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Exploring the Mechanisms underlying the Therapeutic Effect of Shaofu Zhuyu Decoction in Endometriosis using Network Pharmacology and Molecular Docking

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Abstract

The mechanisms underlying the therapeutic effect of Shaofu Zhuyu Decoction (SFZY) on endometriosis (EMs) were examined using a systematic network pharmacology approach and molecular docking in this paper. By screening active ingredients of SFZY, targets of EMs and SFZY, sequentially to construct a protein-protein interaction (PPI) network. Kyoto Encyclopedia of Genes and Genomes (KEGG) pathway enrichment analysis and Biological Process (BP) were conducted. 173 different active ingredients and 995 targets of SFZY were screened, and 1500 EMs-related and 274 drug-disease intersection gene targets were obtained for further analysis. The results showed that 45 BP and 88 KEGG terms were enriched. The docking targets with the two active components of baicalein and EGFR show good binding force. The results show that SFZY plays an important role in the treatment of EMs by “multi-component, multi-target, and multi-pathway”.

Keywords

Shaofu Zhuyu Decoction, endometriosis, network pharmacology, molecular docking

Endometriosis (EMs) is a debilitating disease with features of chronic inflammation and is defined as the presence of functional endometrial glands and stroma outside the uterine cavity. According to the comprehensive literature, there are about 176 million women in the world suffering from endometriosis, 71-87% of them have chronic pelvic pain, and 20%-50% have infertility ^[1]. Shaofu Zhuyu Decoction (SFZY) is used for promoting blood circulation, removing blood stasis, warming the meridian, and relieving pain as referred to Yilin Gaicuo of Wang Qingren. The recipe is composed of 10 herbs, including fennel, dried ginger, rhizoma chuanxiong, angelica, corydalis, cinnamon, radix paeoniae, myrrh, wulinzhi and ctyphus, which affect reducing the volume of ectopic lesions ^[2], anti-inflammatory, spasmolysis, analgesia, decomposition adhesion and anticoagulation ^[3].

Network pharmacology methods are effective for studying and clarifying the mechanisms underlying drug actions, which is including cheminformatics, bioinformatics, network biology, and pharmacology ^[4]. In this study, we utilized a network pharmacology approach to explore the main bioactive components of SFZY and predict their effective molecular targets and potential mechanisms in the treatment of EMs.

Objective

The mechanisms underlying the therapeutic effect of SFZY on EMS were examined using a systematic network pharmacology approach and molecular docking.

Materials and methods

The TCMSP database was used to screen active ingredients of SFZY. The corresponding SMILE structures were found in the PubChem database. The targets of SFZY were obtained by using the Swiss Target Prediction databases. The disease targets of “endometriosis” were collected by using TTD, GeneCards, and DisGeNET databases, and the targets were standardized by the UniProt platform. To study the interactions between the active components of SFZY and their target proteins, drug-disease intersection target genes were searched by the interaction database platform STRING v.11.0 and to construct a protein-protein interaction (PPI) network. The targets of SFZY among EMS-related proteins identified using STRING were further analyzed using the Cytoscape (3.7.2) software to visualize and analyze the interaction network. We used the network analysis plug-in of the software to count the nodes in the network and analyze their roles in the network. Cytoscape (3.7.2) software was also used to construct the network of the “herb-component-target.” Kyoto Encyclopedia of Genes and Genomes (KEGG) pathway enrichment analysis and Biological Process (BP) were conducted using the Cytoscape plug-in ClueGO. The candidate EMS-related genes targeted by SFZY were entered into the ClueGO plug-in, with P set to <0.01 and the K score set to $\geq .53$. The core active ingredients and action targets of the drug were verified by molecular docking using AutoDock(1.5.6) and PyMol software.

Results

By searching the TCMSP database, 173 different active ingredients of SFZY were screened. Venn analysis was performed by the 995 targets of SFZY active components and 1500 EMS-related target genes, 274 drug-disease intersection gene targets were obtained for further analysis. A total of 274 targets were imported into the STRING platform to establish a PPI network. By importing the PPI network information that obtained from the STRING platform into Cytoscape (3.7.2) software for visualization. Then, 325 nodes and 326 edges were obtained from this platform as well. The double median of “Degree” that is, “Degree ≥ 10 ,” was used to screen the intersection targets. By importing the PPI network information that obtained from the STRING platform into Cytoscape (3.7.2) software for visualization. The top 10 compounds were screened, including MOL002714, Styrene, MOL000358, MOL002464, MOL002501, trans-Cinnamic Acid, Anethole, MOL001009, MOL001040, MOL000217. They may be the key compound of SFZY in the treatment of EMS. The Analyze Network plug-in of Cytoscape 3.7.2 was used to screen 19 targets larger than average center DC: 36.79, average BC: 287.30, and average CC: 0.49. To reveal the potential mechanism underlying the therapeutic effect of SFZY in EMS, the results showed that 45 BP terms were enriched, including the regulation of chemokine production, regulation of acute inflammatory response, positive regulation of vascular endothelial growth factor production, regulation of nitric-oxide synthase activity, negative regulation of oxidative stress-induced cell death, positive regulation of receptor signaling pathway via JAK-STAT, response to reactive oxygen species, smooth muscle cell proliferation and regulation of smooth muscle cell proliferation. 88 KEGG terms were enriched, including Toll-like receptor signaling pathway, Th17 cell differentiation, Choline metabolism in cancer, VEGF signaling pathway, and T cell receptor signaling pathway. According to PPI results, such as IL6, AKT1, TNF, EGFR and ESR1 play important roles in the

biological network of SFZY for EMs intervention. The docking targets with the two active components with the highest degree of baicalein and EGFR in SFZY were docking less than $-5.0 \text{ kcal}\cdot\text{mol}^{-1}$, showing good binding force. The docking results were visualized by PyMol. The main compounds of SFZY acting on EMs are baicalein, Styrene, beta-sitosterol, Sexangulare-tin, [(1S)-3-[(E)-but-2-enyl]-2-methyl-4-oxo-1-cyclopent-2-enyl](1R,3R)-3-[(E)-3-methoxy-2-methyl-3-oxoprop-1-enyl]-2, 2-dimethylcyclopropane-1-carboxylate, trans-Cinnamic Acid, Anethole, (S)-Scoulerine.

Discussion

In this study, we used the network pharmacology research method to predict the chemical composition, target, and signal pathways at multiple levels. The prediction results were verified by molecular docking technology. The results show that SFZY plays an important role in the treatment of EMs through “multi-component, multi-target, and multi-pathway”, which provides a new theoretical basis for further experimental research and clinical treatment.

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Clinical Study of Scalp-acupuncture Combined with Needling-warming Therapy in the Treatment of Secondary Amenorrhea

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Abstract: **Objective:** To observe the clinical effect of scalp-acupuncture combined with needling-warming moxibustion on secondary amenorrhea of the pattern of liver qi stagnation, and to explore its influence to artery and blood flow of the ovary and uterine. **Methods:** 60 patients were randomly divided into the observation group (n = 30) and the control group (n = 30), the observation group was treated with scalp-acupuncture combined with needling-warming moxibustion and the control group was treated with conventional acupuncture. The clinical effect of the two groups were compared from the aspect of menstrual cycles symptoms relief, the artery blood flow of ovary and uterine, such as the values of PSV, RI, PI (being monitored by color doppler ultrasound). **Results:** The total effective rate of the observation group was 87.6%, which is significantly higher than 74.3% of the control group ($P < 0.05$). The value of PSV was greatly increased and the values of RI and PI were both greatly decreased in both groups after the treatment ($P < 0.05$). **Conclusion:** The therapy of scalp-acupuncture combined with needling-warming moxibustion is better than conventional acupuncture on the treatment of secondary amenorrhea of the pattern of liver qi stagnation, which can obviously improve the artery blood flow of ovarian and uterine.

Key words: Scalp-acupuncture; Needling-warming moxibustion; Amenorrhea; Pattern of liver qi stagnation; uterine; ovarian; artery blood flow

Secondary amenorrhea is a common endocrine disease in gynecological department, the age of onset between is 23-40 years old according to domestic and international epidemiological statistics, it's relevant to female reproductive tract and pelvic infection. [1]. The main symptoms are menoliposis with chronic pelvic pain, abnormal vaginal discharge, a series of emotional and psychological disorders, which often leads to infertility and other variety of complications. It is intractable and has a high recurrence rate which distress females and increase the economic and social burden of the family and the society.

1. Clinical data

This study collected 60 cases met the diagnostic criteria of secondary amenorrhea, 60 patients were randomly divided into two groups, the observation group (30 cases with scalp acupuncture and needling-warming moxibustion), the control group ((30 cases with conventional acupuncture). The age, duration, etc. of the patients in 2 groups are not statistically different. The patients are without any other chronic (heart, cerebrovascular, kidney disease, etc.), infectious (such as tuberculosis, hepatitis etc.) and organic diseases who volunteered to participate in this test.

2. Treatment methods

2.1 The acupoints of observation group : Touwei, Sishencong, Baihui, uterine points, ovary points, belt vessel, Zhongji, Ciliao, Sanyinjiao, Taichong

Method of operation: (1) Scalp point: after the outer circumferential annular wipe disinfection with

75% alcohol cotton ball in the operating part of the center, select Andy steriled acupuncture needles 0.25 * 40mm(made by Guizhou Andy Medical Device Co., Ltd.No. 2009 2270726), puncture the points at a degree of 30 slowly push the needle into the scalp by the depth of 0.8-1.5cun, to wait the arrival of qi and retain the the needle for 60 minutes.(2) Body points: take a supine position, with the same disinfection method of scalp acupuncture, select the uterine point, ovary point, Sanyinjiao, Zhongji,Taichong and belt vessel, insert the needle at adegree of 90, after 30 minutes, change to prone position and puncture Ciliao point to wait the arrival of qi and place the moxa on these points, operate once a day, 14 days as a course.

2.2 The control group: Acupoints: Touwei, Sishencong, Baihui, uterine points, ovary points, belt vessel, Zhongji, Ciliao, Sanyinjiao,Taichong

The same operation method were manipulated as the observation group apart from the moxibustion

3. Observation index:

3.1 Symptom score standard: reference "clinical research and guiding principle of new Chinese medicine" (Trial Implementation) Nimodipine score is calculated using the method, that is, [(points before treatment - after treatment points) ÷ before treatment integral] × 100% is displayed as a percentage.

3.2 The ovarian, uterine artery blood flow were measured of both observation group and the control group, and the values of PSV, RI and PI as well. All these courses were monitored by color doppler ultrasound apparatus.

4. Statistical methods

SPSS 20 was used to process the statistical software, and the measurement data were expressed by the standard deviation (S).Among the groups were compared using the test; Efficacy percentage statistics.Count data using χ^2 test.P <0.05 was considered statistically significant.

5.Result

Table 1 Comparison of the two groups of patients overall clinical efficacy

Group	cases	Cured	Excellent	Effective	Invalid	Total efficiency (%)
Observation group	30	3	8	14	5	83.33%
Control group	30	2	7	12	9	70.0%

Ps: Compared with the control group*P<0.05

Table2 Compare ovarian of two group's artery blood flow changes ($\bar{x} \pm s$)

Hemodynamic Parameters	Comparative group		Treatment group		Normal group
	Before treatment	After treatment	Before treatment	After treatment	
PI	2.06±0.37	0.93±0.76*	2.08±0.40	0.89±0.67 ^{▲△}	0.90±0.18

RI	0.82±0.09	0.71±0.09*	0.82±0.09	0.68±0.08 ^{▲△}	0.65±0.05
PSV	13.26±0.92	13.66±1.24*	13.35±0.95	14.06±1.24 ^{▲△}	14.01±1.13

Ps: Comparison before and after treatment ★P<0.05. The difference between observation group and the control group, P<0.05. Compared with women of childbearing age △P<0.01

The result shows patients' uterine artery PSV patients was significantly lower than the control group. PI, RI were significantly higher than the control group. The ovarian blood flow becomes more abundant. The value of PSV, RI, PI were statistically significant (P<0.05)

Table3 Comparison of blood flow changes in two groups of uterine arteries ($\bar{x} \pm s$)

Hemodynamic Parameters	the control group		Observation group		Normal group
	Before treatment	After treatment	Before treatment	After treatment	
PI	2.74±0.67	2.40±0.45*	2.71±0.85	2.23±0.45 ^{▲△}	2.21±0.67
RI	0.80±0.04	0.78±0.04*	0.79±0.05	0.78±0.05 ^{▲△}	0.78±0.04
PSV	229.05±3.28	37.85±3.96*	30.05±3.46	39.20±4.71 ^{▲△}	41.75±2.28

Ps: Comparison before and after treatment ★P<0.05, ▲P<0.05, The difference between before and after the treatment group and the control group comparison P<0.05, Compared with women of childbearing age △P<0.01.

The result shows :The uterine artery PSV in patient group was significantly lower than the control group, PI and RI are significantly higher than the control group.

After treatment the blood perfusion of uterine artery of patients in both two groups increase, uterine artery PSV increase as well, RI and PI decrease. All of these were of statistically significance (P<0.05) and after comparing the treatment of the two patient groups, the improvement uterine artery blood flow in the observation group is better than the control group.

6. Conclusion

Abdomen is an important part of the human body it is the "second brain" and responsible for mediating the visceral function (rhythm, absorption, secretion, and nutrition) [5] as well as mutual transmission of the brain sensation and perception of human body. Owing to the abdominal and pelvic vessels are these nutrients transmission channel, improving blood flow to the pelvic and abdominal visceral disease is significant. Modern medical research shows that scalp acupuncture is a positive stimulus which can improve blood circulation of the cerebral cortex area, enhance cortical local oxygen supply, awaken brain cells which is under the focus of oppression and shock or hibernation, and quickly restore its excitability, thereby promoting visceral function and activity dominating corresponding region to gradually recover [6]. So scalp acupuncture may improve pelvic blood flow by improving blood circulation. In recent years, the pathogenesis of SA in documents increasingly emphasized the importance of pelvic peripheral blood circulation disorder. This method is simple and easy to operate and it is a good way to improve patients' compliance and acceptance.

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Huo-Gu Formula for the Treatment of 5-HT Induced Suppression of the Bone Marrow Mesenchymal Stem Cells (BMSCs) Osteogenic Differentiation in Alcohol-induced Osteoporosis (AIO)

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Abstract

The previous study has shown that overdrinking for the long-term can lead to the increase of serum serotonin (5-HT) in alcohol-induced osteoporosis (AIO), and the change of 5-HT content is significantly related to bone metabolism. In this study, we used network pharmacology and molecular biology technology methods to verify that 5-HT significantly inhibited the cell viability, osteogenic differentiation, and mineralization of bone marrow mesenchymal stem cells (BMSCs), which was related to cell apoptosis. Huo-Gu formula could effectively decrease BMSCs apoptosis induced by 5-HT and restored BMSCs cell viability, osteogenic differentiation, and mineralization ability.

Keywords: 5-HT, BMSCs, Huo-Gu formula, Alcoholic Osteoporosis

Long-term heavy drinking can lead to osteoporosis, and animal study has shown that the level of serum 5-HT is elevated in alcoholic osteoporosis [1,2]. The inhibitory effect of serum 5-HT on bone formation has been reported [3], while the specific mechanism remains unclear. How to antagonize the osteogenic inhibition of 5-HT effectively is still the direction for us to explore the treatment of AIO. At present, traditional Chinese medicine (TCM) is significant in disease intervention due to its multi-target and multi-channel treatment characteristics. Therefore, we chose Huo-Gu formula, a TCM prescription that has been applied in clinical to treat AIO for a long time, to represent the account of BMSCs osteogenesis inhibition caused by 5-HT and the cause of effective antagonism of Huo-Gu formula.

Objective

To evaluate the antagonistic effect of Huo-Gu formula on BMSCs apoptosis, osteogenic differentiation, and mineralization reduction induced by 5-HT in the AIO.

Materials and methods

String (<http://cn.string-db.org>) and David (<http://david.ncifcrf.gov>) databases were used for analyzing and predicting the network of the protein-protein interaction (PPI) and to prove the biological function of the Huo-Gu formula for the treatment to the AIO. MTS was used to detect the effect of Huo-Gu formula and 5-HT on BMSCs cell viability. ALP staining, ARS staining, and

Western Blot were used to verify the antagonistic effect of the formula, which renovated BMSCs injury induced by 5-HT.

Results and discussion

Although the pathogenesis of AIO has not been clear, the core pathological process is the disruption of the balance of bone formation and bone resorption^[4]. The status of bone formation depends on a variety of osteogenic differentiated cells, while BMSCs are important preosteogenic cells in bone regeneration. In this study, cell viability was significantly inhibited in BMSCs, which intervened with 10 mM 5-HT for 3 days (Figure 1). However, the 2⁻³ concentration of Huo-Gu formula stock solution had no impact on BMSCs cell viability and could antagonize the damaging effect of 5-HT (Figure 2a, 2b). These results suggest that a high concentration of 5-HT can induce the activation of the programmed cell death (PCD) pathway in BMSCs. Through network pharmacology studies, we identified 99 intersecting proteins between the formula and disease (Figure 3a), and the biological functions can occur in the activation and inhibition of apoptosis, aging, cell proliferation, and so on (Figure 3b). We also found that the intervention of 5-HT could enhance the activation expression of caspase-3, a critical determinant of the apoptosis program, while Huo-Gu formula could reduce the activation level of caspase-3 (Figure 4). Moreover, 5-HT can reduce the ALP staining and ARS staining of BMSCs, while the Huo-Gu formula can enhance its staining ability (Figure 5,6). ALP staining reflects the strength of osteogenic differentiation ability, while ARS staining reflects the level of osteogenic mineralization ability^[5].

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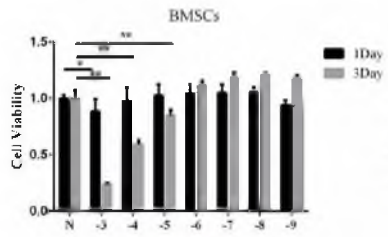


Figure 1

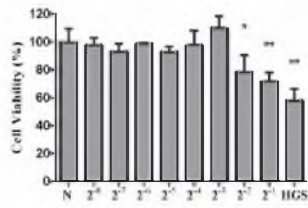


Figure 2a

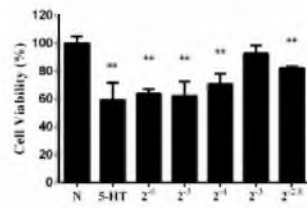


Figure 2b



Figure 3a

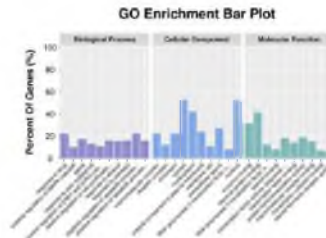


Figure 3b

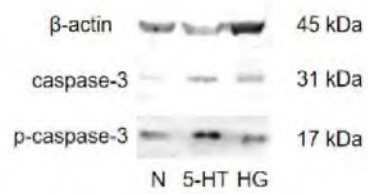


Figure 4

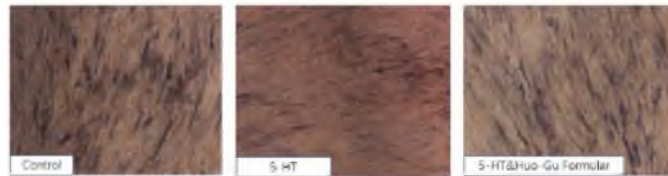


Figure 5

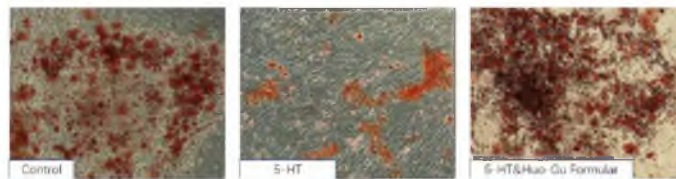


Figure 6

Up-regulation of Caveolin 1 Mediated by Chitosan Activates Wnt/ β -catenin Pathway in Chronic Refractory Wound Diabetic Rat Model

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Abstract

Diabetes mellitus (DM) can be implicated in the perturbations of vascular integrity and the dysfunction of angiogenesis. Chitosan has the advantage of promoting vascular endothelial cell proliferation. However, the molecular mechanism of action in the promotion of wound healing by chitosan derivatives is still debated. In the current study, DM with chronic wound (CW) model rats were prepared and treated with chitosan. Vascular endothelial cells isolated from granulation tissues were conducted RNA sequencing. 2,316 genes were up-regulated, while 1,864 genes were down-regulated after chitosan treatment compared to the CW group. Here, we observed that caveolin 1 (CAV1) was highly expressed and induced by chitosan. Furthermore, we observed that CAV1 knockdown could compromise the activation of the Wnt pathway by reduction of β -catenin in rat aortic endothelial cells (RAOECs) and brain endothelium 4 cells (RBE4s). Moreover, we determined a direct interaction between CAV1 and β -catenin by IP assay. The C-terminus of CAV1 and β -catenin (24 to 586 amino acids) contributed to the interaction of these two proteins. Finally, the protein docking analysis indicated that the fragments of β -catenin might be affected by the structure of CAV1 and facilitated the resistance to degradation. In general, the study demonstrates that chitosan can up-regulate CAV1 expression, and CAV1 can interact with β -catenin for the promotion of canonical Wnt signaling pathway activity. The results have deepened the molecular mechanism of the Wnt pathway in vascular endothelial cells and area benefit to developing new targets to assist in enhancing the pharmacological effect of chitosan on wound healing and angiogenesis against DM.

Keywords: CAV1, β -catenin, chitosan, Wnt pathway, angiogenesis, diabetes mellitus

As a chronic condition, diabetes mellitus (DM) has become a major public health issue worldwide. In 2017, International Diabetes Federation reported that 425 million people suffered from diabetes and 5 million people died from diabetes with more than 800 billion USD for diabetic care. DM2 is associated with numerous co-morbidities, including, but not limited to, cardiovascular disease, stroke, chronic renal failure, peripheral neuropathy, and diabetic skin wounds or ulcerations.

Objective

In this study, we investigated the molecular role of chitosan in wound healing against DM. RNA sequencing (RNA-seq) was conducted to study RNA profiles of chronic refractory wound DM rat model with chitosan treatment. The expression of candidate gene FAM83F and activity of the WNT signaling pathway was found to be associated with chitosan. The results determined a novel therapeutic mechanism of chitosan for promoting wound healing in DM.

Materials and methods

Adult male Sprague-Dawley rats (200-220g) acquired from Shanghai SLAC Laboratory Animal Co. Ltd. (Shanghai, China) were enrolled in this study. DM rats were then anesthetized with 10% pentobarbital sodium 1 mL/100g and removed the back hair at the area of 4cm x 4cm and cut away the skin to the fascia as a chronic wound model. 0.5g chitosan antibacterial gel was evenly applied to the wound area and changed every two days. The wound was covered and bandaged for two weeks. After that, wound and granulation tissues were obtained for the consequent experiments.

Granulation tissue was fixed in 4% formaldehyde solution, dehydrated with gradient alcohol, paraffin-embedded, cut into slices of 5 μ m and HE stained. The pathological changes of fibrosis, inflammatory infiltration, vessel angiogenesis, and cell regeneration were observed and captured in images using Olympus BX-51 light microscope with 200x amplification.

Isolated vascular endothelial cells were conducted as previously described, and the concentration and quality of RNA were measured using a Nanodrop 2000 (Thermo Fisher Scientific) and an Agilent Bioanalyzer 2100. A total of 5 μ g of RNA from each group was used for library preparation using the NEBNext Ultra Directional RNA Library Prep Kit for Illumina (NEB, USA) following the manufacturer's instructions, and sequenced on an Illumina HiSeq platform. CAV1 siRNA was synthesized from GenePharma (Shanghai, China), and transfected using Lipofectamine RNAiMAX according to the manufacturer's instructions. Immunoprecipitants were washed with IP buffer three times and resuspended with 20 μ L lysis buffer. The protein lysate was subjected to a western blot assay.

The protein lysate was then analyzed by SDS-PAGE and transferred to PVDF membranes (Bio-Rad Laboratories, USA). The blotting bands were developed with ECL plus immunoblotting detection reagents (Thermo Fisher Scientific), UVP ChemstudioPlus System (Analytik Jena, Germany), and captured by Image J.

Results and discussion

HE stains indicated a phenotype of numerous infiltrated inflammatory cells, visible necrotic zones, bleeding, sparse fibroblasts, as well as a few narrow blood vessels in DW. While chitosan could enhance the proliferation of fibroblasts in granulation areas with many new blood vessels (Figure 1A). Moreover, the overall expressions of vascular endothelial growth factor B (VEGFB), fibroblast growth factor 1 (FGF1), and platelet-derived growth factor subunit B (PDGFB) were all elevated in

the wound area of DWC compared to DW (Figure 1B). In conclusion, the therapeutic effect of chitosan on angiogenesis was confirmed by our system.

A total of 722 genes were up-regulated, while 709 genes were down-regulated in DWC compared to DW. The expression and the nucleus-localization of β -catenin could be elevated by chitosan indeed, but compromised by CAV1 knockdown, suggesting that CAV1 might participate in the chitosan-mediated activation of the Wnt/ β -catenin pathway in vascular endothelial cells *in vitro*.

The C-terminal domain of CAV1 and β -catenin (24 to 586 amino acids) contributed to the interaction of these two proteins. Protein docking analysis between CAV1 and β -catenin by the Z-DOCK system showed that fragments of 253-261 “FYAITTLHN” as well as 292-303 “KFLAITTDCLQI” of β -catenin were two major fulcrums to support the protein binding surface.

In summary, our study demonstrates that chitosan can up-regulate CAV1 expression, and CAV1 can interact with β -catenin to promote the activity of the canonical Wnt signaling pathway. The conclusion deepens the molecular mechanism of the Wnt pathway in vascular endothelial cells and is beneficial to developing new targets to assist in enhancing the pharmacological effect of chitosan on wound healing and angiogenesis against DM.

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Observation on Clinical Efficacy of Qihuangtongluo Tang in Treatment of Type 2 Diabetic Peripheral Neuropathy (Deficiency of Qi Yin or Yin with Stasis)

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Abstract:

In this paper, 60 patients with type 2 diabetic peripheral neuropathy were studied by clinical observation in the Department of Endocrinology, The Second Affiliated Hospital of Heilongjiang University of Traditional Chinese Medicine.

Objective:

To investigate and analyze the clinical efficacy of Qihuangtongluo Tang combined with methylcobalamin in the treatment of type 2 diabetic peripheral neuropathy.

Methods:

The patients were divided into a control group (n=30) and an observation group (n=30) by randomization of clinical numbers, and the patients in the control group were treated with methylcobalamin alone, and the observation group was treated with Qihuangtongluo Tang combined with methylcobalamin for 8 weeks, and the clinical effects of the two groups of patients after different treatment were compared.

Results:

The observation groups of the total peroneal nerve, median nerve motor conduction velocity (MNCV), and sensory conduction velocity (SNCV) before and after treatment were more clinically effective than the control group, and the difference between groups was statistically significant ($P<0.05$).

Conclusions:

It is shown that Qihuangtongluo Tang combined with methylcobalamin has a synergistic effect in the treatment of diabetic peripheral neuropathy and has a better clinical effect than the use of methylcobalamin alone, which can improve the speed of nerve conduction and is worthy of clinical promotion and application.

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Clinical Observation on Treatment of Cervical Spondylosis of Vertebral Artery Type with Thread Embedding Needle Knife

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Abstract

Objective: To observe the clinical efficacy of this study in the treatment of cervical spondylosis of vertebral artery type (CSA). **Methods:** 60 cases of CSA in our unit were selected. Two groups, 30 cases each, were randomly assigned. The patients were treated with embedding needle knife and routine acupuncture respectively. The dizziness scores of the two groups were compared before and after treatment; Vertebral basilar artery blood supply level. **Results:** (1) The degree of dizziness in the observation group was better than that in the control group ($P < 0.01$); (2) The blood supply of vertebrobasilar artery in the observation group was better than that in the control group ($P < 0.05$); **Conclusion:** the curative effect of embedding needle knife neck clip ridge in the treatment of CSA is significant and improves its clinical curative effect.

Key words: Embedding needle knife; Acupuncture; Neck clip ridge; Vertebral artery; Cervical spondylopathy;

1. Data and methods

1.1 General data the subjects of the study selected 60 patients diagnosed with CSA in our unit. Compared with the general data of the two groups, the difference was not statistically significant ($P > 0.05$).

1.2 Inclusion criteria

1.2.1 Inclusion criteria: (1) patients who meet the diagnostic criteria of CSA; (2) no other treatment before treatment; (3) support treatment and sign informed consent; (4) 18-65 years old; (5) $20\text{mm} \leq \text{VAS score} \leq 70\text{mm}$.

1.2.2 Exclusion criteria: (1) patients who are not consistent with the diagnosis of this type of cervical spondylosis; (2) organic lesions; (3) patients who cannot be treated by catgut embedding;

1.3 Therapeutic method:

Control group: Operation method: the patient takes the lying position and selects sterile acupuncture needle (0.35mm×40mm) routine acupuncture. Keep the needle for 30min, once a day, 6 days a week, 2 weeks as a course of treatment.

Observation group: In the prone position, put the No. 4 PGA suture body with tweezers into the front end of the No. 7 embedding needle 1.5cm, one needle for each point. After disinfection, hold the needle in the right hand, along the Jiaji point of the second cervical vertebra, hold the knife in the right hand, the cutting edge line is parallel to the longitudinal axis of the cervical vertebra, the

needle body is vertical to the spinous process of the second cervical vertebra, quickly penetrate the skin, and reach the outer upper edge of the spinous process of the cervical vertebra, the needle body breaks through to the outer edge of the spinous process of the axis on one side, loosen the muscles for 3-5 times, and then leave the thread body there. Other acupoints are the same as above. Once a week, two weeks is a course of treatment.

1.4 Observation index:

1.4.1(1) Dizziness degree score: choose visual analog scoring method (VAS): 0 (no dizziness) 10 (heaviest dizziness); (2) improvement of vertebral basilar artery blood supply: measured by Transcranial Doppler (TCD);

1.4.2 Efficacy evaluation: curative effect evaluation refers to the curative effect evaluation standard of vertigo formulated in the diagnosis and curative effect standard of traditional Chinese medicine [1]: recovery: dizziness and neck discomfort are eliminated, and the improvement rate is $\geq 75\%$; Remarkable effect: dizziness is significantly improved, $50\% \leq$ improvement rate $< 75\%$; Effective: improve dizziness, slightly affect daily life and learning, $25\% \leq$ improvement rate $< 50\%$; Invalid: unable to study and work normally, and the improvement rate is less than 25%.

1.5 Statistical methods:

SPSS20.0 software is used for statistical analysis, in which the measurement data is displayed by ($\bar{x} \pm s$). If the data is normally distributed, the paired data t-test and two independent sample t-test are used for the comparison of the data before and after treatment and between groups in the same group. If the data is not normal, the data before and after treatment and between groups are compared by nonparametric test, in which $P < 0.05$ means statistically significant.

2. Treatment results

2.1 Comparison of clinical efficacy between the two groups the total clinical effective rate of the observation group was 96.67%, and that of the control group was 80.00%. The comparison between groups ($P < 0.05$) was statistically significant, and the treatment of the observation group was better than that of the control group.

2.2 Comparison of dizziness scores between the two groups before and after treatment. After statistical analysis, there was no significant difference in the VAS score of dizziness between the two groups before treatment ($P > 0.05$). After treatment, the difference between the two groups was statistically significant (both $P < 0.01$), indicating that the two treatment methods were effective. After treatment, the difference between the two groups was statistically significant ($P < 0.01$), and the treatment group was better than the control group.

2.3 Comparison of the improvement of blood supply level of vertebral basilar artery between the two groups before and after treatment. The peak systolic blood flow velocity (VP) and peak diastolic blood flow velocity (VD) of vertebral basilar artery in the two groups before treatment were analyzed, ($P > 0.05$), which was comparable. After treatment, there was statistical difference between the two groups ($P < 0.05$), and there was statistical significance between the two groups ($P <$

0.05). See Table 1.

Table 1 Comparison of VP and VD of vertebral basilar artery between the two groups before and after treatment($\bar{x}\pm s$)cm/s

Group	Number of cases	Vp / (cm/s)		Vd/ (cm/s)	
		Before treatment	After treatment	Before treatment	After treatment
Control group	30	59.53±4.44	62.06±1.36 ^a	33.00±1.66	35.03±2.31 ^a
Observation group	30	60.40±4.68	65.26±1.60 ^{ab}	32.63±1.99	36.72±1.76 ^{ab}

Note: compared with that before treatment, ^a $P < 0.05$; Compared with the control group^b $P < 0.05$.

3. Discussion

As a new treatment method, "thread embedding needle knife" has three characteristics of "acupuncture, thread embedding and Acupoint Injection" [2,3,4]. The mechanism of thread embedding needle knife can be summarized in three points: first, long-term acupoint stimulation. The implantation of thread into acupoint points will continue to stimulate acupoints on the body. Once, it is equal to or more than the effect of acupuncture for about 7-10 days, which is also the most important therapeutic effect of thread embedding therapy; The second is tissue therapy. The thread body used for embedding thread is equivalent to antigen, which can regulate the emergency ability and viscera of the body; Third, blood pricking effect. When embedding thread, stab it to dredge meridians and regulate blood; Finally, through the physical effect of the blade of the tip of the needle, the adhesion is loosened, and the symptoms such as headache and dizziness disappear [5,6]. Therefore, this method is a relatively less painful and effective treatment.

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Effect of Nape Acupuncture Combined with Swallowing Training on Dysphagia in Patients with Parkinson's Disease

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ABSTRACT

To explore the effect of acupuncture combined with swallowing training in patients with Parkinson's disease with swallowing dysfunction. From August 2017 to August 2019, a total of 120 patients with Parkinson's dysphagia with grades II to IV of the "Kubota Water Swallowing Test" were selected and randomly divided into treatment group (n=60) and control group (n=60). The control group was treated with swallowing training, and the treatment group was treated with nape acupuncture combined with swallowing training, 30 min each time, 6 times a week for 4 weeks. Standardized Swallowing Assessment (SSA), Videofluoroscopic Swallowing Study (VFSS) were used to evaluate swallowing, and Swallowing-related Quality of Life (SWAL-QOL) was used to evaluate quality of life before and after 4 weeks' treatment. There was no significant difference in the SSA, VFSS and SWAL-QOL scores before treatment between the two groups ($P > 0.05$). After 4 weeks' treatment, the SSA scores of the two groups were lower than those before treatment, and the VFSS and SWAL-QOL scores were all higher than those before treatment ($P < 0.05$). At end of treatment, the SSA scores of the treatment group were (21.67 ± 3.34), which were lower than those of the control group (25.16 ± 3.82), and the difference was statistically significant ($P < 0.05$). The VFSS and SWAL-QOL scores were (7.68 ± 1.03) and (137.24 ± 12.97), which were all higher than those of the control group (5.94 ± 1.72) and (121.98 ± 9.32), and the differences were statistically significant ($P < 0.05$). Nape acupuncture combined with swallowing training can effectively improve the swallowing function and quality of life of patients with Parkinson's dysphagia, which were better than the single swallowing training.

KEY WORDS Parkinson's disease; dysphagia; nape acupuncture; swallow training

Parkinson's disease (PD) is a common clinical central nervous system disease, mainly characterized by resting tremor, myotonia, bradykinesia, motor symptoms of postural and gait abnormalities, and other non-motor symptoms^[1]. Dysphagia is one of the common non-motor symptoms in PD patients, with an incidence rate as high as 35%-82%, and patients with hidden dysphagia account for a high proportion^[2]. Dysphagia can occur at any stage of PD, mainly manifested as difficulty in eating, followed by different degrees of dehydration, malnutrition and decreased resistance, and even aspiration pneumonia and choking and asphyxia in severe cases^[3]. Nape acupuncture is a special acupuncture method for treating head and nape diseases by needling acupoints on the neck, which has remarkable curative effect on bulbar paralysis^[4]. Sixty PD patients with dysphagia were treated by nail needle combined

with swallowing training. The changes of swallowing function were observed before and after treatment, in order to provide new ideas for clinical rehabilitation treatment of PD.

Objective

To explore the effect of acupuncture combined with swallowing training in patients with Parkinson's disease with swallowing dysfunction.

Methods: From August 2017 to August 2019, a total of 120 patients with Parkinson's dysphagia with grades II to IV of the "Kubota Water Swallowing Test" were selected and randomly divided into treatment group (n=60) and control group (n=60). The control group was treated with swallowing training, and the treatment group was treated with nape acupuncture combined with swallowing training, 30 min each time, 6 times a week for 4 weeks. Standardized Swallowing Assessment (SSA), Videofluoroscopic Swallowing Study (VFSS) were used to evaluate swallowing, and Swallowing-related Quality of Life (SWAL-QOL) was used to evaluate quality of life before and after 4 weeks' treatment.

Results and discussion:

There was no significant difference in the SSA, VFSS and SWAL-QOL scores before treatment between the two groups ($P > 0.05$). After 4 weeks' treatment, the SSA scores of the two groups were lower than those before treatment, and the VFSS and SWAL-QOL scores were all higher than those before treatment ($P < 0.05$). At end of treatment, the SSA scores of the treatment group were (21.67 ± 3.34), which were lower than those of the control group (25.16 ± 3.82), and the difference was statistically significant ($P < 0.05$). The VFSS and SWAL-QOL scores were (7.68 ± 1.03) and (137.24 ± 12.97), which were all higher than those of the control group (5.94 ± 1.72) and (121.98 ± 9.32), and the differences were statistically significant ($P < 0.05$).

There is still a lack of sufficient sample size for the targeted treatment of PD patients with dysphagia by needle. We will further carry out a multi-center and large-sample controlled clinical study in the future, in order to achieve the best effect in the treatment of this disease and provide more new ideas for the clinical non-drug treatment of dysphagia in PD patients.

Conclusion: Nape acupuncture combined with swallowing training can effectively improve the swallowing function and quality of life of patients with Parkinson's dysphagia, which were better than the single swallowing training.

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Effect of fire needle combined with acupoint catgut embedding on spasm degree and motor function of upper limb in patients with stroke

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Abstract: **[objective]** to study the effect of fire needle combined with catgut embedding at acupoints on spasm degree (MAS) and motor function (FMA) of upper limb in patients with stroke. **[methods]** 120 patients with stroke upper limb spasm hospitalized in the fifth ward of acupuncture in the second affiliated Hospital of Heilongjiang University of traditional Chinese Medicine from January 2019 to February 2021 were randomly divided into treatment group (n = 60) and control group (n = 60). The control group was treated with fire needle, and the treatment group was treated with catgut embedding at acupoints on the basis of fire needle acupuncture in the control group. the patients in the two groups were treated for 4 weeks. The indexes of MAS, FMA, neurological deficit score (CSS), γ -aminobutyric acid (GABA), glycine (Gly), self-rating anxiety scale (SAS) and activities of daily living (ADL) were measured. **[results]** after treatment, the scores of CSS and SAS were lower than those before treatment, and the scores of FMA, Gly, GABA and ADL were higher than those before treatment, and the score of MAS in the treatment group was better than that in the control group, while the scores of CSS and SAS in the treatment group were lower than those in the control group, while the scores of FMA, Gly, GABA, ADL and clinical efficacy in the treatment group were better than those in the control group. **[conclusion]** Fire needle combined with catgut embedding at acupoints is effective in the treatment of spasm and motor function of upper limb in patients with stroke, which can reduce the degree of spasm and improve the motor function of upper limb.

Key words: fire needle; acupoint catgut embedding; stroke upper limb spasm; spasm degree; upper limb motor function

In recent years, studies have found that the incidence of hemiplegia in stroke is the highest. Most patients will have spasm of hemiplegic limbs within 20 days of onset, resulting in spastic hemiplegia. The symptoms of limb spasm are sudden muscle tension, involuntary convulsions and dyskinesia, joint pain^[1-2]. The common sequela of stroke is upper limb spasm, which will not only affect the quality of life of patients, but also bring anxiety to patients^[3]. In recent years, acupuncture is widely used in clinic and has a good effect in the treatment of upper limb spasm after stroke^[4]. Fire needle therapy can regulate qi and blood deficiency and dredge blocked meridians^[5].

Catgut embedding at acupoints can achieve the effect of nourishing muscles and veins and dredging channels and collaterals [6]. The purpose of this paper is to study the effect of fire needle combined with acupoint catgut embedding on spasm degree and motor function of upper limb in patients with stroke, so as to provide reference for clinical application [7].

Stroke has the characteristics of acute onset, high fatality rate and high disability rate, which will affect the patient's physical strength, perception, or inability to speak, walk, and blurred vision [8]. Spastic hemiplegia of upper limb is one of the common complications of stroke, which directly affects the quality of life of patients. The main reason that hinders recovery is muscle spasm. Muscle spasm lasts for a long time will make the affected side of the upper limb contracture deformity, serious cases will lead to hemiplegia [9]. Therefore, how to effectively treat muscle spasm after stroke is of great significance. Fire needle therapy of traditional Chinese medicine has a long history, and its main characteristics are simple implementation, good curative effect and quick effect [10]. From the point of view of traditional Chinese medicine, the imbalance of yin and yang and the imbalance of qi and blood are the main factors affecting stroke, while yin prosperity and yang decline, deficiency and excess are the results of upper limb spasm after stroke [11]. "Lingshu ·functional ability" said: "both yin and yang are empty, and fire should be taken care of." The importance of Yang Qi and warming method is emphasized, and the stimulation amount of fire needle acting on acupoints is much larger than that of ordinary acupuncture. Jiaji acupoint should be in Zang-fu organs and reflect the shape of Zang-fu organs, which is the same as back-Shu acupoint, which is the acupoint of direct transfer and flow of human meridians and viscera. Acupoint catgut embedding is a kind of immunotherapy which integrates acupoint stimulation and catgut alloprotein. catgut embedding stimulates back acupoints Dazhui, Feishu (Taiyuan), Ganshu (Taichong), Pishu (Taibai), Shenshu (Taixi), Mingmen, Yaoyangguan and other acupoints, in order to recuperate qi and blood deficiency, nourish muscles and veins, and dredge channels and collaterals. Moreover, catgut, as a heterogeneous protein, can cause allergic immune reaction in human body and sensitize lymphoid tissue, which can be as long as 20 days or longer by decomposing and liquefying catgut into peptides and amino acids, compared with acupuncture. Catgut embedding at acupoints has the advantages of short time, easy to consolidate the curative effect and not easy to relapse. The residual or emerging neurological deficit in stroke patients with upper limb spasm is mainly targeted at CSS, which reflects the improvement of neurological impairment in stroke sequelae [12]. The results of this study show that fire needle combined with catgut embedding at Jiao acupoint can reduce the MAS score of stroke patients with upper limb spasm, increase the score of FMA and CSS, thus reduce the degree of spasm and improve the motor function of upper limb.

In this study, fire needle combined with catgut embedding at Jiao acupoint can increase the levels of Gly and GABA in serum [14-15], so as to control the development of patients' disease and improve their muscle spasm. and this study found that fire needle

combined with catgut embedding at Li acupoint can reduce SAS score, increase ADL score, improve anxiety, improve quality of life, and further improve the therapeutic effect of patients.

To sum up, fire acupuncture combined with catgut embedding at acupoints has a significant effect on spasm degree and motor function of upper limb in patients with stroke, reduce MAS score and SAS score in patients with spasm of upper limb, increase the levels of FMA, CSS, ADL and serum Gly, GABA, improve upper limb movement function and improve patients' quality of life, which is of great significance to patients.

Study on Effect and Mechanism of Kangzhi Syrup Suppressing Airway Remodeling in cough variant asthma based on TGF- β 1/Smads Signaling Pathway

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ABSTRACT: Objective: To investigate the effect of Kangzhi syrup on ovalbumin (OVA)-induced airway remodeling in guinea pig model of cough variant asthma (CVA) and its mechanism. It aims at providing the basis for the clinical application of Kangzhi syrup, hence contribute to the addition of supplementary or alternative treatment for the disease.

Key words: Cough variant asthma; Airway remodeling; Cytokines; TGF- β 1/ Smads signal pathway; Kangzhi syrup

Methods: Sixty healthy male guinea pigs were randomly divided into four experimental groups: blank control group, model group, dexamethasone group, Kangzhi syrup group, 15 in each group. The model of CVA airway remodeling was established by OVA sensitization and stimulation in guinea pigs. The drug intervention of the two treatment groups was given by gavage from the 15th day of the experiment, and the blank group and the model group were given by gavage with physiological saline of the same amount as Kangzhi syrup for 42 days. During the experiment, we should pay attention to observe and record the general changes of guinea pigs in each group. To detect the classification and count of inflammatory cells in bronchoalveolar lavage fluid (BALF) by Gimesa staining. To measure and calculate the characteristic morphometric indexes representing airway remodeling by Masson staining and microscopic analysis system, then to further observe and calculate the changes of lung tissue morphology. To detect the content of hydroxyproline in trachea by alkaline hydrolysis. To detect the expression of TGF- β 1, Smad3 and Smad7 in lung tissue by Real-time PCR. Finally, they are used to verify the modeling situation, as well as the therapeutic effect and mechanism of Kangzhi syrup.

Results:

1. Classification and count of inflammatory cells in BALF: Compared with the blank group, the count of WBC and EOS in BALF of model group increased significantly ($P < 0.05$), the percent of EOS and LYM increased significantly ($P < 0.05$). Compared with the model group, the count of WBC and EOS and the percent of EOS and LYM in BALF of Kangzhi syrup group and dexamethasone group decreased significantly ($P < 0.05$). There was no significant difference between the two treatment groups ($P > 0.05$).

2. Results of Masson staining in lung tissue: In the model group, there were a lot of

blue collagen deposition around the bronchial wall and vascular wall. The subdermal fibrosis, basement membrane thickening, smooth muscle hyperplasia and airway remodeling were obvious. In the Kangzhi syrup group and dexamethasone group, the deposition of collagen around the bronchial wall and vascular wall was significantly reduced, and subepithelial fibrosis, basement membrane thickening, smooth muscle hyperplasia were improved to varying degrees.

3. Masson staining image analysis results: Compared with the blank group, the thickness of subepithelial basement membrane, bronchial wall, airway smooth muscle, IOD and deposition thickness of collagen in the model group increased significantly ($P < 0.05$). Compared with the model group, the thickness of the subepithelial basement membrane, the thickness of the bronchial wall, the thickness of the airway smooth muscle, the IOD value of collagen deposition and the thickness of deposition in the Kangzhi syrup group and dexamethasone group were significantly reduced ($P < 0.05$). There was no significant difference between the two treatment groups ($P > 0.05$).

4. Determination of hydroxyproline in trachea: Compared with the blank group, the content of hydroxyproline in the model group increased significantly ($P < 0.05$). Compared with the model group, the content of hydroxyproline in the trachea of Kangzhi syrup group and dexamethasone group decreased significantly ($P < 0.05$). There was no significant difference between the two treatment groups ($P > 0.05$).

5. Expression level of TGF- β 1mRNA, Smad3mRNA and Smad7mRNA in lung tissue: Compared with the blank group, the expression of TGF- β 1mRNA and Smad3mRNA in the lung tissue of the model group increased, and the expression of Smad7mRNA decreased ($P < 0.05$). Compared with the model group, the expression of TGF- β 1mRNA and Smad3mRNA in lung tissue of Kangzhi syrup group and dexamethasone group decreased, and the expression of Smad7mRNA increased ($P < 0.05$). Between the two treatment groups, the expression levels of TGF- β 1mRNA, Smad3mRNA and Smad7mRNA in lung tissue were significantly different ($P < 0.05$).

Conclusions: Kangzhi syrup can inhibit the airway remodeling of cough variant asthma by changing the pathomorphological degree of airway remodeling model and blocking the process of pulmonary fibrosis. Kangzhi syrup can regulate the TGF- β 1/Smads signaling pathway by inhibiting the expression of TGF- β 1, inhibiting the activation of Smad3 downstream, and promoting the production of Smad7 protein in the downstream, thereby inhibiting the airway remodeling of cough variant asthma.

Molecular Mechanism of Jiawei Simiao Yong'an Decoction combined with Bone Transport in the Treatment of Diabetic Foot Ulcer through RAGE/PI3K-Akt Pathway Based on Network Pharmacology

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Abstract

In this study, the molecular mechanism of Jiawei Simiao Yong'an Decoction in the treatment of diabetic foot ulcer was preliminarily predicted by network pharmacology and molecular docking technology. Then, the fasting plasma glucose (FPG) and weight of diabetic foot ulcer rabbits were measured by animal experiments, the wound healing rate was calculated, the pathological changes of wound tissue were observed by HE staining, ELISA, RT-PCR and Western-Blot. Expression of key targets in RAGE/PI3K-Akt signaling pathway.

Key words: Diabetic foot ulcer, Bone transport, Traditional Chinese medicine, Repair and regeneration

Diabetic foot ulcer is a lower extremity infection, ulcer and destruction of deep tissue caused by neuropathy and various degrees of peripheral vascular disease in diabetic patients. It is estimated that every 20 seconds in the world, 1 diabetic patient is amputated due to diabetic foot. The mortality rate of diabetic foot amputation patients is as high as 22%, and the annual mortality rate of ulcer patients is as high as 11%.

The Ilizarov technique mainly includes annular external fixation technique, bone elongation technique, bone transfer technique and the biological principle of "tension-stretch" principle (law of tension stress, LTS) which guides the application of these techniques. Among them, bone transport technology (bone transport, BT) was first created by Dr. Ilizarov in Russia in the 1970s, and was gradually applied to the clinic after the 1980s. In China, Professor Hua Qikai and other scholars applied the Ilizarov tibial lateral bone transfer technique to treat diabetes, thromboangiitis obliterans and chronic ulcers caused by arteriosclerosis obliterans and other diseases and achieved good clinical results, effectively saving many patients who were on the verge of amputation.

Objective

In this study, network pharmacology and molecular docking technology were used to explore the therapeutic mechanism of Jiawei Simiao Yong'an Decoction combined with bone transfer technology on the healing of diabetic foot wounds by regulating the RAGE/PI3K-Akt signaling pathway.

Materials and methods

In this study, network pharmacology was used on the TCMSP platform to determine the active ingredients and targets of nine Chinese herbs (Scrophulariaceae, Honeysuckle, Angelica, Licorice, Chishao, Chuanxiong, Rehmannia glutinosa, Achyranthes, and Tuckahoe) in Jiawei Simiao Yong'an Decoction. Points were searched, and disease-related targets were collected through GeneCards, OMIM, TTD, PharmGkb, and DrugBank databases. Cytoscape 3.6.1 software was used to build a "compound-target" network, and the STRING platform was used to build an intersecting target-protein interaction network, and Cytoscape 3.6.1 software was used to perform topological

analysis on the network to obtain core genes, and perform GO enrichment through R language. Analysis and KEGG pathway enrichment analysis, and finally use molecular docking technology to conduct molecular docking verification between the active ingredients in Jiawei Simiao Yong'an Decoction and the core target of DFU, and predict the mechanism of action of Jiawei Simiao Yong'an Decoction in the treatment of DFU. Jiawei Simiao Yong'an decoction combined with bone transfer technique in the treatment of diabetic foot ulcer was verified by animal experiments.

Results and discussion

It was predicted that there were 141 active ingredients of Jiawei Simiao Yong'an Decoction in the treatment of DFU, corresponding to 257 targets. Topological analysis obtained 5 core genes, including AKT1, TNF, CASP3, VEGF, and EGF. GO enrichment analysis involved a total of 3057 biological processes (BP), 32 cellular components (CC), 16 molecular functions (MF), and 180 were screened by KEGG pathway enrichment analysis. Pathways related to DFU mainly include AGEs-RAGE signaling pathway, lipid and atherosclerosis signaling pathway, neurodegeneration pathway in diabetic complications-various disease signaling pathway, MAPK signaling pathway, etc. In conclusion, the active ingredients of Jiawei Simiao Yong'an Decoction mainly participate in the glycosylation process of DFU, regulate the expression and release of pro-inflammatory factors and vascular endothelial growth factor, and affect chronic cell activation and continuous cell damage to achieve therapeutic effects. Molecular docking results showed that the main active compounds could bind to the core target with good affinity.

The results showed that after 14 days of treatment in each group, compared with the control group, the FPG of the rabbits in the model group was significantly increased ($P < 0.01$); compared with the model, the FPG values of the rabbits in the JSM group and the JSM+GB group were significantly decreased ($P < 0.01$). Compared with the control group, the body weight of the rabbits in the model group decreased significantly ($P < 0.01$). Compared with the model, the body weights of the rabbits in the JSM group, GB group and JSM+GB group increased significantly ($P < 0.01$). Rabbit wound healing rate Model group < JSM group < GB group < JSM+GB group ($P < 0.01$). The above results show that the healing effect of Jiawei Simiao Yong'an Decoction combined with bone transport in the treatment of DFU is better than that of single treatment, and it is more significant at 14 days. It may be because 14 days is a complete cycle of traditional Chinese medicine treatment, and the microcirculation caused by bone transport is reconstructed. Apparently active at 14d.

The contents of IL-6, IL-8 and TNF- α protein in serum were detected by ELISA; compared with the control group on 7d and 14d, the IL-6, IL-8 and TNF- α protein in the wound tissue of the rabbits in the model group increased ($P < 0.05$); compared with the model group, the levels of IL-6, IL-8 and TNF- α in the JSM group, GB group, and JSM+GB group were decreased, among which the JSM group < GB group < JSM+GB group ($P < 0.05$). The above results indicate that both Jiawei Simiao Yong'an Decoction and bone transfer have the effect of intervening inflammation, and the combined treatment of the two is better than the single treatment, and may have a synergistic anti-inflammatory effect. RT-PCR and Western-Blot were used to detect the expressions of RAGE and Akt mRNA and protein. Compared with the Control group, the expressions of RAGE, Akt mRNA and protein in the wound tissue of the Model group were up-regulated at 7d and 14d ($P < 0.05$). Compared with the Model group, the expressions of RAGE mRNA, Akt mRNA and protein in the JSM group, GB group and JSM+GB group were all down-regulated ($P < 0.05$), among which

the JSM group < GB group < JSM+GB group ($P < 0.05$). The above results indicate that Jiawei Simiao Yong'an Decoction combined with bone transfer may inhibit the occurrence of inflammation by activating the PI3K-Akt pathway through the glycosylation target RAGE, and promote the healing of diabetic foot ulcer wounds.

Therefore, this study pointed out that Jiawei Simiao Yong'an Decoction can promote the healing of DFU foot ulcer wounds, which may be related to its ability to reduce the fasting blood glucose level and serum IL-6, IL-8 and TNF- α levels in DFU model rabbits. Jiawei Simiao Yong'an Decoction combined with bone transfer therapy can regulate RAGE and activate the downstream PI3K-Akt pathway to exert hypoglycemic and anti-inflammatory effects, which is helpful for wound healing in DFU rabbits. The effect of Jiawei Simiao Yong'an decoction combined with bone transfer technique in promoting wound healing of DFU rabbits is better than that of single treatment, and the combination of the two may have a synergistic therapeutic effect.

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The Effects of Bunaozhixian Power on the Expression of IL-1 β and IL-6 in Hippocampus of Epileptic Rats Induced by Pentylenetetrazol Based on Theory of “Inanition of the Brain”

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Abstract

Epilepsy is a chronic disease which has a group of temporary due to recurrent abnormal discharge of neurons of the central nervous system dysfunction. It belongs to the category of "epilepsy" of traditional Chinese medicine. Chinese medicine has a long history and rich experience of epilepsy, and Chinese medicine treatment in clinical practice with its curative effect is stable and no obvious side effects. This research team relying on the outpatient and ward patients from the Acupuncture Department of First Affiliated Hospital of Heilongjiang University of Chinese Medicine. According to my team for many years clinical experience, summed up the "sui hai kong xu, nao shen shi yang" the fundamental pathogenesis of epilepsy syndrome, and thus created Bunaozhixian powder. It has been used in clinic for many years and can significantly reduce the number of seizures in patients with epilepsy. In this study, by observing the effects of Bunaozhixian powder on the behavioral changes and inflammatory factors IL-1 β and IL-6 in the hippocampus of pentatetrazolium induced epileptic rats, explore the anti-epileptic effect of Bunaozhixian powder and its mechanism.

Key words: Epilepsy; Pentylenetetrazol; Bunaozhixian Power; IL-1 β ; IL-6

Objective

To observe the changes of Bunaozhixian power on general state, behavior, IL-1 β and IL-6 expression in hippocampus of epileptic rats induced by pentylenetetrazol. To investigate the mechanism of Bunaozhixian power in the treatment and prevention of epileptic diseases based on theory of “Inanition of the Brain”.

Methods

7 days before modeling, the experimental rats were randomly selected as Bunaozhixian power control group and were given Bunaozhixian power intragastric administration. After 7 days, except for the control group, rats were randomly selected as blank group. Epilepsy model was ignited in other rats and control group. The rats successfully ignited were randomly and evenly allocated to model group and Bunaozhixian power group. Except for blank group, other rats were treated by gavage. Record the general state and epileptic seizures of rats before and after treatment. The number of IL-1 β and IL-6 positive cells in the hippocampus was detected by immunohistochemistry, and the average gray value of the positive cells was calculated.

Results

After the ignition of the epilepsy model, compared with the blank group, the body weight of the model group, the prevention and treatment group and the tonifying brain and antiepileptic group were significantly decreased. The number of IL-1 β and IL-6 positive cells in the hippocampus were significantly increased, and the mean gray value was significantly decreased, all of which showed

highly significant differences ($P < 0.01$). After intragastric administration, compared with the model group, the body weight of rats in the prevention and treatment group and the Bunaozhixian powder group were significantly increased, the onset latency was significantly prolonged, and the onset grade was significantly decreased, and the differences were highly significant ($P < 0.01$). The number and average gray value of IL-1 β and IL-6 positive cells were significantly different between control group and model group ($P < 0.01$). There were significant differences in the number of IL-1 β and IL-6 positive cells and average gray values between Bunaozhixian powder group and model group ($P < 0.05$).

Discussion

Epilepsy is a common disease in the department of neurology, because of its complex pathogenesis, treatment is more difficult, and the current prevention of epilepsy disease is still lack of exact and effective means. Therefore, preventing the formation of epilepsy is a key difficulty for the department of neurology. At present, based on our preliminary research, we have carried out animal experimental studies on Bunaozhixian powder, and found that Bunaozhixian powder can adjust the balance of Glu and GABA content in serum and hippocampus of pentatetrazolium induced epileptic rats in order to suppress seizures. The above research on the mechanism of Bunaozhixian powder in treating epilepsy provides theoretical basis for clinical application of Bunaozhixian powder in treating epilepsy.

In this study, it was found that Bunaozhixian Powder could significantly improve the general state of epileptic rats induced by pentatetrazolium, correct the weight loss, significantly prolong the seizure latency of epileptic rats, and reduce the grade of epileptic seizures. In particular, there was no significant difference in seizure grade and seizure latency between the control group, Bunaozhixian powder group and model group before treatment ($P > 0.05$). However, after intraperitoneal injection of PTZ, the seizure grade of rats in the model group and Bunaozhixian powder group were all grade 4 or 5, and the control group could occasionally have grade 3 seizures. Moreover, the latency time of seizure was longer than that of model group and Bunaozhixian powder group, which may be related to Bunaozhixian powder's preventive effect on epilepsy. After treatment, although there was no significant difference in seizure level and seizure latency between the prevention and treatment group and the Bunaozhixian powder group ($P > 0.05$), the observation of statistical results showed that the seizure level of the prevention and treatment group was slightly lower than that of the Bunaozhixian powder group, and the seizure latency was slightly longer than that of the Bunaozhixian powder group. And the improvement of the control group, the body quality of epilepsy is and check for brain scattered groups had no significant difference ($P > 0.05$). But the data of its value for brain epilepsy check scattered closer to the blank group, the treatment before the results may be related to check scattered the prevention of epilepsy for brain function, after treatment results may be related to the control group treatment schedule is longer.

Conclusion

Bunaozhixian powder can obviously improve the general state of epileptic rats induced by pentylenetetrazol and alleviate epileptic seizures in rats. It can reduce the expression of IL-1 β and IL-6 cytokines in the hippocampus of epileptic rats and inhibit the inflammatory response. Its

treatment and prevention of epilepsy disease may be related to this mechanism.

Effect on the Mincle/Syk Pathway by Acupuncture through Baihui to Qubin in Model Rats of Intracerebral Hemorrhage (ICH)

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Abstract

Macrophage-inducible C-type lectin (Mincle) recognizes self-ligands released by dead cells, with subsequent downstream activation of spleen tyrosine kinase (Syk), and the increased expression of inflammatory cytokines. It can cause destruction of the blood brain barrier and the occurrence of cerebral edema. Repairing brain damage by inhibiting the Mincle/Syk signaling pathway is a potential new target for treating cerebral hemorrhage. In this study, the authors aimed to verify whether acupuncture is an effective treatment for ICH through this pathway. A total of 234 male rats were divided into 4 groups: sham, model, piceatannol, and acupuncture. The ICH rat model was established using autohemic blood infusion. More specifically, piceatannol was intraperitoneally injected and the acupuncture group was treated with hand-twist acupuncture of Baihui to Qubin (DU20 through GB7 on the lesion side). Modified neurological severity scores (mNSS) and brain water content was assessed at 6, 12, 24 and 72 h after establishment of the ICH model. Expression of Mincle, Syk, and CARD9 (a member of the caspase-associated recruitment domain [CARD]) was detected using immunohistochemistry and western blot. The levels of interleukin (IL)-1 β mRNA were measured using a real-time polymerase chain reaction assay. Results revealed that acupuncture significantly decreased the mNSS, brain water content ($p < 0.05$), and the expression of Mincle, Syk, CARD9, and IL-1 β .

Key Words: nerve protection; intracerebral hemorrhage; acupuncture; Baihui (DU20) ; Qubin (GB7) ; inflammation; Mincle; CARD9; Syk; IL-1

Objective

To investigate the effect of acupuncture through “Baihui ”to“ Qubin” on the Mincle/Syk pathway in model rats of intracerebral hemorrhage .

Materials and Methods

A total of 234 male, Sprague-Dawley rats were divided into 4 groups: sham, model, piceatannol, and acupuncture. The ICH rat model was established using autohemic blood infusion. More specifically, piceatannol was intraperitoneally injected and the acupuncture group was treated with hand-twist acupuncture of Baihui to Qubin (DU20 through GB7 on the lesion side). Modified neurological severity scores (mNSS) and brain water content was assessed at 6, 12, 24 and 72 h after establishment of the ICH model. Expression of Mincle, Syk, and CARD9 (a member of the caspase-associated recruitment domain [CARD]) was detected using immunohistochemistry and western blot. The levels of interleukin (IL)-1 β mRNA were measured using a real-time polymerase chain reaction assay.

Results and Discussion

Mincle is a pattern-recognition receptor primarily expressed on myeloid cells, especially antigen-presenting cells. Expression levels of Mincle are under normal circumstances. However, during infection and tissue damage, Mincle is upregulated and binds to endogenous antigen, and

subsequently recruit and activate Syk. Syk can activate protein kinase C- δ , which phosphorylates downstream CARD9. This activates NF- κ B pathway via CARD9/BCL10, which generates biologically active IL-1 β [1,2]. As a mediator of immune response and activation point of inflammation, the expression level of IL-1 β directly reflects the grades of inflammation after cerebral hemorrhage. Research investigating the Mincle/Syk signaling pathway has demonstrated that this pathway is involved in a variety of innate immune responses, including ischemic stroke, traumatic brain injury, and subarachnoid hemorrhage^[3,4,5]. Our study showed that acupuncture significantly suppressed protein expression in the Mincle/Syk pathway in rat brain tissue with hemorrhage, and decreased the expression of IL-1 β . These results suggest that acupuncture Baihui to Qubin may mitigate cerebral hemorrhage injury neuritis and improve neural function by suppressing the Mincle/Syk pathway, which further downregulates the expression level of downstream inflammatory cytokines.

Several groups have demonstrated that piceatannol, which is a Syk inhibitor, can suppress expression of Syk/CARD9 during ischemic stroke and subarachnoid hemorrhage (SAH), reduce IL-1 β levels, improve neural function, and facilitate therapy of brain edema [5,6]. Our study found that, compared with the piceatannol group, rats treated with acupuncture through Baihui to Qubin exhibited no significant difference in the effects of therapy, further suggested that acupuncture through Baihui to Qubin can, in fact, affect the Mincle/Syk pathway, mitigate inflammatory injury of brain, improve neural function, and alleviate brain edema.

Collectively, our data suggests that acupuncture through Baihui to Qubin may suppress the Mincle/Syk pathway, and reduce the release of proinflammatory cytokines, and, therefore, mitigate neurological damage after cerebral hemorrhage. However, mechanism on why blocking Mincle improves ICH outcomes and the connections between Mincle and other signaling pathways after ICH require further studies in the future.

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Clinical Observation: Treatment of Sanweiwufa for Cervical Radiculopathy

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Abstract

At present, there are many means and methods for the treatment of radiculopathy cervical spondylosis, but in the clinic, these methods are often used alone, and the effect is uneven. Sanweiwufa Treatment for cervical radiculopathy, which can quickly control the disease, both shortening the course of the disease and alleviating the physical and psychological pain suffered by the patient. Therefore, this treatment deserves to be widely disseminated in clinical practice.

Key words: Sanweiwufa; cervical radiculopathy

Radiculopathy is a type of clinical syndrome in which bilateral or unilateral spinal nerve roots are compressed or stimulated, followed by dysfunction of the corresponding innervated site. Most cervical radiculopathies have clinical manifestations such as reflex disorders and movement disorders. The range of motion of the cervical spine is greatly affected, and it is accompanied by a pronounced feeling of pain, seriously affect the normal life of the patient^[1].

Objective

To observe the clinical effect of Sanweiwufa Treatment for cervical radiculopathy, for the clinical application of traditional Chinese medicine comprehensive therapy to treat the disease to provide objective basis. Meanwhile, at the same time, we actively responded to the guideline of the comprehensive reform of urban public hospitals issued by the general office of the state council, to reduce the proportion of drugs.

Materials and Methods

60 patients who met the diagnostic criteria for radiculopathy were randomly divided into two groups: treatment group and control group, 30 patients in each group. Treatment group was treated with Sanweiwufa therapy, acupoints selected Fengchi, Gongxue, Tianzhu, Jingjiaji, Jianjing, Quchi, Waiguan, Hegu and Houxi; while the meridian is dominated by SI, BL, GB; the sinew is dominated by the fascial SI, BL; the comprehensive treatment of Guasha, cupping, acupuncture, moxibustion and traditional Chinese medicine. Control group was treated with single acupuncture. Respectively, before and after therapy compared two groups of patients of VAS pain score, the Tianzhongjingjiu symptom scale score, electromyography F wave frequency, and evaluated the clinical effect of two groups patients before and after treatment.

Results and discussion

When it comes to the gender, age and course comparison of the two groups before treatment, the difference was not statistically significant ($P > 0.05$), and it was comparable. 2 weeks after treatment, we compared the VAS pain score, the Tianzhongjingjiu symptoms scale score, the electromyography F wave frequency of these two groups, the difference was statistically significant ($P < 0.05$), which explain in alleviating pain, improving symptoms, the treatment group is superior

to the ordinary acupuncture control group. Compared with pretreatment, the total effective rate of the treatment group was 96.67%, and the control group was 90.00%. This trial showed there was a statistically significant difference between them in the effect ($P < 0.05$).

Sanweiwufa Treatment of radiculomotor cervical spondylosis is superior than that of acupuncture alone. In the course of treatment, each therapy is targeted and penetrates into each other. Scrapping is the use of a certain tool to scratch some acupoints of the body to produce a certain stimulation, which is able to achieve the meridian dredging and harmonize Ying and Wei, and can effectively relieve pain^[2]. Cupping is mainly aimed at the lesions of the tendons, and the adsorption effect and traction effect of the fire can on the muscle tissue can alleviate the condition of muscle spasm and tension, so that the muscles can be relaxed while improving blood supply. In addition, the warming effect of the fire tank can speed up local blood circulation, promote the excretion of metabolites, and give evil a way out^[3]. Acupuncture is mainly aimed at lesions with blocked and damaged meridians. From the perspective of traditional Chinese medicine, acupuncture can dredge the meridians, regulate Qi and blood, reduce stasis and stagnation, reduce swelling and relieve pain. From the perspective of Western medicine, acupuncture mainly has analgesic effects, and clears peripheral blood vessels, increases blood flow, accelerates energy metabolism, and improves the ischemia and hypoxia of diseased tissue. Moxibustion is applied to specific parts of the body with appropriate temperature and heat stimulation. It can stimulate the acupuncture points and meridians from the surface, which can warm the meridians, activate the blood and dissolve the stasis, and promote the recovery of damaged nerves^[4-5]. Take the Chinese medicine-Jitongxiao, which made in our hospital, has the effect of activating blood and dissolving stasis, clearing heat and water, dispelling wind and relieving pain, and replenishing Qi and fixing the surface. After years of clinical application, it is effective in treating cervical spondylosis.

Sanweiwufa is a treatment method that uses five kinds of traditional Chinese medicine methods of Guasha, cupping, acupuncture, moxibustion, and traditional Chinese medicine to comprehensively act on the acupuncture points, meridians, and sinews. Sanweiwufa Treatment of cervical spondylosis, is a synergistic relationship, the five therapies are not a simple superposition of effects, its efficacy is remarkable, easy to operate, safe, and a variety of treatments are carried out at the same time, easy to be accepted by patients.

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Study on the Mechanism of Neuroprotective Effect of Scalp Acupuncture in Rats with Cerebral Hemorrhage

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Objective

The purpose of this study was to observe the effect of scalp acupuncture "Baihui" penetrating "Qubin" treatment on the improvement of nerve function in rats with acute cerebral hemorrhage. This study will further investigate the possible mechanisms by which scalp acupuncture activates the "P62/keap1/Nrf2" signaling pathway to antagonize the lipid peroxidation damage of ferroptosis^[1] in neuronal cells.

Materials and methods

Several healthy 6-week-old Sprague-Dawley male rats (280±10g) were selected. 160 healthy male rats were randomly divided into control group, sham group, model group, acupuncture group and inhibitor group after one week of acclimatization feeding, where each group was further randomly divided into 4 subgroups of 6 hours, 1 day, 3 days and 7 days, with 8 rats in each group. The control group did not undergo any intervention. The model group was replicated using the autologous blood injection method to replicate the rat model of cerebral hemorrhage. The sham group received the same operations as the model group, with a microinjector at the same location, but without blood injection. In the acupuncture group, the acupuncture point "Baihui" was penetrated through the "Qubin", and the acupuncture point was penetrated with 0.35×40mm needles at a depth of 0.8 inch. The acupuncture treatment was performed once a day. The inhibitor group was treated with once daily intramuscular injection of deferoxamine 100mg/kg. The neurological deficits in each group were evaluated by the Ludmila Belayev scale, and the morphological changes of brain tissue were observed by HE staining. Mitochondrial morphological and structural changes in rat brain tissue were observed by transmission electron microscopy. Iron kit was used to measure the iron content of rat brain tissue. Malondialdehyde (MDA) kit was used to detect lipid peroxide MDA in rat brain tissue. The expression of neuron-specific nuclear protein (NeuN), P62, keap1, Nrf2, FTH1 and GPX4 protein in rat brain tissue was detected by immunoprotein blotting. Finally, the above results were analyzed by statistical software.

Results

1. Neurological function scores: The rats in the control group and sham group showed no significant neurological deficits at any time point. Compared with the control and sham group, the rats in the model group showed significant neurological deficits at 6 h ($P<0.05$), which gradually increased at

1 d ($P < 0.05$), reached a peak at 3 d ($P < 0.05$) and gradually recovered at 7 d ($P < 0.05$). The degree of neurological deficits in the acupuncture group was significantly less than that in the model group at all time points ($P < 0.05$). There was no significant difference between the neurological function scores of the rats in the acupuncture group and the inhibitor group at each time point ($P > 0.05$).

2. HE staining results: In the control group and sham group, all kinds of cells were relatively intact. No obvious pathological changes were found. The ICH rats had a large number of inflammatory cells, red blood cells, and broken cells, which was accompanied by edema in neurons, disordered cellular architecture, severe vacuolation of the intercellular space, neuronal karyopyknosis, and anachromasis. However, SA improved pathological injury post-ICH, the blood was absorbed obviously and a small amount of red blood cells and inflammatory cells infiltrated.

3. TEM results: In the sham operated group, there was no obvious change in the morphology of mitochondria, but swelling mitochondria were scattered; Neuronal soma show a large number of shrunken mitochondria at 3 days post-ICH even with increased mitochondrial membrane density and the rupture of outer mitochondrial membrane. Compared with the ICH group, neuronal soma showed scattered shrunken mitochondria with thickened and ruptured outer mitochondrial membrane at 3 days after SA treatment and DFX administration.

4. Results of iron Kit and MDA Kit: Compared with the control group and the sham group, the Fe content and MDA content in the model group increased significantly at each time point ($P < 0.05$). With the extension of time, the Fe content and MDA content of the model group increased gradually, reaching the peak in 3 days, and maintaining a high level in 7 days. Compared with the model group, the content of Fe in acupuncture group decreased significantly at the time points of 1d, 3d and 7d ($P < 0.05$). The MDA content of acupuncture group at each time point was significantly lower than that of the model group ($P < 0.05$). There was no significant difference in Fe content and MDA content between acupuncture group and inhibitor group at each time point ($P > 0.05$).

5. Western blot results:

Results of NeuN protein expression: Compared with the sham group, the expression of NeuN protein in the model group decreased significantly ($P < 0.05$) at 1day, 3days and 7 days after ICH, reached the peak at 3days ($P < 0.01$), and the death of nerve cells was the most serious, and recovered at 7 days ($P < 0.05$). Compared with the model group, the expression of NeuN protein in acupuncture group increased significantly ($P < 0.05$) at 1day, 3days and 7 days after ICH. There was no significant difference in the expression of NeuN protein between acupuncture group and inhibitor group ($P > 0.05$).

Results of P62、Nrf2 protein expression : The expression of p62、Nrf2 protein in the model group increased significantly at the time of 1day, 3days and 7days after cerebral hemorrhage ($P < 0.05$). The expression of p62 began to increase on the first day after ICH, peaked on the third day, and

maintained on the seventh day. In the model group, Nrf2 protein expression began to increase at 6h, peaked at 3d and decreased at 7days. Compared with the model group, the expression of p62 protein in the acupuncture group was significantly higher at each time point ($P<0.05$). The expression of Nrf2 in acupuncture group increased at 6h, 1d and 3d ($P<0.05$), and decreased significantly at 7d ($P<0.05$).

Results of Keap1 protein expression: Compared with the sham group, the expression of Keap1 protein in the model group decreased significantly at 1 day, 3 days and 7days after cerebral hemorrhage ($P<0.05$). In the model group, the expression of Keap1 began to decrease at 1 day, peaked at 3 days, and increased at 7 days. Compared with the model group, the protein expression of Keap1 in the acupuncture group decreased significantly ($P<0.05$).

Results of GPX4 protein expression: Compared with sham group, GPX4 protein expression in model group decreased significantly at different time points ($P<0.05$); In the model group, GPX4 began to decrease at 1 day and reached the peak at 3 days, and the expression of GPX4 protein increased at 7 days. Compared with the model group, GPX4 protein expression in the acupuncture group increased significantly at 3d and 7d ($P<0.05$).

Results of FTH1 protein expression: The expression of FTH1 protein in the model group increased significantly at all time points ($P<0.05$). In the model group, the content of FTH1 began to increase at 6h, continued to increase at 1d and reached the peak at 3days. Compared with the model group, the expression of FTH1 protein in acupuncture group was significantly higher at the time of 1d, 3days and 7days ($P<0.05$).

Conclusion

1. Scalp acupuncture "Baihui" penetrating "Qubin" treatment can significantly improve neurological deficits and limb motor functions in rats with cerebral hemorrhage.
2. Scalp acupuncture "Baihui" penetrating "Qubin" treatment can significantly improve the pathological morphology of brain tissue in rats with cerebral hemorrhage, reduce the free iron content and MDA content of lipid peroxidation products in brain tissue with hemorrhage, improve the mitochondrial ultrastructure of brain tissue with hemorrhage, and inhibit the occurrence of ferroptosis in brain tissue of rats with cerebral hemorrhage.
3. Scalp acupuncture "Baihui" penetrating "Qubin" treatment can obviously up regulate the protein expression of p62 and down regulate the protein expression of Keap1, promote the increase of Nrf2 into the nucleus, thus activating "p62 / Keap1 / Nrf2" signal pathway, and enhancing the ability of anti-lipid peroxidation.

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Research and Development Prospect of *Inonotus Obliquus* under the Background of Health Industry Integration between China and Russia

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Abstract

This paper reviews the research progress of chemical constituents and pharmacological actions of *Inonotus obliquus* in recent years, shows its broad development prospects, and provides new ideas for further study of *Fusarium betulatus* and its development and application in large health industry.

Key words: *Inonotus obliquus*, Chemical composition, Pharmacological action, Development

At present, China and Russia are deeply integrated in cross-border medical care, health tourism, health care integration, food and drug development and other related fields, providing strong health guarantee for the Chinese and Russian people. *Inonotus obliquus* is a precious medicinal and edible fungus, widely distributed in temperate continents between 40° and 50° north latitude and in China, Russia and other countries and regions in temperate monsoon climate^[1]. It has antioxidant, hypoglycemic, hypolipidemic, immune regulation, anti-tumor and other functions. In this paper, chemical composition and pharmacological action of the fungus were summarized, and the prospect of its development was put forward.

Objective

To research progress of chemical constituents and pharmacological action of *Inonotus obliquus* was summarized, and the prospect of its development was put forward.

Materials and methods

Using the key words "*Inonotus obliquus*, chemical constituents and pharmacological effects", we searched the relevant literature of *Foramina betulinus* from Web of Science, PubMed, China National Knowledge Infrastructure and Wanfang database from 2000 to 2022. The research progress of chemical constituents and pharmacological effects of *Inonotus obliquus* was summarized.

Results and discussion

1 Main components

At present, the chemical constituents of *Inonotus obliquus* mainly include polysaccharides, terpenoids, flavonoids, steroids and phenols.

1.1 Polysaccharide

The polysaccharides of *Inonotus obliquus* are mainly composed of monosaccharides linked by-glycosidic bonds, such as galactose, glucose, mannose, rhamnose, arabinose, glucuronic acid and galacturonic acid, and are mainly acidic polysaccharides^[2].

1.2 Terpenoids

The terpenoids of *Inonotus obliquus* were lanosterol, inotodiol, Trametenolic acid, 3 β -hydroxylanosta-8,6 β -hydroxy-trans-dihydroconfertifolin etc [3].

1.3 Flavonoids

The flavonoids in *Inonotus obliquus* are mainly flavonoid glycosides composed of quercetin, naringin, kaempferol and isorhamnetin [4].

1.4 Nonsteroidal

The nonsteroidal in *Inonotus obliquus* are ergosterol, ergosterol peroxide, cholesterol, stigmasterol, β -sitosterol and other steroidal compounds [5].

1.5 Phenolic

The phenolic in *Inonotus obliquus* including hispolon, Hispidin, Inonoblin A, Inonoblin B, Inonoblin C and p-hydroxybenzoic acid, etc [6].

2. Studies on pharmacological effects

2.1 Antioxidant effect

Inonotus obliquus had antioxidant effect. Hong N et al. [7] found that polysaccharides from *Inonotus obliquus* showed significant reducing ability for DPPH and hydroxyl radicals, which could stimulate the production of nitric oxide and phagocytosis activity of RAW 264.7 macrophages.

2.2 Hypoglycemic effect

Inonotus obliquus plays a hypoglycemic role by regulating insulin level and improving glycogen synthesis. Wang et al. [8] studied the anti-diabetic effect of polysaccharide and chromium (III) complex of *Inonotus obliquus* on streptozotocin (STZ)-induced type 2 diabetic mice, and showed that it had significant hypoglycemic effect.

2.3 Hypolipidemic effect

Several studies have shown that *Inonotus obliquus* also has certain effects on lipid metabolism. Zhang et al. [9] confirmed in vitro that *Inonotus obliquus* could reduce the lipid accumulation and triglyceride content of Hep G2 cells.

2.4 Regulation of immune function

The polysaccharide of *Inonotus obliquus* has obvious immunomodulatory function. Jiang et al. [10] found that polysaccharide from *Inonotus obliquus* could significantly improve the immune ability of diabetic mice.

2.5 Anti-tumor effect

Inonotus obliquus can inhibit the cell cycle of tumor cells and induce the apoptosis of tumor cells. Baek et al. [11] proved that triterpenoids from *Inonotus obliquus* have pro-apoptotic activity on human lung cancer cells under different p53 states.

3 Thinking about development prospects

Inonotus obliquus is widely used in food and medicine because of its anti-oxidation, hypoglycemic, hypidemic, immunological and anti-tumor effects, low toxicity and high safety. At present, many kinds of medicament and health care products have been developed, such as essence powder, tea

decoction, aerosol and injection. According to the existing literature, the polysaccharides of *Inonotus obliquus* is one of the most effective active components of *Inonotus obliquus*. However, in China, the related research on polysaccharides of *Inonotus obliquus* is still in the field of basic research. In Russia, polysaccharides of *Inonotus obliquus* have been used in clinical studies on antitumor and hypoglycemic effects, but they have not yet become large-scale and industrialized. Under the background of health industry integration between China and Russia, how to carry out clinical transformation research on the existing research results of *Inonotus obliquus* polysaccharide and promote its industrialization is the key link to be solved in the development of *Inonotus obliquus* polysaccharide. Concrete ideas can further use modern high-tech to improve the yield and purity of products; Determine the industrial production technology for the extraction and preparation of polysaccharides from *Inonotus obliquus*, realize industrial production, enrich the market product types, such as oral liquid, freeze-dried powder and other corresponding preparations.

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Effect of Nourishing Liver and Kidney Medicated Diet on Perimenopausal Obesity Patients with Liver and Kidney Yin Deficiency

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Abstract

Objective To explore the effect of nourishing liver and kidney medicated diet plan on TCM syndrome and obesity in perimenopausal obesity patients with liver and kidney Yin deficiency. **Methods** 72 patients were randomly divided into 2 groups. The control group was given nutrition education, the intervention group was given intermittent fasting therapy and nourishing liver and kidney medicated diet on the basis of the control group. **Results** At the 4th and 8th week of intervention, there was statistical difference in TCM syndrome scores between the two groups($P<0.01$).The TCM syndrome score of the intervention group was gradually decreased,and the pairwise comparison at each time point showed significant difference($P<0.01$).Waist circumference, hip circumference, waist height ratio and other obesity indexes in the intervention group were significantly lower than those before intervention and control group($P<0.05$). **Conclusion** Nourishing liver and kidney medicated diet can not only improve TCM syndrome effectively, but also reduce the degree of central obesity in patients, which is safe and reliable.

Key words: Nourishing liver and kidney; TCM syndrome; Intermittent fasting; Perimenopausal obesity

Perimenopausal obesity refers to a simple obesity in which perimenopausal women change their body fat into a central distribution due to abnormal secretion of sex hormones, accompanied by a series of symptoms such as glucose and lipid metabolism disorders^[1]. Studies show that the prevalence rate of obesity among women aged 40-60 is as high as 65%,which not only aggravates hot flashes and induces urinary tract infection,but also increases the prevalence of cardiovascular diseases with the increase of waist circumference^[2].Studies have shown^[3]that liver-kidney Yin deficiency is the most common clinical syndrome type.At present,there is no specific effective therapy in the comprehensive intervention.Dietary therapy is a relatively safe and effective non-drug therapy. Modern nutrition can control calories and reduce obesity by changing the dietary pattern and structure of patients.TCM medicated diet is used according to syndrome differentiation, and intervention is carried out according to individual syndrome type of patients to improve physical fitness.Integrated traditional Chinese and Western medicine diet therapy is widely used in the treatment of perimenopausal obesity.

Objective

To explore the effect of plan of nourishing liver and kidney medicated diet combined with light fasting therapy on TCM syndrome and obesity of perimenopausal obesity patients with liver and kidney Yin deficiency. To verify its effectiveness and safety, in order to provide a more scientific basis for the clinical promotion of non-drug therapy for perimenopausal obesity.

Materials and Methods

Seventy-two patients with perimenopausal obesity were selected as the research objects by random

sampling method in the nutrition outpatient department of a grade A Hospital of Traditional Chinese Medicine in Heilongjiang. Patients corresponding to even numbers were divided into intervention group and patients corresponding to odd numbers were divided into control group by random number table, with 36 cases in each group. Inclusion criteria: ①meeting the diagnostic criteria of perimenopausal and obesity; ②patients with liver-kidney Yin deficiency syndrome differentiated by clinical TCM experts according to "Guiding Principles for Clinical Research of New Chinese Medicine"^[4]; ③volunteers and informed consent without cognitive dysfunction; Exclusion criteria: ①allergic to the food materials involved in this study; ②patients with secondary obesity and pathological obesity caused by other reasons; ③patients receiving other interventions during the process; ④suffering from heart, liver, kidney and other serious diseases or endocrine diseases, uterine and ovarian diseases.

The control group carried out nutrition and health education, with reference to the Dietary Guidelines for Chinese Residents^[5] and taught the patients to calculate the reasonable daily intake of calories according to their weight and height, followed by low-fat and light diet, and forming good living habits. On the basis of the control group, the intervention group took medicated porridge with light fasting; The patients were instructed by the uniformly trained and qualified members of the research group to eat normally for 5 days a week according to their height and weight, avoid greasy diet, and the rest 2d (generally not continuous) were given light fasting, with the intake of calories of about 2,093kJ on light fasting days^[6], drinking more water and eating more vegetables and fruits; Medicinal porridge compatibility for licorice 5g, floating wheat 10g, lotus leaf 5g, hawthorn 3g, Poriacocho 3g, 3 jujube, mulberry 3g, wolfberry 3g, 50g japonica rice boiled to porridge, do staple food.

Results and Discussion

After two courses of intervention, waist circumference of patients in the intervention group decreased from 92.33 ± 6.73 to 87.70 ± 6.17 , median hip circumference decreased from 102.5 to 98.8, waist height ratio decreased from 0.57 ± 0.04 to 0.53 ± 0.03 . There was no difference in the control group before and after intervention, and there was significant difference between the two groups ($P < 0.05$). It is suggested that medicated porridge combined with light fasting therapy can effectively reduce waist circumference, hip circumference and waist-height ratio, and effectively reduce central obesity. Based on the analysis of its causes, light fasting mode can regulate energy metabolism, accelerate body fat mobilization^[6], regulate the diversity of intestinal flora and thus reduce obesity. The lotus leaf in medicated meal congee can strengthen the spleen and drain dampness, Poriacocho can promote urination and percolate dampness, hawthorn can nourish the stomach and eliminate food, and have the effect of draining dampness and reducing fat together.

The TCM syndrome score in the intervention group showed a gradually decreasing trend, which was 16.48 ± 3.62 before intervention, 12.76 ± 2.91 after the first course, and 6.70 ± 1.40 after the second course, indicating that the decrease level was the largest in the second course. The difference between the two time points was extremely significant ($P < 0.01$). The control group scores per point in time was 17.09 ± 4.30 , 16.97 ± 4.02 , 16.79 ± 3.85 , and there was no statistical difference at each time point ($P > 0.05$). There were significant differences in the fourth and eighth week of intervention in 2 group ($P < 0.05$). The interaction of time factor and time factor*group and the difference between

groups were statistically significant ($P < 0.01$), indicating that the TCM syndrome score of patients had a trend of change over time, and the trend of change over time was different between the two groups. It shows that the medicated diet can effectively improve the syndrome of deficiency of liver and kidney Yin, and the longer the implementation time, the more obvious the effect. Analysis of its reasons: floating wheat in medicated meal porridge can remove trouble and calm the mind, wolfberry can nourish liver and kidney, mulberry can nourish blood and Yin, improve the syndrome of deficiency of liver and kidney Yin; In addition, modern studies have shown that light fasting can regulate the immune system and significantly reduce the stress state of overweight people by reducing the level of C-reactive protein^[7], which is conducive to stability of internal environment. In conclusion, the nourishing liver and kidney medicated diet program can effectively improve TCM syndrome and reduce the central obesity degree of patients through multiple systems and multiple targets.

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Research Progress in Rehabilitation of Prevention and Treatment of Senile Dementia

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Abstract

Senile dementia is a group of degenerative diseases of the central nervous system, which often leads to severe impairment of the patients' ability to work and activity, and their inability to take care of themselves in life bringing great pressure to their families and society. This article mainly focuses on the targeted treatment of clinical manifestations of senile dementia by rehabilitation, searches relevant Chinese and foreign literature, and summarizes the prevention and treatment of senile dementia by rehabilitation in order to slow down the process of senile dementia by means of rehabilitation.

Key words: Rehabilitation Alzheimer's disease Prevention and treatment

Statistics show that there are 30 million patients of Alzheimer's disease worldwide, and the prevalence of Alzheimer's disease is expected to increase by 2050^[1]. Some of the symptoms of dementia in the aged, such as long-term and short-term memory loss, visual space difficulty, cognitive ability, judgment and calculation ability decline on the original basis, can be improved with the help of speech therapy and job therapy in rehabilitation training. In the late stage of dementia caused by various complications such as bedsores, fractures caused by falling, physical therapy in rehabilitation therapy can play a good role in alleviating.

Objective

By searching for the literature related to senile dementia, to find the positive role of rehabilitation in senile dementia, in order to improve the quality of life quality of senile dementia patients and their families through the relevant rehabilitation treatment technology, reduce their family expenditure.

Materials and methods

For Alzheimer's patients, the cognitive decline is generally irreversible, and there is currently no specific treatment for the disease. This paper searched the relevant literature on rehabilitation treatment of senile dementia in recent years from CNKI, Wanfang, VIP and PubMed, and summarized and extracted the application of rehabilitation in senile dementia.

Results and discussion

Rehabilitation refers to the adoption of a variety of measures to reduce or eliminate the physical, mental and social dysfunction of patients, so that patients can achieve and maintain their various functions at the best level, improve the quality of life, enhance their self-care ability, and help patients return to society^[2]. When treating patients like Alzheimer's, the principles of rehabilitation are patience, simplicity, family involvement, appropriate help, and patient-centered care.

Cognitive function training: for patients with cognitive impairment, all kinds of training to improve their basic cognitive ability and activities of daily living are collectively referred to as cognitive function training. PQRST can improve the memory ability of senile dementia patients. Memories are reinterpreted and unify the role of the unsolved problems in the past, to help patients solve their

psychological conflict, rebuild their cognitive, give new meaning to life, overcome the reality of depression, promote self-repair and integrate^[3].

Exercise therapy: exercise therapy mainly improves patients' quality of life by enhancing muscle strength and reducing muscle tension. Moderate physical exercise can relax the patient's spirit, which is conducive to better recovery. Training patients' ADL abilities such as washing face, brushing teeth, dressing and going to the toilet can help patients better adapt to life and realize self-care at an early date. Exercise training is feasible for the treatment of patients with Alzheimer's disease and their caregivers, and exercise training has the potential to benefit both cognitive and non-cognitive outcomes in patients with Alzheimer's disease. Literature has shown that dual exercise can enhance patients' functional independence and reduce the burden of caregivers, and dual exercise training can improve balance and functional outcomes of patients with senile dementia and reduce the risk of falls in the aged^[4].

Occupational therapy: Occupational therapy include many kinds of treatment of Aalzheimer's disease, according to their specific clinical symptoms, develop the corresponding occupational treatment plan.

Behavioral and psychological treatment: Senile dementia patients are prone to anxiety and restlessness. Recent studies have found that neuropsychological rehabilitation or cognitive rehabilitation combined with drug therapy is very feasible. At the same time, personalized treatment for senile dementia patients can stimulate the enthusiasm of senile dementia patients to participate in training.

Speech rehabilitation: the therapist demonstrates the patient's mouth movements by having the patient repeat them and instructing the patient to organize their own speech. Freezing point stimulation and picture reading are also commonly used in speech rehabilitation.

ADL activities: to the patient's causal ability and judgment, comprehensive practical ability, choice ability, calculation ability, social coordination ability, etc., the implementation of treatment intervention. Aerobic exercise engages large muscle groups to work in a repetitive and rhythmic manner. It has been reported that the cognitive ability of the elderly with mild cognitive impairment will be improved when they participate in aerobic exercise training, and aerobic exercise training may have an effect on the elderly dementia patients through neuropathological cognitive pathway and physiological cardiopulmonary health^[5].

Rehabilitation of senile dementia and rehabilitation education: Helping dementia patients establish regular habits and gradually develop muscle memory can help reduce anxiety in dementia patients. When we treat senile dementia patients, we should not only pay attention to the patients themselves, but also carry out communication and education for the caregivers of patients, so as to better treat the patients.

Physical therapy: Studies have shown that interventions that promote neuroplasticity can significantly improve cognitive performance in alzheimer's patients, especially those at risk or with mild alzheimer's. Non-invasive techniques transcranial magnetic stimulation and transcranial direct current stimulation induce significant and lasting changes in both focal and non-focal neuroplasticity. Literature has shown that repetitive TRANSCranial magnetic stimulation has a good effect on hearing sentence comprehension^[6].

Drugs retain symptoms and side effects existing in drugs to a large extent, and non-drug

intervention in Alzheimer's disease has become a new research hotspot ^[7]. In conclusion, rehabilitation can improve our physical function, slow down the progression of Alzheimer's disease, improve our ability of daily living activities, and help Alzheimer's patients better return to society and integrate into their families.

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Effect of Acupuncture on Cerebral Hematoma Volume and HO-1 Expression in Rats with Acute Cerebral Hemorrhage

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Abstract

In this study, autologous blood injection was used to create a rat model of ICH, and subsequently, a needle was used to stimulate the acupoint Qubin (GB7) through the acupoint Baihui (GV20). The effects of acupuncture on neurological function scores, hematoma absorption, and HO-1 expression in a rat model of ICH were observed to examine the protective mechanisms of acupuncture on hematoma absorption. Through experiments, we come to the conclusion that acupuncture may promote the expression of hemeoxygenase-1 protein, reduce the volume of hematoma and the score of neurological deficit in rats with intracerebral hemorrhage, improve the performance of neurological deficit, and play a role in brain protection.

Key words: Acupuncture, Baihui, Qubin, Cerebral hemorrhage, Hemeoxygenase-1, Modified neurological severity score

Intracerebral hemorrhage (ICH) refers to nontraumatic hemorrhage in the brain parenchyma. The mortality rate for early ICH is 49.4% and the survivals always have unfavorable prognosis with kinds of neurological sequelae.

Hemoglobin entering the brain tissue will cause secondary damage, such as disrupting the blood-brain barrier, causing focal edema, and inducing neuroglial apoptosis. Heme, the degradation product of hemoglobin, generates oxygen free radicals and oxidative stress responses, which can cause neuronal death. Heme oxygenase-1 (HO-1), which is heme-degradation enzyme and rate-limiting enzyme, can catalyzes the degradation of heme to carbon monoxide, catalytic iron and bilirubin.

Previous studies have shown that acupuncture can improve the neurologic impairment symptoms of rats with acute ICH, alleviate pathological and ultrastructure damage, and promote restoration of neurological function. However, there are few studies on the use of acupuncture as an intervention for ICH.

Objective

To explore the effect of acupuncture on the expression of heme oxygenase-1 in rats with acute cerebral hemorrhage.

Materials and methods

108 Wistar male rats were randomly divided into sham operation group, model group, and acupuncture combined with model group (referred to as acupuncture group). Each group was divided into 3 subgroups according to 1d, 3d and 7d, with 6 rats in each subgroup. The rat model of cerebral hemorrhage was established by autologous blood injection. Acupuncture was given at Baihui (GV20) and Qubin (GB7). Separately, at the 1st, 3rd and 7th day, modified neurological severity score was used to evaluate the neurological function of rats, HE staining was used to measure the volume of cerebral hematoma and western blot was used to detect the expression of heme oxygenase-1 protein in cerebral hematoma tissue.

Results and discussion

Compared with the model group, at each time point, the modified neurological severity score of the acupuncture group was significantly reduced ($P < 0.01$); at the two time points of 3rd and 7th day, the cerebral hematoma volume of the acupuncture group was significantly reduced ($P < 0.05$) and the expression of heme oxygenase-1 protein in brain tissue was significantly increased ($P < 0.05$).

Acupuncture may promote the expression of heme oxygenase-1 protein, reduce the volume of hematoma and the score of neurological deficit in rats with intracerebral hemorrhage, improve the performance of neurological deficit, and play a role in brain protection.

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Clinical Observation on the Treatment of Mild Late-life Depression by Acupuncture with Shu Yuan Tiao Du

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Abstract

A total of 84 patients with late-life depression who met the inclusion criteria were included in this study, they were divided into 42 cases each in the test group (Shu Yuan Tiao Du acupuncture therapy) and the control group (conventional acupuncture) using a randomized controlled trial. After treatment, the total clinical efficacy of the Shu Yuan Tiao Du acupuncture therapy group was 92.5%, and the total effective rate of the conventional acupuncture group was 82.1% ($P < 0.01$). The HAMD-24, GDS-30, HAMA, TCM symptom score, item score for somatic symptoms in HAMD-24 of the Shu Yuan Tiao Du acupuncture therapy group were significantly lower than those of the conventional acupuncture group ($P < 0.05$). 1 month after the end of treatment, the follow-up recurrence showed that the recurrence rate was 7.5% in the group of Shu Yuan Tiao Du acupuncture therapy and 17.9% in the group of conventional acupuncture ($P < 0.01$). The Shu Yuan Tiao Du acupuncture therapy group was superior to the conventional acupuncture group in improving patients' depressive symptoms, anxiety symptoms and somatic symptoms, and had more advantages in long-term efficacy.

Key words: Acupuncture; Shu Yuan Tiao Du Acupuncture Therapy; Mild Late-life Depression; Clinical Observation

Late-life depression (LLD) is a kind of depression occurring at the age of more than 60 years old. In addition to typical depression, LLD is mainly characterized by somatic symptoms, hypochondriacal tendency and irritability^[1]. According to WHO statistics, the increase of age is positively correlated with the increase of LLD prevalence, and the prevalence of LLD in elderly women is higher than that in men^[2]. In addition, studies have shown that LLD patients have a much higher probability of developing vascular dementia or Alzheimer's disease within 5 years than normal elderly people^[3], and increase the morbidity and mortality of hypertension, coronary heart disease and diabetes^[4]. LLD has become one of the most intractable problems in aging due to its insidious onset, easy to be missed or misdiagnosed, high morbidity, low attendance rate, easy to miss and misdiagnosed, and high suicide rate. Acupuncture not only solves the drug resistance and withdrawal syndrome caused by long-term medication, but also has the advantages of low side effects and low treatment cost. Therefore, it has significant advantages in the treatment of LLD.

Objective

To compare the clinical effect of Shu Yuan Tiao Du acupuncture therapy and conventional acupuncture therapy in the treatment of late-life depression.

Methods

A total of 84 patients with late-life depression were randomized into an testgroup(42 patients, 2 case dropped off) and a control group (42 patients, 3 case dropped off).

The test group used Shu Yuan Tiao Du acupuncture therapy, in which du meridian acupoint selection: Baihui(GV20), Yintang(GV29), Shenting(GV24), shuigou(GV26). (1) Liver-kidney Yin Deficiency : Add Ganshu(BL18), Taichong(LR3), Shenshu(BL23), Taixi(KL3). (2) Liver Depression and Spleen Deficiency: Add Ganshu(BL18), Taichong(LR3), Pishu(BL20), Taibai(SP3). (3) Heart-spleen Deficiency: Add Xinshu(BL15), Shenmen(HT7), Pishu(BL20), Taibai(SP3). (4) Spleen-kidney Yang Deficiency: Add Pishu(BL20), Taibai(SP3), Shenshu(BL23), Taixi(KL3).

The control group used conventional acupuncture therapy. (1) Liver-kidney Yin Deficiency : Add Ganshu(BL18), Shenshu(BL23). (2) Liver Depression and Spleen Deficiency: Add Ganshu(BL18), Pishu(BL20). (3) Heart-spleen Deficiency: Add Xinshu(BL 15), Pishu(BL20). (4) Spleen-kidney Yang Deficiency: Add Pishu(BL20), Shenshu(BL23).

Both groups were treated for 30min, once a day, 7 days as a course of treatment, every 6 days of treatment for 1 day rest, a total of 6 courses of treatment. Observation indicators included Hamilton Depression Inventory (HAMD-24), Geriatric Depression Scale (GDS-30), Hamilton Anxiety Scale (HAMA), TCM Symptom Score Scale and item score for somatic symptoms in HAMD-24, and the efficacy was evaluated by the subtraction rate of HAMD-24 total score.

Results and discussion

The total clinical efficacy of the Shu Yuan Tiao Du acupuncture therapy group was 92.5%, and the total effective rate of the conventional acupuncture group was 82.1% (P<0.01). The HAMD-24, GDS-30, HAMA, TCM symptom score, item score for somatic symptoms in HAMD-24 of the two groups was significantly lower than that before treatment (P<0.01), and the HAMD-24, GDS-30, HAMA, TCM symptom score, item score for somatic symptoms in HAMD-24 of the Shu Yuan Tiao Du acupuncture therapy group were significantly lower than those of the conventional acupuncture group (P<0.05). 1 month after the end of treatment, the follow-up recurrence showed that the recurrence rate was 7.5% in the group of Shu Yuan Tiao Du acupuncture therapy and 17.9% in the group of conventional acupuncture (P<0.01).

Table 1 Comparison of scores between the two groups (Score, $\bar{x}\pm s$)

Group	case	HAMD-24		GDS-30		HAMA		TCM symptom score		item score for somatic symptoms	
		Before	After	Before	After	Before	After	Before	After	Before	After
Test group	40	27.05±	12.48	15.50±	7.80±	21.05	11.48	21.03±	11.45	8.50±	2.58±
		3.75	±7.09	2.26	3.90	±3.27	±6.66	3.42	±6.79	2.26	1.47
control group	39	26.92±	16.23	15.30±	10.54	20.62	14.85	21.18±	15.41	8.31±	4.56±
		3.89	±6.04	2.36	±4.44	±3.11	±5.12	3.34	±5.36	2.36	2.54

In conclusion, Shu Yuan Tiao Du acupuncture therapy can effectively treat late-life depression, and has more advantages in long-term efficacy. The Shu Yuan Tiao Du acupuncture therapy combines

back-shu point with yuan point to adjust and nourished the Zang-fu organs, and takes du meridian point to tong du and awaken the brain, taking into account the somatic symptoms, reflecting the overall concept, syndrome differentiation and treatment, both tong and supplement, specimen treatment characteristics. Our research group plans to explore the therapeutic effects of different syndromes of late-life depression in the next step, so as to provide more accurate treatment plans and higher-level evidence for clinical treatment.

Conclusion

Both the Shu Yuan Tiao Du acupuncture therapy group and the conventional acupuncture group were effective in the treatment of mild late-life depression. The Shu Yuan Tiao Du acupuncture therapy group was superior to the conventional acupuncture group in improving patients' depressive symptoms, anxiety symptoms and somatic symptoms, and had more advantages in long-term efficacy.

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Clinical Observation on the Treatment of Post-stroke Fatigue with Awn Needle Penetrating DU Meridian

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Abstract

Post-stroke fatigue (PSF) is a relatively common complication of stroke that seriously affects the rehabilitation and long-term prognosis of stroke patients due to the long-term presence of mental and physical fatigue^[1]. Epidemiological surveys have shown that the prevalence of PSF has reached 25%-85%^[2], suggesting that it has become an important part of the recovery process for stroke patients that cannot be ignored. Currently, PSF is mainly treated with oral medications and rehabilitation training, but long-term medication has adverse effects such as drug dependence and headache^[3], and the persistence of somatic fatigue can greatly reduce the effectiveness of rehabilitation training. According to traditional medicine, the deficiency of Yang Qi after stroke, resulting in the loss of the use of the mind, and the loss of both the body and the spirit are important causes of PSF fatigue symptoms. Therefore, stimulating Yang Qi and harmonizing the body and spirit is the key to treating PSF. The awn needle penetrating DU meridian gives full play to the effect of the DU meridian to raise Yang Qi and regulate the brain and spirit, combined with the awn needle penetrating stabbing to multiply the needle sensation, which has the effect of awakening the brain and opening the orifice, raising Yang Qi, harmonizing Yin and Yang, and helping to remove fatigue. Therefore, in this study, the clinical efficacy of the treatment of post-stroke fatigue with awn needle penetrating DU meridian was evaluated in terms of the degree of fatigue relief and improvement of symptoms of post-stroke neurological deficits by using conventional acupuncture as a control.

Keywords : Post-stroke fatigue; Awn needle penetration; DU meridian; Clinical efficacy observation.

Objective

To compare the clinical effect of awn needle penetrating DU meridian and conventional acupuncture in the treatment of post stroke fatigue.

Methods

A total of 66 patients with post-stroke fatigue were randomized into an observation group (33 patients, 1 case dropped off) and a control group (33 patients, 2 case dropped off). In the control group, conventional acupuncture was applied at Pishu(BL20), Ganshu(BL18), Shenshu(BL23), Baihui(GV20), Guanyuan(CV4), Zusanli(ST36), Sanyinjiao(SP6). The observation group was treated with awn needle penetrating DU meridian (The specifications of 0.40×150mm awn-needle (length 6 inches, no. 26) were selected for needling operation, from Baihui (GV20) to Shenting(GV24), Zhiyang (GV9) to Dazhui (GV 14), Mingmen(GV4) to Zhiyang(GV9).) The needles were retained for 30 min, once a day, continuous treatment for 6 days per week, 4 weeks

were required in the two groups. Before and after treatment, the fatigue severity scale(FSS) score, multidimensional fatigue index-20 (MFI-20) score, modified barthel index(MBI) score and national institute of health stroke scale(NIHSS) score,were compared in the two groups.

Results and discussion

Compared before treatment, the FSS, MFI-20 and NIHSS scores after treatment were decreased in the two groups ($P < 0.05$), and those in the observation group were lower than the control group ($P < 0.05$). Compared before treatment, the MBI scores after treatment was increased in the two groups ($P < 0.05$), and that in the observation group was higher than the control group ($P < 0.05$) (Table 1,2,3) .

The treatment results of this study showed that the FSS score, MFI-20 score and NIHSS score decreased and the MBI score raised in both groups of PSF patients, and the observation group was significantly better than the control group in reducing the FSS score, MFI-20 score and NIHSS score and improving the MBI score after treatment, suggesting that the therapeutic effect of awn needle penetrating DU meridianfor PSF patients significantly better than conventional acupuncture therapy.

Table 1 Comparison of general data between two groups of patients with post-stroke fatigue

Group	Case	Sex		Age			Disease duration(Days)		
		Man	Woman	Min	Max	Mean	Min	Max	Mean
observation group	32	19	13	48	73	60.53±8.24	15	120	43.84±28.42
control group	31	20	11	44	72	59.81±7.19	15	175	41.55±30.74

Table 2 Comparison of FSS and MFI-20 scores between two groups of patients with post-stroke fatigue before and after treatment (Score, $\bar{x} \pm s$)

Group	Case	FSS score		MFI-20 score	
		Before	After	Before	After
observation group	32	45.41±5.31	20.50±4.59 ¹⁾²⁾	59.19±6.10	45.16±3.23 ¹⁾²⁾
control group	31	44.48±4.44	25.00±5.09 ¹⁾	58.68±5.05	47.10±3.31 ¹⁾

Note: Compared with the group before treatment, 1) $P < 0.01$; Compared with control group after treatment, 2) $P < 0.05$

Table 3 Comparison of MBI and NIHSS scores between the two groups of patients with post-stroke fatigue before and after treatment (score, $\bar{x} \pm s$)

Group	Case	MBI score		NIHSS score	
		Before	After	Before	After
observation group	32	47.50±9.42	65.31±8.88 ¹⁾²⁾	7.50±1.95	3.41±1.43 ¹⁾²⁾
control group	31	47.90±8.04	59.68±8.06 ¹⁾	6.87±1.84	4.71±1.35 ¹⁾

Note: Compared with the group before treatment, 1) $P < 0.01$; Compared with control group after treatment, 2) $P < 0.05$

To sum up, in this study, the use of awn needle penetrating DU meridian in the treatment of post-stroke fatigue has a significant effect, effectively reduce the fatigue degree of patients with post-stroke fatigue, relieve a variety of fatigue symptoms, improve the ability of post-stroke fatigue in daily life, improve the neurological function defect symptoms of patients with post-stroke fatigue, shorten the neurological function rehabilitation process of patients with post-stroke. It is worthy of further clinical application. The disadvantage is that the research time is relatively short. In the future, more comprehensive long-cycle, multi-center and multi-study studies will be carried out to increase the observation of relevant laboratory indicators and further explore the mechanism of its action.

Conclusion

The efficacy of awn needle penetrating DU meridian for post-stroke fatigue was better than that of conventional acupuncture in reducing the severity of fatigue, relieving fatigue symptoms and enhancing the ability to perform daily activities.

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Exploration on Regularities and Characteristics of Differentiation and Treatment of Multiple Myeloma Based on Ancient Chinese Medicine Books

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Abstract

Objective: To explore the related empirical formula for multiple myeloma from ancient books, so as to provide more references for its traditional Chinese medicine (TCM) treatment.

Materials and methods

Since there is no relevant record of "myeloma" in ancient literature of traditional Chinese medicine (TCM), and the disease was mostly detected with bone-related symptoms as the initial symptom, we took bone arthralgia^[1] and bone erosion^[2] as searching terms and screened the search results with the help of the 5th edition of Chinese Medical Dictionary.

Results

A total of 560 articles were obtained.

Conclusion

It is considered that on the basis of patterns of both qi and blood deficiency, yin deficiency of liver and kidney, yang deficiency of spleen and kidney, obstruction of phlegm and blood stasis, and invasion of evil and toxin, the treatment of bone pain should focus on promoting nutrient and defense smoothing, and the exogenous pathogenic factors should take cold and heat as the total classification, and then according to the symptoms of the sub-classification, the yang qi of spleen and kidney should be protected specially. The struggling relationship between healthy qi and pathogenic factor should be paid more attention to. For acupuncture and moxibustion treatment, we should choose different acupuncture methods according to syndrome and symptoms, combine with modern equipment and select the corresponding meridians and acupoints suggesting that the clinical treatment proportion of acupuncture and moxibustion for myeloma should be increased as appropriate^[3-8]. In terms of treatment, external treatment can be combined, and draw lessons from the homology of medicine and food so as to achieve the result of internal and external integrated treatment as well as comprehensive conditioning. The appropriate amount of aconite herbs corresponding to the pathogenesis can be considered in the prescriptions for medication, and the idea of sweat therapy to boost yang in the treatment of the pathogenesis of spleen and kidney is worth learning and thinking for doctors. The prognosis is usually unfavorable.

Keywords: multiple myeloma, ancient TCM books, bone arthralgia, bone erosion, TCM syndrome differentiation

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Determination of Five Chemical Constituents in *Paeony alba*

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Abstract

Objective: To determine the contents of 5 active components (paeoniflorin, paeoniflorin, catechin, paeonol and gallic acid) in *Radix paeoniae alba* by HPLC. **Methods:** Diamonsil C18 column (250 mm×4.6 mm, 5 μm) was used. The mobile phase consisted of acetonitrile and 0.1% phosphoric acid in water in gradient elution with a volume flow rate of 1.0 mL/min. The detection wavelength was 230 nm and the column temperature was 30 °C. **Results:** The contents of paeoniflorin, paeoniflorin, catechin, paeonol and gallic acid were 3.17%, 2.06%, 0.39%, 0.19% and 0.22% respectively, and had a good linear relationship with the peak area at 0.01~2 mg/ml and reproducibility. **Conclusion** This method is efficient and accurate for the determination of 5 active components in *Paeoniae paeoniae*, providing ideas for the further improvement of the quality control of *Paeoniae paeoniae*.

Introduction

Paeonia lactiflora Pall is a plant of Ranunculaceae.^[1] Paeony is used to treat painful symptoms, such as dysmenorrhea of blood deficiency pattern, muscular pain caused by liver stagnation and blood deficiency, abdominal pain caused by liver and spleen disharmony and headache caused by hyperactivity of liver Yang. It is one of the most commonly-used traditional Chinese medicine in clinical practice^[2, 3].

1. Materials

1.1 Instruments and reagents

Paeoniflorin (batch number: DST180103-070), Paeoniflorin (batch number: DST170419-071), catechin (batch number: DST180128-001), paeonol (batch number: DST180312-048) Gallic acid (batch number: DST180312-048) Dst180226-008) standard was purchased from Chengdu Durst Biotechnology Co., LTD.

2 method

2.1 Preparation of standard

10 mg of paeoniflorin, paeoniflorin, catechin, paeonol and gallic acid were accurately weighed and placed in a volumetric flask, shaken with methanol, and the volume was fixed to 5 ml to prepare the reserve solution of the mixed reference. At this time, the mass concentration of the five reference substances was about 2 mg/ml. Store at 4 °C and set aside.

2.2 Sample preparation

Take peony fresh products, wash sediment, boil with clear water for half an hour, slice, air dry, flour. The above crude powder was placed in a 50 ml flask, diluted with 35 ml dilute ethanol solution, shaken well, and ultrasonic was carried out in a 40 °C tank for 1 h. The liquid was filtered, and the filtrate was taken for later use.

2.3 Optimization of chromatographic conditions

The determination was performed on a Diamonsil C18 column (250 mm×4.6 mm, 5 μm) with a

flow rate of 1.0 ml/min and an injection volume of 10 μ L. The detection wavelength was 230 nm and column temperature was 30 $^{\circ}$ C. Mobile phase: acetonitrile (A) and 0.1% phosphoric acid in water (B), gradient elution conditions were 0 min: 0% acetonitrile; 0-40 min: 0%~50% acetonitrile; 40-42 min: 50%-0% acetonitrile; 42~50 min: 0% acetonitrile.

2.4 Measuring Item

1. Linearity test; 2. Precision test; 3. Stability test; 4. Repeatability test.

3 Result

The determination results of paeony samples are shown in Table 1. According to the experimental data, the calculated RSDS of peak areas of the five active ingredients were 2.85%, 1.27%, 2.79%, 2.42% and 2.18%, respectively. It indicated that the precision of the established HPLC was good. The chemical properties of the paeony test solution were stable within 24 hours. The recovery rate of paeony was 95.93%-98.25%, RSD \leq 1.40%;

Table 1. Determination of 5 components to be tested in Paeony test solution (n=3)

name	mass fraction (%)				
	paeoniflorin	albiflorin	gallate	catechinic	paeonol
radix paeoniae alba	3.175	2.064	0.2205	0.3900	0.1960

4 Discussion

In this study, a new HPLC-DAD method was established for the rapid determination of five effective components of *Paeoniae paeoniae*, which optimized the method of using only one index component, paeoniflorin, in the 2020 edition of Chinese Pharmacopoeia. Using this method for quality control, the quality of *paeoniae paeoniae* could be evaluated more comprehensively and accurately. This study provides reference for quality control and evaluation of *Paeony*.

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Innovation and Development of Health Management under the Background of Health Industry

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Abstract

With the development of health industry and the improvement of social health awareness, the demand for health management industry increase gradually . In order to promote better development of health management industry, it is very important to seek institutional innovation and development of health management. This paper introduces the development status of Chinese health management and its existing-problems, puts forward useful ideas for the development of health management industry which provides a certain reference for the health management industry with Chinese characteristics.

Keywords: health management; innovation and development ; Chinese characteristics

1. The Current Situation of the Health Management Industry

Health management is based on modern health and medical concepts, guided by the concept of "Preventive disease" in traditional Chinese medicine, collects and evaluates the health status and health risk factors of individuals or groups, and formulates health management plans to achieve prevention and control. disease, the purpose of improving the quality of life. my country's health management industry has begun to take shape and has become an important part of the medical service system, which has played a certain role in effectively improving people's health and reducing medical expenses. However, the current industry development is still in the growth stage, and there are mainly the following problems^[1].

The current health management service is mainly an additional service of the health examination center, and there is no clear business scope and supervision standards. The main goal of the medical examination center business is disease detection rather than disease prevention. Internet new media provides insufficient services such as health risk assessment, health planning, and intervention. The entry threshold for health management practitioners is low, and the knowledge system is not sound enough.

The health management market has a relatively narrow audience, mainly high-income people. The public has not yet established the concept of health management, pays less attention to health management, and does not recognize the importance of disease prevention.

At present, health management is mainly reflected in the management of chronic diseases, the prevention features are not prominent, and the health management of healthy people is relatively weak.

2. Health management industry innovation and development measures

In order to improve the level of health management, a health management center will be established relying on the powerful medical resources of public hospitals. Develop health management APPs and physical examination equipment^[2]. Increase the health management services of community hospitals or private hospitals, and give full play to the advantages of wide coverage and good

service attitude. Through the new media of the Internet, medical information sharing is realized, and services such as online health examination appointments, health consultation, conditioning and rehabilitation, and health care are increased.

Establish a health management major to cultivate health management talents with comprehensive medical knowledge. Standardize the access standards for "health managers", improve the difficulty of obtaining health managers certificates, and make them truly capable of providing reliable health management services to the population.

Expand the service objects of health management, and adopt hierarchical management for groups with different needs. For healthy and sub-healthy people, it is necessary to "prevent the disease before it occurs, and treat it before the disease", and give scientific health guidance before the disease occurs, so as to achieve the purpose of disease prevention. For the sick population, it is necessary to "prevent the disease and treat it at the beginning of the disease". Early detection and early treatment can effectively slow down the development of the disease, improve the probability of disease cure, and alleviate the pain. In the face of people who are about to be cured, it is necessary to "do everything in their power to eliminate evil and prevent relapse", and pay attention to preventing recurrence and promoting functional recovery in the treatment of diseases. With the increasing number of health management audiences, the concept of health has been gradually changed from treatment-oriented to prevention-oriented.

The society should strengthen health education and raise awareness of health management. Increase health lectures by means of Internet new media, and enrich the channels and means for the public to learn health knowledge. Primary and secondary schools have added health knowledge courses to provide students with early health education.

3. Improve service content and links

3.1 Health monitoring

Measure the health information of the service recipients, including the history of present illness, past history, family history, marriage and childbearing history, bad habits, etc. These health information is the premise of health management.

3.2 Health assessment

Health assessment refers to the purpose of preventing disease by analyzing health risk factors. Health risk factors refer to various factors including environment, lifestyle, genetics, etc. that endanger health and increase the risk of disease and death. By combining health risk factors with health information, a health risk factor model is established to predict the possibility of various diseases, so as to carry out targeted preventive interventions.

3.3 Health intervention

According to health information and health assessment results, risk factors are intervened, including diet, exercise, psychology, nutrition, etc., to find self-management and health care methods suitable for individuals to achieve the purpose of reducing disease risk[3].

4. Pay attention to the role of traditional Chinese medicine in health management

Based on the guiding ideology of "preventing disease" in traditional Chinese medicine, through traditional Chinese medicine methods such as physical therapy, acupuncture, massage, medicated bath, and fumigation, it can help righteousness, balance yin and yang, and improve the body's

ability to prevent disease. Study the Chinese's unique health risk intervention methods, and establish a health management model with traditional Chinese medicine characteristics.

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Study on the Anti-depressant Mechanism of Zhizigancaochi Decoction Combined with Moutan Bark

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Abstract: In order to investigate the affect of Gancaozhizichi decoction combined with Moutan bark, on rats with depression model. The rat model of depression was established by the methods. That was "solitary care and chronic unpredictable mild stress"(CUMS). Animal models were treated with fluoxetine or Gancaozhizichi decoction combined with Moutan bark by intragastric administration for 30 days. After 30 days' treatment, analysis of the behavioral indexes of rats was examined by the weight growth, the glucose water consumption test, open field test, forced swimming test and the tail suspension test. Simultaneously the behavioral indexes of rats were detected the content of 5-hydroxytryptamine/serotonini (5-HT) and Dopamine (DA) in the hippocampus and serum. The results showed that the Gancaozhizichi decoction combined with Moutan bark could promote the weight growth rate and the glucose water preference of rats with depression; it could reduce the immobility time, tail suspension time of model rats; increase the total distance, average exercise, speed and the number of climbing and standing of model rats. It also could increase the 5-HT, DA content in hippocampus and serum of model rats. Gancaozhizichi decoction combined with Moutan bark had a significant improvement of depression on model rats. The mechanism was related to the levels of 5-HT and DA in serum and hippocampus.

Keywords: Depression; Gancaozhizichi Decoction Combined with Moutan Bark; Behavioral Indexes; 5-HT; DA

Objective: Adding licorice to Zhizichi Decoction can moderate the nature of medicinal sand boost qi, which combines with Moutan bark to all eviate vexation. In this study, a rat depression model was established by "solitarycare+CUMS"^[1-3], the changes of 5-HA and DA contents in serumand hippo campus being detected through behavioral analysis, clarifying the effect and mechanism of GancaoZhizichi Decoction combined with Moutan bark on depression.

Materials and Methods:

Materials: Experiment animals:40 clean grade Wistar rats, male, with a body weight of 200±20g. **Drug sander agents:** ZGCM: Firs to fall, add 900mL of distilled water to gardenia15g,licorice30gandmoutanbark15g, which is decocted until the solution is about 500mL. Next,50g of fermented soy bean were added, decocting similarly until the solution is 300mL. Besides, take the filtrate and concentrate it to 110ml with the cruded rug amount 1g/mL, and storeitat-20°C forstand by. Finally, fluoxetine was added to distilled water to prepare a suspension of 0.5mg/ml.

Methods: Animal grouping and modeling methods: the rat depression model was establish ed by solitary care and CUMS^[3]. At the same time of modeling, the positive control group was perfused with fluoxetine suspension at the weight of1.8mg/kg per day, likewise, the Z GCM group with the volume of 9.9mL/kg per day likewise (converted according to the dail y dosage of adults). **Animal behaviortest**^[3-7]: including syrup preference test, rat weight gro w thrate, forced swimming test, tail suspension test and open field test. **The contents of 5-**

HT and DA in serum and hippocampus of rats: 30 Days after administration, serum and hippocampus homogenate supernatant were collected, the contents of 5-HT and DA (ng/g) in serum and hippocampus of rats being detected by ELISA. **Statistical analysis:** the data were calculated by Microsoft Excel 2007, plotted by GraphPad Prism 6, and compared with each other by SPSS 26.0 for one-way ANOVA. $P < 0.05$ was statistically significant.

Results and Discussion:

The effect of ZGCM on the weight growth rate, syrup preference, swimming immobility time and tail suspension immobility time of depression model rats: As shown in FIG 1, the weight growth rate of normal rats is higher than that of model, fluoxetine and ZGCM group, while the weight growth rate of rats in fluoxetine group and ZGCM group was similar and higher than that in model group

Effects of swimming immobility time and tails suspension immobility time: Compared with the blank group, the swimming immobility time and tail suspension immobility time of model group rats increased significantly ($P < 0.01$), while the time of fluoxetine group and ZGCM group increased, but the difference was not statistically significant ($P > 0.05$). Compared with the model group, the immobility time of rats in fluoxetine group and ZGCM group decreased significantly ($P < 0.01$).

Effects of syrup preference and open field exercise: The results are shown in FIG 1. Compared with the blank group, the syrup preference, total distance, average exercise speed and vertical standing time so rats in the depression model group were significantly reduced ($P < 0.01$). The syrup preference, the total distance, exercise speed and standing times of fluoxetine group and ZGCM group, in which the difference was not statistically significant ($P > 0.05$). Compared with the model group, the sugar preference, total distance and exercise speed of fluoxetine group and ZGCM group increased significantly ($P < 0.01$ or $P < 0.05$), and the number of standing increased, but the difference was not statistically significant ($P > 0.05$).

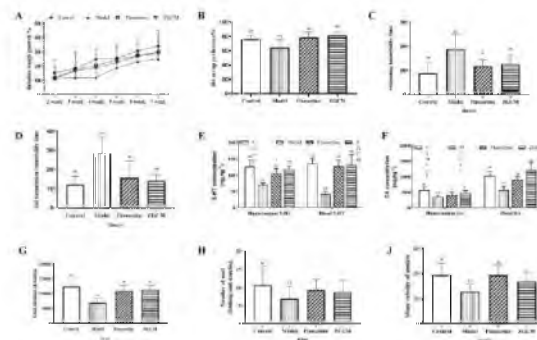


FIG. 1 Behavioral changes and the concentration of 5-HT and DA of rats in different groups

Note: A: weight growth rate, B: sugar preference, C: immobilization time of rat swimming, D: immobilization time of rat tail suspension, E: 5-HT concentrations in hippocampus and serum, F: DA concentrations in hippocampus and serum, G: Total distance of motion, H: Number of wall climbing and standing, I: Mean velocity of motion

Note: Compared with blank group, $**P < 0.01$, $*P < 0.05$; Compared with the model group, $##P < 0.01$, $#P < 0.05$

Effect of ZGCM on the concentration of 5-HT and DA in serum and hippocampus of model rats: Compared with the blank group, the content of 5-HT and DA in hippocampus and serum of

model rats decreased observably($P<0.01$). And compared with the model group, the contents of ZGCM group were significantly increased($P<0.05$ or $P<0.01$),and the contents of fluoxetine group were markedly increased($P<0.01$), but the content of DA in hippo campus was increased, there being no statistical significance($P>0.05$).

The experimental results showed that the syrup preference of the model rats decreased, the total exercise distance, average exercise speed, number of upright, etc. decreased signally, and the forced swimming immobility time and tail suspension immobility time increased strikingly, the behavior of the rats simulating the main characteristics of human depression. In this study, based on Zhizichi Decoction, licorice and moutan bark were added to investigate its effect on depression model rats. The results revealed that ZGCM can improve the behavior of depression model rats, and Zhizichi Decoction combined with Moutan bark has a certain anti depressant effect, whose possible mechanism is related to the upper regulation of 5-HT, DA and other mono amine neurotransmitters.

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Lignan-Amides of Datura Metal Seeds Attenuates Neuroinflammation and Cognitive Decline through TREM2/Dap12-Mediated Activation of Multiple Signalings and Neurotrophin

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Abstract

Alzheimer's disease (AD) is a common neurodegenerative disease characterized by the aggregation of amyloid-beta ($A\beta$) and hyperphosphorylated tau. We previously reported that lignan-amides of Datura metal seeds (LDS), improved neuroinflammation and increased TREM2 aggregation in BV2 cells. To explore the mechanism of LDS improving the learning and memory ability of SAMP8 mice and its potential effect on AD. LDS attenuated memory impairments in the Morris water maze. LDS treatments prevented brain atrophy and improved morphological changes in the hippocampus and cortex, as evidenced by IHC and H&E staining for neuron damage and loss. LDS treatments increased TREM2/Dap12 and reduced TLR4 signals. The cognitive impairment, neuronal aging, damage, and loss of SAMP8 mice were protected by LDS. The mechanisms could be attributed to increased activation of anti-neuroinflammation activity, and upregulation of TREM2/Dap12, also involving the levels of neural factors, and inflammatory factors.

Keywords: Lignan-amides of Datura metal seeds, TREM2, neuroinflammation.

Alzheimer's disease (AD) is a progressive and irreversible neurodegenerative disorder leading to cognitive, memory, and behavioral impairments. Brain regions involved in learning and memory processes, including the temporal and frontal lobes, were reduced in AD patients induced by degeneration of synapses and death of neurons. The pathogenesis of AD was complex and involved diverse physiological, cellular, and molecular pathologies. Accumulating evidence increasingly indicated that the inflammatory process was encountered in the pathology of AD. Examination of postmortem brains of AD patients revealed an abundant presence of pro-inflammatory cytokines and chemokines [1]. TREM2 was a cell surface receptor of the Ig superfamily that was expressed on microglia in the CNS. Recent genetic studies have identified a rare variant of TREM2 that was a risk factor for nonfamilial AD, which was the most common form of late-onset dementia. Coincidentally, the lignan-amides have represented outstanding effects for AD treatment involving acetylcholinesterase inhibitory activity, anti-oxidation, and anti-inflammatory in previous modern pharmacological studies [2]. Simultaneously, the rich lignin-amides existed in the seeds of Datura metal including cannabisin D-H [3]. In our previous study, they were associated with TREM2 protein. Therefore, we have carried out relevant research

Objective

It is worth noting that although our previous studies have shown that LDS has an anti-neuritis effect, and explored its potential molecular mechanisms, but the treatment of AD has not been reported. Through this study we investigated the effect and the possible mechanisms of action of LDS in SAMP8 mice of AD.

Materials and methods

In our previous study we found that the sample contains 27 lignan-amides that have been [3]. Male mice of SAMP8 purchased from Peking University Health Science Center were used in this study to avoid the interference of estrogen on neuroinflammation and cognitive function. All procedures were approved by the regulations (permit no. 2019110101). References were used for other test methods [2].

Results and discussion

The water maze was designed to examine spatial learning for rodents and evaluate hippocampus-dependent navigation and memory. The normal control, the SAMP8 (model), the SAMP8-Donepezil (positive), and the SAMP8-LDS groups were subjected to the MWM test. Compared with the model group, the swimming distance was significantly decreased in the SAMP8 mice after feeding with either Donepezil or LDS. We observed that mice with a high dose of LDS treatment restored the ability to navigate the platform, indicating that LDS was beneficial to the learning and memorial memory abilities. Compared with the model group, the SAMP8 treated with either Donepezil or the high dose of LDS, the cerebral cortex and hippocampus morphologies showed various degrees of recovery. Neurons were arranged orderly into a compact structure, uniformly distributed, and showed normal histological staining. This result of IHC indicated that LDS improved the A β , TREM2, and IBA-1 deposition in SAMP8 mice (Fig. 1A-C).

Additionally, TREM2 has been demonstrated to have a positively suppressive effect on TLR4. In the present study, the expression changes of TREM2/Dap12 and TLR4/MyD88/NF- κ B/p65/NLRP3/Caspase-1 were determined in the SAMP8 mice. Western blot results indicated that the protein levels of TREM2/Dap12 were increased and TLR4/MyD88/NF- κ B/p65/NLRP3/Caspase-1 were lower in the cortex and hippocampus of the SAMP8 mice after LDS and DPZ dispose of ($P < 0.05$). However, the increased expression of TREM2 as a potential compensatory response suppresses the activity of TLR4 (Fig. 1D-E).

As one of the important factors in the occurrence of Alzheimer's disease, neuroinflammation can lead to the overexpression of pro-inflammatory cytokines such as interleukin (IL-6, IL-1 β) and TNF- α , resulting in neurological dysfunction, neuronal vacuolation, and growth factor inhibition. Therefore, the release levels of TNF- α , IL-6, and IL-1 β , the classic indicators of inflammation, were detected experimentally. The results showed that the release levels of TNF- α , IL-6, and IL-1 β were overexpressed in the model group, while the release levels of TNF- α , IL-6, and IL-1 β were inhibited in the positive drug group and the LDS high-dose group (Fig. 1F).

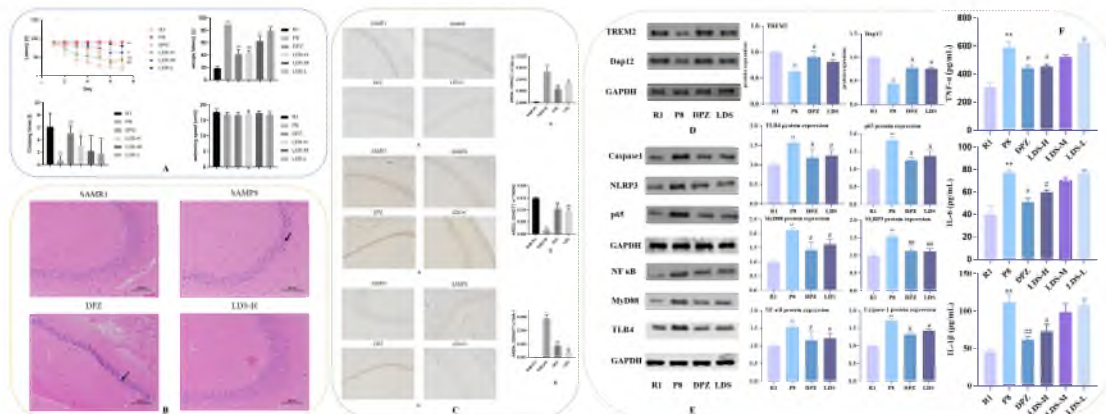


Fig.1 (A) The results of the MWM test; **(B)** The results of the HE staining; **(C)** The results of the IHC staining; **(D)** The protein levels of TREM2/DAP12; **(E)** The protein levels of TLR4/MyD88/NF- κ B/p65/NLRP3/Caspase-1; **(F)** Expression of inflammatory factor.

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Metal-organic Framework IRMOFs Coated with a Temperature-sensitive Gel (IRMOF-3-Gel) Delivering Norcantharidin (NCTD) to Treat Liver Cancer

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Abstract

NCTD is suitable for the treatment of primary liver cancer, especially early and middle stage of primary liver cancer. However, the side effects of NCTD have limited its application. Therefore, we aimed to establish a liver-targeting therapy in which NCTD is loaded into IRMOF-3 coated with a thermosensitive gel (NCTD-IRMOF-3-Gel), which can be efficiently delivered to liver cancer cells and slowly released. The results reveal that this thermosensitive gel-encapsulated IRMOF-3 has great advantages as an antitumor drug carrier and provides some ideas for passive targeting therapy of tumors.

Keywords: NCTD; Metal-organic frameworks; IRMOF-3; Anticancer; MTT; Liver cancer

In recent years, a large number of studies have been carried out to reduce the side effects and increase the efficacy of NCTD^{[1]-[2]}. This project aims to develop a multifunctional metal-organic framework (IRMOF-3) that can play an important role in drug carrying and delivery. Because of the special topological structure of IRMOF-3, drugs can be loaded into the spatial structure to the maximum extent, and it plays great role in control release^{[3]-[5]}. However, when NCTD-IRMOF-3 enters the body, burst release will be caused due to endocytosis or gastrointestinal absorption. Therefore, we aimed to establish a liver-targeting therapy in which NCTD is loaded into IRMOF-3 coated with a thermosensitive gel (NCTD-IRMOF-3-Gel), which can be efficiently delivered to liver cancer cells and slowly released. In this study, NCTD-IRMOF-3-Gel was prepared, and the in vitro targeting behavior was explored. It showed that the combination of IRMOF-3 and the thermosensitive gel could decrease the toxicity and increase the bioavailability of NCTD, representing an effective method for the chemotherapy of liver cancer. This study lays a foundation for the liver-targeting ability of NCTD-IRMOF-3-Gel. The results reveal that this thermosensitive gel-encapsulated IRMOF-3 has great advantages as an antitumor drug carrier and provides some ideas for passive targeting therapy of tumors.

Objective

To develop a nanomaterial carrier, NCTD-IRMOF-3-Gel (NCTD-loaded metal-organic framework IRMOF-3 coated with a temperature-sensitive gel), aiming to improve the anticancer activity of NCTD and reduce the drug dose.

Materials and methods

NCTD-loaded IRMOF-3 (a kind of metal-organic framework) coated with a temperature-sensitive gel (NCTD-IRMOF-3-Gel) was obtained by a coordination reaction. The apparent characteristics and in vitro release of NCTD-IRMOF-3-Gel were investigated. Cell cytotoxicity assays, flow cytometry and apoptosis experiments on mouse hepatoma (Hepa1-6.) cells were used to determine the anti-liver cancer activity of NCTD-IRMOF-3-Gel in in vitro models.

Results and discussion

The particle size of NCTD-IRMOF-3-Gel was 50~100 nm, and the particle size distribution was uniform. The release curve showed that NCTD-IRMOF-3-Gel had an obvious sustained-release effect. The cytotoxicity assays showed that the free drug NCTD and NCTD-IRMOF-3-Gel treatments markedly inhibited Hepa1-6 cell proliferation, and the inhibition rate increased with increasing drug concentration. By flow cytometry, NCTD-IRMOF-3-Gel was observed to block the Hepa1-6 cell cycle in the S and G2/M phases, and the thermosensitive gel nanoparticles may inhibit cell proliferation by inducing cell cycle arrest. Apoptosis experiments showed that NCTD-IRMOF-3-Gel induced the apoptosis of Hepa1-6 cells.

Based on the results of this study, NCTD-loaded IRMOF-3 nanoparticles incorporated into a thermosensitive gel appeared to be a useful tool for cancer treatment because of the enhanced inhibition rate of cancer cells and controlled release of drugs from these nanocarriers. Our future studies will focus on elucidating the activity of the drug delivery system and its effects on the mechanism of action of the encapsulated anticancer drug.

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Study on Preparation of Health Medicine Clove Formula Granules

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Abstract

Objective : To explore the best technology of clove formula granules. **Methods**: Orthogonal test was used to investigate three factors: the dosage of ingredients A, the proportion of auxiliary materials B and the concentration of wetting agent C. **Results**: The optimum preparation conditions of granules were as follows: 40% of auxiliary materials, 1:1 ratio of starch dextrin and 75% of ethanol concentration. Conclusion The clove formula granules prepared according to the above technological conditions have high molding rate, good solubility and suitable hygroscopicity.

Keywords: clove, granule, technological investigation

1 Introduction

Clove plays a significant role in the treatment and prevention of many chronic diseases. Clove, a traditional Chinese medicine, plays a significant role in the treatment and prevention of many chronic diseases^[1-2]. The unique component of clove, has anticancer, antioxidant, antipyretic, analgesic and antibacterial effects^[3]. In this study, the best preparation technology was selected according to the investigation of molding technology.

2 Materials and methods

2.1 Materials and reagents: Clove slices, Starch, Anhydrous, Ethanol (Tianjin Tianli Chemical Reagent Co., Ltd.), Purified water (Watsons Co., Ltd.)

2.2 Methods: Soak 100g clove slices in 12 times of water for 30min, extract with volatile oil extractor for 1.5h, filter with 150 mesh sieve while it is hot, repeat for three times, combine the filtrates, concentrate at 46°C under reduced pressure to 100ml, and freeze-dry to obtain clove formula granule dry paste powder. Take 100g dry paste powder, starch dextrin as auxiliary material and ethanol as wetting agent, and adopt orthogonal $L_9(3^4)$ test to select three factors: auxiliary material dosage, auxiliary material ratio and wetting agent concentration. See Table 1 for the level table. The molding rate, hygroscopicity and solubility were investigated according to Chinese Pharmacopoeia.

2.3 According to the best process, 15 batches of clove formula granules were prepared, and the chromatogram was recorded, as shown in Figure 1. Three batches were selected to determine the molding rate, solubility and moisture absorption rate.

Table 1 Level Table of Process Investigation Factors

level	factors			
	A adjuvant dosage (%)	B adjuvant proportion (starch: dextrin)	C ethanol concentration (%)	D blank
1	30	0.3	75	1
2	40	1:1	85	2
3	50	1:2	95	3

3 Results and discussion

Table 2 Orthogonal design and experimental results

serial number	factor				index			
	A	B	C	D	Molding rate (%)	Melting rate (%)	Moisture rate in 24h (%)	Comprehensive score
1	1	1	1	1	79	81	5.16	92.72
2	1	2	2	2	82	85	5.35	96.17
3	1	3	3	3	86	80	5.12	94.60
4	2	1	2	3	90	89	5.24	99.23
5	2	2	3	1	93	92	5.22	101.94
6	2	3	1	2	90	91	5.37	99.12
7	3	1	3	2	84	86	5.36	96.42
8	3	2	1	3	87	91	5.28	98.89
9	3	3	2	1	85	87	5.19	97.19
K ₁	94.703	95.723	96.740	97.363				
K ₂	100.101	99.260	97.825	97.107				
K ₃	97.155	96.877	97.331	97.540				
R	5.214	3.457	0.874	0.403				

Table 3 Variance analysis of experimental results

Variance source	Sums of squared deviations	freedom	Mean square	F	P
A	41.350	2	20.675	153.148	P<0.05
B	16.588	2	8.294	61.437	P<0.05
C	5.327	2	2.6635	19.730	P<0.05
D (error)	0.27	2	0.135	1	

Table 4 Best process validation test

Component	Molding rate	Melting rate	Moisture rate	Comprehensive score
1	93	95	5.24	102.02
2	96	94	5.26	101.95
3	94	95	5.24	102.08
Mean	93	93	5.21	102.02
RSD%	1.64	0.62	0.19	0.06

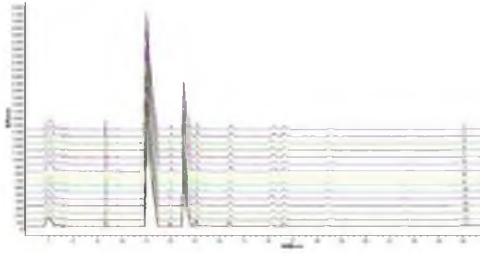


Fig. 1 Clove particle chromatogram



Fig. 2 product of clove granules

According to the results, the optimum technological conditions were determined as follows: 40% of auxiliary materials, 1:1 ratio of starch dextrin and 85% of ethanol concentration. The finished granule product is shown in Figure 2. The preparation method is as follows: starch and dextrin are mixed at a ratio of 1:1, the ratio of dry paste powder to auxiliary materials is 1:0.4, and the concentration of ethanol is 85%. After uniform mixing, dry granulation is carried out, and sieving is carried out. The molding rate of granules prepared by this method is 94.33%, with good solubility and suitable hygroscopicity.

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The Development of Medicinal Properties of Fructus Cannabis in Past Dynasties

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Fructus Cannabis is the dried ripe fruit of *Cannabis sativa* L. that belongs to Moraceae. It is a typical medicine that is homologous in medicine and food, with a long history in China. The medicinal use of this product was first seen in "Shennong Herbal Scripture". There are many names of Fructus Cannabis in the ancient books of *Materia Medica*, which are mixed but not very clear. The name of Fructus Cannabis "Hu Ma Ren" was first found in the "Daily *Materia Medica*" written by Wu Rui in the Yuan Dynasty [1]. Its Gan and Ping are recorded in the "Chinese Pharmacopoeia". Fructus Cannabis belongs to the spleen, stomach and large intestine meridians, with moistening the intestines and relieving defecation, for blood deficiency and fluid deficiency, intestinal dryness and constipation. However, by sorting out the records of Fructus Cannabis in previous dynasties, we can see that the medicinal properties and classics of Fructus Cannabis have undergone great changes. The purpose of this study is to make a textual research on the medicinal properties and functions of Fructus Cannabis in order to systematically clarify the evolution of the medicinal properties and meridian tropism of Fructus Cannabis.

Textual Research on Sweet in Flavor

The medicinal flavor of Fructus Cannabis was first included in "Shennong Herbal Scripture", and the qualitative analysis of flavor of Fructus Cannabis in successive dynasties was basically the same. The reasons for the analysis may be as follows: first, the theory of thin and thick smell of Yin and Yang [2], and it is recorded in the fifth chapter on the appearance of Yin and Yang: "the flavor is sweet and divergent into Yang, acid and bitter gush into Yin", and "the taste of Yin goes out of the lower body and Yang qi goes out of the upper body. Thick taste is Yin, while thin is Yin and Yang. If the taste is thick, it will leak, and if it is thin, it will pass." "Pharmaceutical Dharma Xiang" recorded: "bitter medicine rises, and so does the slight cold." Sweet and pungent medicine is flat, sweet cold and purging fire. "Gan Xin flavor medicine has the effect of inhibiting the decline, but also because the sweet and pungent taste is thin, like the Yang of the earth, has a rising trend. Fructus Cannabis belongs to the medicine of tonifying middle qi, tonifying blood and Yin, relieving spleen and moistening dryness, which can treat spleen and stomach weakness, qi deficiency and fever, and eat less abdominal distension, which is in line with the method of "sweet and slow acid harvest". Second, according to the theory of pre-tonifying and reducing the pain of the five internal organs [3], "the theory of plain asking about the method of storing qi" said: "the desire for the spleen is slow, urgent food is sweet to ease it, with bitter diarrhea, and willing to supplement it." Fructus Cannabis can relieve spleen moistening dryness, cure Yang Ming disease, spleen brought by sweat, stomach heat, it is difficult, can specialize in the treatment of intestinal

dryness and constipation, stroke sweating, irregular menstruation, and Buzhong Yiqi. Therefore, Fructus Cannabis can be regarded as "sweet". Third, according to the theory of the efficacy of the five flavors^[4], Sweet in flavor has the effect of relieving pain, tonifying the deficiency of yin and yang, reconciling medicinal properties and alleviating toxicity. Hemp kernel can tonify qi, replenish deficiency and fatigue, tonify blood and tonify Yin, slow down the function of erysipelas, which can be regarded as the role of "sweet".

Textual Research on Neutral in Nature

The understanding of "neutral in nature" of Fructus Cannabis in previous dynasties is basically the same, which is based on the following points: first, the medicinal property of Fructus Cannabis is peaceful^[5]. The nature of Fructus Cannabis is neither hot nor cold, its kernel quality is Yin, and there is no taste of Fructus Cannabis^[4]. In the works of Traditional Chinese Medicine, most of them are "non-toxic" taste, and because the mild medicine is mostly sweet, sweet flavor can be replenished, can be balanced, can be slow, sweet and peaceful, and there are no significant side effects. Through the inspection of previous dynasties of Materia Medica, it is proved that Fructus Cannabis is just in line with the above characteristics of mild medicinal properties^[6]. The second is that Fructus Cannabis has a conciliatory effect. Traditional Chinese Medicine takes advantage of the mild nature of cold and heat to adjust the "disharmony" of the body and the "excessive deviation" of the drug, which is very close to the meaning of "harmony in harmony"^[7]. Fructus Cannabis has the effect of tonifying qi, tonifying blood and tonifying Yin, which is in line with the characteristics of calming drugs to reconcile qi, blood, Yin and Yang. The medicinal characteristics of Sanping drugs "two-way application, conditional dominance"^[8]. Through the inquiry and textual research of this herb, it is found that Fructus Cannabis acts on intestinal dryness and constipation, and the disease of stomach heat and sweating shows the action characteristics similar to those of cold medicine rhubarb, while it is used to replenish qi or act on blood deficiency and fluid deficiency, and irregular menstruation shows the action characteristics similar to those of warm medicine *Atractylodes macrocephala*. It is preliminarily proved that hemp kernel is bidirectionally applicable, so it can be judged to be "neutral".

Conclusion

From "Shennong Herbal Scripture", which was first recorded in Fructus Cannabis, to the classics of Materia Medica in the Ming and Qing dynasties, we gradually have a supplementary understanding of the nature, taste and efficacy of Fructus Cannabis. For the nature and taste of Fructus Cannabis, whether in most ancient books or contemporary pharmacopoeia, it is considered to be sweet and neutral. A few works, such as "Dietotherapy Materia Medica", locate the slightly cold characteristics of Fructus Cannabis, which may be beneficial to the dryness and hot shower of large intestine, and it is determined to be slightly cold according to the theory of treating heat and cold.

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Schisandrin B improves anxiety-like behaviors in fear-conditioned rats via the Hypothalamic-Pituitary-Adrenal Axis

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Abstract: Objective: This study aims to explore the anti-anxiety effect of Schisandrin B (Sch B) and its mechanism. **Methods:** The four randomized groups are made including control group, model group, diazepam group and Sch B group. To establish an improved conditioned fear model by the plantar electric shock method, the administration group was given Sch B solution (10mg/kg, 1mg/ml), diazepam solution (3.6mg/kg, 1mg/ml), rats in the blank group and model group were given normal saline. The elevated plus maze (EPM) and the open field test (OFT) were used to investigate the effect of Sch B on anxiety behavior. And ELISA was used to detect changes in serum indicators related to Hypothalamic-Pituitary-Adrenal (HPA) axis. **Results:** The freezing time was used as an indicator to verify the successful replication of the modified conditioned fear model. On the 4th day after replication, compared with the blank group, the freezing reaction time of the rats in the model group ((1.87±0.36) s, (55.37±3.51) s, $P<0.01$) was significantly prolonged, indicating that the conditioned fear model was successfully replicated. The results of the EPM and the OFT further confirmed that the model rats had anxiety-like behaviors. Compared with the model control group, after Sch B intervention, the results of the EPM experiment showed that the percentage of open-arm entry times ((12.29±4.93) %, (26.71±5.89) %, $P<0.01$) and the percentage of open-arm residence time ((2.24±0.97) %, (15.09±3.74) %, $P<0.01$) increased significantly. In addition, the number of times, time, standing, and modification times of entering the central grid in the OFT experiment increased. The test results of serum HPA axis showed that the levels of corticosterone (CORT), adrenocorticotrophic hormone (ACTH), and corticotropin releasing hormone (CRH) were all reduced. Compared with the blank group, the indicators of the model group all increased, but not all of them were significant. Compared with the model group, the contents of CORT in the HPA axis of the Sch B group decreased significantly ((61.07±0.41) $\mu\text{g}\cdot\text{L}^{-1}$, (45.12±1.29) $\mu\text{g}\cdot\text{L}^{-1}$, $P<0.05$). Compared with the model group, the results of the contents of ACTH in the HPA axis of the Sch B group also showed significant decrease ((101.13±9.31) $\text{ng}\cdot\text{L}^{-1}$, (79.98±4.12) $\text{ng}\cdot\text{L}^{-1}$, $P<0.05$). And the results of the contents of CRH in the HPA axis showed that compared with the model group, the Sch B group decreased significantly ((46.37±5.22) $\text{ng}\cdot\text{L}^{-1}$, (42.54±1.08) $\text{ng}\cdot\text{L}^{-1}$, $P<0.05$). **Conclusion:** Sch B has a significant improvement effect on anxiety-like behaviors caused by conditioned fear, which is speculated to be related to the expression of CORT, ACTH, CRH and other indicators that regulate the HPA axis. The above results have laid a theoretical foundation for China and Russia of the development and utilization of Schisandra chinensis, the in-depth study of the anti-anxiety mechanism of these components and the development of new anti-anxiety drugs. It provides the possibility to maintain the mental health of the people of China and Russia.

Key words: Sch B; Conditioned fear; Anti-anxiety

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Preparation of postoperative supplementary oral nutrient emulsion

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Abstract: The paper is to discuss the preparation of oral nutritional emulsion. As a drug delivery system, oral nutritional emulsion could improve the solubility and bioavailability of drugs. It's an oil-in-water emulsion system made of protein, carbohydrates, vitamins and minerals. Oral nutritional milk plays an important role in maintaining life energy and nutrition in patients with malnutrition, chronic wasting disease and patients who cannot eat normally during postoperative recovery^[1].

Keywords: oral nutritional; medium-chain triglyceride; Sucrose; Xanthan gum; average particle size

Purpose: Through screening the appropriate prescription and equipment parameters, the oral nutritional emulsion was obtained by high-speed shear emulsification with quality evaluated. The purpose was to control the viscosity and droplet size of oral nutritional lotion, improve its stability, make it suitable for drinking and improve the taste of drinkers.

Materials and Method:

The structure of raw materials were shown in the figure 1 below.

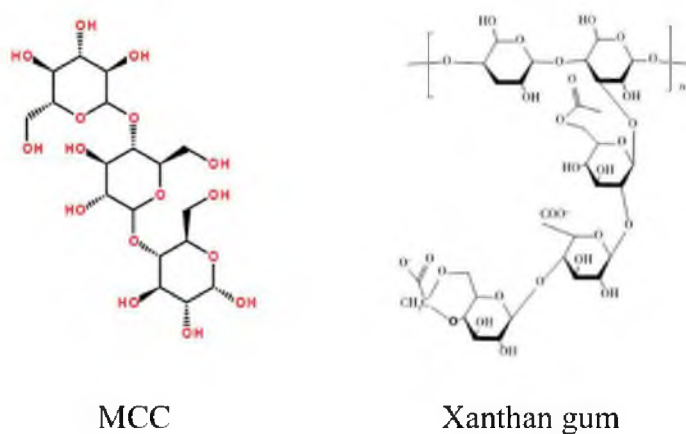


Figure 1 The structure of raw materials

Oral nutritional emulsion's preparation method was shown in Figure 2.

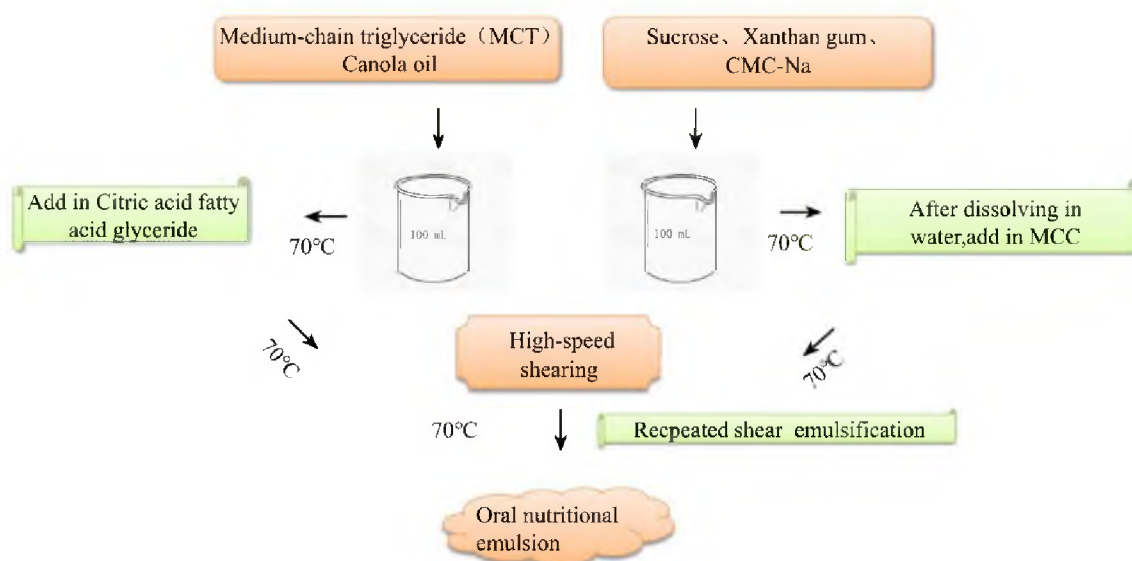


Figure 2 Preparation method of oral nutritional emulsion

Oral nutritional emulsions were left at room temperature to study their stability and viscosity at different speeds with a Viscometer. After diluting according to emulsion: water = 1:9, observe it with microscope and analyze its particle size. Select the appropriate prescription through the above survey results^[2].

Results and Discussion:

Prescription 1 was formulated and characterized by consulting literatures. The results showed that the oral emulsion prepared according to formula 1 had good particle size but with high viscosity. Therefore, the contents of MCC and CMC Na were reduced to obtain prescription 2 and prescription 3. It was found that the reduction of MCC and CMC-Na had little effect on the viscosity, and the particle size of the droplets increased^[3]. Therefore, the contents of MCC and CMC-NA in prescription 1 were maintained and the amount of Xanthan gum in the prescription and formulate prescription 4 and prescription 5 were reduced. Prescription and viscosity data are shown below.

Table 1 Prescription 4 and 5

Composition	Prescription 4	Prescription 5
Medium-chain triglyceride	7g	7g
Canola oil	20g	20g
Citric acid fatty acid glyceride	1g	1g
Sucrose	2g	2g
MCC	0.2g	0.2g
CMC-Na	0.035g	0.035g

Xanthan gum	0.03g	0.015g
Water	Add to 50g	Add to50g

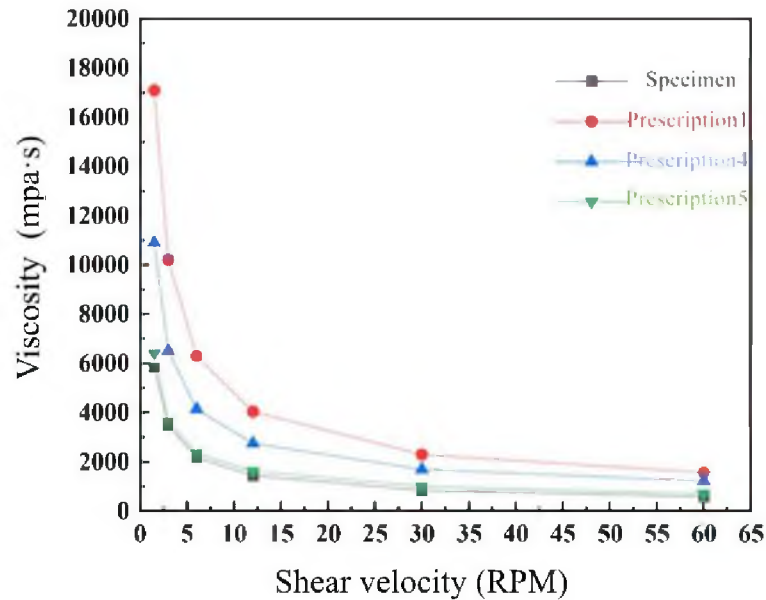


Figure3 Relationship Between Shear rate and viscosity

It has significant impacts on the stability of the ratio of MCC, CMC-Na, xanthan gum and other raw materials. The reduction of MCC and CMC-Na's content has little effects on the viscosity while the particle size of lotion drops will increase. Reducing the xanthan gum content can significantly reduce the viscosity of the prepared oral nutritional emulsion.

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The effect of antibiotics on the efficacy of immune checkpoint inhibitors in cancer patients

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Abstract: As a new type of anti-tumor drug, immune checkpoint inhibitors (ICIs) play an important role in the immunotherapy of malignant tumors due to their good efficacy and controllable safety. Clinical experiments have shown that gut microbes play an important role in regulating the efficacy and toxicity of cancer immunotherapy. Thus, the response of cancer patients to ICIs may be influenced by conditions that alter the composition of the gut flora, including dysbiosis caused by antibiotic (ATB) use. It was compared that the clinical results of the type of antibiotics used and the exposure time of tumor patients, and the result was shown that both of them affect the overall survival (OS) and progression-free survival (PFS) of patients, which in turn affects the treatment effect of ICIs. Through relevant research, fecal bacteria transplantation and probiotics have been found to reduce the effect of antibiotics on ICIs treatment.

Keywords: immune checkpoint inhibitors; antibiotic; gut flora; cancer patients

The expression of immune checkpoint molecules on immune cells could inhibit the function of immune cells, preventing the body from producing an effective anti-tumor immune response, and these "checkpoints" may be used by tumors in tumor tissues to form immune escape. Immune checkpoint inhibitors, also known as immune system counterpoint inhibitors, act on immune checkpoints to enhance immune responses or relieve immune suppression. Representative drugs include programmed cell death protein 1 antibody (PD-1), programmed cell death ligand 1 (PD-L1) and cytotoxic T lymphocyte-related antigen 4 (cytotoxic T lymphocyte-associated antigen 4, CTLA-4) antibody^[1].

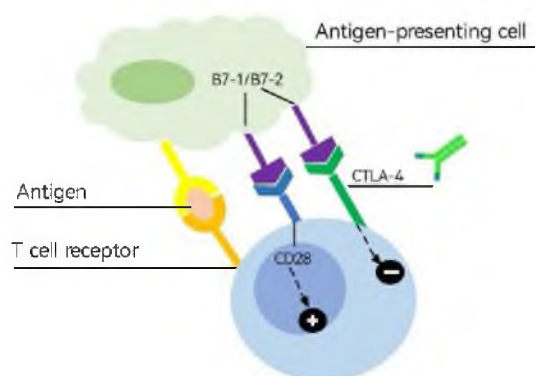


Fig 1 Immune checkpoint inhibitors mechanism of action. Take anti-CTLA-4 inhibitors as an example. After the antigen-presenting cells bind to T cells, co-stimulatory molecules on T cells such as CD28 bind to co-stimulatory molecules on antigen-presenting cells such as B7 and activate T cells. T cells express CTLA-4 which competitively bind to B7. Unlike CD28, CTLA-4 sends an inhibitory signal to T cells, and anti-CTLA-4 antibodies block the inhibitory signal.

Objective

To investigate the effect of antibiotics on the therapeutic effect of ICIs and how to reduce this effect.

Materials and Methods

In this study, immune checkpoint inhibitors, intestinal flora, antibiotics, and cancer patients were selected as the key words for the literature regarding the type of cancer being non-small cell lung cancer, melanoma, colon cancer, or renal cell carcinoma. Case studies of post-treatment infection with ICIs and their relevance were interpreted from selected literature. To interpret the mechanism and influencing factors of antibiotics in the treatment of cancer with ICIs, and find ways to reduce the influence of antibiotics in the treatment of cancer.

Results and Discussion

Immune checkpoint inhibitors bind to receptors on T cells or cancer cells to prevent the production of immunosuppression, enabling T cells to recognize cancer cells and mobilize the systemic immune system to eliminate tumor cells. Ruminococcus and Lachnospiraceae in the gut flora can produce short-chain fatty acids such as butyrate to regulate the production of cytokines, affect the function of antigen-presenting cells and then affect the recognition of tumors by T cells, and indirectly affect the therapeutic effect of immune checkpoint inhibitors.

It was conducted that an experiment to select 60 colon cancer patients with urinary tract infection before and after ICIs treatment and give them antibiotics. The results showed that the overall survival time and progression-free survival time of patients were shortened. Other studies have also shown that the use of broad-spectrum antibiotics such as β -lactams and quinolones can also shorten the overall survival time and progression-free survival time of patients. Broad-spectrum antibiotics given to patients may have exhausted the microorganisms involved in stimulating immune response and expanded the microorganisms inducing inhibitory immune response, thus reducing the effect of ICIs. However, narrow-spectrum antibiotics have no obvious effect on the therapeutic effect of ICIs^[2].

It was found that the overall survival (OS) and progression-free survival (PFS) were significantly shortened by using antibiotics in the immunotherapy window for cancer. It was studied that 196 patients with NSCLC (n = 119), melanoma (n = 38), and other tumor types (n = 39). These results suggested that exposure to antibiotics may increase the risk of complications during treatment, making patients more likely to discontinue ICIs therapy due to disease progression while receiving ATB^[3].

It was evaluated that melanoma growth in mice treated with Bifidobacterium in combination with anti-PD-L1. The result was shown that this combination eliminated tumor growth. The lactic acid and acetic acid produced by the probiotics reduce the luminal pH and inhibit overgrowth of other undesirable species. In addition, they increase the expression of tight junction proteins and improve the barrier function of the intestinal tract to help restore the efficacy of immune checkpoint inhibitors^[4].

Fecal microbiome transplantation (FMT) is to inject the treated feces collected by screened healthy donors into the intestines of affected patients, with the aim of restoring the diversity, composition and function of intestinal microbiome. In a study, a 50-year-old woman with high-grade metastatic

urothelial cancer which is difficult to be cured by standard chemotherapy and a 78-year-old man with prostate cancer were selected. The female patients were treated with CTLA-4 and PD-1, and the male patients were treated with two doses of ipilimumab. As a result, they all suffered from diarrhea and urinary tract infection. After a single dose of FMT was given to them, the infection was obviously improved, which showed that FMT can eliminate ICIs-related toxicity.

To sum up, the use of antibiotics may greatly affect the effect of ICIs in the treatment of cancer, but modern technology proves that these effects can be avoided. The future research direction may be to use probiotics, intermittent FMT and microbial specific antibiotics to enhance immune stimulation or down-regulate the immunosuppression of some intestinal organisms. In patients who need antibiotics, we should also consider carefully choosing antibiotics and avoid using antibiotics that regulate immune response.

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Nitrogen-doped mesoporous carbon and carbon nanotube composite electrode for dopamine detection

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Abstract

In this paper, nitrogen-doped mesoporous carbon nanospheres (N-MCS) were used as the matrix material and composited with carbon nanotubes (CNT) to successfully detect dopamine. Cyclic voltammetry (CV) experiments prove that N-MCS@CNT nanocomposite has better electrocatalytic activity. Differential pulse voltammetry (DPV) experiments demonstrate that the nanocomposite has a good linear range and detection limit for the oxidation of dopamine. After testing with real samples, it is found that the sensor can be used for the detection of dopamine in human serum, which shows that the sensor has certain practical application.

Key word: Nitrogen doped mesoporous carbon; Electrochemical detection; Dopamine

Dopamine (DA) is a common neurotransmitter that improves hormone levels and regulates physiological functions of the nervous and cardiovascular systems^[1]. In human body fluids, the imbalance of DA levels can easily lead to a series of psychiatric diseases^[2]. Compared with traditional detection methods, electrochemical detection^[3] has the advantages of simplicity, rapidity and high sensitivity, showing great potential in the detection of dopamine-related diseases.

Mesoporous carbon is a new type of carbon material with large pore volume, specific surface area and more active sites. The introduction of nitrogen atoms can change the physicochemical properties of mesoporous carbon materials, such as pH, electron transfer ability, and dispersibility. Electrodes modified with mesoporous carbon materials exhibit excellent electrochemical activity towards many electroactive species.

Carbon nanotubes have many excellent properties, such as unique tubular structure, large specific surface area, and high electrical conductivity, which make them ideal electrode materials in the field of electrochemical sensors^[4-5]. Functionalized carbon nanotubes contain hydroxyl (-OH), carboxyl (-COOH), and carbonyl (C=O) groups, which further enhance their catalytic performance and increase the electron transfer rate^[6]. The combination of carbon nanotubes and N-MCS further expands the dispersibility, increases the active sites, and optimizes the electrochemical properties of the composite material, making it more effective for the detection of small molecules in drug analysis.

Objective

To prepare a high performance dopamine electrochemical sensor based on mesoporous carbon material and carbon nanotubes.

Materials and methods

Synthesis of nitrogen-doped mesoporous carbon (N-MCS): Nitrogen-doped mesoporous carbon nanospheres (N-MCS) were prepared by the method in the literature^[7].

Preparation of nitrogen-doped mesoporous carbon composite carbon nanotube electrodes: 0.01 g of the prepared N-MCS and 0.01 g of acidified carbon nanotubes were added to 15 mL of deionized water, stirred for 40 minutes, and hydrothermally reacted at 120 °C for 18 h. The resulting product

was centrifuged, washed three times with methanol and deionized water, and dried in an oven at 60 °C for 16 h to obtain the final product N-MCS@CNT. The material was fixed on the pretreated electrode surface by drop coating and dried in an oven at 60 °C for 5-8 min.

Three-electrode system used to perform electrochemical studies. CHI-760E electrocatalytic workstation was functional to carry out the electrochemical measurements. The experimental temperature was 20 - 25 °C, and the solution in the system was 10 ml of 0.1 M phosphate (PBS) buffer with different pH. After repeated scans until the baseline stabilized, analytes were added for detection. In this paper, the electrochemical performance of the composite electrode was evaluated by differential pulse voltammetry and cyclic voltammetry.

Results and discussion

1. Electrochemical activity of N-MCS@CNT composite

The cyclic voltammetry curves of the electrode at different scan rates (10-100 mV·s⁻¹) were measured by CV method, and its electroactive surface area was further calculated. The linear equation of the square root of current and scan rate is $I_{pa} = -46.294 + 22.666 V^{1/2}$, $R = 0.997$, according to the Randles-Sevcik equation, the calculated active area is 6.113 cm², far exceeding the active area of 0.0707 cm² of the blank glassy carbon electrode, which proves that the composite electrode has better electrochemical activity.

2. The linear range and detection limit

Using DPV method, the linear range and detection limit of N-MCS@CNT electrode were investigated in pH = 6.0 PBS buffer solution. With the increase of dopamine concentration, the response current increases linearly within a certain range, and the current changes linearly within the dopamine concentration of 5-115 μM. Through calculation, the detection limit (S/N = 3) is 0.006 μM, the detection range and detection limit of the composite electrode are better than some published articles, and have certain practical value.

3. Real sample analysis

The composite electrode was tested in real samples of human serum, and the content of dopamine in human serum was determined by standard addition method. Human serum was obtained from a local hospital blood bank, and 100 μL of serum was made up to 10 mL with pH = 6 PBS in a 10 mL pipette as a stock solution. Using the DPV method, the actual detected dopamine concentration is compared to the added known concentration. The results showed that the recoveries of the composite electrode in actual serum samples were 93.33 % - 107.78 %. This proves that this sensor has application potential for detecting dopamine in human serum.

Given to these results, as an electrode material for sensor, the N-MCS@CNT nanocomposite manifests wide linear range and low detection limit, making it a promising candidate as a sensing nanomaterial for dopamine detection.

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Identification of stem barks of *syringa reticulata* as potent inhibitors for the SARS-CoV-2 3CL protease

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Abstract

3CL protease of SARS-CoV-2 is a highly conserved cysteine protease that plays an important role in the viral life cycle and host inflammation, providing an ideal target for developing broad-spectrum antiviral drugs. Here we describe the discovery of stem barks of *syringa reticulata*, mainly used to treat chronic bronchitis and asthma in clinical, as a specific and potent inhibitor of the SARS-CoV-2 3CL protease. Fluorescence resonance energy transfer (FRET) assay demonstrated 70% ethanol extract of stem barks of *syringa reticulata* dose-dependently inhibited the cleavage activity of 3CL protease with IC_{50} value of 0.0018 mg/ml, but little effect on pseudovirus-based cell entry assay and luciferase-based RNA-dependent RNA polymerase (RdRP) activities. These results suggest that stem barks of *syringa reticulata* will be a potential leading candidate for COVID-19 treatment.

Keywords: stem barks of *syringa reticulata*, SARS-CoV-2, 3CL protease, high throughput screening

Since SARS-CoV-2 emergence in December 2019, it has not only distressed medical services but also resulted in enormous economic losses, marking an urgent to develop safe, effective, and cost-efficient drugs^[1]. Various activity assays combined with high throughput screening (HTS) target different viral proteins have been used to develop new inhibitors^[2, 3]. Up to now, many leading compounds have shown potential antiviral activity in the pre-clinical stage, but their application and safety in clinical remain to be confirmed.

Traditional Chinese medicine (TCM) herbs and formulae have exhibited extraordinary advantages by directly inhibiting SARS-CoV-2 replication and reducing the expression of inflammatory factors^[4]. In addition, TCM has unique advantages with rich resources, low price, and few side effects, which makes itself an ideal library to develop leading candidates against SARS-CoV-2.

Objective

To develop broad-spectrum anti-coronavirus drugs, FRET-based 3CL protease cleavage activity assay was used to screen potential herbs against SARS-CoV-2 TCM produced in Heilongjiang province.

Materials and methods

70% ethanol extract of sixty-one dried herbs produced in Heilongjiang province were selected in this study. 2019-nCoV Mpro/3CLpro Inhibitor Screening Kit (Beyotime, Shanghai) was used to initially confirm the inhibitory activity of 3CL protease according to the manufacturer's instructions. To determine whether stem barks of *syringa reticulata* has a specific antagonistic effect on 3CL protease, pseudovirus-based neutralization assay and Gaussia luciferase (Gluc) based RdRP activity assay were proceeded based on the standard protocol developed by our laboratory. Data analysis was performed with the GraphPad Prism 7 software. Differences among the different groups were

determined based on one-way analysis of variance (ANOVA) followed by Tukey's multiple comparisons. $p < 0.05$ was considered significant.

Results and discussion

Viral protease is an attractive antiviral drug target for RNA viruses including SARS-CoV-2. In response to the COVID-19 pandemic, great efforts have been made to evaluate the possibility of various protease inhibitor drugs for the clinical treatment of this disease. Unfortunately, Remdesivir and other approved viral protease drugs failed in a clinical trial without showing benefit compared with the standard of care. To address this unmet need, 61 herbs produced in Heilongjiang province were screened at 5 mg/ml in the high-throughput, initial screening. Among these 61 herbs, twenty-seven potentially active herbs were found (inhibition $> 75\%$), including eight drugs with superior inhibitory activity against SARS-CoV-2 3CL protease (inhibition=100%). The eight best active SARS-CoV-2 3CL protease inhibitors are listed in Figure 1, with their IC_{50} values. Notably, the best of eight herbs has similar activity to inhibit 3CL protease activity at initial screening, but stem barks of *syringa reticulata* led to 50% inhibition of SARS-CoV-2 3CL protease activity at 0.0018 mg/ml.

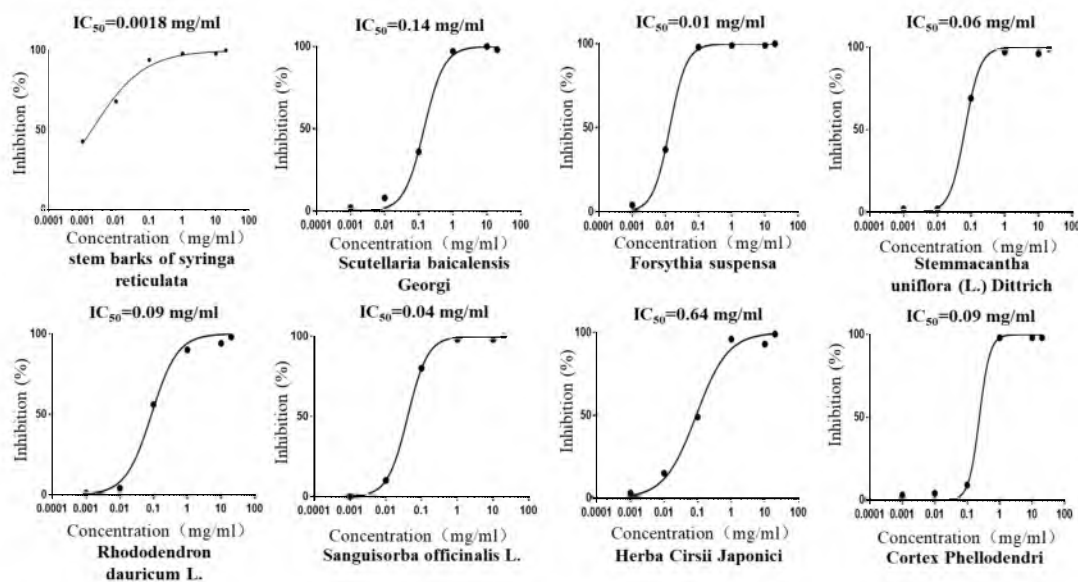


Figure 1. IC_{50} value of SARS-CoV-2 3CL protease activity of best of eight herbs.

Spike-ACE₂ interaction mediated virus entry and RNA-dependent RNA polymerase, which have a crucial role in the viral life cycle, were also the important drug development target. To elucidate whether stem barks of *syringa reticulata* could inhibit RdRP activity or block virus from entering the target cell, we first used a cell-based assay to determine the inhibitory activity of stem barks of *syringa reticulata* on SARS-CoV-2 RdRP. As shown in Figure 2A, when the Gluc reporter-expressing cells were transfected with RdRP, the activity of Gluc dramatically increased compared with that of cells expressing the reporter alone, but stem barks of *syringa reticulata* (5 mg/ml) had a little inhibitory effect on RdRP activity. To demonstrate if stem barks of *syringa reticulata* could prevent infection by blocking SARS-CoV-2 cell entry, a pseudovirus-based neutralization assay was carried out. We incubated pseudovirus with 5 mg/mL of stem barks of *syringa reticulata* or vehicle control (DMEM) and then infected human ACE₂ over-expressing cells, after 24 h post-infection. We found no obvious difference in cells treated with stem barks of *syringa reticulata*

compared to vehicle control (Figure 2B).

Taking together, we have identified stem barks of *syringa reticulata* as a specific and potent drug of SARS-CoV-2 3CL protease which provides critical information for further discovery of leading compounds from stem barks of *syringa reticulata* against the SARS-CoV-2 virus.

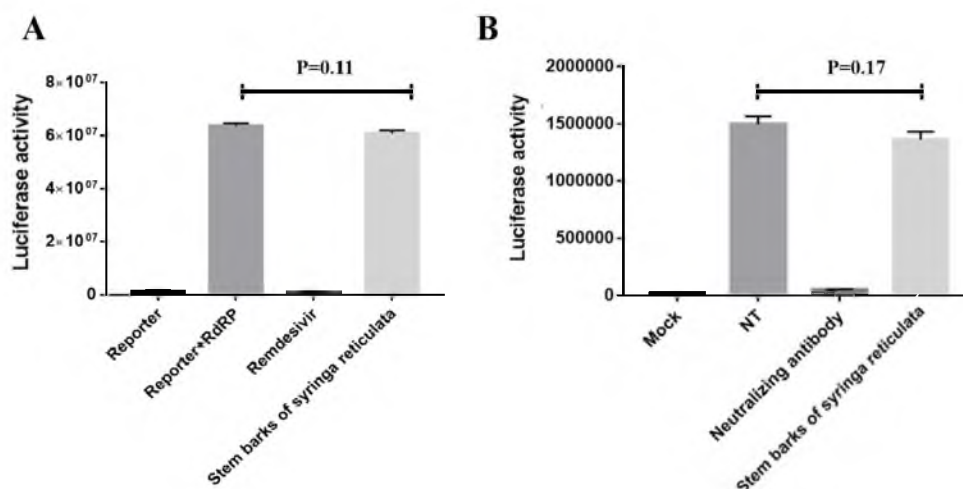


Figure 2. stem barks of *syringa reticulata* has little effect on pseudovirus based entry or RdRP activity. A, RdRP activity assay, B, Pseudovirus-based neutralization assay, NT means No treatment

Funding

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Pharmacological effect and mechanism of Radix Paeoniae Rubra for asthma treatment

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Abstract

In this paper, the network pharmacology method was used to analyze the active ingredients, targets, and pathways of Radix Paeoniae Rubra in treating asthma. Molecular docking between the active ingredients and therapeutic targets of asthma was performed. Through the allergic asthma model of rats induced by ovalbumin, the improvement of asthma symptoms and the reduction of pulmonary inflammation by RPR were confirmed, and the mechanism of RPR in the treatment of asthma was initially discussed.

Keywords: Radix Paeoniae Rubra, Asthma, Network pharmacology, Molecular docking

Radix Paeoniae Rubra (RPR) is Heilongjiang genuine medicinal herb, mainly derived from *Paeonia lactiflora* Pall. Shaoyao-Gancao Decoction with Shaoyao as the sovereign medicine has been proved to be effective in treating asthma^[1]. Pharmacological study shows that RPR has anti-inflammatory, immune regulation, nerve regulation, and other effects^[2-3]. However, the therapeutic effect, active ingredients, targets, and mechanism of RPR on asthma are still unclear.

Objective

The therapeutic effect, active ingredients, targets, and mechanism of RPR on asthma were studied based on network pharmacology, molecular docking, and animal experiment.

Results and discussion

The active ingredients of RPR were searched by TCM pharmacological database based on the absorption, distribution, metabolism, and excretion properties. Finally, 16 active ingredients (including monoterpene glycosides, flavonoids, and sterols) were determined, and 234 targets of RPR were involved. A total of 1249 targets related to asthma were obtained in the relevant database. By matching the targets of the active ingredients of RPR with those of asthma treatment, the Venn diagram of intersection targets was obtained (Fig 1), in which there were 78 intersection targets. A Protein-Protein-Interaction network was constructed using the String database, the results showed that IL6, CXCL8, VEGFA, TNF, and EGFR might be important potential target proteins of RPR for asthma treatment. Through the enrichment analysis of 78 common targets on the Metascape platform, 1129 GO biological processes (BP) items were collected and clustered by the platform. Results showed that the main BP involved blood circulation, inflammatory response, and positive regulation of cell migration. KEGG analysis revealed 186 enrichment pathways, which were mainly related to Neuroactive ligand-receptor interaction, CGMP-PKG, AGE-RAGE, IL-17, and other signaling pathways. It was found that lactiflorin and paeoniflorigenone of the monoterpene glycosides in RPR had lower binding energy to the anti-inflammatory target proteins by molecular docking. Based on the results of network pharmacology and molecular docking, we used the asthma model of rats induced by the ovalbumin for preliminary experimental verification. The effects of RPR on asthma symptoms and pulmonary inflammation were evaluated by behavioral score and HE

staining, respectively. The levels of IgE, IFN- γ , IL-4, and IL-17 in serum were investigated by ELISA. The results showed that the high-dose group of RPR(RPRH) decreased the behavioral score (Fig 2), alleviated pulmonary inflammation (Fig 3), increased levels of IFN- γ , and decreased levels of IgE, IL-4, IL-17 after the last asthma provocation (Fig 4).

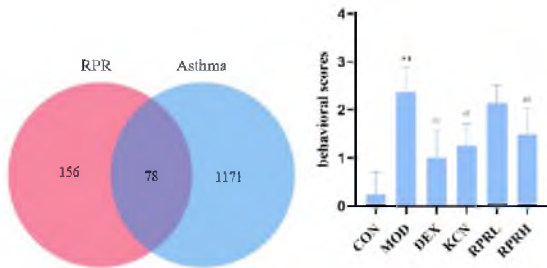


Fig 1 Venn diagram of disease and targets Fig 2 Behavioral scores

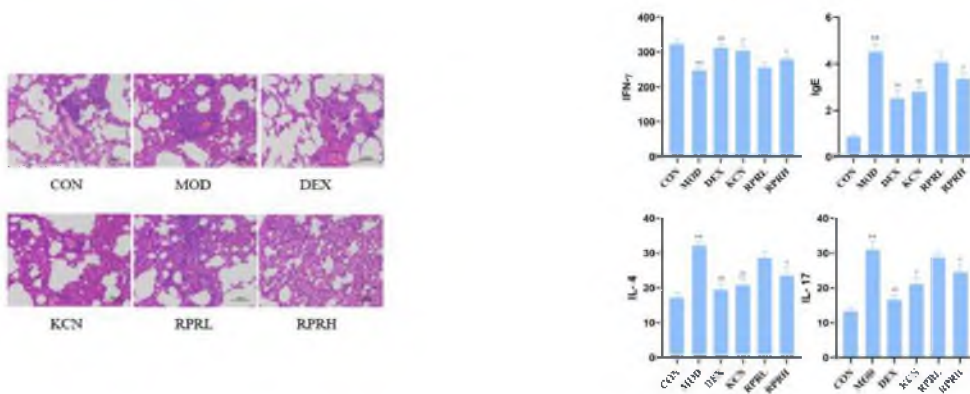


Fig 3 HE staining of lung tissue(200 \times) Fig 4 IgE, IFN- γ , IL-4, and IL-17 in serum

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Effect of *Acanthopanax Senticosus* on Body Surface Temperature in Mice

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Objective: To observe the effects of different concentrations of *Acanthopanax senticosus* decoction on body surface temperature of male and female mice. **Methods:** Kunming mice were randomly divided into four groups: blank group, high group, middle group, and low group. The mice were given water decoction of *Acanthopanax senticosus* at the dosage of 0g/kg, 32g/kg, 16g/kg and 8g/kg respectively for 7 days. And 30 minutes after the seventh day, the infrared thermography (back and abdomen) of each group was taken by thermal imager, then the data were analyzed. **Results:** Compared with the blank group, the head temperature of female rats in the low concentration group decreased significantly ($P < 0.01$). The temperature of caudal root, liver, stomach, small intestine, large intestine and bladder of female rats in high concentration group decreased significantly ($P < 0.01$). And the temperature of heart decreased significantly ($P < 0.05$). Compared with middle dose group, the temperature of small intestine and large intestine in high dose group decreased significantly ($p < 0.01$). Compared with the blank group, the trunk temperature of male rats in the low concentration group increased significantly ($P < 0.01$). The trunk temperature of male rats in high concentration group increased significantly ($P < 0.01$). The trunk temperature of male rats in middle concentration group increased significantly ($P < 0.01$). **Conclusion:** *Acanthopanax senticosus* can regulate the body surface temperature in mice. And the regulation effect is different with different genders. After one week of administration, the body surface temperature in female rats decreased, and different doses had different effects. However, The body surface temperature in male rats increased, and there was no obvious change at different doses.

Keywords: *Acanthopanax senticosus*, mouse, body surface temperature, infrared thermal imaging

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Research advances in herbs couples of anemarrhenae rhizoma and phellodendron amurense

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Abstract

“Herbs couples” is the clinical prescription of relatively fixed two drug combination, and is a prescription compatibility of traditional Chinese medicine with the most basic, the most simple, the most common of traditional medicine dosage forms. Among them anemarrhenae rhizoma and phellodendron amurense in clinical on commonly used reducing asthenia heat is one of herbs couples. Through consulting the literature in recent years, the classical herbs couple is studied in the round such as chemical constituents, pharmacological action, and clinical application are reviewed.

Keywords

Phellodendron amurense; Anemarrhenae rhizoma; chemical constituents; pharmacological action; clinical application

Phellodendron amurense and anemarrhenae rhizoma are one of the commonly used herbs couples in clinic. The herbs couples come from the 《Lan shi mi zang》 by Li Dongyuan, a famous medical scientist in the Jin Dynasty. They have many pharmacological effects, such as nourishing yin and reducing fire, removing dampness and clearing heat, reducing asthenia heat and inducing efficiency downward.

1. Influence of herbs couples on chemical composition

Phellodendron amurense, a well known herbal medicine in China, its main chemical components are alkaloids, limonin, flavones, terpenes, sterols, phenolic acid, and others, such as Berberine、Phellodendrine、Magnoflorine、Jatrorrhizine and Palmatine^[1-2]. Anemarrhenae rhizoma is the dry rhizome of *Anemarrhena asphodeloides* Bge, with the pharmacological effects of clearing heat and purging fire, nourishing yin and moistening dryness. The main active components are steroidal saponins, flavonoids, diphenylpyrones, lignin and others, such as Mangiferin, Anemarrhenasaponin I, Timosaponin B II, Anemaran A^[3]. Nowadays, the changes in the material basis of the compatibility of Phellodendron amurense and Anemarrhenae rhizoma are mostly focused on the changes in the content of their active ingredients, and the compatibility ratio is mainly concentrated in 1:1. There are few reports on the compatibility of different proportions and whether there are new substances after compatibility compared with the original medicinal materials. Therefore, Xu et al. used HPLC to determine the content changes of the main components of anemarrhenae rhizoma and phellodendron amurense in different proportions. The research results showed that the decocting amount of mangiferin and berberine were significantly reduced in different proportions compared with the same amount of compatibility. When the same amount of compatibility was used, the content of berberine and mangiferin was basically the same or higher than that of anemarrhenae rhizoma and phellodendron amurense decoction alone. And the content of berberine decocted with the two drugs was significantly higher than that decocted alone, However, there was no difference in the content of neomangiferin under different proportions with the different decocting methods.

UPLC-TQD-MS/MS was used for detecting the blood concentration of mangiferin. Results show that the blood concentration of mangiferin in anemarrhenae rhizoma decoction was significantly higher than that in the monomer administration group, but when compatibility with phellodendron amurense, the absorption of mangiferin in vivo was reduced, and the retention time of mangiferin in vivo was prolonged^[4]. To sum up, anemarrhenae rhizoma and phellodendron amurense are more conducive to the dissolution of the three effective ingredients under the conditions of equal proportion and decoction, and it provided the strong experimental evidence for the equal compatibility of anemarrhenae rhizoma and phellodendron amurense in prescriptions and clinical application.

2. Pharmacological action and clinical herbs couples after compatibility

In anemarrhenae rhizoma and phellodendron amurense herbs couple, anemarrhenae rhizoma is with the effect of clearing heat and purging fire, and phellodendron amurense is with the effect of heat clearing and dampness drying. The herbs couples of anemarrhenae rhizoma and phellodendron amurense are commonly used heat-clearing, with the effect of clearing away heat, purging fire and improving thirst symptoms. The herbs couple is mainly used for dizziness, yin deficiency tidal fever, bone fever and sweating. And it is widely used in modern clinical practice and has definite curative effect. Both anemarrhenae rhizoma and phellodendron amurense are cold and bitter, and entering the kidney meridian. Thus combination of the two herbs can not only enhance the effects of clearing away heat and purging fire, relieving deficiency and heat, but also nourishing and strengthening yin. Modern clinical research shows that it has significant clinical effects in the treatment of nephrotic syndrome and allergic rhinitis heat syndrome. The prescriptions commonly used in clinic consisting of anemarrhenae rhizoma and phellodendron amurense are Da-bu-yin pills, Zi-shen pills, Liao-ben-zi-shen pills, Zhi-bai-tian-di decoction, Zhi-bai-kun-cao decoction, Zheng-qi decoction, Zhan-meng dan, Zhi-bai-shen-dong decoction, Zhi-bai-bu-xue decoction, Si-zhi-huang-bai pills and so on. Because of the functions of removing heat and purging fire, nourishing yin and reducing fire, it is widely used in clinical diagnosis and treatment, and has remarkable curative effect. Such as huochong dizziness, dream ejaculation, ureaplasma urealyticum prostatitis combined with low sperm motility, female climacteric syndrome, precocious puberty etc.

3. Conclusion

Anemarrhenae rhizoma and phellodendron amurense, the classic antipyretic herbs couples are widely used in modern clinical practice because of their significant changes in the effective components, pharmacological effects, pharmacodynamics, pharmacokinetics and other aspects through the compatibility of different traditional Chinese medicines.

In recent years, research on the combination of anemarrhenae rhizoma and phellodendron amurense has mainly focused on the determination of chemical components, the evaluation of quality standards, and the mechanism of treatment under the same proportion. Our research team believes that there are still many problems to be discussed about the drug pair, such as the change of chemical components compared with single drugs, the influence of the drug pair on the pharmacokinetics and tissue distribution of active components of pharmacodynamic substances in the body, the analysis of chemical components under different proportions, the study of active components in different prescriptions, the analysis and research of metabonomics, the scope of clinical application, etc. It is believed that through the in-depth research of anemarrhenae rhizoma

and phellodendron amurense, a new foundation will be laid for the compatibility law of this classic antipyretic drug pair, and more reliable experimental data for its clinical application will be provided.

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The effect of Danggui-Shaoyao-San polysaccharide on type 2 diabetes mellitus via bile acid

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Abstract

Diabetic patients often suffer from abnormal lipid metabolism. Danggui-Shaoyao-San polysaccharide can regulate glucose metabolism by regulating bile acids and relieve diabetes symptoms. The study finds that Danggui-Shaoyao-San polysaccharide mainly affects the type and abundance of intestinal flora in patients with T2DM, and affects the release of related signaling pathways and inflammatory factors to regulate bile acid metabolism, thereby achieving the purpose of relieving diabetes.

Key words: Danggui-Shaoyao-San polysaccharide, T2DM, bile acid, intestinal flora, signaling pathway, inflammatory response

Type II diabetes (T2DM) is a group of metabolic diseases characterized by hyperglycemia. In recent years, some scientists have found that Danggui-Shaoyao-San (DSS) has a positive effect in the treatment of DM. Its main component, Danggui-Shaoyao-San polysaccharide (P-DSS), can relieve diabetes-related symptoms by participating in bile acid metabolism. This provides a new research idea for TCM treatment of diabetes. Bile acids originate from the catabolism of cholesterol in the liver. First, primary bile acids such as CDCA and CA are generated from cholesterol through the classical and alternative pathways, and then secondary bile acids such as DCA and LCA are generated under the action of food and intestinal flora. Bile acids can participate in glucose metabolism and energy regulation by activating the TGR5 receptor, while hepatic insulin resistance and hyperglycemia can increase bile acid synthesis, resulting in changes in bile acid composition. Therefore, regulation of bile acid metabolism has important implications for glucose metabolism and energy regulation.

Objective

Traditional Chinese medicine polysaccharides affect glucose metabolism and energy regulation by regulating bile acid anabolism, which will provide new investigative ideas for traditional Chinese medicine treatment of T2DM.

The effect of P-DSS on bile acids

Through the study of a hydroxymethylated Poria polysaccharide, it was found that it can enhance the ability to bind bile acids in vitro, inhibit the reabsorption of bile acids, and increase their excretion. In addition, theabrownin (TB) combined with Poria polysaccharide (PCP) showed an overall lipid-lowering function, which could modulate bile acid and fatty acid metabolism. Atractylodes polysaccharide and angelica polysaccharide can regulate the composition and activity of intestinal flora. Atractylodes polysaccharide promotes the growth of Bifidobacterium while Angelica polysaccharide can reduce the abundance of Bifidobacterium. Bifidobacterium combined with bile acid hydrolase can convert various Combined with the hydrolysis of bile acids into free bile acids, Atractylodes polysaccharides can also promote the growth of lactic acid bacteria and affect the esterification of bile acids. [1] Alisma polysaccharide can effectively regulate the

Adiop R2/PPAR α signal transduction pathway in the liver, [2] promote the degradation of fat by lipase into glycerol, fatty acids and other products contained in bile acid particles, increasing bile acid secretion. Paeoniflorin can regulate bile acid metabolism, alleviate cholestatic liver injury, and regulate glucose and lipid metabolism by up-regulating the expression of SIRT1/FXR and inhibiting NF- κ B/NLRP3 inflammasome. [3] Angelica polysaccharide can inhibit NF- κ B and JAK2/STAT3 pathways by regulating miR-10a and miR-223 in HT22 cells, and reduce endotoxins such as lipopolysaccharide; at the same time, Angelica polysaccharide can also reduce the production of inflammatory mediators and down-regulate TLR4 , mRNA expression of MyD88 and some pro-inflammatory chemokines (CCL2, CCL20, CXCL2, CXCL8, CXCL10), inhibiting NF- κ B and MAPK signaling pathways. Bile acid metabolite 3-oxoLCA can inhibit the development of Th17 cells in vivo while isoalloLCA can enhance Treg cells and affect related inflammatory responses.[4] Chuanxiong pectin polysaccharide (LCP-II-I) can block the NF- κ B pathway and upstream signals, and activate the Nrf2 pathway. Through the study of caspase-3, Bax family, MAPK family and their upstream signaling in different cell types, it was found that LCP-II-I can increase the number of intestinal stem cells in the mouse intestine under the action of bile acids, and through the TGR5-involved mechanisms promote intestinal regeneration and regulate intestinal apoptosis, thereby protecting mice from acute colitis.

Conclusions and perspectives

Therefore, P-DSS can regulate glucose metabolism and energy metabolism by regulating intestinal flora, affecting related signaling pathways and inflammatory responses to participate in bile acid synthesis and metabolism. It can be seen that traditional Chinese medicine polysaccharides still have significant advantages and practical potential in the treatment of T2DM. This provides a new research idea for the treatment of T2DM.

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Effect of polysaccharide from Danggui-Shaoyao-San on treatment of type II diabetes mellitus in female rats

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Abstract

This study investigated the effect of polysaccharides from Danggui-Shaoyao-San (DSSP) on type II diabetes mellitus (T2DM) rats. After treatment with DSSP for 4 weeks, the results showed that DSSP can decrease fasting blood glucose, liver weight index, and kidney weight index, and improve insulin resistance in STZ-induced diabetic female rats. In summary, DSSP has an anti-diabetic effect on T2DM in female rats.

Key words: Danggui-Shaoyao-San, type II diabetes mellitus

According to the International Diabetes Federation (IDF) [1], today, there are more than 500 million cases of diabetes worldwide, and this number is expected to reach 783 million by 2045. About 541 million people are estimated to have IGT (impaired glucose tolerance) globally and about 6.7 million people (20–79 years old) died of diabetes and its complications in 2021. Further, globally the proportion of undiagnosed diabetes is high, standing at 45%, and most of them are type 2 diabetes mellitus (T2DM). T2DM is characterized by chronic hyperglycemia due to defective insulin secretion or action and disturbances in protein and lipid metabolism. Therefore, more studies are still required to find an effective treatment for this disease.

Empty and out solid, empty of liver, spleen and kidney is a reason, phlegm turbidity and congestion is outer phenomenon, which is the basic TCM pathogenesis of this condition. Danggui-Shaoyao-San (DSS) is a famous prescription in the Synopsis of the Golden Chamber written by Zhang Zhongjing, a famous doctor in the Han Dynasty. DSS has the advantages of activating blood, invigorating the spleen and eliminating dampness, tonifying deficiency and removing reality, dispelling blood stasis, and resolving phlegm. So, DSS may have a therapeutic effect on diabetes.

Objective

To investigate the effect of lowering blood glucose and improving insulin resistance in T2DM rats.

Materials and methods

DSS, composed of Radix Angelicae sinensis (Dang Gui, 45g, root of Angelica sinensis (Oliv) Diels.), Radix Paeoniae alba (Bai Shao, 240g, root of Paeonia lactiflora Pall.), Poria Cocos (Fu Ling, 60g, sclerotium of Poria cocos (Schw.) Wolf.), Rhizoma Atractylodis macrocephalae (Bai Zhu, 60g, rhizome of Atractylodes macrocephala Koidz.), Rhizoma Alismatis (Ze Xie, 120g, rhizome of Alisma orientalis (Sam.) Juzep.) and Rhizoma Chuanxiong (Chuan Xiong, 120g, rhizome of Ligusticum chuanxiong Hort.) was purchased from Local medicine wholesale market. Using 10, 8, and 6 times the quality of water to decoct successively these drugs 3 times, each time for 1.5 hours. The filtrate was combined three times and concentrated into an extract via decompression. Then the

four-fold volume of ethanol (95%, v/v) was added to the extract and stored at 4 °C. After 12 hours, the precipitations were collected and washed by absolute ethanol. Finally, the sample was dried to obtain crude polysaccharides of Danggui-Shaoyao-San (DSSP). 1 g of DSSP is equivalent to 7.5 g of crude drug.

36 healthy female (6 weeks of age, mass: 150±20g) Sprague–Dawley (SD) rats were purchased from Heilongjiang University of Chinese Medicine, Heilongjiang, China. The controlled animal area was maintained at 22 ± 2 °C and 55 ± 10% relative humidity under a 12-hour light/dark cycle (7:00 am–7:00 pm). All animal experiments were performed in accordance with the Guidelines for the Care and Use of Laboratory Animals of Heilongjiang University of Chinese Medicine.

T2DM rats were induced by the combination of high-fat diet feeding and low-dose STZ injection according to the method described previously with some modifications [2]. Briefly, after adaptive feeding for one week, rats were randomly divided into the control group and the T2DM group. The control group was fed with standard normal diet (ND), while the T2DM group was fed with high sugar and fat diet (HFD, powdered normal pellet diet, 73.5%; lard, 10 %; sucrose, 10 %; cholesterol, 5 %; protein, 1%; sodium cholate, 0.5%) for 4 weeks. HFD–treated rats were injected intraperitoneally (i.p.) with a single dose of STZ (40mg/kg) dissolved in citrate buffer (pH 4.5). ND-treated rats only received an equivalent volume of citrate buffer. During the 2 weeks after injection, blood glucose concentrations were monitored from the tail vein using blood glucose meter after a 12-hour fast. Rats with fasting blood glucose (FBG) over 11.1 mmol/L were considered as successful T2DM models. Successful T2DM model rats were randomly divided into model, metformin (50mg/kg), and DSSP (220mg/kg) groups, Each group contained 9 rats. The body weight and fasting blood glucose of rats were monitored every 7 days until the end of the experiment.

At the end of the experiment, glycated hemoglobin (GHb) and serum Fasting insulin (FINS) were measured using the ELISA Kit (Mei mian, Jiangsu, China).

Results and discussion

Compared with control group, the weight change of model control group was significantly decreased ($P < 0.0001$), and liver weight index and kidney weight index were significantly increased ($P < 0.0001$); Compared with model control group, body weight change of metformin group was significantly increased ($P < 0.0001$), liver weight index and kidney weight index were significantly decreased ($P < 0.0001$ or $P < 0.001$); Compared with the control group, the weight change of the rats in the DSSP group was increased, but there was no significant difference ($P > 0.05$), while the liver weight index and kidney weight index were significantly decreased ($P < 0.0001$ or $P < 0.01$).

Table 1. Effects of DSSP on body weight change, liver weight index and kidney weight index in T2DM rats (±s). (Control vs. Model, ##### $p < 0.0001$; Model vs. Metformin and DSSP, **** $p < 0.0001$, *** $p < 0.001$, ** $p < 0.01$)

Group	n	Body weight change (g)	Liver weight index (%)	Kidney weight index (%)
Control	9	30.31±9.725#####	2.412±0.1231#####	0.5656±0.1051#####
Model	9	-8.922±10.34	5.039±0.5269	1.091±0.0953
Metformin	9	19.80±11.28****	3.319±0.6794****	0.7778±0.1943***
DSSP	9	2.844±15.03	3.373±0.5053****	0.8367±0.1438**

Compared with control group, FBG, GHb, FINS, and HOMA-IR were significantly increased in model group ($P < 0.0001$). FBG, GHb, FINS and HOMA-IR were significantly decreased in metformin group and DSSP group ($P < 0.0001$ or $P < 0.001$ or $P < 0.01$).

Table 2. Effects of DSSP on FBG, GHb, FINS, and HOMA-IR (Homa insulin-resistance) in T2DM rats (\pm s). (HOMA-IR= FBG \times FINS/22.5, Control vs. Model, ##### $p < 0.0001$; Model vs. Metformin and DSSP, **** $p < 0.0001$, *** $p < 0.001$, ** $p < 0.01$)

Group	n	FBG (mmol/L)	GHb (ng/mL)	FINS (mU/L)	HOMA-IR
Control	9	7.311 \pm 1.462#####	1930 \pm 193.9#####	5.883 \pm 1.104#####	1.932 \pm 0.5942#####
Model	9	30.92 \pm 2.174	6945 \pm 119.8	10.64 \pm 0.1771	14.62 \pm 1.061****
Metformin	9	14.30 \pm 8.624***	3422 \pm 502.5****	7.034 \pm 0.5775****	4.514 \pm 2.806****
DSSP	9	16.27 \pm 6.276**	4349 \pm 187.8****	7.905 \pm 0.7142****	5.607 \pm 1.910****

As a result, DSSP can decrease the levels of liver weight index, kidney weight index, FBG, GHb and FINS, and improve insulin resistance.

Thus, traditional Chinese formula Danggui Shaoyao San may be considered a potential therapeutic approach for T2DM.

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Study on the evolution of Manyprickle Acanthopanax Root

GUAN Zihe

Abstract: Manyprickle Acanthopanax Root, as the representative drug of "longjiuwei", is highly praised by Chinese medicine scholars at home and abroad because it can strengthen the foundation, replenish qi and strengthen the spleen, tonify the kidney and calm the mind. It enjoys the reputation of "helping sleep, replenishing qi and calming the mind, although it is a plant but a treasure". However, due to the relevant records and the origin are unclear in herbal literature, it leads to the frequent mixing of similar drugs in clinic, which seriously affects the modern research and development of traditional Chinese medicine of it. In order to carry forward the quintessence of China and inherit the culture of traditional Chinese medicine, the author conduct traceability research of theoretical literature on Manyprickle Acanthopanax Root and its similar drugs, find "Jackal Stem" in ancient herbal literature is the present Manyprickle Acanthopanax Root, and extract and summarize the related discussion of Manyprickle Acanthopanax Root from the documentation of Acanthopanax Cortex, enriched the materia medica research data of it. The research ideas and methods of this paper not only provide a direction for the inheritance and innovation of genuine Longjiang medicinal materials, but also provide a reference for other controversial research on the traceability of traditional Chinese medicine.

Keywords: Manyprickle Acanthopanax Root; Acanthopanax Cortex; Jackal Stem; Traceability of traditional Chinese Medicine

Acanthopanax senticosus (rupr.maxim.), as a representative drug of "dragon nine flavor", was first described in the national collection of Chinese herbal medicine The dried roots and rhizomes or stems of harms) are used as medicine [1]. Due to the lack of ancient literature, it leads to the confusion of similar drugs in clinic, which seriously affects its modern research and development. In the initial research, the author found that the ancient literature of Acanthopanax senticosus, which is similar to Acanthopanax senticosus, is rich. This paper traces and discriminates the ancient drug name, origin, function and many other aspects of Acanthopanax senticosus, in order to explore whether Acanthopanax senticosus is included in the ancient literature of Acanthopanax senticosus, so as to clarify the development context of Acanthopanax senticosus and guide clinical practice.

1. Reasons for the lack of Acanthopanax senticosus literature

The name of traditional Chinese medicine is related to the shape, color and smell of traditional Chinese medicine, which embodies the philosophy of taking images and comparing classes and the unity of heaven and man. In the early times, the ancients used their typical morphological characteristics to name and remember the traditional Chinese medicine of Acanthopanax senticosus, For example, the famous doctor's special record says, "five Jiapi, five leaves are good. [2]" song Hongmai's Rongzhai essays says: "five flowers, five Jiapi also. The leaves are male and female, the three leaves are male, and the five leaves are female. [3]" Ming Yang Shen's Dan lead general record says: "a five leaf branch is good. [4]" Ming Li Shizhen's Compendium of Materia Medica says: "the five leaves are good, so it is called five Jias, also known as five flowers. [4]" five leaves ", " five flowers " Terms such as "five leaves intersection" can be used to identify the general characteristics of this kind of traditional Chinese medicine, but the ancients did not distinguish their

differences. Such confusion was also common in ancient times, such as "red peony and white peony are called peony", "Cang and *Atractylodes macrocephala* are called Shu", etc. The author speculates that the lack of ancient literature of *Acanthopanax senticosus* is related to its confusion with the skin of *Acanthopanax senticosus*, a similar drug. From this, this paper combs and explores the ancient literature of *Acanthopanax senticosus*, and reversely confirms it with modern literature.

2. Differentiation of ancient medicinal names of *Acanthopanax senticosus*

2.1 differentiation of jackal lacquer and jackal festival form

There are mainly two kinds of ancient drug names of *Acanthopanax senticosus*. The Shennong herbal classic says: "a jackal lacquer.

2.2 identification of the origin of jackal lacquer and jackal Festival

So far, there are more than 30 species of *Acanthopanax* worldwide, and the proportion of China is larger than that of other countries, with as many as 27 species, and more than 13 medicinal varieties, all over the country [9]. Due to the similar morphology of Acanthaceae plants, it is easy to be confused. Since ancient times, there has been a discussion that "jackal lacquer" and "jackal Festival" belong to *acanthopanax* bark, which also confused the origin and distribution of the two. In order to confirm the above judgment that "jackal Festival" is *Acanthopanax senticosus*, the author discriminates the origin of the two from ancient to modern times.

3. Ancient literature analysis of the function of *Acanthopanax senticosus*

According to the above analysis, "jackal Festival" is *Acanthopanax senticosus*. However, when further searching its ancient documents, the author found that there were few documents corresponding to "jackal Festival", and most of the contents were confused with "*Acanthopanax senticosus*". Therefore, in order to further explore the function of *Acanthopanax senticosus*, this paper analyzed it from the ancient documents of *Acanthopanax senticosus*, and obtained the following three views.

4. Differentiation and analysis of Chinese Pharmacopoeia on the functions of *Acanthopanax senticosus* and similar drugs.

In the vast number of modern Chinese herbal medicine books, "Chinese Pharmacopoeia" as the core of the national drug standard system [30], is highly respected. Under the common guidance of traditional Chinese medicine theory and modern medicine, it remains scientific, progressiveness, normative and authoritative, and has become a code to ensure the quality and standards of drugs in China. Based on this, this paper first discriminates the contents of Chinese Pharmacopoeia of *Acanthopanax senticosus* and its similar drugs.

5. Correspondence between ancient literature views of *Acanthopanax senticosus* and modern varieties

Through the cognition of the Chinese Pharmacopoeia on the toxicity and function of *Acanthopanax senticosus* and its similar drugs *Xiangjiapi* and *Ciwujia*, and the reverse confirmation of the three viewpoints of the ancient literature of *Acanthopanax senticosus*, it can be seen that the relevant discussion on the efficacy of "expelling wind and dampness, activating blood and diuresis" adhering to the viewpoint of the book of *Materia Medica* is consistent with the modern function of *Acanthopanax senticosus*; The viewpoint of "adverse reaction and toxicity" is consistent with the modern toxicological cognition of *cortex Periplocae*; The efficacy characteristics of "entering the five internal organs and tonifying" are consistent with the modern functions of *Acanthopanax*

senticosus. It can be seen that the ancient document view of *Acanthopanax senticosus* covers the functions of modern *Acanthopanax senticosus*, fragrant *Acanthopanax senticosus* and *acanthopanax senticosus*. The ancient document content of *Acanthopanax senticosus* should belong to the herbal books corresponding to the theory of "entering the five internal organs and tonifying", which should be extracted from the ancient herbal document discussion of traditional *Acanthopanax senticosus* so as not to confuse the application.

6. Conclusion

Through the ancient alias "jackal lacquer" and "jackal Festival" of *Acanthopanax senticosus*, the drug name interpretation, plant morphology description, and the ancient and modern confirmation of the main origin, it can be concluded that "jackal Festival" is *Acanthopanax senticosus*. Its shape is characterized by brown skin of stems or rhizomes with black spots, clumps of stem nodes, and dense burrs between nodes. The northeast three provinces, mainly in Heilongjiang, are the most widely distributed. Through the analysis of ancient documents on the function of *Acanthopanax senticosus*, three ancient views can be obtained, namely, "dispelling wind and dehumidification, activating blood and benefiting water"; The theory of "adverse reactions and toxicity" and the theory of "entering the five internal organs can be beneficial". Through the reverse confirmation with the functions of *Acanthopanax senticosus* and its similar drugs *Xiangjiapi* and *Ciwujia* in the Chinese Pharmacopoeia, it can be concluded that the theory of "entering the five internal organs and tonifying" is consistent with the functions of *Ciwujia*, which separates its ancient literature from the bark of *Acanthopanax senticosus*, and then clarifies the source and flow.

The author believes that the ancient literature of *Acanthopanax senticosus* is not short-lived. It was confused by the ancients because it is similar to *Acanthopanax senticosus* bark and other drugs in morphology. In addition, due to the joint influence of irresistible factors such as historical dating and regional changes, its ancient literature was buried in *Acanthopanax senticosus* bark. After tracing and analyzing the origin of *Acanthopanax senticosus*, its ancient literature is relatively rich, and the functional difference between it and similar drugs is also relatively clear, that is, *acanthopanax senticosus*, compared with *Acanthopanax senticosus* bark and *Xiangjiapi*, has increased tonic effect, which can nourish the heart and spleen, replenish the spleen, improve the zongqi, benefit the kidney qi, and treat "insufficient heart and spleen, insomnia and dreams; body deficiency and fatigue, loss of appetite; long cough and asthma, kidney deficiency, waist and knee pain" and other diseases.

The research ideas and methods of this paper not only provide a direction for the inheritance and innovation of Longjiang genuine medicinal materials, but also provide a reference for other controversial research on the traceability of traditional Chinese medicine.

A Review for the Nano Preparations of Paeoniflorin, a Monoterpene Glycoside of Paeonia

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Abstract

Paeoniflorin is an important compound rich in genus Paeonia plants, it is also the quality marker of Chinese herbal medicine red paeony root (*Paeoniae Radix Rubra*, Chinese Chishao) and white paeony root (*Paeoniae Radix Alba*, Chinese Baishao) stipulated by the Chinese Pharmacopoeia. Paeoniflorin has a variety of pharmacological activities, including antidepressant, neurodegenerative diseases, antithrombotic, antitumor, cardiovascular and cerebrovascular diseases, diabetes and its complications, anti-inflammatory and antioxidant, immune regulation, anti fibrosis, to name just a few. However, the poor bioavailability of paeoniflorin limits its application, sustained release and nano medication schemes can effectively improve the bioavailability and disease treatment effect of paeoniflorin. Therefore, this paper reviews the research of paeoniflorin nano preparations, in order to provide reference for the application and preparation research of paeoniflorin in the field of pharmacy and clinical.

Key words: Paeoniflorin, nano preparations

Paeoniflorin (PF; C₂₃H₂₈O₁₁; CAS: 23180-57-6) is a monoterpenoid glycoside, and paeoniflorin content of Chishao is the highest among Paeonia plants. A large body of research evidence shows that paeoniflorin can exert pharmacological effects through multiple pathways and multiple mechanisms. For example, paeoniflorin can treat inflammatory pain, rheumatoid arthritis, cardiovascular, cerebrovascular diseases and neurological diseases by mechanism of inhibiting the inflammatory factors.

Although paeoniflorin has a wide application prospect, its poor fat solubility limits its clinical application. With the development of nanotechnology, new nano-formulations of paeoniflorin have been developed, including nanoparticles, liposomes, micelles, polymers, etc. These regimens can effectively improve the bioavailability of peony, enhance the efficacy and reduce damage to normal tissues.

Objective

Review the types, preparation methods and application value of paeoniflorin nano preparations, to provide basis and reference for broadening the clinical application of paeoniflorin and speeding up its popularization.

Methods

The information was searched from the scientific literature published on the online databases (including PubMed, CNKI, and Web of Science) and other bibliography (e.g. the Chinese Pharmacopoeia, 2020 edition).

Results and discussion

Liposome

Paeoniflorin-loaded pH-sensitive liposomes (Pae-LS) which was prepared according to the lipid film hydration method alleviate inflammation had been confirmed, which exhibited physical stability, sustained release, long cycling, pH-responsive properties, and higher uptake by active macrophages than free paeoniflorin. In addition, the paeoniflorin lipopolymer hybrid nanoparticles prepared by emulsion polymerization had significant liver targeting properties after modification with glycyrrhetic acid.

Preparation of paeoniflorin solid lipid nano topical preparation by hot melt emulsification homogenization method. Paeoniflorin is a drug with poor water solubility and fat solubility, which is not conducive to drug percutaneous absorption when being used as an external preparation. A new drug carrier system composed of solid lipid as matrix, which wraps drugs in its core or adsorbs them on its surface, can improve the permeability of drugs and prolong the action time, which is a new scheme to promote the percutaneous absorption of paeoniflorin.

Microspheres

Zeng Linru et al. used a modified emulsion polymerization method to prepare paeoniflorin-poly(n-butyl cyanoacrylate) microspheres, and investigated the in vitro sustained release properties of the microspheres. The drug loading of paeoniflorin N-butyl cyanoacrylate microspheres could reach 12.6% and it had a small sudden release effect, which can reduce the number of clinical administration and improve the curative effect.

Micelles

In order to further improve the liver protecting pharmacological effect of paeoniflorin, paeoniflorin phospholipid composite micelles were prepared and researched their protective effect of 17 α -ethinyl estradiol (EE)-induced cholestatic liver injury. The results showed that paeoniflorin micelles could further promote the inhibition of inflammation, and its molecular mechanism was through the inhibition of tlr4/myd88/nf- κ B signaling pathway.

Nanoparticles

Solid and hollow zein-paeoniflorin nanoparticles prepared by phase separation, the encapsulation rate of nanoparticles was 55.65%, and the average particle size was 50nm. The advantage of hollow nanoparticles was that they can improve the encapsulation efficiency and enhance the sustained release effect.

Lipid liquid crystal nanoparticles have a unique double channel structure and a large membrane surface area, which can encapsulate drugs of various polarity (hydrophilic, lipophilic or amphiphilic). It has high biocompatibility, simple preparation process, easy surface modification and spontaneous emulsification-ultrasound is common preparation method of lipid nanoparticles. The intestinal absorption characteristics of paeoniflorin lipid liquid crystal nanoparticles were studied by eversion intestinal sac method. It was found that the nanoparticles were better absorbed in the intestine than the drug granules, and were absorbed in different intestinal segments, and the absorption rate constant K_a of each intestinal segment increased with the increase of drug concentration, which was obviously concentration dependent, suggesting that it may be passive absorption.

The above research results confirm that nano-formulation is an effective method to improve the bioavailability of paeoniflorin, however, there are still few studies on this aspect. In fact, there are

many carriers that can be selected in the research and development of nano-formulations, especially for drugs with extremely poor lipid solubility such as paeoniflorin, many polymers, organic materials and inorganic materials, all can be used as excellent carrier. Therefore, the research on nano-formulations loaded with paeoniflorin has great exploration value, which will also provide technical support for the clinical research of paeoniflorin.

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Anti-inflammatory Steroids Form the Leaves of *Datura Stramonium L.*

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Abstract

Eight new steroids, designated mantuoluosides A-H (**1-8**), were obtained from the enrichment of steroids by HPD-BJQH macroporous resin of the leaves of *Datura stramonium L.* The elucidation of their respective structures were based on spectroscopic methods and comparison data with literature. The anti-inflammatory activities of these compounds were evaluated on (LPS)-induced BV-2 cells with IC₅₀ value. It was found that compounds **1**, **5**, **7**, and **8** showed different degrees of anti-inflammatory activity with IC₅₀ less than 50 μM.

Key words: *Datura stramonium L.*, Steroids, Withanolides, Anti-inflammatory

Datura stramonium L. is an annual herb of the Solanaceae family, which is widely distributed in temperate, tropical and subtropical regions^[1]. This plant has been used in the treatment of epilepsy, depression, rheumatoid arthritis, convulsions, bruises, and other diseases. Sifting of the literature shows that steroids, flavonoids, sesquiterpenes, and alkaloids have been reported from this genus^[2]. Out of interest in the chemical structural diversity of steroids, we used HPD-BJQH macroporous resin for enrichment, separation of methanol extracts from the dried leaves of *Datura stramonium L.* and other chromatographic columns, as a result, a series of new steroids, including three ergostane-type steroids (**1-3**) and five withanolide-type steroids (**4-8**), were isolated and identified. Meanwhile, the anti-inflammatory activities of these isolated items were evaluated and reported for the first time.

Objective

To clarify the pharmacodynamic foundation of the anti-inflammatory effect of the leaves of *Datura stramonium L.*, the constituents from its methanol extract of it were systematically and thoroughly studied, which could provide the theoretical basis for further research on the pharmacodynamics and mechanism of action, quality evaluation, and clinical medication of *D. stramonium* leaves.

Materials and methods

In this experiment, maceration and conventional column chromatography, such as HPD-BJQH macroporous resin, silica gel, and ODS column chromatography, were used to systematically separate 95% ethanol components of methanol extract of *D. stramonium* leaves, and then analyze and purify them with HPLC. Finally, their structures were determined according to NMR, UV, MS, and other spectral data.

Results and discussion

Mantuoluoside A (**1**) with the molecular formula C₃₄H₅₆O₁₀ (HRESIMS). The 1D NMR spectra of **1** showed general features similar to those of the daturmeteside C^[3], except for an additional

β -glucosyl moiety at C-3 in **1**. The HMBC correlations from H-1' (δ_{H} 4.38) to C-3 (δ_{C} 74.7) established a 3-O- β -D-glucopyranoside structure. Hence, the structure of **1** was identified as (20S,22R,24Z)-1 α ,7 α ,22,26-tetrahydroxyergost-5,24-diene-3-O- β -D-glucopyranoside (**Fig. 1**).

The 1D NMR spectra of mantuoluoside B (**2**) showed general features similar to those of the known daturmeteside D^[3], except for an additional β -glucosyl moiety at C-27 in **2**. The HMBC correlations from H-1' (δ_{H} 4.28) to C-27 (δ_{C} 70.8) unambiguously established 27-O- β -D-glucopyranoside structure. Thus, the structure of **2** was identified to be (20S,22R,24E)-1 α ,3 β ,7 α ,22 α -tetrahydroxyergost-5,24-diene 27-O- β -D-glucopyranoside (**Fig. 1**).

Mantuoluoside C (**3**) with the molecular formula C₃₄H₅₆O₁₀. The 1D NMR spectra of **3** were extremely similar to the compounds **2**, except for one more β -glucosyl moiety in **3** and the loss of hydroxy at C-1 in **3**. The HMBC correlations confirmed that the β -glucopyranosides were located at C-3 and C-27, respectively. Therefore, the structure of **3** was identified as (20S,22R,24E)-7 α ,22 α -dihydroxyergost-5,24-diene-3,27-O- β -D-glucopyranoside (**Fig. 1**).

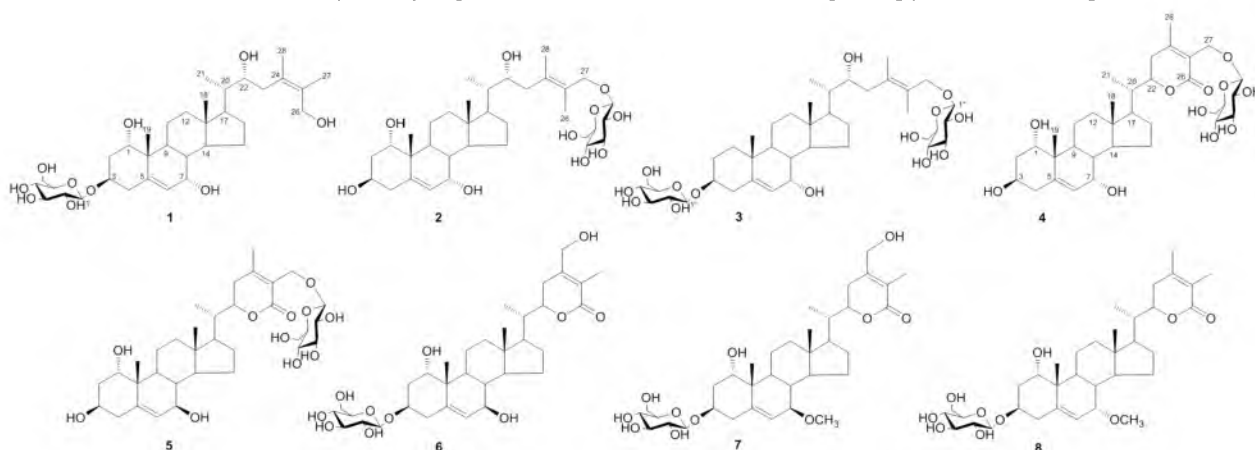


Fig. 1 Structures of compounds 1-8.

Mantuoluoside D (**4**) with the molecular formula of C₃₄H₅₂O₁₁, deduced by the HRESIMS. The comparison of the 1D-NMR data with those of daturmetelide K suggested that these two compounds featured a similar carbon framework^[4], except for an additional β -glucosyl moiety in **4**. The HMBC correlations from H-1' (δ_{H} 4.33) to C-27 (δ_{C} 63.6) confirmed that the β -glucosyl was located at C-27. Therefore, the structure of **4** was considered to be 1 α ,3 β ,7 α -trihydroxy-(20S,22R)-witha-5,24-dienolide-27-O- β -D-glucopyranoside (**Fig. 1**).

Mantuoluoside E (**5**) with the molecular formula C₃₄H₅₂O₁₁ (HRESIMS). By comparing the ¹³C-NMR data of compounds **5** and **4**, it was found that they have the same planar structure, the major differences were the signals for carbons around C-7, which indicated that these two compounds should be the different orientation of 7-OH and by NOESY spectrum, together with the large coupling constants ($J = 8.2$ Hz), suggesting the β -orientation of the 7-OH group. Consequently, the structure of **5** was established as 1 α ,3 β ,7 β -trihydroxy-(20S,22R)-witha-5,24-dienolide-27-O- β -D-glucopyranoside (**Fig. 1**).

Mantuoluoside F (**6**) was assigned the molecular formula C₃₄H₅₂O₁₁ by HRESIMS. Analysis 1D

NMR spectra data revealed that the structure of **6** was similar to that of **5**. The obvious differences between **6** and **5** were the location of the β -glucosyl moiety group and the presence of 28-OH. The key correlations observed in the HMBC spectrum from H-1' (δ_{H} 4.38) to C-3 (δ_{C} 74.8) indicated that the β -glucosyl was attached at C-3. The stereochemistry of **6** was quite similar to **5**. Given this evidence, the structure of **6** was assigned as 1 α ,7 β ,28-trihydroxy- (20S,22R)-witha-5,24-dienolide 3-O- β -D-glucopyranoside (**Fig. 1**).

Mantuoluoside G (**7**) with the molecular formula of C₃₃H₅₄O₁₁ (HRESIMS). The NMR spectroscopic data of **7** were closely related to those of **6**. The main difference between them was a methoxy group of **7** at δ_{H} 3.27 (3H, s), instead of the hydroxyl group at C-7. The coupling constant of H-7 (8.3, 2.1) suggested the β -orientation of 7-OMe. The rest of the configurations of **7** were determined to be the same as those of **6**. Consequently, the structure of **7** was established as 1 α ,28-dihydroxy-7 β -methoxy-(20S,22R)-witha-5,24-dienolide-3-O- β -D-glucopyranoside (**Fig. 1**).

Mantuoluoside H (**8**) with the molecular formula C₃₆H₅₅O₁₂ (HRESIMS). The NMR spectroscopic data of **8** were closely related to those of **7**. The main difference between them was the relative configuration of H-7, and the β -orientation of H-7 was verified by NOSEY. The remaining configuration of **8** is determined to be the same as that of **7**. Consequently, the structure of **8** was established as 1 α ,28-dihydroxy-7 α -methoxy-(20S,22R)-witha-5,24-dienolide-3-O- β -D-glucopyranoside (**Fig. 1**).

All isolated compounds were evaluated for their inhibitory effects on NO production in LPS-induced BV-2 microglial cells. Compounds **1**, **5**, **7**, and **8** were found to show obvious anti-inflammatory activity with IC₅₀ values of 5.9-39.9 μ M.

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Based on the textual research of classic prescriptions of Jinshui Liujun Decoction

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Abstract

Traditional Chinese medicine (TCM) culture is a great treasure and a unique health resource in our country. However, due to serious constraints on inheritance and development, the scientific and technological foundation of TCM is relatively weak, which restricts the expansion and strength of the traditional Chinese medicine health industry. As a result, it is difficult for TCM to go abroad and go international. At present, the state attaches great importance to the development of TCM and has issued a series of laws and regulations to support the culture of TCM. The cause of TCM is going to be bright step by step. In order to respond to the call of the country, this paper sorted out the textual research of the classic famous recipe Jinshui Liujun decoction, and lays a theoretical foundation for the development of the health industry of the classic prescription.

Keywords: classic famous prescription, Jinshui Liujun Decoction, textual research of prescription drugs, health industry

Jinshui Liujun decoction is the catalogue of ancient classic prescriptions (the first batch) issued by the State Administration of traditional Chinese medicine, which has extremely curative effect in the treatment of cough, bronchial asthma and other respiratory diseases. The traditional empirical prescription is the treasure of Chinese traditional medicine culture, which should be widely publicized on the basis of rectifying the source. Future generations should know the idea of prescription well before using it, and excavate the essence of drug pairing.

Objective

This paper mainly focuses on the collation and research of the classic medical books of traditional Chinese medicine related to the classic famous prescription Jinshui Liujun decoction. On the premise of full collation and textual research of classical medical books, we should strengthen the combing of the essence of classical medical books, and integrate modern science and technology to improve the clinical efficacy and service rate of classic prescriptions. Simultaneously, it lays a substantial foundation for the development and utilization of the next step preparation of the classic famous prescription-- Jinshui Liujun decoction.

Materials and methods

By going to traditional Chinese medicine libraries to consult ancient books, as well as through modern scientific and technological means, such as through CNKI, TCM ancient books search and other websites, search with the keywords of classic famous prescriptions, Jinshui Liujun decoction, evolution of prescription analysis, historical evolution, etc., it is summarized and discussed the prescription source, rule of prescription change, historical evolution, prescription dose, decoction method and objection of Jinshui Liujun Decoction.

Results and discussion

The classic famous prescription Jinshui Liujun decoction is still widely accepted and used by the later physicians, and it has a miraculous effect on treating phlegm, cough, asthma and other diseases caused by deficiency of lung and kidney. It is found that it is not a precedent for Jinshui Liujun Decoction to use Yin-nourishing medicine to resolve phlegm, and it is very reasonable. The dosage and decocting method of prescription Chinese medicine were determined to provide a theoretical basis for the next preparation process development of Jinshui Liujun Decoction, and at the same time to make the original Chinese medicine prescriptions clear and to spread the correct culture of Chinese medicine to the public.

TCM civilization is a precious heritage left by our ancestors. We should take it as our duty to promote it. We should cherish, protect, and strive to develop the treasure of TCM, which will be transformed into the development advantage of China's TCM industry. Win more discursive power for China's TCM industry, and create a comprehensive revitalization of China's TCM health industry!

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The third-generation non-small cell lung cancer specific drug-osimertinib

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Abstract

As a third-generation TKI, Osimertinib can target both EGFR TKI sensitizing mutations and T790M. In addition, some wild-type EGFR mutation patients are also suitable for this drug. Osimertinib was first approved by the U.S. FDA as a clinical drug for NSCLC in 2015 and was approved by the European Medicines Agency the following year as an EGFR T790M mutation therapy for NSCLC patients. The results of the latest phase of clinical trials show that osimertinib is superior to platinum chemotherapy drugs in many aspects for advanced EGFR T790M positive mutation NSCLC patients. This article will review the mechanism of action and therapeutic application of osimertinib.

Keywords : osimertinib, T790M mutation, epidermal growth factor receptor, tyrosine kinase inhibitor

Lung cancer is a cancer with a high mortality rate, and about a quarter of cancer deaths in 2016 were in lung cancer patients ^[1]. Non-small cell lung cancer (NSCLC), which includes adenocarcinoma, squamous cell carcinoma, and large cell lung cancer, accounts for approximately 85% of lung cancer patients, and NSCLC is usually diagnosed as locally advanced or metastatic secondary. For patients with advanced NSCLC, platinum-based chemotherapy has always been one of the main methods of clinical treatment ^[2]. Research on epidermal growth factor receptor (EGFR) mutations and anaplastic lymphoma kinase (ALK) rearrangements has led to the development of specific molecularly targeted drugs that have fundamentally improved the treatment of patients with advanced NSCLC ^[3, 4]. Compared with platinum chemotherapy drugs, some EGFR TKIs such as gefitinib, erlotinib and afatinib can significantly improve the therapeutic effect of patients ^[5]. These targeted drugs are currently more effective for patients with advanced NSCLC. medicine. The combination therapy of erlotinib and bevacizumab is also one of the ideal treatment options for patients with EGFR-mutant NSCLC^[6]. For patients with advanced EGFR-mutant NSCLC, the emergence of the third-generation precision therapy drug osimertinib provides them with an opportunity to prolong their survival and improve their quality of life.

Osimertinib design and mechanism of action

Osimertinib (TAGRISSOTM, ADZ9291, AstraZeneca) is a monoanilinopyrimidine compound that irreversibly and selectively targets EGFR TKI sensitization and EGFR T790M resistance mutations, and also it can target some patients with wild-type EGFR mutation (see Figure 1) ^[8]. Binding of osimertinib to EGFR kinase targets cysteine 797 residues of the ATP-binding site and is formed by a covalent bond. While WZ4002 and rociletinib share some common structural features, osimertinib has a unique chemical structure. In the EGFR recombinase assay, osimertinib was nearly 200-fold more potent against L858R/T790M than wild-type EGFR, thus confirming that it is more sensitive to mutant EGFR^[7]. In the in vitro model tests for the specificity evaluation of different EGFR TKI mutations, osimertinib has broad therapeutic prospects for the EGFR T790M resistance mutation. In an in vivo study in mice, the metabolism of osimertinib resulted in two products, AZ5104 and

AZ7550, of which only AZ7550 was more potent and sensitive than the original compound, while AZ5104 was more specific for Formation of mutant and wild-type EGFR with partial loss of selectivity. Osimertinib exhibited minimal off-target kinase activity when co-tested with a variety of other kinases. At 1 μ M, the compound exhibited >60% inhibition, limiting other kinases such as ErbB2/4, ACK1, ALK, BLK, BRK, MLK1 and MNK2, so osimertinib was more preferred. In vivo, osimertinib does not exhibit activity at the IGF-R and insulin receptors, and is located in the kinase domain with a methionine gate, thus suggesting a low dose risk, and unlike rociletinib, osimertinib limits Toxicity associated with hyperglycemia ^[8]. Figure 1 Osimertinib inhibits EGFR phosphorylation of sensitized EGFR-mutated EGFR in EGFR cell lines similar to the previous generation of reversible TKIs. However, unlike the first-generation TKIs, it inhibited EGFR phosphorylation more efficiently in T790M cell lines (H1975: L858R/T790M and PC-9VanR: ex19del/T790M) than wild-type EGFR. The ability of osimertinib to induce inhibition of downstream signaling (pAKT, pERK) was also stronger in mutant EGFR cell lines than in EGFR wild-type cell lines. In cell line studies transfected with other mutated EGFR and HER2 mutated cfDNA, EGFR TKI-related resistance was developed, suggesting that AZ5104 has some activity against EGFR VIII mutations and that osimertinib has an effect in inhibiting the growth of HER2 cell lines. Therefore, depending on clinical studies, osimertinib and AZ5104 may inhibit these targets ^[8]. Once-daily doses of osimertinib induced significant dose-dependent regressions in both TKI-sensitized and T790M-resistant EGFR mutant models studied in mutant EGFR xenograft models. Significant tumor shrinkage was seen at low doses, complete and durable responses were seen in EGFR-mutant xenograft tumors when osimertinib was administered at long-term daily oral doses, and there was no evidence of tumor progression to 200-day-treated animals. It is well tolerated and begins to lose less than 5% of body weight ^[7]. Finally, in an in vivo transgenic mouse tumor model, osimertinib has antitumor activity against EGFR L858R or L858R+T790M mutations.

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Analysis of Acupuncture and Moxibustion Methods to Prevent and Cure Infectious Illness of SUN Si-miao's Qianjinfang

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Abstract

The Qianjinfang of SUN Si-miao collects numerous clinical achievements of traditional Chinese medicine before the Tang Dynasty. His thoughts and methods of acupuncture and moxibustion for preventing and curing diseases are significant. Moxibustion was taken to prevent and cure diseases. He uses moxibustion for both dispelling filth and reinforcing the healthy qi. The amount of moxibustion depends on the condition. He focuses on selecting specific points to reinforce the healthy qi and dispel pathogenically. The site of moxibustion will vary if the same disease starts at different sites which reflects the principle of seeking the source of the disease. It is the first record Er-Zhong point to treat the infectious illness meanwhile summarize experience points in the process of treatment. SUN Si-miao also promotes acupuncture in combination with Traditional Chinese Medicine to prevent and treat infectious illnesses. Through the analysis of the characteristic methods of acupuncture which are from the prevention and treatment of infectious illness of SUN Si-miao, excepting to open ideas for the prevention and treatment of infectious illness in the future.

Keywords: SUN Si-miao; Beiji Qianjin Yaofang; QianJin Yifang; Infectious illness; Acupuncture and moxibustion.

SUN Si-miao has extensive knowledge in the prevention and treatment of disease with acupuncture. He also pays attention to the application of acupuncture and moxibustion in infectious illnesses. His theory plays an immeasurable role in the development of TCM infectious illness. He makes some innovations based on inheriting the theory of his predecessors which include prevention before getting sick, early treatment after infection, focusing on diet, acupuncture, and other methods of preventing and treating infectious illness. All the above theories have a profound impact on offspring doctors.

The history of acupuncture in the prevention and treatment of infectious diseases is almost if the development of acupuncture. Acupuncture and moxibustion played an indelible role in the human struggle against the infectious illness for thousands of years. Although it is not directly dispelled filth like Traditional Chinese Medicine, the occurrence of the disease is nothing but a conflict between health and pathogen. According to the theory of traditional Chinese medicine, the deficiency of healthy qi is the basis of the disease, pathogenic qi invasion is the main cause of the disease. Acupuncture and moxibustion indirectly dispel evil by enriching the healthy qi of the human body. Strengthening the healthy qi without leaving the pathogenic qi, and dispelling pathogenic qi without harming the healthy qi, have the dual functions of tonifying method and purgation, which is incomparable with medicines.

Objective

Providing ideas and contributing methods for treatment of infectious illness prevention by analyzing the characteristic methods of acupuncture which are from the prevention and treatment of infectious illness of SUN Si-miao.

Materials and methods

This article is based on the 2014 editions of *Beiji Qianjin Yaofang* and *Qianjin Yifang*, which is proofread by Li-Jingrong et al. Finding the articles related to acupuncture and moxibustion for the prevention and treatment of infectious diseases throughout the whole book. Inducting and arranging related diseases, points, and operation methods. Statistics on the frequency and characteristics of points. Summarizing the characteristic methods of SUN Si-miao's acupuncture and moxibustion in the prevention and treatment of infectious illness.

Results and discussion

The *Qianjinfang* of SUN Si-miao uses acupuncture and moxibustion to prevent and treat diseases, using moxibustion more than acupuncture. Using scar moxibustion to "open the door and drive away thieves" to prevent infectious illness. In the treatment, moxibustion is used according to the disease, and the number is not limited to avoid filth and reinforce the healthy qi and pay attention to the use of specific points in the selection of points such as raising points, original acupoints, and seeking the source of disease at the same time. The same disease, different initial site, different treatment methods. It also recorded extraordinary points and empirically effective points, acupuncture in combination with Traditional Chinese Medicine for preventing and treating infectious illnesses.

The reason, methods, prescriptions, and points in an orderly manner of the acupuncture and moxibustion for preventing and treating infectious illness of Qian Jin Fang. There are rules to follow in the selection of points and prescriptions in accordance with the treatment method. And its acupuncture application forms are various, flexible, and operation specific. It will be very meaningful for us to improve the efficacy of clinical infectious illness in the future by inheriting and carrying forward the experience of using acupuncture to prevent and treat the infectious disease of SUN Si-miao.

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Analysis of concentration of attention and sensorimotor reactions in patients with mild and moderate traumatic brain injury

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Abstract

On the basis of the Amur Regional Neuropsychiatric Dispensary and the Amur Medical Academy, a controlled open randomized study was conducted to study cognitive functions in 20 patients with a history of traumatic brain injury in comparison with practically healthy volunteers (n=20). Concentration of attention and sensorimotor reactions were evaluated using the "Schulte Table" method. The results of the study showed that in patients in the long-term period of traumatic brain injury, the efficiency of work decreases by 3 times relative to healthy volunteers and mental stability. It is concluded that it is necessary to conduct a mandatory neuropsychological examination in patients with traumatic brain injury in the long term in order to timely and pathogenetically justified pharmacocorrection.

Keywords: traumatic brain injury, remote period, work efficiency, degree of development, mental stability, patients.

The problem of cognitive impairments leading to a decrease in the quality of life in patients who have suffered a traumatic brain injury remains a priority today, taking into account the annual statistical increase in the number of brain injuries [2, 8]. The untimely diagnosis of cognitive disorders that form in the long-term period of traumatic brain injury, the possibility of transforming into post-traumatic dementia determines the need for early diagnosis and adequate pathogenetically based therapy in order to correct neuropsychological symptoms and preserve the habitual lifestyle of patients for as long as possible [5, 7]. In this regard, it is of interest to study of concentration of attention and sensorimotor reactions in patients with mild and moderate traumatic brain injury.

Materials and methods

On the basis of the Amur Regional Neuropsychiatric Dispensary, a prospective controlled open randomized study was conducted with the participation of 20 patients aged 36 to 58 years with a history of mild and moderate traumatic brain injury (S06 according to the tenth revision of the International Classification of Diseases). The properties of switching and distribution of attention, tempo and sensorimotor reactions were diagnosed using the "Schulte Tables" method [1, 3]. When processing the results, work efficiency (average task completion time), the degree of workability (an indicator reflecting how quickly the subject is included in the task), mental stability (an indicator reflecting how long the subject can concentrate on a specific search task) were evaluated. The statistical analysis of the obtained results was carried out using the Statistica statistical software package.

Results and discussion

Considering that the time to complete the tasks of the "Schulte Tables" test is normally 40-50 seconds, it should be noted that in patients with a history of traumatic brain injury, the average time spent on one table and indicated by the indicator "Work efficiency" was 3.2 times higher than the same parameter in healthy volunteers and amounted to 141.8 seconds. The value of the indicator

"Degree of workability" was equal to 1.00 conventional units, which indicated sufficient workability, in contrast to the assessment of mental stability in patients with post-traumatic cognitive disorders - the time spent with the fifth (last) Schulte table exceeded the average time spent on the task as a whole, which allowed registering an indicator equal to 1.02 conventional units, and to state the impossibility of the subjects to concentrate for a long time on a specific search task. Thus, in patients with mild and moderate traumatic brain injury, a decrease in concentration, pace and sensorimotor reactions is recorded in the anamnesis, which allows us to consider neuropsychological examination as an obligatory element of diagnostic measures in patients who have suffered traumatic brain injury, regardless of the severity of the injury, and suggests the addition of post-traumatic therapy with the appointment of medications, having neurometabolic, nootropic and antioxidant activity [4, 6].

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Search for TRPM8 ligands by *in silico* methods

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Abstract

The strategy for predicting potential ligands to TRPM8 based on *in silico* methods had been proposed. Of the 10 potential ligands predicted by the neural network, eight showed a high minimum binding energy and a greater number of conformations compared to the classic TRPM8 ligand, menthol, when verified by the AutoDock program. Using *in silico* methods, it was possible to modify the 3D structure of menthol and obtain a ligand that binds to TRPM8 differently than the natural one. The modified ligand does not bind to the key amino acid of the active center TRPM8 Y745 and, therefore, should exhibit antagonist properties. The proposed approach allows to perform preliminary screening of potential drug candidates and separate protein ligands into agonists and antagonists.

Keywords: TRPM8, bronchial hypersensitivity, cold, *in silico* methods, neural network.

In the development of bronchial hypersensitivity to low temperatures, an important role belongs to the TRPM8 receptor protein [1], which can become a target for drugs intended for the prevention and treatment of bronchial hyperreactivity to cold [2]. The aim of the study – to select potential ligands for TRPM8 with a help of *in silico* methods.

Materials and methods

To select potential ligands for TRPM8, we created a PyTorch neural network [3] with a hybrid architecture and used intermolecular docking methods [4, 5]. The developed network accepts two types of input data simultaneously and passes these data independently through different layers. Information about receptors passes through convolution layers and fully connected layers. Regardless of receptors, information about ligands passes through fully connected layers. Then information about receptors and ligands was combined and passes through fully connected layers. The network outputs probability distribution included two classes: a pair of molecules interacts, or a pair does not interact. To dock TRPM8 with potential ligands we used a set of tools of the graphic molecular laboratory MGLtools [6] and a special program Autodock [7]. Virtual modification of the menthol structure was carried out using the PyMol program [8]. To identify the features of the docking of menthol and its modified derivative in the TRPM8 molecular pocket, the service of the Galaxy7TM virtual molecular laboratory was used [9].

Results and discussion

Using the neural network, 10 potential ligands were detected: A17 (Gibberellin), FAD (Flavinadenine Dinucleotide), FDA (Dichlorophenylarsine), G4M, 57-83-0 (Progesterone), 52-39-1 (Aldosterone), 65807-02-5 (Goserelin), 526-36-3 (Xylometazoline), 53-06-5 (Cortisol) and III (Dexamethasone). The obtained potential ligands were verified by the AutoDock program for the ability to form complexes with three amino acid residues of the TRPM8 active center - Tyrosine 745 (Y745) - critical center for TRPM8, Phenylalanine 1008 (R1008) and Alanine 1009 (L1009). Upon completion of docking, 8 stable complexes were obtained out of 10 at each site. The data on the minimum docking energy and the number of stable conformations are presented in the table. Of the 10 potential ligands predicted by the neural network, eight showed a high minimum binding

energy and a greater number of conformations compared to the classic TRPM8 ligand, menthol, when verified by the AutoDock program. FAD and G4M revealed the largest number of possible conformations (five out of five) with Y745 and R1008 centers. For the L1009 center, FAD demonstrated successful docking for four of the five conformations given. It should be concluded that it is these ligands that have the highest affinity for TRPM8. Two of the predicted FDA ligands and 65807-02-5 (Goserelin) failed to dock, which may be due to insufficient allocated memory of the computing device for successful docking or other technical problems.

Table. Minimum binding energies for the identified conformations of ligands when docked with three centers (kcal/mol).

Ligands	Docking center														
	Tyrosine 745					Phenylalanine 1008					Alanine 1009				
	Revealed conformations of the ligand														
	1	2	3	4	5	1	2	3	4	5	1	2	3	4	5
A17 (Gibberellin)	-4.4	-4.1	-	-	-	-5.8	-5.6	-5.6	-	-	-5.5	-5.4	-5.0	4.	5.-
FDA (Dichlorophenylarsine)	-4.7	-4.7	-4.7	-4.7	-1.9	-11.9	-10	-9	-8.3	-5	-12	-10.4	-6.7	-3.4	-
G4M	-9.5	-8.4	-8.4	-5.4	-4.8	-10	-9.6	-7.6	-6.5	-3.4	-10.3	-9.3	-9.1	-9.1	-7.1
57-83-0 (Progesterone)	-5.5	-	-	-	-	-6.3	-	-	-	-	-5.6	-	3.-	4.-	5.-
52-39-1 (Aldosterone)	-8.7	-6.9	-	-	-	-8.8	-8.5	-	-	-	-9.2	-8	3.-	4.-	5.-
526-36-3 (Xylometazoline)	-5	-	-	-	-	1.-5.18	-4.9	-	-	-	-5.6	-5.4	-5.4	-	-
53-06-5 (Cortisol)	-8	-	-	-	-	1.-8.40	-8.2	-	-	-	-10.1	-8.7	-8.2	-	-
III (Dexamethasone)	-5.7	-5.6	-	-	-	1.-9.62	-9.3	-	-	-	-11.3	-10.1	-	-	-
Menthol	-4.69	-4.45				-4.94	-				-5.41	-			

To answer the question of whether the ligands we found are TRPM8 agonists or antagonists, we used a virtual modification of the structure of the classic TRPM8 agonist menthol, removing the hydroxy group in the meta-position and adding two new hydroxy groups to the ortho-positions (Figure 1).

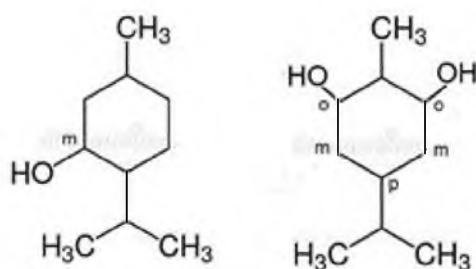


Figure 1. Menthol (left) and its modified derivative (right). o, m, p – positions in the cycle. [5]. Menthol interacts with the receptor through a molecular pocket, which includes Y745 and R842 [5]. Upon the formation of the complex, a hydrogen bond arises between the hydroxyl group of menthol in the meta position and the residue Y745. The docking of the receptor and menthol showed its characteristic agonist properties, namely, the formation of hydrogen bonds between the hydroxyl group in the meta position and the Y745 amino acid residue in several possible conformations (Figure 2, left). Intermolecular docking between the receptor and the modified menthol derivative also revealed the formation of a complex in this molecular pocket, but other amino acid residues rather than Y745 were involved in the formation of the complex. Due to the symmetrical arrangement of hydroxyl groups in the ortho-positions of the modified molecule, the ligand is forced to form bonds with nearby amino acid residues (aspartic acid 802, phenylalanine 839 or R 842), ignoring Y745 (Figure 2, right). Due to the formation of hydrogen bonds with the

indicated amino acid residues, the ligand blocks access to Y745, the main amino acid in the active site responsible for the operation of the ion channel, and behaves as an antagonist, a competitive inhibitor of the natural ligand (menthol). Since the binding energy of the modified ligand to the receptor is higher than that of menthol, it can be concluded that the modified ligand will bind to the receptor more efficiently than the natural one and prevent the action of menthol as a TRPM8 agonist.

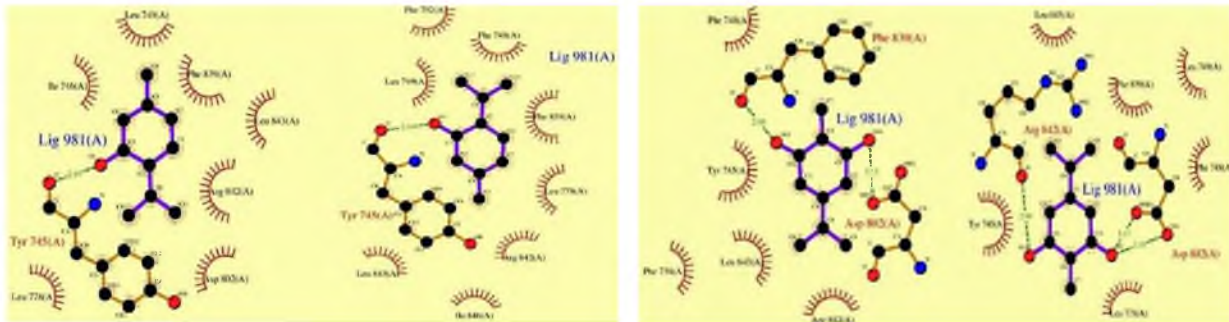


Figure 2. Schematic representation of the possible conformations of menthol (left) and its modified ligand (right) with TRPM8. The green dotted line indicates hydrogen bonds between the hydroxy groups of the ligand and amino acid residues located near tyrosine Y745 [5].

The proposed strategy for predicting potential ligands to TRPM8 *in silico* allows for a preliminary screening of potential drug candidates. Of the 10 potential ligands predicted by the neural network, eight showed a high minimum binding energy and a greater number of conformations compared to the classic TRPM8 ligand, menthol, when verified by the AutoDock program. Using *in silico* methods, it was possible to modify the 3D structure of menthol and obtain a ligand that binds to TRPM8 differently than the natural one. The modified ligand does not bind to the key amino acid of the active center TRPM8 Y745 and, therefore, should exhibit antagonist properties. The proposed approach can be used to separate protein ligands into agonists and antagonists.

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Results of assessment of cognitive dysfunction in patients in the long-term period of traumatic brain injury

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Abstract

On the basis of the Amur Regional Neuropsychiatric Dispensary and the Amur Medical Academy, a controlled open randomized study was conducted to study cognitive functions in 16 patients with a history of traumatic brain injury (men aged 32 to 54 years, the main group). The control group consisted of 20 practically healthy volunteers. In accordance with the purpose of the study, the parameters of the neuropsychological status were determined. The results of the study showed that in the long-term period of traumatic brain injury, patients experience the formation of moderate cognitive impairments, a decrease in work efficiency, mental stability and concentration of attention against the background of a decrease in memory compared with similar parameters in healthy volunteers. It is concluded that in the long-term period of traumatic brain injury, it is necessary to carry out pharmacocorrection of cognitive dysfunction.

Keywords: post-traumatic cognitive dysfunction, traumatic brain injury, work efficiency, degree of workability, auditory memory, patients.

The consequences of traumatic brain injury are a problem of modern medicine in general and neuropsychiatry in particular, since the statistical growth of injuries, especially among people of young working age, annually maintains a tendency to steady growth [2, 8]. This potentiates a high level of temporary disability and disability of victims and forces researchers to look for pathogenetically justified pharmacocorrection aimed at maximizing the restoration of neurological and neuropsychological status in the long-term period of traumatic brain injury [5, 7]. In this regard, it is of interest to study the parameters of cognitive dysfunction in patients with a history of traumatic brain injury.

Materials and methods

A prospective controlled open randomized trial was conducted with the participation of 16 patients aged 32 to 54 years with a history of traumatic brain injury (S06 according to the tenth revision of the International Classification of Diseases) with a trauma prescription of up to 6 years. The comparison group consisted of 20 practically healthy volunteers who, in parallel with patients with traumatic brain injury, performed tasks included in the minimum neuropsychological examination. Cognitive functions were assessed according to The Montreal Cognitive Assessment (MoSA-test), the properties of switching and distribution of attention, pace and sensorimotor reactions were diagnosed using the "Schulte Table" method; the assessment of mnemonic disorders was performed using the "10 words" test [1, 3]. The statistical analysis of the obtained results was carried out using the Statistica statistical software package.

Results and discussion

When assessing cognitive disorders on the Montreal Cognitive Assessment (MoSA-test) in patients with a history of traumatic brain injury, none of the patients (0%) scored 26-30 points corresponding to the normal range, which differed from similar indicators in healthy volunteers who

effortlessly performed tasks included in screening testing. Patients with traumatic brain injury experienced the greatest difficulties in passing the Montreal Cognitive Assessment (MoSA-test) in tasks for memorizing and reproducing information, including delayed, concentration of attention, abstract thinking. The time spent on average on completing tasks according to the Schulte tables was 3 times higher than the same parameter in healthy volunteers. Testing using the "10 words" method in patients who suffered trauma allowed us to establish on average the reproduction of three words out of ten, which corresponds to moderate short-term memory disorders, while by 4-5 presentation all 10 words (norm) were not reproduced by any patient (0%) at 100% in healthy volunteers.

Thus, the results of the study allow us to state the formation of cognitive disorders in patients with traumatic brain injury in the long-term period, which implies the appointment of pharmacocorrectors of post-traumatic cognitive dysfunction [4, 6].

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History of the study of endemics of the Far East and South-East Asia – relevance of integration

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Abstract

Clonorchiasis belongs to the topical natural focal trematodosis of the Russian Far East and Southeast Asia. The purpose of the study was to present the results of clonorchiasis research by the staff of the Amur State Medical Academy (ASMA) and to attract the attention of scientists to study the problem in order to integrate efforts aimed at devastating clonorchiasis. An analysis of scientific sources from the databases (WoS, PubMed, Google Scholar, eLIBRARY) was carried out, concerning the epidemiology, biology of the parasite and parasite fauna of endemic foci, historical data on the study of nosology by the staff of the ASMA for 70 years. It has been established that in the countries of East Asia, 200 million people are at risk of infection with clonorchiasis, and 15-20 million are already infected. In Russia, 12.2-36.7% of the indigenous inhabitants of the lower and middle Amur are infected with clonorchiasis. On the territory of the Amur Region as foci of epidemiological risk according to the results of a retrospective analysis (2015–2020). Unresolved endemic problems historically unite Russian scientists from the Far East and the countries of Southeast Asia, become the subject of biological and medical education, contributing to a competent approach to the biology of the parasite, its diagnosis, treatment and prevention of clonorchiasis.

Keywords: Clonorchiasis, endemics, endemic disease, Far East, Amur Region, South-East Asia.

Clonorchiasis is a topical natural focal trematode disease of the Far Eastern Federal District of Russia and South-East Asia. More than 19 mln. people are affected by it on the globe. High population infestation rate in these countries is connected with the consumption of raw, thermally improperly treated fish. In Russia, clonorchiasis occurs in the Far East, mainly in the Amur River basin and its tributaries. Each year, about 50% of the cases of clonorchiasis registered in the Russian Federation occur in the Amur Region, Khabarovsk Territory, and Primorskii Territory [1, 2].

The aim of study to substantiate the urgency of studying the parasitic invasions, including natural focal helminthiasis, among the problems of the XXI century world infectiology; to prove the expediency of studying the epidemiology of clonorchosis in the endemic regions of Russia, China, Vietnam, Korea; to reflect the historical perspective of clonorchosis research by employees of the ASMA; to draw the attention of scientists, doctors and teachers of the system of biological and medical education of the Russian Federation and South-East Asia to studying the general problem in order to integrate efforts aimed at the de-vast.

Material and methods

The authors used modern scientific resources on the problem of clonorchiasis (numerous database sources Web Science, PubMed, Google Scholar, eLIBRARY), concerning the epidemiology and biology of the parasite and the parasitofauna of endemic foci, as well as historical data on the study

of nosology by the ASMA staff for 70 years. An illustrated module of the curriculum of the Biology discipline «Far Eastern trematodeases» was developed for both full-time and distance teaching.

Results

About 56 million people in the world are infested with helminths of Trematodes class - suckers. Among 17 species of trematodes, *Clonorchissinensis*, first described by McClonnel in 1874 and studied in detail by Kobajashi in 1910, deserves special attention. Clonorchiasis is an endemic disease affecting the hepatobiliary system and the human pancreas. In many East Asian countries, 200 million people are at risk for clonorchiasis, and 15-20 million have already been infected. Of this number, more than 50% are from China, and the rest are from Korea and Vietnam [3, 4]. In Russia, 12.2-36.7% of the natives of the lower and middle Amur River are infected with clonorchosis. The custom of eating raw fish (tala, stroganina, etc.), which is a national tradition, is widespread among the Nanai, Ulchi, Udegei, and other indigenous ethnic groups of the Amur River. Among Russians, clonorchiasis is relatively rare [5]. However, given that a persistent focus of clonorchiasis has been formed in the Amur Region, the nosology remains an urgent problem. The incidence rate of this trematodeosis in 2020 was 3.4 per 100 thousand population, which is 42.4% lower than last year (2019 - 5.9, 2018 - 10.27). Based on the results of retrospective analysis (2015-2020), Bureisky (15.47), Mikhailovsky (15.26), Arkharinsky (7.16), Blagoveshchensky (6.99) districts and Raichikhinsk city (3.8) were defined as the epidemiological risk hot spots in the Amur region with more than 2-fold excess of the average regional level of population invasion by clonorch.

In the 20th century, the beginning of a systematic study of the human helminth fauna of the Far East was laid about 100 years ago by the 60th Union helminthological expedition organized by Academician K.I. Skryabin in 1927, whose members systematically surveyed over a thousand of the Amur River's natives from Khabarovsk to the Amur estuary. The peculiarity of the Amur River hydrofauna, caused by the presence in it of shellfish and fish species ecogenetically connected with the South Asian areas, was a natural prerequisite for the clonorchosis foci formation.

In the system of medical education, clonorchiasis has been singled out as the most active natural focal trematodeosis in the Far East endemics, which has been studied by the ASMA staff since the institute was founded. The results of research by biologists V.A. Kirilov and V.A. Dymin, published in the Proceedings of the Annunciation Medical Institute, testify to the presence of all clonorchosis nosoarea participants in the Upper Priamurie [6]. On the basis of the materials of expeditions, a detailed characterization of a natural outbreak of clonorchosis from 1954 to 1963 in the Upper Priamurie, from the village of Grodekovo to the village of Bibikovo, and along the Zeya River, from Blagoveshchensk to the village of Moskvitino, was given, with studies of not only rivers, but also floodplain lakes and oxbow lakes. Proof detection and substantiation of the presence of outbreaks were made by examining different fish species (16 species), the 2nd intermediate host, for their infection with *Clonorch'smetacercariae*. Infestation of the final host, cats, was verified: autopsies of 150 animals revealed parasite mariters in the liver of 2% of them. Up to 20% of fish caught in lakes were infested. Localization of metacercariae corresponded to muscles, pectoral fins, and head section of the body.

The researchers confirmed that the metacercariae belonged to the species *Clonorchissinensis* not only microscopically, but also biologically, by feeding the kittens of one litter with 25 specimens of

larvae, after which mature clonorchids were found in their livers 35 days later. The priority data obtained indicated the presence of a natural focus of clonorchiasis in Upper Priamur'ye and allowed us to significantly supplement the information on the geographical distribution of the endemic. The studies were continued with the participation of not only biologists and histologists (A.S. Shatrov, A.D. Chertov, P.P. Prokhorov, I.M. Cheremkin, R.N. Podolko) [7], but also clinicians of ASMA: V.A. Figurnov, V.A. Gavrilov, I.S. Katin, R.S. Mateisen, L.V. Krugliakov, P.K. Soldatkin [7]. Relevant data from the Department of Hospital Therapy of ASMA: Head of the Department Prof. Y.S. Landyshev, N.I. Georgievsky, M.V. Pogrebnaya ("A case of clonorchiasis occurring under the hematological mask of chronic myeloleukosis").

Studies of clonorchiasis in the Amur Region continue in the 21st century [7]. The role of the 1st and 2nd intermediate hosts of *C. sinensis*, which is performed by Parafossarulusmanchouricus mollusks and fish – numerous carp species of mainly Amur-Ussuriichthyocomplex, to which the larval stages of the parasite show increased specificity, is studied. Priamur'ye is the northern area of their ranges on the Asian continent, therefore they are concentrated in the southern regions of the Far East – in the Ussuri water basins, and in the Priamur'ye – in the waters of Zeya-Bureya watershed up to 52° of northern latitude along the Amur valley in the greatest quantities. The study of these peculiarities of the distribution of intermediate hosts of the pathogen, which determine the boundaries of the clonorchosisnosoareal and influence the character of its structure, does not lose its relevance and attracts the attention of parasitologists, ichthyologists, and ecogeneticists.

The relevance of studying the natural focal infestation, clonorchiasis, is undoubted in the XXI century. Various aspects and unresolved problems of the endemic have historically united Russian scientists of the Far East and Southeast Asian countries, becoming a subject of biomedical education [8], contributing to a competent approach to the biology of the parasite, its diagnosis, treatment and prevention of clonorchosis due to the dynamics of ecological and climatic factors, and extensive international tourist and business contacts, actively developing our countries and peoples.

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The relationship between the parameters of the antioxidant system and dermatological indices in patients with Rosacea

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Abstract

The analysis of correlations between the parameters of the antioxidant system and dermatological indices in patients with rosacea is presented. There were 25 women aged 26 to 54 years with erythematous-telangiectatic and papulo-pustular forms of rosacea who received standard therapy according to Clinical guidelines for the management of rosacea patients. The comparison group consisted of 21 practically healthy women. The study of the relationship between quantitative traits was carried out using the paired Pearson linear correlation coefficient (r). The analysis of correlations between markers of oxidative stress and dermatological indices allowed us to establish strong direct links between malondialdehyde and the Investigator's Global Assessment (IGA) criteria, the dermatological index of the symptom scale. Moderate direct connections were registered in the pairs of lipid hydroperoxide and IGA, lipid hydroperoxide and the dermatological index of the symptom scale. Thus, a close interdependence was established between dermatological indices and parameters of antioxidant status in patients with rosacea.

Key words: correlations, rosacea, dermatological indices, antioxidant system, patients.

Our previous studies have shown that with rosacea, patients have disorders of the prooxidant-antioxidant balance towards the accumulation of lipoperoxidation products [4, 8]. These markers of oxidative stress (malondialdehyde, lipid hydroperoxides, diene conjugates), the concentration of which increases by the end of the remission period, were designated by us as predictors of relapses of rosacea [6, 7]. The establishment of correlations between the parameters of the antioxidant system and dermatological indices in patients with rosacea will determine the adequate pharmacocorrection of changes in rosacea [2, 3, 5, 9, 10]. Objective – to analysis of correlations between the parameters of the antioxidant system and dermatological indices in patients with rosacea.

Materials and methods

There were 25 women aged 26 to 54 years with erythematous-telangiectatic and papulo-pustular forms of rosacea who received standard therapy according to Clinical guidelines for the management of rosacea patients. The comparison group consisted of 21 practically healthy women. In women, the parameters of the antioxidant status – lipid hydroperoxides, diene conjugates, malondialdehyde were determined in blood plasma with subsequent processing of the results using the Student's criterion (t) [1, 6, 7]. The severity of clinical manifestations was assessed according to the criteria of the Investigator's Global Assessment (IGA) and using the dermatological index of the scale of symptoms. The study of the relationship between quantitative traits was carried out using the paired Pearson linear correlation coefficient (r). In all statistical analysis procedures, the critical significance level was assumed to be 0.05.

Results and discussion

Evaluation of the severity of clinical manifestations using the dermatological index of the scale of

symptoms in patients with rosacea allowed to register the presence of erythema in 19 patients, telangiectasia – in 16, papules and pustules – in 11, 19 patients complained of dryness and peeling against the background of a significant increase in the concentration of lipid hydroperoxides and diene conjugates in blood plasma in women with dermatosis 25%, malondialdehyde – by 42% compared with similar parameters in practically healthy women ($p < 0.05$). The analysis of correlations between markers of oxidative stress and dermatological indices allowed us to establish strong direct links between malondialdehyde and IGA, malondialdehyde and the dermatological index of the symptom scale ($r = 0.82$ and $r = 0.79$, respectively, $p < 0.05$), which indicates the predominance of the severity of clinical manifestations of rosacea with the accumulation of a secondary product of lipoperoxidation. Interactions in pairs of lipid hydroperoxide and IGA, lipid hydroperoxide and the dermatological index of the symptom scale ($r = 0.59$ and $r = 0.54$, respectively, $p < 0.05$) were registered similar in direction and moderate in strength.

Thus, in patients with erythematous-telangiectatic and papulo-pustular forms of rosacea, a close interdependence between dermatological indices and parameters of antioxidant status is recorded, which implies pharmacocorrection and the inclusion of drugs with antioxidant activity in order to optimize rosacea therapy.

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Tactics of managing patients with thermal inhalation trauma

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Abstract

The article carried out a retrospective analysis of the results of treatment of 18 patients with thermal inhalation injury on the basis of the Amur Regional Clinical Hospital (Blagoveshchensk), and also analyzed the percentage of tracheostomy performed in these patients. According to the results of the study, the complex of treatment of patients with TIT and skin lesions included therapy aimed at arresting acute respiratory failure, prevention of purulent-septic complications of the respiratory tract, treatment of burn disease, surgical treatment in the amount of autoplasty for deep burns, and tracheostomy. Tracheostomy was performed in 55.5% of patients with thermal inhalation injury (TII) in combination with skin burns.

Keywords: thermal inhalation injury, patients, combinationskin burns, tactics of managing TII includes inhalation injury, skin burns, and combined injury. Patients with TII belong to the category of patients with critical injuries [1]. According to modern literature, the combination of with respiratory tract lesions occurs in 30% of victims with deep flame burns [2]. Soot particles, inhaled with inhaled air and deposited on the surface of the mucous membrane of the respiratory tract, have both thermal and chemical effects on the ciliated epithelium, which leads to its death. The presence of TIT in burned patients significantly affects the course of burn disease, aggravating the severity of burn shock and leading to the development of life-threatening conditions. Mortality in TIT ranges from 33.3 to 82.2%, which determines the relevance of the problem under study [3]. All therapeutic measures for thermal inhalation injury are aimed at preventing and combating bronchospasm, edema and death of the mucous membrane of the respiratory tract. Leading in the treatment of acute respiratory lesions is repeated sanitation fibrobronchoscopy (FBS) [4]. Patients of this category, with an increase in the phenomena of respiratory failure, are intubated and artificially ventilated. Given the long stay of patients on the endotracheal tube, due to the severity of the patient's condition, the course of the burn disease, it is advisable to subsequently perform a tracheostomy. The aim of the study was a retrospective analysis of the results of treatment of patients with thermal inhalation injury and the percentage of tracheostomy performed in this category of persons.

Materials and methods

Analysis of the results of treatment of 18 patients with TII in the period from 2017-2021 was carried out on the basis of Amur Regional Clinical Hospital (Blagoveshchensk) Men - 10 (55.5%) and women - 5 (27.8%) aged 25-70, of which 3 children (16.7%) aged 8-11 years. Etiology of TII: fire in a closed room. Classification of TII: isolated lesion in 4 people (22.2%), in 14 people (77.8%) in combination with skin burns. The degree of TIT involvement was mild in 6 patients (33.3%), moderate in 10 patients (55.5%), severe in 2 patients (11.2%). Skin lesion area: less than 10% of the body surface (b.s.) - in 4 people (22.2%), 10-30% b.s. - in 8 victims (44.6%), 50% -90% b.t. - in 6 people, respectively (33.3%). The degree of skin damage is II-III degree. Patients in 83.3% were

hospitalized in the department no later than 6 hours from the moment of injury. Lethal outcome was 33.3% (6 patients).

Results and discussion

Comprehensive treatment of patients with TII in 100% of cases included infusion, antishock, antibacterial therapy, sanitation FBS. 14 patients with skin burns were regularly dressed with antiseptic solutions and wound dressings. The skin was restored by autoplasty in 7 patients with deep burns.

4 patients with isolated TII underwent oxygen therapy, inhalation of mucolytics, antibiotic therapy, with a positive effect. Of the 4 victims with burns less than 10%, 2 patients had a clinic of acute respiratory failure on the 3rd day after the injury, sanitation fibrobronchoscopy without effect, intubation, and tracheostomy was performed 3 days later.

3 patients from the group with burns with an area of 10-30% b.s. on the 7th day after the injury, intubation and tracheostomy were required. TII led to an aggravation of the burn disease.

6 patients with burns 50-90% b.s. were treated in the RAO ward, taking into account the degree of burn shock, the area and depth of the lesion, and the presence of TII.

Patients were put into drug-induced sleep. 5 out of 6 patients with burns 50-90% b.s. a tracheostomy was performed, because for these categories of persons, an endotracheal tube was installed in the first hours after the injury, taking into account their severity of the condition, long-term stay in RAO conditions and prolonged sanitation FBS. A patient with TII and 90% burns did not undergo a tracheostomy, because life expectancy after injury was less than a day.

Complications of TII were observed in 10 patients in the form of purulent bilateral endobronchitis (50%), polysegmental pneumonia (30%) and acute respiratory distress syndrome (20%). In 3 out of 10 patients with tracheostomy, late complications were detected in the form of tracheal stenosis, 2 of them were children.

Thus, treatment of patients with isolated TII includes a set of measures aimed at stopping respiratory failure, preventing purulent-septic complications of the respiratory tract, in combination with skin burns - treatment of burn disease and restoration of the skin. TII aggravates the course of the burn disease. Mortality was 33.3%. In 55.5% of patients with TII in combination with skin burns, tracheostomy was performed, 2 of them with a clinic of acute respiratory failure, the rest with a severe course of burn disease. Complications after tracheostomy were observed in 16.7% (3) of patients in the form of tracheal stenosis.

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Evaluation of correlations between markers of oxidative stress and hematological parameters in patients with ovarian cancer

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Abstract

The analysis of correlations between markers of oxidative stress and some hematological parameters in patients with ovarian cancer on the background of polychemotherapy is presented. 30 patients with stage III ovarian cancer who received platinum preparations were under observation. The presence of strong feedbacks between the concentration of malondialdehyde and the number of erythrocytes, monocytes, platelets has been established. Moderate feedbacks were registered in pairs of malondialdehyde and leukocytes, lipid hydroperoxidation and monocytes, lipid hydroperoxidation and platelets, catalase and average erythrocyte volume. A direct relationship was established between malondialdehyde and the average volume of an erythrocyte, between ceruloplasmin and monocytes. Thus, the presence of a sufficient number of reliable correlations between the parameters of the antioxidant status and hematological indicators indicates the pathogenetic component of complications of polychemotherapy on the part of the blood system induced by the prooxidant action of platinum preparations.

Key words: correlations, ovarian cancer, platinum preparations, markers of oxidative stress, hematological indicators, patients.

The main result of the scientific research is the establishment of relationships between individual parameters, followed by the study of the possibility of influencing the established dependencies by various chemical, pharmacological and other factors [3, 5, 6, 7,9]. Among the most popular methods of parametric statistics, a special place is occupied by the Pearson correlation criterion, which allows determining the change in one indicator in response to the dynamics of another [4]. Considering that our previous studies proved the formation of oxidative stress in patients with ovarian cancer on the background of polychemotherapy [1], the identification of correlations between markers of oxidative stress and some hematological indicators will allow us to assess the possibility of pharmacocorrection of side effects of platinum preparations[10]. Objective – to evaluation of correlations between markers of oxidative stress and some hematological parameters in patients with ovarian cancer on the background of polychemotherapy.

Materials and methods

30 patients with stage III ovarian cancer who received platinum preparations (cisplatin, carboplatin) were under observation. During polychemotherapy, hematological parameters (leukocytes, erythrocytes, hemoglobin, hematocrit, platelets), leukocyte, erythrocyte and platelet indices were evaluated using an automatic hematological analyzer Horiba ABX Micros ES60 (France). Lipid peroxidation products – lipid hydroperoxides, diene conjugates, malondialdehyde and the main components of the antioxidant system – ceruloplasmin and catalase were determined in the blood plasma of the patients, with subsequent processing of the results using the Student's criterion (t)[2, 8]. The study of the relationship between quantitative signs was carried out using a paired Pearson linear correlation coefficient (r), where $r = 0.7 - 1.0$ – strong dependence; $r = 0.69 - 0.3$ – moderate

dependence; $r < 0.29$ – weak dependence. In all statistical analysis procedures, the critical significance level was assumed to be 0.05.

Results and discussion

As a result of correlation analysis, it was found that in patients with ovarian cancer on the background of polychemotherapy, there is a relationship between the degree of accumulation of lipoperoxidation products and some hematological parameters: a strong feedback between the concentration of malondialdehyde and the number of red blood cells ($r = -0.73$, $p < 0.05$), malondialdehyde and monocytes ($r = -0.89$, $p < 0.05$), malonic dialdehyde and platelets ($r = -0.74$, $p < 0.05$), which indicates a decrease in the indicated hematological parameters in response to the accumulation of a secondary peroxidation product. The relationship between malonic dialdehyde and leukocytes was similar in direction and moderate in strength ($r = -0.56$, $p < 0.05$). In the pairs of lipid hydroperoxides and monocytes, lipid hydroperoxides and platelets, catalase and average erythrocyte volume, moderate feedbacks were established ($r = -0.67$, $r = -0.65$ and $r = -0.56$, respectively, $p < 0.05$). A direct relationship was recorded between malonic dialdehyde and the average volume of erythrocytes ($r = 0.67$, $p < 0.05$), between ceruloplasmin and monocytes ($r = 0.69$, $p < 0.05$).

Thus, in patients with stage III ovarian cancer, a sufficient number of reliable correlations between markers of oxidative stress and hematological parameters are formed against the background of polychemotherapy, which indicates the pathogenetic component of complications of polychemotherapy from the blood system and confirms the pro-oxidant effect of platinum preparations.

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Vitamin D levels in pregnant women with bronchial asthma in a changing climate

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Abstract

A special role of vitamin D in the prevention of asthma has been identified. In this regard, it is of interest to study the characteristics of the course of bronchial asthma during gestation, depending on the level of vitamin D. Of the 150 pregnant women with bronchial asthma participating in a prospective study, 62 were followed up from the moment of registration in the antenatal clinic until the moment of delivery. The content of vitamin D in the blood serum was analyzed. The average level of vitamin D in 150 pregnant women with asthma was significantly lower - 18.79 ± 4.83 than in 50 pregnant women of the comparison group - 25.43 ± 3.65 ng/ml ($p=0.00001$). At the same time, the level of vitamin D in women with the onset of the disease during pregnancy was significantly lower and amounted to 15.38 ± 5.69 ng / ml than in women with asthma duration of more than 10 years - 22.58 ± 6.57 ng / ml ($p = 0.03$). Therefore, low vitamin D levels may be one of the risk factors for developing asthma. Vitamin D deficiency is a marker of worsening asthma during pregnancy ($r = -0.54$, $p = 0.0002$), and also leads to more and more severe exacerbations ($r = -0.42$, $p = 0.0003$).

Keywords: vitamin D, bronchial asthma, pregnant women, deficiency, marker of worsening.

The winter period in the Amur region is 6-7 months. In the Amur region, the UV index for 6-7 months of the year is 0 or 1, which undoubtedly leads to a low production of vitamin D in the body. It is also known that during pregnancy, the need of the woman's body and the fetus for vitamin D increases, while the consumption of vitamin D also increases.

Bronchial asthma is widespread among pregnant women: in Europe it is about 4% [4], in the Russian Federation it ranges from 1.0% to 5.2% [2]. A screening examination conducted in St. Petersburg revealed the presence of symptoms of bronchial asthma in 11.8% of pregnant women [3]. In Blagoveshchensk, asthma among pregnant women occurs in 4.8 per 1000 people [3]. A special role of vitamin D in the prevention of asthma has been identified [4,5,6]. Interest in multi-organ effects and vitamin D deficiency has become particularly evident in the last decade; it manifested itself in scientific studies evaluating the role of vitamin D throughout a person's life [7]. However, contradictions in understanding the role of vitamin D still persist in scientific publications [6]. Thanks to the studies of many scientific groups [7], ideas about the role of vitamin D in the body have changed significantly over the past decades. The potential effect of vitamin D on the course of asthma is due to its ability to influence cellular and humoral immunity, thereby reducing the inflammation process [8]. This mechanism is due to gene expression and cytokine synthesis, vitamin D receptors and vitamin D metabolic enzymes found in many cells: T- and B- lymphocytes, macrophages, including pulmonary alveolocytes, and bronchial smooth muscle cells [9]. A high prevalence of vitamin D deficiency has been identified, including among pregnant women, children and adolescents [9]. In this regard, it is of interest to study the characteristics of the course of bronchial asthma during gestation, depending on the level of vitamin D, which was the purpose of this study.

Materials and methods

Of the 150 pregnant women with bronchial asthma participating in a prospective study, 62 were followed up from the moment of registration in the antenatal clinic until the moment of delivery. The comparison group consisted of 50 pregnant women without bronchopulmonary pathology and other chronic diseases. The content of vitamin D in the blood serum was analyzed using a high performance liquid chromatography analyzer Liason Dia Sorin Pleutschland GmbH Germany, sn-22290044. According to the latest data that the level of vitamin D should increase during pregnancy, the level of vitamin D ≥ 30 ng/ml was regarded by us as sufficient, within 29-20 ng/ml – insufficient, ≤ 20 ng / ml – its deficiency [7,10]. Statistica 10.0 application package and Excel 2013 spreadsheets was used.

Results

Over the past 4 years, a worsening of the course of asthma in pregnant women has been revealed in the Amur Region, which is associated with a change in climatic conditions (large-scale flooding in 2021). The average duration of the disease was 6.58 ± 0.8 years. In recent years, the percentage of patients with asthma duration less than 5 years has increased and the manifestation of the disease in the gestational period has increased by 3%. The debut of asthma during pregnancy was noted in 42 patients, while a mild course of the disease was observed in 22 cases (52.38%), moderate - in 17 (40.47%), severe - in 3 (7.14%), i.e., almost $\frac{1}{2}$ had a moderate and severe course of the disease. 20 (47.6%) pregnant women with newly diagnosed asthma noted the onset of symptoms of the disease in the first trimester, more often at a period of 5-6 weeks, 19 (45.2%) - in the II at a period of 18-20 weeks and 3 (7.1%) - in the III trimester. At the same time, 20 patients with mild asthma noted the appearance of the first attacks of suffocation after contact with the allergen. At the same time, 16 patients with moderate asthma and 2 pregnant women with severe asthma recorded the first symptoms at 6, 14, 20 and 29 weeks of gestation after an acute viral infection. The worsening of asthma may be associated with a large-scale flood that occurred in the Amur region in 2021, pollution of the river. Cupid and the spread of a new coronavirus infection COVID-19. In the Amur region, compared with other regions of the Russian Federation, mycogenic sensitization has acquired a significant place - in 25.3%, which is possibly associated with a large-scale flood in the Amur region.

The average level of vitamin D in 150 pregnant women with asthma was significantly lower - 18.79 ± 4.83 than in 50 pregnant women of the comparison group (without bronchopulmonary pathology) - 25.43 ± 3.65 ng/ml ($p=0.00001$). At the same time, the level of vitamin D in women with the onset of the disease during pregnancy was significantly lower and amounted to 15.38 ± 5.69 ng / ml than in women with asthma duration of more than 10 years - 22.58 ± 6.57 ng / ml ($p = 0.03$). Therefore, low vitamin D levels may be one of the risk factors for developing asthma.

The content of vitamin D in the body was significantly lower in the group of pregnant women with severe asthma than in other groups. At the same time, the minimum content of vitamin D in a pregnant woman with severe asthma was 5.25 ng / ml, which is a severe vitamin D deficiency and requires correction. The indicators of vitamin D were determined depending on the level of disease control in pregnant women. There is a statistically significant difference between the level of vitamin D in pregnant women with controlled asthma, which was 25.33 ng / ml and in pregnant

women with uncontrolled asthma, 19.76 ng /ml ($p=0.02$). At the same time, there were no significant differences between allergic and non-allergic asthma.

When evaluating the effectiveness of treatment, it was found that patients with moderate uncontrolled asthma, taking basic therapy during pregnancy, were able to achieve control and noted an improvement in the dynamics of the disease in the absence of exacerbations during the gestation period, accounting for 20.5% of all pregnant women who noted improvement and 25% from pregnant women with an uncontrolled form ($p<0.05$), while the level of vitamin D in these patients was significantly higher and amounted to 22.3 ± 3.65 ng / ml than in patients who did not achieve asthma control - 19.76 ng /ml ($p<0.05$).

Vitamin D deficiency is a marker of worsening asthma during pregnancy ($r = -0.54$, $p = 0.0002$), and also leads to more and more severe exacerbations ($r = -0.42$, $p = 0.0003$). Vitamin D deficiency affects the development of exacerbations, while the lower its concentration in the body, the higher the risk of exacerbations over several trimesters. Correlations between FEV₁ and vitamin D concentration were determined ($r = 0.38$; $p = 0.01$). The revealed links confirm the results of studies on the effect of vitamin D deficiency on the course of asthma and prove the presence of receptors for this vitamin in the bronchopulmonary system.

In this article, we have demonstrated the direct involvement of vitamin D in inflammation processes through its effect on the frequency and severity of exacerbations, the dynamics of the course of asthma in pregnant women. According to the study, it was found that lung function indicators correlated statistically significantly with the level of vitamin D in the blood serum. At the same time, there was a confident trend of a decrease in functional indicators against the background of degradation of vitamin D-status indicators. Thus, our results emphasize the role of plasma calcidiol in structural changes in smooth myocytes of the airways, which in turn contributes to impaired lung function, characterized by functional parameters, including FEV₁ and FVC [10]. Summing up the above, we can say with confidence about the importance of vitamin D in the life of both the mother and the fetus. Vitamin D deficiency can be considered a marker of both severe asthma and worsening dynamics in the gestational period, as well as an aggravated course of pregnancy and childbirth, leading to pathology of the fetus and newborn, which requires correction of its level when planning pregnancy.

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Macrophages in the experimental impact in vitro

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Abstract

They say that biological effects of low intensity Red laser radiation are realised on cellular level. The laser radiation along with positive influence can provide the prooxidant effect on cells and emoxipine as a strong effective antiradical inhibitor can reduce negative effect. We used low-intensity laser radiation and emoxipin as factors under the influence of which the nuclear apparatus of the cell, biosynthetic and basic enzymatic systems are activated. Everything which was said above is the basis for conducting the study. The cells under laser radiation reacted to it by several morphological changes such as the increase of morphological cell's rate, the changes of population structure, the remarkable growth of the very huge macrophages which have light vacuolized cytoplasm. The destruction of mitochondrions which are mostly sensitive to the influence of red laser radiation was noticed. Emoxipine added to medium for cultivation have stabilised membrane structure and have reduced the destructive changes in cytoplasm.

Keywords: macrophages, short timed culture of cells, red laser radiation, emoxipine.

The system of mononuclear phagocytes combines various types of cells involved in the protective reactions of the body and regulating between the immune, nervous and endocrine systems during the immune response. Having common features of morphology, metabolism and functions, cells are a heterogeneous population. A special group among them are alveolar macrophages - multifunctional cells, whose role as immunomodulators is combined with a pronounced secretory activity. With their cytotoxic potential and reactivity, alveolar macrophages play an important role in protecting the lower respiratory tract and the respiratory region of the lungs. The study of the morphology of macrophages, their functional activity and quantitative ratio is important for determining the level of local immunity and reactivity of the body. The basis of the interaction of macrophages, both among themselves and with other cell populations, is their heterogeneity, and due to the secretion of biologically active substances by them, macrophages are an important link in maintaining homeostasis in the body in normal conditions and during inflammatory and reparative processes. Macrophages can exhibit the activity of a wide range of genes, the expression of which changes under the influence of various stimuli. In this regard, it is of interest to study to evaluate the changes of alveolar macrophages under the influence of the red laser radiation in vitro and with the presence of emoxipine in the incubation medium.

Materials and methods

Experimental studies were conducted on short timed culture of lungs macrophages of outbred rats. Bronchoalveolar liquor for experimental studies was taken in standart conditions. Then it was placed and centrifuged in microcameras at 800 turns during 5 min for getting cells monolayer. This macrophages monolayer was influenced by red laser radiation waved 0,63 mcm and dosed 0,2 J/cm and it was also radiated by red laser dosed 0,2 J/cm and incubated in cultural medium with emoxipine. The specimen of short timed culture was colored by hematoxilin and eosin for color

microscopy and morphometrical study. Macrophages morphology was studied by transmission electronic microscope.

Results and discussions

The influence of red laser radiation can lead to the changes of morphology, numeral characteristics and population composition of alveolar macrophages. In this connection the number of huge cells increased 4,5times during the red laser radiation and the was the changes of several numeral characteristics. The macrophages area was increased 2,48 times. Besides the area we can notice the statistically important increase of the length, width and circumference of cells. The red laser radiation dosed 0,2 J/cm showed the strong influence on cytoplasm structure. There is the swelling of mitochondriones which is the sign of energetical depletion of cells and it correspond to the opinions of several authors that laser influence dosed 0,63 mcm increases the membrane capacity of mitochondriones and of the Proton gradient. Analysing the recieved data the high degree of the red laser radiation on macrophages causing destructive changes in cells was revealed. During the combined action of emoxipine and red laser radiation statistically important decrease of the numeral characteristics of macrophages such as the area and the circumference of the cells was revealed. Growths and invaginations of plasmolemas were revealed during the Electronic microscope study. The destructive changes of mitochondriones were not registered. The number of degenarative cells was decreased. Adding the emoxipine to the incubation medium during the red laser radiation of macrophages lead to the decrease of degenarative changes in cytoplasm of cells and this decrease the side effects of red laser radiation at this dosage.

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Emergency medical care: stages of formation and improvement of competence

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Abstract

The purpose of the research reflected in this article is a systematic analysis of the formation of competence to provide medical care in emergency and urgent forms for students on the basis of the Accreditation and Simulation Center of the Amur State Medical Academy based on the study of work programs of disciplines and practices implemented using simulation technologies and the results of an anonymous survey of students. As a result of the analysis, the main problems were identified and ways to eliminate them were proposed, both on the part of students and on the part of the teaching staff of the Academy.

Keywords: formation of competence, emergency medical care, improvement of competence, higher education, residency.

Analysis of the system of formation and improvement of the competence to provide assistance in emergency and urgent forms for students of the Amur State Medical Academy under the programs of higher education – specialty (specialty Medicine) and residency, programs of additional professional education – advanced training programs and professional retraining. Identification of existing difficulties on the part of the organization of the educational process and on the part of students. Determination of reference points for improving the quality of mastering this competence. The purpose of the research – is a systematic analysis of the formation of competence to provide medical care in emergency and urgent forms for students on the basis of the Accreditation and Simulation Center of the Amur State Medical Academy based on the study of work programs of disciplines and practices implemented using simulation technologies and the results of an anonymous survey of students.

Materials and methods

We conducted an analysis of the work programs of disciplines and practices under the higher education and additional professional education programs implemented by the Academy, as well as an analysis of the number of classes aimed at the formation of the above competence in the Accreditation and Simulation Center of the Amur State Medical University (Center) for 2017-2022. An analysis of the anonymous questionnaire of students after the end of the training simulation cycle was also carried out ^[4]. The main questions of the questionnaire were aimed at identifying the motivating components of effective learning, evaluating classes using simulation technologies, comments and suggestions.

Results and discussion

The main documents regulating the provision of emergency and emergency medical care by specialist doctors are Federal Law No. 323-FZ "On the basics of protecting the health of citizens of the Russian Federation" with amendments and additions (Article 11, paragraph 2 "Emergency medical care is provided by a medical organization and a medical worker to a citizen immediately

and free of charge. Refusal to provide it is not allowed"), professional standards and federal state educational standards of higher education [1,3].

Having analyzed the work programs of disciplines and practices in higher education programs – specialty programs, in the process of mastering the competence of providing medical care in emergency and emergency forms at the Academy, 3 main stages can be distinguished. The first stage (30 hours of practical classes at the Center) is the training of 2nd and 3rd year students in general medical, general medical skills (necessary for the formation of competence) in the framework of mastering the program "General Surgery", "Propaedeutics of internal diseases" and the program of industrial practice "Clinical practice – assistant ward nurse". The second stage is the formation of clinical skills for the diagnosis (including differential) of urgent and emergency conditions, the definition of therapeutic tactics, the formation of the skill of basic life support (BLS) for 4th year students (30 hours of practical classes at the Center) – mastering the work programs of the disciplines "Faculty surgery", "Faculty therapy", "Emergency conditions in therapy". The third stage is the formation and improvement of the competence to provide medical care in emergency and urgent forms, including teamwork skills, an expanded BLS complex for 6th-year students (70 hours of practical classes at the center) – as part of the development of the programs "Emergency conditions in the practice of a district therapist", "Current problems of cardiology" and "Anesthesiology, intensive care, intensive care".

All the programs of the residency program include the discipline "First aid in critical conditions", the purpose of which is to form competencies for cardiopulmonary resuscitation and emergency medical care. The complexity of this program is 36 hours, 24 of which are allocated to practical classes at the Center. The module "First aid in critical conditions", which provides 24 hours of practical training.

The Department of Anesthesiology, Intensive Care, Intensive Care and Emergency Medicine at the Center implements more than 20 advanced training programs for doctors of almost all specialties. When developing these programs, the staff of the department included in the curriculum classes on the algorithm for diagnosing critical conditions and conducting extended CPR in the amount of at least 6 hours. In addition, programs are being implemented that include 18 hours of a training simulation course, fully aimed at improving the competence of providing medical care in emergency and emergency forms for a wide range of specialties: "Emergency medical care", "Diagnostics and emergency therapy of acute coronary syndrome", "Diagnostics and emergency therapy of life-threatening rhythm disorders", etc.

The problems and difficulties identified by us during the analysis can be divided into 2 groups: organizational and pedagogical and personal (on the part of the student). The basic principles of andragogy, presented by M. Knowls back in 1967, speak about the need for motivation and the need to acquire knowledge from a student, as well as about the practical component – as a leading one in acquiring a skill [2]. During the implementation of simulation courses at the Academy, teachers try to simulate the situation consistent with the level of education and specialty of the student. This provision is confirmed by a positive assessment based on the results of an anonymous questionnaire. In addition, 75% of respondents consider the personality of the teacher to be the leading one when studying the material. In this way, for the successful development of competence, the personal motivation and interest of the teacher is no less important than the student.

For an effective simulation learning process, in our opinion, high-tech equipment is needed (in order to minimize "conditionalities"), functionally allowing the patient to simulate the entire spectrum of the clinical picture of the condition, as well as interaction with real medical equipment, which imposes on the teacher the need for technical knowledge and skills to script and control robot simulators during classes.

All of the above revealed the need for special training of teachers engaged in simulation training. Partially this problem can be solved by the seminar "Specialist of medical simulation training" of the Russian public organization ROSOMED. The staff of the Center, the teachers of the Academy who have been trained under this program, additionally received training under the advanced training program "Simulation teaching methods" (36 hours), implemented by the Center. 10 hours of practical training in this program is devoted to mastering the skill of debriefing as the main component of training, working with "difficult" students, team formation issues. This method of training teachers of simulation training (seminar "Specialist of medical simulation training" together with the development of the developed advanced training program) allowed to improve the quality of training at the Center. More than 90% of respondents have a positive attitude to simulation classes, consider them necessary and most significant in the process of mastering the competence of providing assistance in emergency and urgent forms.

Thus, the formation of competence to provide medical care in emergency and urgent forms is a complex multi-level process that requires gradual development and continuous improvement. The main difficulties associated with insufficient motivation of students at all stages of education, low involvement in the learning process can be solved by including training simulation courses in the educational process, additional training of teachers in the programs "Specialist of medical simulation training" and "Simulation teaching methods" implemented by the Accreditation and Simulation Center of the Amur State Medical Academy of the Ministry of Health of Russia.

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The role of oxidative stress and inflammation in the development of cataracts in chronic non-infectious diseases

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Abstract

Among 128 patients with cataracts, who underwent surgical treatment, cardiovascular diseases were most often associated with cataract. Oxidative stress may be a factor contributing to the development of cataracts in patients with COPD, cardiovascular diseases and diabetes mellitus as follows from the study of products of free radical oxidation of lipids in the blood plasma, lacrimal and intraocular fluids. The increased content of pro-inflammatory IL-8 and IL-18 in the blood plasma indicates a possible role of inflammation.

Keywords: cataracts, patients, oxidative stress, pro-inflammatory cytokines, cardiovascular diseases, COPD, diabetes mellitus.

The most important and cellular mechanisms involved in cataract formation are inflammation and oxidative stress [1]. Cataracts often occur in patients with diabetes mellitus (DM) and cardiovascular disease (CVD) [2]. The results of a number of studies indicate that cataract is a comorbid disease for COPD [3]. The aim of the study – to compare the role of these three groups of diseases as causative factors in the development of cataracts and to find out the intensity of oxidative stress and inflammation in these diseases.

Materials and methods

The study involved 128 patients with cataracts who underwent surgical treatment. Of this number, 80 patients developed cataracts due to concomitant CVD, 23 due to COPD, and 18 due to DM. 7 participants developed cataracts due to other diseases. The control group consisted of 64 people without clinical signs of acute and chronic diseases comparable in age and sex. In blood plasma, lacrimal and intraocular fluids, the content of oxidized forms of lipids was determined based on the registration of UV absorption spectra of lipid extracts, namely, diene conjugates (DC) by absorption at 233 nm, conjugated trienes and ketodienes by absorption at 278 nm. Relative indicators were calculated: the ratio of absorption of oxidized forms of lipids to unoxidized E_{233nm}/E_{204nm} and $278nm/E_{204nm}$ [4]. In blood plasma the content of lipid hydroperoxides (HL) was determined by the ability to oxidize Fe^{2+} ions [5] and malondialdehyde (MDA) by the reaction with thiobarbituric acid [5]. The content of interleukins and C-reactive protein was determined by ELISA using diagnostic kits from Vector Best.

Results and discussion

Tables 1-2 show the results of determining the content of lipid oxidation products and pro-inflammatory cytokines in blood plasma in the examined groups. In all groups of patients in relation to healthy people in the blood plasma, the content of DC, GL and MDA was increased. With the exception of the group of patients with CVD, in the remaining groups of patients, conjugated dienes and ketodienes were increased (Table 1).

Among the determined cytokines, only IL-18 was significantly increased in all groups of patients, and a significant increase in IL-8 was characteristic of patients with CVD and other diseases (Table 2).

The UV spectroscopy method is highly sensitive and allows the analysis of lipid extracts from lacrimal and intraocular fluids. It is impossible to obtain intraocular fluid from healthy people. The content of unoxidized lipids (204nm) in the intraocular fluid in patients with COPD and DM was higher, and in patients with CVD it was lower in relation to the lacrimal fluid of healthy people. The ratio of the content of oxidized forms of lipids to non-oxidized ones (233/204 and 278/204) was significantly higher in patients with COPD and CVD in relation to healthy people. In patients with COPD, the content of non-oxidized lipids, conjugated trienes and ketodienes had significant differences with the group of CVD patients (Table 3).

Table .1 Indices of blood plasma lipid oxidation in the examined groups

Groups	№	204nm	233nm	233/204	278nm	278/204	DC (nmol/ml)	HL (nmol/ml)	MDA (nmol/ml)
Healthy people (n=26)	1	0,586± 0,046	0,037± 0,029	0,057± 0,0076	0,013± 0,002	0,0212± 0,0025	7,12± 0,85	27,5± 1,73	4,79± 0,158
COPD (n=23)	2	0,761± 0,051 P _{2,1} = 0,014	0,067± 0,014 P _{2,1} = 0,021	0,090± 0,021 P _{2,1} = 0,160	0,020± 0,005 P _{2,1} = 0,013	0,029± 0,0043 P _{2,1} = 0,123	16,1± 2,95 P _{2,1} < 0,001	42,3± 2,67 P _{2,1} < 0,001	5,75± 0,22 P _{2,1} = 0,001
CVD (n=80)	3	0,694± 0,0290 P _{3,1} =0 ,892	0,041± 0,0038 P _{3,1} = 0,942	0,067± 0,0069 P _{3,1} = 0,66	0,0128 ±0,001 P _{3,1} = 0,26	0,0202± 0,0042 P _{3,1} = 0,49	11,3± 1,05 P _{3,1} < 0,004	38,3± 0,86 P _{3,1} < 0,001	5,40± 0,076 P _{3,1} = 0,001
DM (n=18)	4	0,733± 0,055 P _{4,1} = 0,048	0,041± 0,058 P _{4,1} = 0,965	0,051± 0,006 P _{4,1} = 0,553	0,0094 ±0,001 P _{4,1} = 0,111	0,013± 0,005 P _{4,1} = 0,011	11,2± 1,58 P _{4,1} < 0,001	38,5± 1,72 P _{4,1} = 0,001	5,66± 0,254 P _{4,1} = 0,007
Other diseases (n=7)	5	0,802± 0,121 P _{5,1} = 0,133	0,032± 0,011 P _{5,1} = 0,497	0,033± 0, P _{5,1} = 0,048	0,080± 0,0020 P _{5,1} = 0,088	0,011± 0,0026 P _{5,1} = 0,011	8,86± 2,94 P _{5,1} = 0,329	36,9±0 ,71 P _{5,1} < 0,001	5,88± 0,257 P _{5,1} = 0,005

Table 2. The content of interleukins and CRP in blood plasma in the examined groups

Groups	№	IL-6	IL-8	IL-10	IL-18	CRP
Healthy people (n=64)	1	2,36±0,33	4,30±0,67	4,23±0,67	157±16	3,12±0,32
COPD (n=17)	2	2,16±0,38 P _{2,1} >0,802	6,58±1,58 P _{2,1} =0,224	3,75±0,64 P _{2,1} =0,519	248±18 P _{2,1} <0,001	3,42±0,68 P _{2,1} >0,664

CVD (n=60)	3	3,15±0,49 P _{3,1} =0,178	12,6±1,68 P _{3,1} <0,001	6,48±0,43 P _{3,1} =0,219	333±26 P _{3,1} <0,001	3,19±0,36 P _{3,1} >0,836
DM (n=17)	4	1,84±0,37 P _{4,1} =0,297	7,58±2,07 P _{4,1} =0,164	4,76±0,87 P _{4,1} =0,775	275±29 P _{4,1} =0,002	3,71±0,75 P _{4,1} =0,466
Other diseases (n=6)	5	3,81±1,26 P _{5,1} =0,308	6,96±0,91 P _{5,1} =0,037	4,62±1,03 P _{5,1} =0,865	309±71 P _{5,1} =0,08	3,53±1,72 P _{5,1} =0,821

Table 3. Indices of lipid oxidation in lacrimal and intraocular fluids in the examined groups

Groups	№	204nm	233nm	233/204	278nm	278/204	DC (nmol/ml)
Lacrimal fluid							
Healthy people (n=30)	1	1,39± 0,113	0,087± 0,014	0,076± 0,010	0,0258± 0,0055	0,0213± 0,0039	2,24± 0,21
Intraocular fluid (patients with cataracts)							
COPD (n=12)	2	0,25± 0,049 P _{2,1} <0,001	0,104± 0,042 P _{2,1} =0,72	0,424± 0,128 P _{2,1} <0,002	0,0292± 0,0056 P _{2,1} =0,672	0,1261± 0,0240 P _{2,1} <0,001	4,11± 1,64 P _{2,1} =0,28
CVD (n=13)	3	1,01± 0,112 P _{3,1} =0,021 P _{3,2} <0,001	0,119± 0,051 P _{3,1} =0,23 P _{3,2} =0,32	0,186± 0,032 P _{3,1} =0,002 P _{3,2} =0,082	0,0036± 0,0152 P _{3,1} =0,51 P _{3,2} =0,04	0,0241± 0,0036 P _{3,1} =0,61 P _{3,2} =0,056	4,57± 1,04 P _{3,1} =0,05 P _{3,2} =0,83
DM (n=7)	4	0,36±0,143 P _{4,1} <0,001 P _{4,2} =0,006	0,132± 0,070 P _{4,1} =0,559 P _{4,2} =0,737	0,236± 0,084 P _{4,1} =0,155 P _{4,2} =0,215	0,0215± 0,0071 P _{4,1} =0,635 P _{4,2} =0,657	0,0786± 0,0202 P _{4,1} =0,124 P _{4,2} =0,153	5,11± 2,7 P _{4,1} =0,341 P _{4,2} =0,760

Thus, cataracts were most often associated with CVD. Oxidative stress may be a factor contributing to the development of cataracts in patients with COPD, CVD and DM. The increased content of pro-inflammatory IL-8 and IL-18 in groups of patients indicates a possible role of inflammation.

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Dynamics of the clinical course of bronchial asthma during the postpartum period

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Abstract

In the last few years, there has been an increasing interest in the problem of diagnosis and treatment of bronchial asthma (BA) in the gestational period worldwide. The aim of the work was to determine the clinical and functional features of the course of asthma during pregnancy and the postpartum period. Observation of 124 patients with asthma was carried out in the dynamics of pregnancy and the postpartum period. In the postpartum period, 35.5% of patients showed an improvement in their condition, 42.7% - without dynamics, 21.8% - worsening of the symptoms of the disease, mainly in patients with moderate and severe BA. The influence of some factors on the dynamics of BA during gestation and in the postpartum period was the following: the severity of the disease, the presence of extrapulmonary allergic diseases, multivalent sensitization, chronic diseases of the upper respiratory tract, ARVI and the degree of patients' compliance with medical recommendations.

Keywords: bronchial asthma, pregnancy, postpartum period, worsening of the course, management of asthma patients.

Bronchial asthma (BA) continues to be a major health problem worldwide. In recent years, there has been a growing interest in the problem of diagnosing and treating asthma in the gestational period worldwide. The period after childbirth is characterized by the occurrence of increased physical and emotional stress. Exacerbation of asthma in the postpartum period can also be associated with autonomic dysfunction - suppressed activity of the sympathetic nervous system and heightened activity of the parasympathetic nervous system. The more severe the course of the disease during pregnancy, the more often exacerbations occur in the postpartum period [1,3,6]. In accordance with the recommendations for the management of asthma patients, the main goal of therapy is to achieve and maintain control over the disease, achieve current control and reduce future risk [2,4,8]. Deterioration of the course of asthma after childbirth can be contributed by the cessation or reduction of the dose of anti-inflammatory drugs due to lactation, fears of the mother and / or doctor, as well as low adherence to therapy [5,6,7].

The aim of the work was to study the clinical and functional features of the course of bronchial asthma during pregnancy and the postpartum period from the standpoint of the level of disease control.

Materials and methods

There were 124 patients with bronchial asthma were observed in the dynamics of pregnancy and the postpartum period from 3 months to 3 years. 27 patients were under observation with repeated childbirths. The comparison group consisted of 70 healthy pregnant women, the mean age and pregnancy parity of whom corresponded to the main group. Clinical and anamnestic data, an asthma control test (ACT), and lung ventilation function research were used.

Results

The dynamics of the course of bronchial asthma in the gestational period in this case of these patients is following: 58 (46.8%) patients have worsening of the course, 50 (40.3%) patients have more often non-allergic and mixed forms of the disease, without significant dynamics - 50 (40.3%), improvement – 16 (12.9%), mainly in the course of a mild form of allergic asthma. The clinical and functional features of the course of BA in 27 patients with repeated pregnancies and childbirths were analyzed. At the same time, mild form of BA was in 14 of them, moderate in 12, severe in 2. Assessing the dynamics of the course of the disease during repeated pregnancies, it should be noted that it remained at the same level in 20 (74%) patients, the severity of symptoms during subsequent pregnancy - in 5 patients with moderate BA, the tendency to improvement - in 2 patients with mild form of BA.

In order to assess the level of BA control in the postpartum period, the Asthma Control Test (ACT) was used. In the first three days after childbirth, exacerbation of bronchial asthma appeared 9 (7.3%) patients, over the next 2-4 weeks - in 38 (30.6%), after 2-4 months - in 28 (22, 5%), after 6 months - in 17 (13.7%), indicating a lack of control of the disease. In the case of 14 (11.3%) patients, the symptoms of bronchial asthma resumed for one year after childbirth. At the same time, 44 (35.5%) patients showed an improvement in their condition after childbirth, 53 (42.7%) patients had no changes. Worsening of the course of BA after childbirth was detected in 27 (21.8%) patients with moderate and severe bronchial asthma. It should be noted that improvement after childbirth was mainly in patients with partially or completely controlled asthma during pregnancy. Only 7 (7.1%) patients with worsening of asthma symptoms during pregnancy indicated an improvement in postpartum condition against the background of adequate basic anti-inflammatory therapy started after childbirth. Worsening of the course of asthma after childbirth was more often observed in patients with exacerbation in the first half of pregnancy and ventilation disorders, which was facilitated by the discontinuation or reduction of the dose of control drugs due to lactation and low adherence to therapy. Worsening of the course of the disease was more often observed in non-allergic BA.

Thus, the deterioration of the course of asthma after childbirth necessitates dynamic monitoring for timely correction of therapy in order to achieve and maintain control.

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Evaluation of factors influencing the clinical course of bronchial asthma in pregnant women

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Abstract

The clinical and functional features of the course of asthma in 70 pregnant women with different duration of the disease (with a debut in childhood and adulthood) were analyzed. Clinical and anamnestic data, the severity and clinical forms of BA, the frequency of exacerbations, the level of BA control, indicators of lung ventilation function and concomitant diseases in pregnant women were studied.

Keywords: bronchial asthma, pregnancy, worsening of the course, respiratory function.

Recently, the problem of diagnosis, treatment and prevention of bronchial asthma (BA) has become increasingly relevant, especially in the gestational period. Previous studies have shown that the course of asthma worsens during pregnancy [2–4]. Lack of BA control is a risk factor for perinatal complications [5–7]. In patients with BA, placental insufficiency, circulatory and inflammatory changes in the placenta were more often observed, especially in the uncontrolled course of BA. The development of placental insufficiency adversely affects the development of the fetus and newborn, which can cause the formation of persistent malformations and pathological conditions [1,8,9].

Purpose and objectives of the study: to analyze the factors influencing the clinical course of asthma in pregnant women, using clinical and anamnestic data, the results of the study of respiratory function.

Materials and methods

180 (62.1%) of the examined pregnant women had mild persistent BA (MildBA), 86 (29.6%) had moderate BA (MBA), and 24 (8.3%) had severe BA (SBA). Most of the pregnant women were of mature childbearing age, including those in the comparison group (respectively, 26.38 ± 3.0 and 24.2 ± 2.5). Allergic BA was diagnosed in 181 (62.4%) patients, non-allergic BA in 30 (10.4%), and mixed BA in 79 (27.2%) patients.

Results

Hereditary burden for allergic diseases (AD) was in 118 (40.7%) patients, while for BA - in 103 (35.5%), of them on the mother's side - in 61 (59.2%). In 15 patients, BA was observed in three generations, of which 12 (80%) on the mother's side, and 3 (20%) on the father's side. The occurrence of the first attacks of asthma in childhood was noted by 97 (33.4%) patients, in the pre- and pubertal period (11-19 years) - 89 (30.7%), in the reproductive period (20-30 years) - 60 (20.7%) women, older than 30 years - 6 (2.1%) patients. In 38 (13.1%) patients, BA was first diagnosed during pregnancy. The age of the patients was 19-41 years, averaging 27.2 ± 2.5 years, that is, there was an older age than that of the general group (26.3 years). A burdened heredity for allergies was observed in 10 of them (26.3%). The structure of allergens was dominated by: household allergens - in 153 (52.8%), pollen - in 125 (43.1%), food - in 62 (21.4%), epidermal - in 56 (19.3%). Of the non-specific factors, the following prevailed: SARS - in 121 (41.7%), psycho-emotional stress - in 174 (60.0%), the influence of weather conditions - in 170 (58.6%), physical

activity - in 88 (30.3%). CVRI during pregnancy was observed in 245 patients with BA, of which 146 (81.1%) - with MildBA, 77 (89.5%) - with MBA and 22 (91.7%) patients with SBA, more often meeting in the II and III trimesters. Extrapulmonary AD was present in 125 (69.1%) patients with MildBA, in 68 (79.1%) patients with MBA, and in 21 (87.5%) patients with SBA. Allergic rhinitis (AR) was noted in 148 patients (51%), pollinosis - in 125 (43.1%), urticaria - in 57 (19.7%) and atopic dermatitis (AD) - in 27 (9.3%) . The presence of atopic BA and AR was noted in 148 (51%) patients, and in 59 (39.9%) of them AR preceded BA, in 89 (60.1%) it manifested simultaneously with BA. The nature of the course of BA is influenced by extragenital pathology, the frequency of which among the observed pregnant women was 3.1 per patient (in the comparison group - 0.3). In 26 patients from the group with BA manifestation in the gestational period, even before the onset of pregnancy, there were concomitant AZs: 10 (26.3%) had urticaria, 8 (21.0%) had AR, 5 (13.2%) had BP, 5 (13.2%) - hay fever, 2 (5.3%) - anaphylactic shock due to drugs. Exacerbation of BA during pregnancy was detected in 218 patients (75.2%). With MildBA - in 124 (68.8%) patients, with MBA - in 70 (81.4%), with SBA - in 24 (100%). The high frequency of exacerbations of BA may be due to the presence of: AR ($r=0.55$, $p<0.001$), CVRI ($r=0.65$, $p<0.001$), exacerbation of chronic diseases of the ENT-organs ($r=0.75$, $p<0.001$), low adherence to therapy, insufficiency of adaptive mechanisms ($r=-0.96$, $p<0.05$ in MildBA, $r=-1.0$, $p<0.01$ in SBA). Thus, worsening of the course of BA in the gestational period was observed in 48.6% of patients, more often with non-allergic and mixed BA, without significant dynamics - in 33.8%, improvement - in 17.6%, mainly with allergic MildBA. Predictors of worsening of the course of BA were: the severity of the disease, the presence of AR, chronic diseases of the upper respiratory tract, common respiratory viral infections, against the background of a tense or unsatisfactory state of the body's adaptive capabilities.

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Analysis of parameters of antioxidants status in patients in the long-term period of traumatic brain injury

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Abstract

On the basis of the Amur Regional Neuropsychiatric Dispensary and the Amur Medical Academy, a controlled open randomized study was conducted to study cognitive functions in 16 patients with a history of traumatic brain injury (men aged 32 to 54 years, the main group). The control group consisted of 20 practically healthy volunteers. In accordance with the purpose of the study, the parameters of the antioxidant status were determined. The results of the study showed that in patients with a history of traumatic brain injury, the content of lipoperoxidation products relative to healthy donors increased by an average of 14-25% in conditions of a decrease in the level of ceruloplasmin by 34% and catalase activity by 14%. It is concluded that in the long-term period of traumatic brain injury, it is necessary to carry out pharmacocorrection of the antioxidant status.

Keywords: traumatic brain injury, lipid peroxidation, antioxidant system, patients.

The fragmentary nature of the results of assessing the antioxidant status in the long-term period of traumatic brain injury suggests conducting additional studies of the prooxidant/antioxidant system in patients with a history of traumatic brain injury in order to substantiate the possibility of optimizing pharmacotherapy [2, 3, 5]. Considering that our previous studies have shown the formation of oxidative stress in trauma conditions, the determination of lipoperoxidation products and the main components of the antioxidant system in patients in the post-traumatic period is advisable from the position of further inclusion in the complex treatment of drugs of antioxidant action [4, 7, 8]. Objective – to study of indicators of antioxidant status in patients with mild and moderate traumatic brain injury.

Materials and methods

A prospective controlled open randomized trial was conducted with the participation of 16 patients aged 32 to 54 years with a history of mild and moderate traumatic brain injury. The comparison group consisted of 20 practically healthy volunteers. In patients with a history of traumatic brain injury and healthy volunteers, the intensity of lipid peroxidation processes was assessed by examining the content of lipid hydroperoxides, diene conjugates in blood plasma according, malondialdehyde by color reaction with thiobarbituric acid, and the main components of the antioxidant system – ceruloplasmin according to the method of V.G. Kolb, catalase according to the method of N.D. Korolyuk [1, 6]. Statistical processing of the results was carried out using the Student's criterion (t) using the Statistica v.6.0 program. The results were considered reliable at $p < 0.05$.

Results and discussion

In patients in the long-term period of mild and moderate traumatic brain injury, there is a shift in the equilibrium of the parameters of the antioxidant status to the pro-oxidant side: the concentration of lipid hydroperoxides increases by 19%, diene conjugates – by 14%, malonic dialdehyde - by 25% compared with similar parameters in healthy volunteers, which indicates an increase in the intensity

of the processes lipoperoxidation. An analysis of the activity of the main components of the antioxidant system indicates a significant decrease in the level of ceruloplasmin by 34% and catalase activity by 14% in the blood of patients with a history of traumatic brain injury relative to the comparison group.

Thus, in patients with mild and moderate traumatic brain injury, a stable excess of the concentration of lipoperoxidation products relative to healthy volunteers is recorded against the background of a decrease in the activity of the components of the antioxidant system, which determines the expediency of prescribing drugs with an antioxidant effect in order to optimize the pharmacotherapy of the consequences of traumatic brain injury.

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Antioxidant activity of Eleutherococcus Extract under magnetic induction

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Abstract

The effect of eleutherococcus extract on the intensity of lipoper oxidati on processes under the influence of a low-frequency alternating magnetic field has been studied. The animals were exposed to a low frequency alternating magnetic field for 3 hours daily for 21 days (control group). In the experimental group, eleutherococcus extract was administered orally daily at a dose of 1 ml/kg to animals before exposure to a low-frequency alternating magnetic field. Exposure of rats to a low-frequency alternating magnetic field was accompanied by an increase in the intensity of lipoper oxidation processes. The introduction of eleutherococcus extract under magnetic induction conditions led to a decrease in the concentration of lipid hydroper oxides by 11-18%, diene conjugates by 12-13%, malondialdehyde by 24-30%, against the background of an increase in ceruloplasmin content by 11-18% and catalase activity by 15-20% ($p < 0.05$). This confirms the presence of antioxidant activity in phytoadaptogen under magnetic induction conditions.

Key words: eleutherococcus extract, low frequency alternating magnetic field, lipid peroxidation, lipid hydroperoxides, diene conjugates, malondialdehyde, ceruloplasmin, catalase, experiment.

Adaptogens are commonly called drugs that create a state of nonspecifically increased resistance to various pathogenic factors and provide an increase in the adaptive capacity of the body [1, 2, 10]. The presence of antioxidant activity in the spectrum of pharmacological effects of adaptogens is noted by many researchers [3, 4, 6]. The uniqueness of the chemical composition of the adaptogen eleutherococcus, represented by a complex of biologically active substances similar in nature to endogenous bioregulatory compounds, determines a wide range of activity and polyvalence of therapeutic action with a gradual increase in effect, low toxicity and absence of adverse reactions with prolonged use [5, 7, 8, 9]. Objective – to study the effect of eleutherococcus extract on the intensity of lipoperoxidation processes under magnetic induction.

Materials and methods

The experiment was carried out on white mongrel male rats weighing 200-220 g for 21 days. The animals were divided into 3 groups, each with 30 rats: 1 – intact group, the animals were in standard vivarium conditions; 2 – control group, the animals were exposed to a low frequency alternating magnetic field for 3 hours daily for 21 days; 3 – experimental group, animals before exposure to a low frequency alternating magnetic field eleutherococcus extract was administered orally daily at a dose of 1 ml/kg. The slaughter of animals was carried out by decapitation on 7, 14, 21 days of the experiment. The intensity of lipid peroxidation processes was assessed by examining the content of lipid hydroperoxides, diene conjugates, malondialdehyde and the main components of the antioxidant system – ceruloplasmin and catalase in blood plasma. Statistical processing of the results was carried out using the Student's criterion (t) using the Statistica v.6.0 program. The results were considered reliable at $p < 0.05$.

Results and discussion

The effect of a low-frequency alternating magnetic field on rats was accompanied by an increase in the intensity of lipoperoxidation processes: in relation to the intact group, control rats had an increase in lipid hydroperoxides by 14-20%, diene conjugates by 14-17%, malondialdehyde by 45-46% against a background of a decrease in ceruloplasmin by 15-17%, catalase by 14-20% ($p < 0.05$). The introduction of eleutherococcus extract under magnetic induction conditions led to a decrease in the concentration of lipoperoxidation products in comparison with the indicators in the control group: the content of lipid hydroperoxides decreased by 11% (day 7 of the experiment), 18% (day 14) and 16% (day 21); diene conjugates – by 13%, 12% and 12% accordingly; malondialdehyde – by 25%, 24% and 30% ($p < 0.05$). The use of phytoadaptogen contributed to an increase in the activity of the antioxidant system in the blood of experimental animals compared with similar indicators in the control: the content of ceruloplasmin increased by 15%, 11% and 18%, respectively, catalase – by 20%, 15% and 17% ($p < 0.05$).

Thus, the introduction of eleutherococcus extract to laboratory animals under conditions of increased intensity of lipoperoxidation processes induced by the action of a low-frequency alternating magnetic field helps to reduce the degree of accumulation of lipoperoxidation products, increases the level of ceruloplasmin, catalase activity and confirms the presence of antioxidant activity in phytoadaptogen.

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Pride of Amur Healthcare - Alexander Porfirievich Eremich

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The history of the city of Blagoveshchensk is about people who have written bright pages in the history of our city. One of such people in the history of Amur healthcare is Alexander Porfirievich Eremich – one of the discoverers of modern intravenous anesthesia. This year marks 112 years of intravenous anesthesia and this year marks the 145th anniversary of the birth of its author - A.P. Eremich. It is known that the very idea of intravascular anesthesia belongs to N.I. Pirogov (however, the use of various means by many experimental surgeons did not give any acceptable results at that time). Nikolai Pavlovich Kravkov tried experimenting with mixed hedonal-chloroform anesthesia — the results of the experiments were encouraging, although they did not completely satisfy the professor. Then he proposed to conduct an experimental clinical study of pure hedonal for intravascular anesthesia. To do this by Professor N.P. Kravkov and Sergey Petrovich Fedorov entrusted their student — a young promising scientist and doctor A.P. Eremich. This research culminated in the creation of a whole technique radically different from previous attempts at intravenous anesthesia, as well as a brilliant defense of a doctoral dissertation in 1910. A dissertation that became an event for the world of surgery, which, in fact, opened a new important page in the history of anesthesia. Intravenous hedonal anesthesia was called "Russian anesthesia", and in all textbooks of medical schools its founders are N.P. Kravkov and St. Fedotov. That's right, but the first one suggested hedonal anesthesia, and Professor Fedorov was a surgeon who performed the first operation under hedonal anesthesia in his clinic. And who was the anesthetist who first performed this hedonal intravenous anesthesia in a clinical setting. Unfortunately, not only medical students, but also most anesthesiologists do not know this. The first publication in the modern central medical press answering this question and resurrecting long-forgotten realities appeared only recently ("Anesthesiology and Resuscitation" No. 3, 2001). It shows that this doctor was Alexander Porfirievich Eremich (1876-1920), a student and employee of the Joint Venture. Fedorova. His role was not limited to testing a new method of anesthesia. Subsequently, he performed 64 successful hedonal anesthesia. According to his grandson (V.P. Eremich), who now lives in Tomsk and works at the Siberian Medical University, Alexander Porfirievich was a high-class surgeon: "In the absence of Prof. SP. Fedorov and on his recommendation, he treated the royal family." (You can't assign such patients to just anyone). He held high medical positions on the fronts of the First World War, was the chief physician of the oncological Yeleninsky Hospital, founded by merchant A.G. Eliseev for the free treatment of poor women suffering from tumors.

There are glorious pages in the history of healthcare in the Amur region that make up the pride of our region. Uncovering them, restoring them and making them public is the duty and task of our generation. An important "detail" in the biography of A.P. Eremich, which struck a chord with the authors in this publication and prompted further searches, was this: "In Petrograd in the winter of 1917-18. A severe famine began. In search of work, A.P. Eremich left for the Far East. In Blagoveshchensk, he was offered the position of chief physician of the city hospital." Here he worked until 1920, when "... during the last operation he became ill. After completing it, he lost

consciousness and died a week later at the age of 44." We managed to establish contact with the Tomsk relatives of A.P. Eremich and get photocopies of their family archive. Many details of his biography have become clear, in particular, the Annunciation period, and, most importantly, the protocols of the first intravenous hedonal anesthesia turned out to be in our hands

On the initiative of the staff of the Department of Anesthesiology and Resuscitation of the Military Medical Academy, on December 13, 2014, a memorial plaque to Eremich Alexander Porfirievich was opened at the expense of the staff of the Department (Fig. 5).

If garages had not been built in our old cemeteries, it might have been possible to preserve the grave of A.P. Eremich and install a monument on it worthy of this man, whose name is undeservedly forgotten in the medical world. It is occasionally mentioned in some places in the domestic medical literature, but always casually and carelessly (initials are mixed up) and certainly does not become level with the names of the joint venture. Fedorov and N.P. Kravkova. There are no words, the merits of these outstanding scientists in the development of intravenous anesthesia are great and undeniable, SP. Fedorov, also taking full responsibility for possible complications of the operation, from the very beginning supervised the preparation, and then operated on patients with this method of anesthesia. But this does not detract from the merits of A.P. Eremich, who directly implemented this method and subsequently defined its clear contours. In fairness, the discoverers of intravenous hedonal anesthesia should be named all three of its creators - N.P. Kravkov, SP. Fedorov and A.P. Eremich. Their names should be on a par with the names of the world-famous pioneers of surgical anesthesia, because the intravenous anesthesia they started, having gone through its evolution, has now taken a central place in the world anesthesiological practice.

Hedonal anesthesia existed until 1926 both in Russia and abroad, however, modern, safer anesthetics appeared, but the principles of intravenous anesthesia established by A. P. Eremich have been preserved to this day in domestic and world anesthesiology.

We have the right to be proud that the glorious name of Alexander Porfirievich Yeremich is connected with the history of Amur healthcare, the history of the first city hospital.

Thanks to a group of public figures of the city of Blagoveshchensk, a section of the abandoned Voznesensky cemetery of the city was explored, where the grave of the famous doctor Alexander Eremich was clearly visible next to the pedestrian path.

I would like to believe that the initiators of the restoration of historical justice, E. Litus, R. Bashmakov, M. Bityak, A. Fedorov, D. Evseev, will be able to return from oblivion the names of the Annunciation who found their last shelter on Voznesenskoye, including the grave of Alexander Eremich, the chief physician of the city hospital, one of the pioneers of intravenous anesthesia, a doctor of medicine who treated the royal family. Alexander Porfirievich died on April 25 (12), 1920 at the age of 44 from pneumonia.

In the obituary published in Amurskaya Pravda, it is said that "up to the last moment he remained at his post – already ill, without noticing the creeping illness, performed the last operations. Alexander Porfirievich Eremich was one of the last Mohicans of the best period of the working intelligentsia of Russia."

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Relationship between adipose tissue biomarkers in chronic obstructive pulmonary disease and metabolic syndrome components

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Abstract

The aim of the study was to study the content of leptin, resistin, adiponectin in the blood serum and to determine their role in the formation of insulin resistance in the comorbid course of chronic obstructive pulmonary disease (COPD). 73 patients with isolated and comorbid course of COPD were examined. In patients with isolated COPD, the levels of leptin and resistin decreased, and adiponectin increased compared to the control. In COPD patients with abdominal obesity, a significant increase in leptin, resistin, insulin resistance index was revealed. In the group of patients with comorbid course of COPD, correlations were found between leptin, the volume of exhaled air at maximum forcing in the first second (FEV1) and the insulin resistance index. The results of the study indicate the involvement of adipokines in the progression of insulin resistance and respiratory failure.

Keywords: chronic obstructive pulmonary disease, COPD, leptin, resistin, adiponectin, abdominal obesity.

A significant predominance of obesity among patients with COPD was established in comparison with the general population of patients. Adipose tissue, primarily visceral fat, is not only an energy depot, but also an active endocrine organ that releases the following adipokines into the blood: leptin, adiponectin, resistin, tumor necrosis factor- α , interleukin-6, which aggravate insulin resistance^[1].

It has been established that despite the higher risk of developing the metabolic syndrome in patients with COPD compared with patients who do not suffer from this disease, only obesity is a component associated with the degree of bronchial obstruction^[2]. Among the numerous comorbidities of COPD, cardiovascular pathology, abdominal obesity and dyslipidemia are currently considered^[3]. An increase in the incidence of metabolic syndrome among COPD patients may be associated with a decrease in physical activity, smoking, and a decrease in insulin sensitivity. The study of biomarkers of adipose tissue in COPD associated with the components of the metabolic syndrome will improve methods for the prevention and treatment of complications of this pathology. In this regard, it is of interest to study the amount of leptin, adiponectin, resistin in comorbid and isolated course of COPD and to evaluate their relationship with insulin resistance, lipid spectrum, anthropometric data.

Materials and methods

The 1st subgroup included 32 COPD patients aged 35 to 72 years of groups A and B according to the risk classification of adverse outcomes according to GOLD 2017. The 2nd subgroup consisted of 41 COPD patients of groups A and B with abdominal obesity and other components of the metabolic syndrome. The control (3rd group) included 19 healthy volunteers with normal anthropometric data. In the 1st subgroup, the Quetelet index and the ratio of the waist circumference to the circumference of the hips were 24.71 (23.38; 26.62) kg/m² and 0.84 (0.74;

0.89), respectively, in the 2nd subgroup - 34.76 (29.37; 37.53) kg/m² and 0.94 (0.84; 1.04). The level of immunoreactive insulin (IRI) and endothelin-1 was determined by enzyme immunoassay. The concentration of leptin, resistin and adiponectin was studied in blood serum by enzyme immunoassay using standard ELISA, Mediagnost and ELISA Biovendor kits. The level of endothelin-1 was determined by enzyme immunoassay with high sensitivity using test systems from BIOMERICA (Australia). The study of the content of tumor necrosis factor-alpha (TNF- α) was carried out using the test systems of CJSC "Vector-Best" by the method of enzyme immunoassay. Using the calculation of the insulin resistance index (IRI) according to the criterion describing the degree of insulin resistance (The Homeostasis Model Assessment - HOMA), we studied the sensitivity of tissues to insulin. Bioimpedancemetry was performed using a body composition analyzer on the Medass apparatus. The principle of this non-invasive study is based on the total electrical resistance of body tissues using a bioimpedance analyzer. Taking into account the age, height, waist and hip circumference of the patient, body fat mass (BMF) normalized for height, skeletal muscle mass, basal metabolism, specific basal metabolism, and total body fluid were determined. The index of the bioimpedance phase angle was determined, which makes it possible to determine the biological age of the patient (correspondence of physical data to actual age). High numbers in the indicator indicate a good condition of cell membranes, the activity of skeletal muscles. Low phase angle values may be a quantitative method using Biochemmack reagents to determine C-reactive protein (CRP) and tumor necrosis factor-alpha (TNF- α). The study of the airflow of the lungs was studied using the spirograph "Erich Jaeger GmbH". In order to increase In order to confirm the reliability of indicators of respiratory function of the lungs, the following indicators were determined: FEV₁, actual vital capacity of the lungs (FVC), Tiffno index-FEV₁ / FVC ratio (%). Statistica 10 software package (StatSoft Inc.) was used for statistical processing.

Results

When examining the 2nd subgroup of patients, arterial hypertension (AH) of the 1st degree was detected in 7 patients (17.1%), AH of the 2nd degree - in 10 patients (24.4%), AH of the 3rd degree - in 9 patients (21.9%). A burdened hereditary history of diabetes mellitus was found in 11 patients (26.8%). Type 2 diabetes mellitus during additional examination was first detected in 8 patients (19.5%), impaired glucose tolerance - in 10 patients (14.6%), impaired fasting glycemia was diagnosed in 6 patients (14.6%). The atherogenic index was 5.81 (4.63; 6.17). The smoking index in COPD was 45.73 (41.25; 51.13) pack-years, in the combined course of COPD - 49.39 (42.54; 53.48). pack-years. In patients with comorbid course of COPD, a greater degree of severity of clinical symptoms of the underlying disease was observed compared to patients with COPD without abdominal obesity. According to the quantitative assessment of the severity of dyspnea on the mMRC scale, the average value of the severity of dyspnea in patients with COPD was 2 (1; 2) points, with a comorbid course of COPD, it tended to increase to 4 (3; 4) points. Statistical analysis revealed significant differences in a number of markers of the metabolic syndrome in patients with COPD comorbidity: FEV₁, FEV₁/FVC, glycated hemoglobin A1C, lipid spectrum, FMT, and total fluid.

In patients with comorbid course of COPD, there was a significant increase in leptin levels by 1.8 times and a decrease in the concentration of adiponectin by 2.3 times compared with the control. Serum concentration of interleukin-6 in subgroup 2 was increased compared to control values. At

the same time, negative correlations were found between the level of leptin and adiponectin ($r = -0.54$; $p = 0.01$). The closest correlations were obtained between serum leptin and body fat mass (BMF), body mass index ($r = 0.64$; $p=0.015$ and $r = 0.82$; $p=0.001$, respectively). We have established a significant correlation between leptin and the volume of exhaled air during the maximum forcing in the first second ($r = 0.96$; $p=0.001$). It is interesting to note that a direct highly significant relationship was found between the resistin index and the insulin resistance index and interleukin - 6 ($r = 0.62$; $p = 0.016$ and $r = 0.51$; $p = 0.012$).

Thus, changes in the content of leptin and adiponectin in the blood serum in comorbid COPD with a low risk of exacerbations and abdominal obesity with components of the metabolic syndrome are multidirectional in the form of an increase in leptin, resistin and a decrease in adiponectin. The established close correlations between markers of adipose tissue, cytokines, and indicators of respiratory function suggest a pathogenetic role of these markers in the progression of insulin resistance in the combined course of COPD.

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Experience of using Moroctokog Alfa for the preventive treatment with hemophilia A patients

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Abstract

The paper presents the experience of using a clotting factor VIII drug with a deleted B domain – moroctocogaalfa (Octofactor, GENERIUM, Russia) for the preventive treatment of patients with severe and moderate forms of hemophilia A living in the Amur Region and in the Khabarovsk Territory of the Far Eastern Federal District of Russia. Based on the observational study, it was concluded that moroctocogaalfa (Octofactor) is not inferior to FVIII plasma concentrates and octocogaalfa in terms of efficacy and safety, and can be effectively used for the prophylactic treatment of bleeding in hemophilia A.

Keywords: hemophilia A, prophylactic treatment, moroctocogaalfa, Octofactor

Hemophilia is a hereditary disease of the blood coagulation system resulting from a deficiency of blood coagulation factor VIII (hemophilia A) or IX (hemophilia B) [1,2,4]. The main manifestation of hemophilia is bleeding and hemorrhage that occurs spontaneously or as a result of trauma. The type of inheritance is recessive (men are sick, and the transmitters of the pathological gene are women). Hemorrhages in the joints that carry the main supporting and motor function in hemophilia lead to the development of deforming arthrosis and ankylosis of large joints and disability of patients [1,2,4]. Extensive intermuscular, intramuscular hemorrhages contribute to the anemia of patients, the development of "pseudotumors". Severe bleeding (gastrointestinal, renal, intracranial) can be fatal. [1,2,4]. The advent of modern coagulation factor VIII (FVIII) concentrates has changed the tactics of management and improved the quality of life of patients with hemophilia A, compared with the period before 2005, when in Russia such patients received cryoprecipitate and fresh frozen plasma (FFP) therapy [3,5,6].

The purpose of the observational study was a retrospective analysis of the effectiveness of the use of a clotting factor VIII drug with a deleted B domain – moroctocogaalfa (Octofactor, GENERIUM, Russia) for the preventive treatment of patients with severe and moderate forms of hemophilia A, living in the Amur Region and in the Khabarovsk Territory of the Far Eastern Federal districts of Russia.

Material and methods

Patients with hemophilia A, aged over 20 years, were divided into 2 groups. In group 1 - 21 patients received replacement therapy with Octofactor; age composition: 40-50 years old (n=10), 30-39 years old (n=6), 20-29 years old (n=5). All of them were diagnosed with hemophilic arthropathy: deforming arthrosis of the knee (n=21), ankle (n=12), elbow (n=16) joints. Group 2 included 21 patients treated with plasma FVIII and octocogaalfa, aged 40-50 years (n=8), 30-39 years (n=8), 20-29 years (n=5). All of them were diagnosed with hemophilic arthropathy: deforming arthrosis of the

knee (n=21), ankle (n=13), elbow (n=17) joints. In both groups, there were 13 patients with severe and 8 with moderate forms of hemophilia A. In both groups, FVIII concentrates at a dose of 20-40 IU/kg of body weight were administered every 2-3rd day (2-3 times a week).

Results

Prior to 2005, when patients in both groups received cryoprecipitate and freshly frozen plasma on-demand, all patients had frequent hemorrhagic complications from 52 to 6 episodes per year, bleeding and hemorrhage were of all severity, including life-threatening ones; patients with a severe form were hospitalized 8-10 times a year, and those with a moderate form - 4 times a year. During the study period, both against the background of the prophylactic use of the Octofactor and other FVIII drugs in group 2, no more than 2 episodes of bleeding (spontaneous and post-traumatic) were noted in 7 patients of the first and 6 patients of the second groups, mild and moderate. Spontaneous bleeding was diagnosed only in patients with low adherence to treatment, was stopped by the administration of the drug in therapeutic doses, mainly on an outpatient basis, and rarely required hospitalization. It was possible to achieve the desired indicators of clinical control – no more than 2 spontaneous hemarthrosis or other bleeding per year. In both groups, a 98% reduction in bleeding was achieved compared to the period prior to 2005, when these patients were treated with cryoprecipitate and freshly frozen plasma on-demand. There were no adverse reactions when using Octofactor in patients.

It has been concluded that the efficacy and safety of moroktokog alpha (Oktofactor) is not inferior to plasma concentrates FVIII and oktokog alpha, and can be effectively used for the preventive treatment of bleeding in hemophilia A.

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Preeclampsia as a complication of pregnancy in women with COVID-19

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Abstract

A systematic review published in 2021 showed that compared with the mild form of COVID-19, the severe form of COVID-19 was closely associated with preeclampsia (4.16 OR, 95% CI from 1.55 to 11.15) [3]. The aim of our study is to study the risks of developing preeclampsia and its complications in pregnant COVID-19 infected women in the Amur region. The analysis of the course of the disease and pregnancy outcomes was carried out according to the medical records of pregnant women, women in labor and maternity women who received medical care in the Clinical Hospitals (Blagoveshchensk), (N=966). The assessment of risk factors was carried out using four-field contingency tables, the risk impact of a particular factor was assessed by the magnitude of the relative risk (RR) and confidence interval (CI), if the CI did not include 1. The average age of pregnant women infected with COVID-19 was 29.6±1.08 years, the body mass index was 27.3±2.6 kg/m². The main complications of pregnancy in the first trimester were threatening miscarriage in 145 (15%), spontaneous and failed miscarriage in 56 (5.8%), in the second and third – premature birth in 113 (11.7%), polyhydramnios in 122 (12.6%), preeclampsia in 126 (13%) and edema with proteinuria at 193 (20%). Thus, the risk of developing preeclampsia, premature birth and fetal growth retardation significantly increased in women with pathological changes in the lungs (moderate and severe) by 1.4, 1.4 and 2 times, respectively.

Keywords: preeclampsia, complication of pregnancy, COVID-19, premature birth, fetal growth retardation

Considering the beginning of the sixth wave of SARS-CoV-2 worldwide, we have to state the fact of the long and constant presence of COVID-19 in our lives. In this regard, the analysis of pregnancy complications in women with COVID-19, the study of mutually conditioning mechanisms affecting pregnancy outcomes, is a promising direction. Pathogenetic mechanisms of pregnancy complications, such as complement activation, release of proinflammatory cytokines, prothrombotic phenomena or endothelial vascular dysregulation, are similar to those in severe forms of COVID-19 [1]. These mechanisms are also involved in the formation of placental disorders, with the subsequent development of preeclampsia, fetal growth retardation and premature birth [2]. A systematic review published in 2021 showed that compared with the mild form of COVID-19, the severe form of COVID-19 was closely associated with preeclampsia (4.16 OR, 95% CI from 1.55 to 11.15) [3]. The aim of our study is to study the risks of developing preeclampsia and its complications in pregnant COVID-19 infected women in the Amur region.

Materials and methods

The analysis of the course of the disease and pregnancy outcomes was carried out according to the medical records of pregnant women, women in labor and maternity women who received medical care in inpatient conditions (form No. 096/1u-20) of the City Clinical Hospital city

(Blagoveshchensk), maternity Hospital (Blagoveshchensk) and Covid Hospital (Blagoveshchensk), (N=966).

The assessment of the severity of COVID-19 was carried out according to the methodological recommendations "Organization of medical care for pregnant women, women in labor, maternity hospitals and newborns with a new coronavirus infection COVID-19". The presence of atypical pneumonia-CoV-2 RNA was established by polymerase chain reaction by sampling material from the nasopharynx and oropharynx in pregnant women.

Statistic 6.1 programs were used for statistical data analysis. For point estimation, continuous values were represented by standard deviations in the format $M \pm SD$, where M is the arithmetic mean, SD is the standard deviation. The assessment of risk factors was carried out using four-field contingency tables, the risk impact of a particular factor was assessed by the magnitude of the relative risk (RR) and confidence interval (CI), if the CI did not include 1, then a conclusion was made about the statistical significance of the revealed relationship between the factor and the outcome with a probability of error $P < 0.05$.

Results

During the two years of the pandemic, COVID-19 was registered in 966 pregnant women in the Amur Region, which accounted for 6.13% of all births during the study period.

In 2021, the number of infected pregnant women increased fivefold compared to 2020 and amounted to 803 against 163 pregnant women. The maternal mortality rate from COVID-19 in the Amur region increased 3 times and amounted to 12.8 and 40.9 per 100 thousand, respectively. COVID-19 was mild in 612 (63.4%) women, moderate in 171 (17.7%) and severe in 11 (1.14%). In 172 (17.8%) pregnant women, COVID-19 had an asymptomatic course.

The average age of pregnant women infected with COVID-19 was 29.6 ± 1.08 years, the body mass index was 27.3 ± 2.6 kg/m².

The main complications of pregnancy in the first trimester were threatening miscarriage in 145 (15%), spontaneous and failed miscarriage in 56 (5.8%), in the second and third – premature birth in 113 (11.7%), polyhydramnios in 122 (12.6%), preeclampsia in 126 (13%) and edema with proteinuria at 193 (20%).

The risk of pregnancy complications significantly increased in women with pathological changes in the lungs (moderate and severe course), compared with pregnant women with mild COVID-19. Pregnant women with moderate to severe COVID-19 had an increased risk of developing preeclampsia (HR – 1.4; 95% CI: 1.05–1.9), premature birth (HR – 1.4; 95% CI: 1.01–1.9) and fetal growth retardation (HR – 2; 95% CI: 1.6–2.4). At the same time, edema with proteinuria had no significant risks (HR – 1.2; 95% CI: 0.8–1.5). Also, in patients with moderate and severe COVID-19, the risk of anemia increased by 1.7 times (HR – 1.7; 95% CI: 1.3–2.23), which could be an additional factor in the development of pregnancy complications.

During the two years of the pandemic, 6.13% of pregnant women in the Amur region were infected with COVID-19. Thus, the risk of developing preeclampsia, premature birth and fetal growth retardation significantly increased in women with pathological changes in the lungs (moderate and severe) by 1.4, 1.4 and 2 times, respectively.

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Peculiarities of blood lipid composition in pregnant women with COVID-19 pneumonia of moderate and severe course.

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Abstract

The aim of the study was to identify the features of the blood lipid spectrum and the ratio of phospholipid fractions in erythrocytes in pregnant women in the third trimester of pregnancy with COVID-19 pneumonia. A case-control study enrolled 65 women in the third trimester of pregnancy, including 30 with moderate or severe COVID-19 pneumonia (treatment group) and 35 without infection (control group). Cholesterol, triglycerides, and high, low, and very low density lipoproteins were determined in blood serum by spectrophotometric method. Phospholipids were determined in erythrocyte membranes by thin-layer chromatography. The main group of pregnant women showed a more pronounced reduction in the blood values of total cholesterol, triglycerides, and high and low density lipoproteins in the subgroup with a severe course of COVID-19; a decrease in the percentage of phosphatidylethanolamine and phosphatidylcholine in erythrocytes; an increase in phosphatidylinositol, phosphatidylserine, and lithophosphatidylcholine in the blood. COVID-19 in pregnant women in the third trimester of pregnancy leads to changes in the blood lipid spectrum and phospholipid ratio of erythrocyte membranes due to metabolic disorders associated with increased lipid peroxidation, which supports inflammation and complicates the disease.

Keywords: COVID-19, pneumonia, pregnancy, lipid metabolism, phospholipids, erythrocytes.

The 2019 coronavirus pandemic (COVID-19) is a global public health problem [1]. COVID-19 and the causative agent, severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), first described in December 2019, are key issues in many countries around the world. At the beginning of the pandemic and based on previous experience with other respiratory viral infections, pregnant women and newborns were considered a high-risk group for SARS-CoV-2, prone to high morbidity and mortality [2]. There is increasing evidence of changes in the lipid spectrum in COVID-19-infected individuals. They serve a number of different functions: structural components, energy molecules and signaling mediators in the human body [3,4]. Pregnant women represent a special population group requiring increased attention. The development of pregnancy is associated with hormonal restructuring and physiological immunosuppression in women, which is the cause of high risk of COVID-19 infection and development of pneumonia, which ranks third in the structure of indirect causes of maternal and infant mortality [5]. Lipids in placental cell membranes play a crucial role in regulating the structure and activity of proteins, especially specific transporters [6]. Disruption of the content and regulation of placental lipid metabolism becomes one of the key pathogenetic pathways affecting adverse pregnancy outcomes. The aim of the study was to investigate the content of total cholesterol, triglycerides, low-density lipoproteins, high-density lipoproteins, and very low-density lipoproteins in peripheral blood serum as well as the

concentration of membrane phospholipids in erythrocytes: phosphatidylcholine, phosphatidylserine, phosphatidylinositol, lysophosphatidylcholine, sphingomyelin, and phosphatidylethanolamine in seropositive women diagnosed with moderate to severe COVID-19-associated pneumonia.

Materials and methods

The CASE CONTROL study enrolled 65 women in the third trimester of pregnancy (28-38 weeks), of whom 30 were COVID-19 seropositive women (the study core group) and 35 were COVID-19 seronegative women (the control group). The main group, in turn, was divided into 2 subgroups depending on the course, area of lung tissue lesion and saturation: moderate and severe COVID-19 pneumonia, respectively. The main inclusion criteria for pregnant women in the experimental group were the presence of signed informed consent to participate in the study, coronavirus infection confirmed by laboratory data at 28-38 weeks of pregnancy, and pneumonia confirmed by CT investigation methods. Exclusion criteria: exacerbation of other inflammatory diseases of extragenital pathology, presence of sexually transmitted infections, and bacterial pneumonia. Peripheral blood serum and erythrocyte membranes were used as study material. Clinical diagnosis of COVID-19 was established by the presence of SARS-CoV-2 coronavirus RNA detected by real-time polymerase chain reaction (PCR) in peripheral blood. SARS-CoV-2 RNA was determined by real-time PCR on a DT-96 machine using NPO-DNA-Technology kits (Russian Federation). Separation of phospholipids (PL) into classes was performed by two-dimensional Kirchner thin-layer chromatography [7], extraction of lipids was performed according to Folch [8], quantification of fractions was performed spectrophotometrically. Concentration of OH, TG, LDL, HDL was determined on spectrophotometer CLARIOstar Plus. To determine very low density lipoproteins we used Friedewald equation: $LDL-C \text{ (mmol/L)} = (\text{Triglycerides}) : 2.2$ [9]. Results were processed using nonparametric statistics using the SPSS 24.0 software package by calculating the median (Me), upper and lower quartiles [Q1 Q2], and Mann-Whitney U-test to assess the significance of differences between groups. Differences were considered significant at $P \leq 0.001$.

Results and discussion

At statistical analysis total cholesterol indices tended to decrease in both experimental groups. In COVID-19 group with pneumonia of moderate severity 1,7 times and 2,2 times in the group with a severe course respectively. Triglyceride values were 1.39 times lower in the group with a moderate degree of severity and 2.1 times lower in the group with a severe course. There was a 4.1fold decrease in HDL in the group with a moderate degree of severity and 2.2fold in the group with a severe course compared to controls. LDL concentration decreased 1.4fold in the moderate group and 1.9fold in the severe group, respectively. There was also a 1.9-2.1fold decrease in LDL-C in the moderate and severe groups. The indicators of phospholipids of erythrocyte cell membranes were also significantly altered. The concentration of phosphatidylethanolamine decreased 1.5fold in the moderate course group and 1.6fold in the severe course group. The concentration of phosphatidylcholine decreased 1.5fold in the moderate and severe groups. The sphingolipid sphingomyelin index was decreased in the moderate and severe course groups. In contrast, the concentration of phosphatidylinositol, phosphatidylserine, and liphosphatidylcholine was elevated. The phosphatidylinositol index increased 1.7fold in the moderate and severe groups, respectively. The concentration of phosphatidylserine was elevated 1.8 and 1.9 times in the moderate and severe

groups, respectively. And lysophosphatidylcholine concentration was elevated 2.2 and 2.3fold in the moderate and severe groups, respectively.

Thus, pregnant women with COVID-19 pneumonia exhibited disease severity-dependent changes in the blood lipid spectrum, characterized by decreased levels of CHL, TG, LDL and HDL, and cell membrane phospholipids (Re, Ps), except for Pi, Ps and Lpc, whose values were elevated. The decrease in OHL and TG may be due to a decrease in their synthesis caused by estrogen deficiency, while LDL and Lpc may be due to increased oxidation of substrates supported by proinflammatory cytokines, which increases their atherogenic effect on vascular endothelium, including Lpc entering the bloodstream from the surface of the erythrocyte membrane. The increase in Pi and Ps fractions in erythrocyte membranes is a marker of metabolic and structural disorganization of cells, which under the conditions of COVID-19 infection leads to hypoxemia and hypoxia, complicating the course of the disease and development of pregnancy complications.

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Prognostic parameters of the negative course of COVID-19 associated with chronic obstructive pulmonary disease

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Abstract

The presented article shows the results of the analysis of the contribution of some laboratory and instrumental parameters to the prediction of the negative course of COVID-19 associated with COPD. The research based on a retrospective analysis of 27 case histories of patients with COVID-19 in the acute period and stable COPD who received inpatient treatment in the infectious diseases hospital of Blagoveshchensk. The diagnosis of COVID-19 confirmed by laboratory polymerase chain reaction (100%). The diagnosis of COPD met the main criteria of the federal clinical guidelines. All patients divided into two groups comparable in age, duration of COPD and smoking history: group 1 (n=12) – patients with COPD and COVID-19 with uncomplicated course of infection; group 2 (n=15) – patients with COPD and COVID-19 with negative course of infection (need for resuscitation support and/or the development of thromboembolic complications). The analysis included the following initial laboratory and instrumental parameters: CRP (mg/l), fibrinogen (g/l), D-dimer (ng/ml), lactate (LAC, mmol/l) of venous blood, ferritin (mcg/l) and blood oxygen saturation (SaO₂, %), measured by pulse oximetry. During the research a mathematical regularity obtained, which was the basis for constructing a model for predicting the negative prognosis of COVID-19 in COPD patients by the logit regression method, taking into account the indicators of CRP, ferritin, LAC blood. An equation proposed, after solving which it is necessary to compare the obtained probability with a value of 0.5. If $P < 0.05$, then in 83.3% of cases uncomplicated course of COVID-19 in COPD patients is predicted. If $P \geq 0.5$ - in 93.3% of cases, a negative course of COVID-19 is predicted in patients with COPD. The proposed model makes it possible to estimate the probability of developing a negative course of COVID-19 in COPD patients using biochemical parameters of blood serum and can be used in determining a personalized approach to patient management both at the outpatient and inpatient stages of treatment.

Keywords: chronic obstructive disease, COVID-19, prediction, logit regression.

Chronic obstructive pulmonary disease (COPD) is a widespread disease among the diseases of respiratory system world over characterized by progressive respiratory failure with the obligatory presence of the episodes of exacerbation and the development of comorbid conditions [1]. According to the results of scientific studies, the incidence of a new coronavirus infection (Coronavirus Disease-2019 (COVID-19)) in COPD patients is low and does not exceed 1.1% [2]. The most common complications such as viral pneumonia with the development of respiratory failure [3], acute respiratory distress syndrome and thromboembolic complications occur in patients with comorbid conditions. The presence of COPD according to the meta-analysis of Chinese scientists significantly increase the risk of a complicated course of COVID-19 [4,5].

In literature, meet research works on prognostic markers of the unfavorable course of COVID-19 in the general population. These include clinical data, C-reactive protein (CRP), neutrophil-lymphocyte ratio, peripheral tissue saturation and body temperature [6]. In addition, scientists

have identified the indicators, which increase the risk of severe and complicated COVID-19 – serum iron, increase in dynamics D-dimer, interleukin-6 and lactate dehydrogenase [7]. However, did not found a model applicable in clinical practice for predicting the adverse course of COVID-19 in COPD patients with using the parameters available in the routine.

The aim of our study – to evaluate the contribution of some laboratory and instrumental parameters to the prediction of the negative course of COVID-19 associated with COPD.

Materials and methods

A retrospective analysis of 27 case histories of patients with COVID-19 in the acute period and stable COPD who received inpatient treatment in the infectious diseases hospital of Blagoveshchensk in 2021 carried out. The group consisted mainly of men (81.5%) aged 62.8 ± 1.39 years. The diagnosis of COVID-19 confirmed by laboratory polymerase chain reaction (100%). The diagnosis of COPD met the main criteria of the federal clinical guidelines [1]. The severity of COVID-19 in 59.3% assessed as severe. The severity of bronchial obstruction according to GOLD II-III (92.5%). The index of a smoking person was 31.7 ± 3.2 packs/years. In 19% of patients, smoking history has not established or not indicated in the medical history. The duration of COPD was 21.0 ± 3.5 years. All patients divided into two groups comparable in age, duration of COPD and smoking history: group 1 (n=12) – patients with COPD and COVID-19 with uncomplicated course of infection; group 2 (n=15) – patients with COPD and COVID-19 with negative course of infection (need for resuscitation support and/or the development of thromboembolic complications). The analysis included the following initial laboratory and instrumental parameters: CRP (mg/l), fibrinogen (g/l), D-dimer (ng/ml), lactate (LAC, mmol/l) of venous blood, ferritin (mcg/l) and blood oxygen saturation (SaO₂, %), measured by pulse oximetry.

The static analysis carried out using the Statistica 10.0 (StatSoft) software package. Descriptive statistics presented as median and interquartile range (Me [Q1-Q3]). The comparative analysis of independent groups was carried out using parametric (Student's criterion) and nonparametric statistics (Mann-Whitney criterion) in compliance with the law on the normality of the distribution of the trait. The possibility of predicting the course of COVID-19 in COPD patients evaluated by constructing a mathematical logit regression model with checking variables for the absence of reliable correlations by Spearman's method. Reliable statistical significance was assumed at $p < 0.05$.

Results and discussion

Established (Table. 1) that the initial level of CP, D-dimer, and ferritin in both groups significantly exceeded the reference values of the indicators. The intergroup analysis showed that in group 2 the content of CRP, ferritin, LAC in blood was significantly higher than in group 1 by 2.14 ($p=0.012$), 2.39 ($p=0.020$), 1.4 ($p=0.018$) times, respectively.

The obtained regularity was the basis for constructing a mathematical model for predicting the negative prognosis of COVID-19 in COPD patients by the logit regression method, which is a classic tool of nonlinear estimation for solving the binary classification problem. Taking into account the results of the comparative analysis, CRP, ferritin, LAC of blood identified as prognostic factors for constructing the equation with a check for the presence of correlation associations. The compiled equation looks like this:

$$P=1/(1+e^{-0,04*X1+2,99*X2+0,01*X3-10,4})$$

Where P is the probability of a negative course of COVID-19 in COPD patients, X1 is CRP in mg/l, X2 is LAC in mmol/L, X3 is ferritin in mcg/l; e is an irrational constant equal to 2.72.

The obtained probability should be compared with a value of 0.5. If $P < 0.05$, then in 83.3% of cases an uncomplicated COVID-19 course is predicted in COPD patients. If $P \geq 0.5$ - in 93.3% of cases, a negative course of COVID-19 is predicted in patients with COPD.

Table 1:

Comparative characteristics of initial laboratory and instrumental parameters in COVID-19 and COPD patients, depending on the course of infection

Indicators	group 1 (n=12)	group 2 (n=15)	p
CRP, mg / l	19,7[14,6-32,1]	42,2[26,0-82,9]	0,012
Fibrinogen, g / l	2,9[2,4-3,6]	3,3[2,4-3,8]	0,580
D-dimer, ng/ml	633,0[478,0-910,0]	844,0[571,5-1276,4]	0,432
Ferritin, mcg / l	209,5[84,3-300,5]	502[295,0-520,0]	0,020
LAC, mmol / l	1,5[1,2-1,8]	2,1[1,6-2,4]	0,018
SpO ₂ , %	94[92;95]	90[85;93]	0,060

Note: The data are presented as Me [Q1-Q3]; p is the coefficient of statistical differences between group 1 and group 2.

Thus, the proposed model makes it possible to assess the probability of developing a negative course of COVID-19 in COPD patients using biochemical parameters of blood serum and can be used in determining a personalized approach to patient management both at the outpatient and inpatient stages of treatment.

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Effect of Sea Buckthorn Oil and Dihydroquercetin on the Intensity of Oxidative Stress and Inflammation in Experimental Diversional Colitis in Rats

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Abstract: Experimental diversion colitis in rats is accompanied by the development of inflammation in the part of the large intestine disconnected from digestion, which is manifested by an increase in the content of IL-10 and IL-18. The introduction of phytochemicals with antioxidant action can reduce the inflammatory response. It is difficult to draw conclusions about the effect of sea buckthorn oil and dihydroquercetin on the state of lipid peroxidation processes in the wall of the large intestine that is disconnected from digestion due to the high content of oxidized forms of lipids in sea buckthorn oil.

Diversion colitis is a nonspecific inflammation of a segment of the large intestine that has been cut off from digestion ^[1]. The development of oxidative stress and inflammatory response in the colonic mucosa are considered as mechanisms underlying the development of diversionary colitis ^[2].

Aim of the study: To assess the intensity of oxidative stress and inflammation in rats with experimental diversion colitis in rats and to find out the possibility of correcting these disorders by introducing phytochemicals of antioxidant action into the section of the large intestine that is disconnected from digestion.

Materials and research methods: Rats were operated on in the volume of laparotomy, separate sigmoidostomy. Under vivarium conditions, a median laparotomy was performed under general inhalation anesthesia. During revision of the abdominal cavity, the descending colon is divided at the level of the middle third. The proximal and distal ends of the descending colon are brought to the anterior abdominal wall through separate incisions, fixed to the muscles and skin. A Nelaton 8CH catheter was placed in the disconnected section (figure). Animals were divided into control and two experimental groups (experimental 1 and 2). Experimental animals were injected twice a day with 1ml of sea buckthorn oil concentrate (BAA "Sea buckthorn oil", Radograd) (experimental group 1) and 1ml of a 0.5% emulsion of dihydroquercetin in sea buckthorn oil (experimental group 2) twice a day in the large intestine disconnected from digestion. After twelve weeks, the animals were withdrawn from the experiment. The content of oxidized forms of lipids was determined in a fragment of the colon and blood plasma disconnected from digestion based on the registration of UV absorption spectra of lipid extracts - diene conjugates (DC) by absorption at 233nm, conjugated trienes and ketodienes by absorption at 278 nm and vitamin E ^[3]. In blood plasma, in addition to the above indicators, the content of lipid hydroperoxides was determined by the ability to oxidize Fe²⁺ ions ^[4] and the content of IL-10, IL-18, and TNF-alpha by ELISA using diagnostic kits from Vector Best.

Results of the study and their discussion: Table 1 shows the results of determining the content of lipid peroxidation products and vitamin E in blood plasma in the examined groups. The



Picture. Catheter for the introduction of phytochemicals into the disconnected section of the large intestine.

content of conjugated trienes, ketodienes and lipid hydroperoxides was significantly increased in the blood of animals of the control group in relation to the intact ones. The values of DC and vitamin E in control animals were higher in comparison with intact ones, but the differences were not statistically significant. The animals of the two experimental groups practically did not differ between themselves and the animals of the control group in terms of the determined indicators.

Table 1. Indicators of blood plasma lipid oxidation in the examined groups.

Examined groups	233nm/ml	278 nm/ml	Lipid hydroperoxides (nmol/ml)	Vitamin E (mkg/ml)
Intact (n=5)	0.233±0.034	0.05±0.009	79.0±13,4	22.8±0.43
Control (n=5)	0.282±0.035	0.082±0.005*	134±29.8*	29.2±0.39
Experimental 1 (n=5)	0.249±0.023	0.089±0.009	129±38.3	25.8±0.90
Experimental 2 (n=5)	0.246±0.075	0.088±0.023	126±38.4	26.7±1.08

* - (p<0.05) significance of differences between the control and intact groups of animals.

In the study of the content of pro-inflammatory cytokines, a statistically significant increase in the content of IL-10 and IL-18 in the blood of animals of the control group in relation to the intact ones was established. In control animals, the content of TNF-alpha was almost two times higher than in controls, but due to the large scatter of values, the changes were not statistically significant. In the blood of animals of the first and second experimental groups, the content of IL-10 was reduced by 63% and 75%, respectively, in relation to the control group, and changes in the content of IL-18 and TNF-alpha were not significant (table 2).

Table 2. The content of interleukins and TNF-alpha in blood plasma in the examined groups (pcg/ml)

Examined groups	IL-10	IL-18	TNF-alfa
Intact (n=5)	15.4±3.63	1.51±0.33	2.56±0.88
Control (n=5)	28.1±3.75*	2.643±0.56*	4.93±1.46
Experimental 1 (n=5)	17.2±2.17**	2.644±1.46	4.606±1.54
Experimental 2 (n=5)	16.1±1.88**	3.56±2.07	3.033±1.66

* - (p<0.05) significance of differences between the control and intact groups of animals.

** - (p<0.05) significance of differences between the control and experimental groups of animals.

In the study of the content of oxidized forms of lipids in the wall of the large intestine disconnected from digestion, there were no significant differences in the content of DC, ketodienes and

conjugated trienes between the examined groups. In contrast, the content of vitamin E in the animals of the experimental groups was significantly 2 times higher than in the intact and control groups (table 3).

Table 3. Indicators of lipid oxidation in the intestinal wall in the examined groups

Examined groups	233nm/g	278nm/g	Vitamin E (mkg/g)
Intact (n=5)	6.30±0.73	1.385±0.199	173.42±41.177
Control (n=5)	7.26±0.80	1.82±0.170	189.2±38.823
Experimental 1 (n=5)	9.32±1.08	3.17±0.713	372.4±39.680*
Experimental 2 (n=5)	10.82±3.9	2.65±0.875	367.8±35.818*

** - (p<0.05) significance of differences between the control and experimental groups of animals.

When analyzing the dietary supplement “Sea buckthorn oil” used by us, it was found that the content of DC and conjugated trienes with ketodienes in it, expressed in units of optical density at 233 nm and 278 nm, amounted to 942 and 362 units, respectively. DC, lipid hydroperoxides 4.5 μmol/ml, vitamin E 2.59 mg/ml were orders of magnitude higher than the values of these indicators in the intestinal wall. Therefore, it is highly probable that, despite the washing with saline solution of the disconnected section of the intestine before removing the animals from the experiment, part of the sea buckthorn oil remained in the intestine and contributed to the measured values.

Conclusions: Experimental diversion colitis in rats is accompanied by the development of inflammation in the part of the large intestine disconnected from digestion, which is manifested by an increase in the content of IL-10 and IL-18. The introduction of antioxidant phytochemicals (sea buckthorn oil, dihydroquercetin) can reduce the inflammatory response and prevent an increase in the content of IL-10. It is difficult to draw conclusions about the effect of sea buckthorn oil and dihydroquercetin on the state of lipid peroxidation processes in the wall of the disconnected section of the large intestine due to the high content of oxidized forms of lipids in sea buckthorn oil.

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Research progress of Traditional Chinese and Western medicine in the treatment of cardiovascular neurosis

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Abstract: In the current environment, the incidence of cardiovascular neurosis is increasing and the onset age tends to be younger. The long-term onset of cardiovascular neurosis will cause cardiac and psychological pressure. Its pathogenesis is mainly related to social influence, personality psychology and changes of vascular endothelial function. The combination of traditional Chinese and western medicine treatment of this disease has achieved good curative effect, help to improve the characteristics of TCM syndrome, cardiovascular, psychological symptoms. In order to provide new thinking and new ideas for the clinical treatment of cardiovascular neurosis, this paper reviewed the research progress of integrated traditional Chinese and Western medicine in the treatment of this disease.

Key words: cardiovascular neurosis; Traditional Chinese and Western medicine; The research progress

Cardiovascular neurosis is with palpitation, bosom frowsty, chest pain wait and accompany nerve function abnormality to wait like anxious state to be main performance, good hair at female, middle-aged and young see more, tend to be younger gradually, combination of traditional Chinese and western medicine treats this disease with good advantage and prospect.

1. Understanding of pathogenesis in modern medicine

The pathogenesis of this disease is still unclear, many viewpoints believe that this disease is mostly related to social factors, psychological factors, vascular endothelial function changes, autonomic nervous dysfunction, coagulation dysfunction, central neurotransmitter dysfunction and other factors.

2. Understanding of etiology and pathogenesis in Chinese medicine

In Chinese medicine, cardiac neurosis can be classified as "heart palpitations", "chest paralysis heartache", "insomnia" and other diseases. Ancient books on the cause of its introduction, such as "Su Ask · Lift pain theory" cloud: "startled heart has no reliance, god has no return, worry has no fixed, so qi chaos." Cheng Wei^[1] believed that the TCM syndromes of this disease mainly included seven syndromes of qi deficiency, blood deficiency, Yin deficiency and qi stagnation, and concluded that qi deficiency was the most common syndrome, followed by blood deficiency and Yin deficiency.

3. Treatment

3.1 Modern medical treatment

At present, the diagnosis and treatment mode of "two-heart medical treatment" is widely adopted to improve patients' mood and relieve symptoms of cardiovascular system. Jiang Weichao et al. [2] pointed out that β -blockers can regulate myocardium by reducing sympathetic activity, thus improving autonomic nervous dysfunction.

3.2 Motherland medical treatment

3.2.1 Traditional Chinese medicine treatment

Proprietary Chinese medicine has the characteristics of controllable quality, safe and reliable, easy to carry, and few adverse reactions. Traditional Chinese medicine decoction has the advantage of compatibility between emperor and minister, and gives full play to the effect of traditional Chinese medicine through special decocting method. Many points of view think that Wenxin granule, Shensong Yangxin capsule and so on have a good effect on the disease, the selection of appropriate Chinese patent medicine can adjust free mood, improve psychological state, easier to improve cardiovascular symptoms. Yan Jianying et al. [3] found significant differences in cardiac autonomic nerve function and serum inflammatory factors in the study group compared with the control group, confirming that Guipi Decoction has great advantages in the treatment of this disease.

3.2.2 Special treatments of TCM

Acupuncture treatment, ear acupoint pressure seed and other traditional Chinese medicine characteristics for this disease also has a good effect. Li Yixia et al. [4] found that this method could improve the symptoms and mood of patients after 2 weeks of treatment by combining acupoints with meridional flow injection and low-frequency acupoint opening. Wang Xuan [5] was treated for 6 weeks with the method of Qiuxu Touzhaohai, Shenmen and Zusanli, and the improvement rate of TCM symptoms, the reduction rate of depression scale and the reduction rate of anxiety scale increased significantly.

3.3 Treatment of cardiovascular neurosis with Traditional Chinese and Western medicine

Combined traditional Chinese and western medicine has obvious advantages in treating this disease. Through research, Song Weiwei et al. [6] concluded that Qishenyiqi dripping pills have the effects of anticoagulation, anti-myocardial ischemia, coronary artery dilation, reducing peripheral vascular resistance and so on. They are used in collaboration with Western medicine and treated with specimens. Cheng Hao et al. [7] concluded that yangxindingpalan capsule combined with Daixin significantly improved the efficiency, effective rate and total effective rate in the treatment of this disease, and combined use was easier to improve cardiovascular symptoms.

Summary and outlook

Traditional Chinese medicine treatment has the advantage of syndrome differentiation and treatment. It can consider the symptoms of patients from a macro perspective. It can not only treat the primary symptoms, but also improve the secondary symptoms by adding and reducing the prescription. Western medicine treatment has the advantage of quick effect and obvious curative effect, but it has the risk of drug dependence and the disadvantage of "treating the symptoms rather than the root

cause". Therefore, the combination of traditional Chinese and Western medicine treatment has become the inevitable trend of the treatment of this disease, through traditional Chinese medicine decoction, traditional Chinese medicine treatment combined with modern medicine psychotherapy and western medicine treatment, not only can quickly improve the existing symptoms of patients, alleviate the pain of patients, but also fundamentally eliminate the cause. At present, many studies have been done on the treatment of cardiovascular neurosis with integrated Traditional Chinese and Western medicine, and great progress has been made. However, further research and practice are still needed to standardize the treatment of cardiovascular neurosis.

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Correlation Among Constitution in Chinese Medicine Questionnaire of the Aged in Harbin and Activity of Daily Living

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Abstract:

Objective: To investigate the Activity of Daily Living (ADL) of the senior citizen in Harbin, to analyze the correlations among the basic factor, constitution in Chinese Medicine questionnaire (CCMQ) of the aged and ADL. **Methods:** The basic information, ADL, TCM constitution of 662 elderly aged 65 and above were analyzed by collecting data of the aged in Harbin. The correlation factors were sifted out by single factor χ^2 analysis, and then analyzed by binary Logistic regression analysis. **Results:** With 662 valid questionnaires, the ADL impairment rate was 31.7 %, and the ADL score is 17.618 ± 0.306 points. TCM constitution distribution is dominated by Balanced Constitution, Qi-deficient Constitution, Yang-deficient Constitution. The binary Logistic regression analysis shows that education, family genetic diseases, bad habit history, Yang-deficient Constitution, Phlegm-dampness constitution, age and elderly ADL are correlated. **Conclusion:** The daily life ability of old people in Harbin area drops. Elderly people over 80 years of age, illiterate, Yang-deficient Constitution and Phlegm-dampness constitution are high-risk groups with daily life disabilities.

Keywords: Activity of Daily Living; elderly; Traditional Chinese Medicine constitution; Harbin

Background:

The population aged 65 and above accounted for 8.93% of the total population in China, and the proportion of population in the northeast region was higher than that in the whole country, and the aging development speed was faster than that in the whole country. The incidence of Activity of Daily Living (ADL) disorders in the elderly is gradually increasing, and the ability of self-care is impaired to varying degrees.

Relevant researches on diseases from the aspect of TCM constitution have been widely recognized. Based on the research of the elderly in Harbin (under the extremely cold environment) and the constitution of traditional Chinese medicine and their daily living ability, this paper provides guiding suggestions for the elderly in Harbin in their daily living ability from the aspects of traditional Chinese medicine nursing and so on.

Materials and methods

Materials

From May to October 2018, the sample size was determined according to 20 times the number of

items in the questionnaire. The basic minimum sample size was 640. The sample size was expanded to 700. 662 valid questionnaires were completed.

Methods:

A unified questionnaire was used for face-to-face survey. The questionnaire includes three parts. The basic population information includes name, age, sex, educational background, nationality, allergy history, family hereditary disease, and 9 items of history of bad habits and surgery. The Activities of Daily Living, ADL) Scale evaluates the healthy function of the elderly. Fourteen items are graded on a four-level scale, namely: they can do it completely (1 point), have some difficulties (2 points), need help (3 points) and cannot do it at all (4 points). If the total score is more than 15 points, they can be judged as dysfunctions of daily living. Chinese medicine constitution scale, referring to "classification and determination of Chinese medicine constitution", divides Chinese medicine constitution into nine kinds of constitutions: peaceful constitution, qi deficiency constitution, yin deficiency constitution, yang deficiency constitution, phlegm-dampness constitution, damp-heat constitution, blood stasis constitution, qi depression constitution and special constitution. The determination of each constitution is divided into three levels: none (0), tendency (1), and yes (2).

Results:

Sample general circumstance:

The number of males (56%) was slightly higher than that of females (44%) of the 662 subjects studied, the average age is 71.675±0.313 years old, of which 45.5% are 65-69 years old. 90.8% of the elderly have the acceptance of primary school education or above. The majority of nationalities are Han (96.2%), while the other minority nationalities are less than 5%, so they are not listed in the table. 21.6% of the elderly have a family history of hereditary diseases. 19.8% of the elderly had a history of alcohol, tobacco and other bad habits. See table 1.

Table 1. 662 general circumstances to research object and ADL function obstacle list factor 2 analysis

Factor	Gender	Age	Education	Allergy History	Familial-dietary	Bad Habits	Operating Theatre
	male/female	65-69/70-74/75-79/ 80-	Illiteracy/Primary School/Junior Middle School/High School /University	Yes/NO	Yes/NO	Yes/NO	Yes/NO
Total	371/291	301/150/105/106	61/141/202/191/67	97/565	143/519	131/531	176/486
Health Disorder	250/202	223/103/68/58	21/93/138/146/54	68/384	88/364	80/372	124/328
	121/89	78/47/37/48	40/48/64/45/13	29/181	155/55	159/51	158/52
χ^2	0.330	14.298	43.193	0.175	3.825	3.919	0.524
<i>p</i>	0.577	0.003**	<0.001***	0.676	0.050*	0.048*	0.469

Marking: **p*<0.05 ***p*<0.01 ****p*<0.001

Sample ADLs and TCM constitution endowment present conditions

The ADL barrier rate of the respondents was 31.7%. The ADL scale score was ($\bar{X} \pm s$)

17.618±0.306, the PSMS scale score was ($\bar{X}\pm s$) 7.243±0.118, and the IADL scale score was ($\bar{X}\pm s$) 10.375±0.198. In PADL, the damage rate except for eating and bathing was lower than the damage rate of IADL. The top three barriers to all projects: use of transportation (22.2%), laundry (18.3%), food cooking (17.4%). See Table 2

The distribution of TCM constitution in the elderly is more than that of the physical constitution. The elderly tend to be temperamental with the highest number of people (43.9%), followed by peace (41.7%) and yang deficiency (39.9%). See Table 3.

Table 2. ADL function damaged circumstance

ADL	PADL							IADL						
	Toilet	Meal	Dress	Wash	Walk	Shower	shop	Coo	House	Laun	Using	Medi	Using	Care
Disorder	55	107	70	58	78	91	98	115	100	121	147	99	92	81

Table 3. The Chinese medicine physical endowment distributes a circumstance

TMC	Balanced	Qi-deficient	Yang-deficie	Yin-deficien	Phlegm-dam	Damp-heat	Stagnant	Stagnant Qi	Inherited
Constitution	Constitution	Constitution	nt	t	pness	Constitutio	Blood	Constitution	Special
			Constitution	Constitution	Constitution	n	Constitution		Constitution
Tendency	95	97	73	59	61	43	85	52	19
Yes	181	193	125	130	88	45	109	62	15

Discussion:

The survey results show that the ADL impaired rate of the elderly in Harbin is 31.7%, higher than the research results in eastern (Guangzhou, Jiangsu, Zhejiang, Shanghai) and central (Hunan, Jiangxi) regions (14.7-25.6%). The serious decline in the ability of the elderly to use tools may be related to the economic situation of the elderly in Harbin, geographical environment, cold climate, lifestyle, unique disease spectrum and other factors.

In Harbin, the elderly should pay attention to warm keeping, reasonable diet and exercise, choose long dragon moxibustion, Baduanjin, warm acupuncture, and other traditional Chinese medicine therapies to improve the constitution of yang deficiency and phlegm dampness in the elderly so as to prevent and improve ADL dysfunction. Reasonable use of acupuncture, traditional Chinese medicine and other traditional Chinese medicine characteristic therapies to adjust the constitution that easily leads to the decline of the elderly's daily living ability. Improving the daily living ability of the elderly so that the elderly can better take care of themselves, is one of the important aspects of the prevention of disease by traditional Chinese medicine.

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Discussion on the influence of signal pathway on RA based on Th17 and Treg

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Abstract:

Rheumatoid arthritis (RA) is an autoimmune disease with aggressive and symmetrical polyarthritis as its main clinical manifestations. The pro-inflammatory effect of Th17, the anti-inflammatory effect of Treg and the close relationship between Th17/Treg cell balance and the occurrence and development of RA have attracted the attention of many medical researchers. Combined with the results of modern medical research, this paper reviews the research progress of Th17 and Treg cell differentiation, balance relationship and signal pathways related to Th17/Treg balance intervention, in order to provide new ideas for the mechanism research and clinical prevention and treatment of RA.

Keywords: RA; Th17/Treg; Signal pathway

RA is an autoimmune disease characterized by chronic synovitis, but its pathogenesis is still unclear. With the in-depth study of RA, it is found that there are important factors in the destruction of immune balance. The abnormal immune regulation of Treg and Th17 cells is the focus of its pathogenesis, and regulating the balance of Th17/Treg has become a new way to treat RA.

1.Th17/Treg

The concept of Th17 cells was proposed by Harrington [1] et al in 2005 according to the differences in the properties of cytokines secreted by CD4⁺ helper T cell subsets. It can induce the expression of pro-inflammatory factors, chemokines, chemotactic protein-1 and matrix metalloproteinases, mediate the excited process of neutrophil mobilization, and cause cell infiltration and tissue destruction. Treg cells, discovered by Gershon et al, play a key role in maintaining immune homeostasis in vivo. Treg cells can inhibit the immune system, reduce the production of inflammatory cytokines and antibody secretion and other negative regulation.

2.Th17/Treg and RA

A large number of literatures have reported that the frequency of Th17 cells in circulation, the serum levels of IL-17A and IL-23, and the content of synovial IL-17 in patients with RA are positively correlated with disease activity. Th17 can stimulate a variety of immune cells to produce pro-inflammatory cytokines, participate in the course of RA all the time, and is closely related to the chronicity of RA. Niu et al. [2] have shown that the increase of the ratio of Th17 cells and the decrease of the ratio of Treg cells in peripheral blood of RA patients lead to the dynamic imbalance of Th17/Treg cells, which may play a key role in the progression of RA. Therefore, the imbalance between Th17 and Treg cells may play an active role in the pathogenesis of RA, and regulating the balance of Th17/Treg cells becomes the key pathway for the treatment of RA.

3.JAK/STAT pathway and Th17/Treg

JAK/STAT pathway and rheumatic immune diseases, and the therapeutic target is effective. Its continuous activation is closely related to inflammatory injury of joint tissue and bone destruction. If the STAT3 signal pathway is blocked, Th17 cells cannot be transcribed and IL-17, a key RA

proinflammatory cytokine, can not be expressed, but can not play its inflammatory effect. The mechanism is that CD4⁺T cells induce the differentiation of Th17 cells and Th17 cells by activating STAT3 pathway in the presence of IL-6 and TGF- β , inhibit the differentiation of Treg cells characterized by the expression of Foxp3+mRNA, and enhance the expression of IL-21 and IL-23R,ROR γ t. It was found that baicalin could promote the shift of Th17/Treg immune balance to Treg in RA rats, inhibit the activation of JAK/STAT3 signal in joint synovium, reduce joint inflammation and improve the clinical symptoms of rats, indicating that the mechanism of baicalin in the treatment of RA may be to inhibit the activation of JAK/STAT3 signal and correct the shift of Th17/Treg immune balance to Th17 [3].

Through animal experiments, Liu Hui et al found that AmGP can improve the diet, mental state and activity of CIA mice, reduce the arthritis index, and reduce the degree of articular cartilage and bone destruction, mainly because AmGP can inhibit JAK-STAT3 signal pathway, reduce ROR γ t expression, inhibit Th17 cell production, and induce the activation of JAK-STAT5 signal pathway, up-regulate Foxp3 expression, increase the proportion of Treg cells, and restore the balance of Th17/Treg cells.

4. Mapk pathway and Th17/Treg

MEKK2 protein play an important role in the pathogenesis of CIA model. LLDT-8 may play a role in the treatment of RA by increasing the expression of MEKK2 protein and affecting the proportion of Th17/Treg. Zhang et al established CIA mice and detected the Th17/Treg ratio of spleen lymphocytes by flow cytometry. The gene and protein expression of Foxp3, RoR- γ t, IL-17A and MEK2 protein were detected by reverse transcriptase polymerase chain reaction (RT-PCR) and Western blotting. It is found that allicin may play a therapeutic role in rheumatoid arthritis (RA) by up-regulating the expression of MEKK2 protein in MAPK signal pathway and affecting the ratio of Th17/Treg.

5. Smad pathway and Th17/Treg

Xinfeng capsule can reduce joint inflammation by up-regulating Foxp3 and Treg, down-regulating the expression of TGF- β 1, regulating TGF- β 1/Smads signal pathway and improving joint symptoms. Glycyrrhizin may repair cartilage injury in OA rats by inhibiting TGF- β /Smad1 signal pathway, inhibiting cartilage degradation and apoptosis, correcting Th17/Treg cell imbalance and reducing immune inflammatory response.

6. PI3K/Akt pathway and Th17/Treg

PTEN gene are natural pathway inhibitors of PI3K/Akt axis, which can change the imbalance of Th17/Treg to improve the symptoms of RA.

Discussion:

Further deepen the understanding of traditional Chinese medicine, find a more accurate target and mechanism, and make new contributions to the clinical application and promotion of traditional Chinese medicine in the treatment of RA. Regulating Th17/Treg cell balance from different levels, such as cytokine level, transcriptional regulatory factor level and epigenetic level, can provide new ideas and methods for clinical treatment and make the treatment of diseases more individual and accurate.

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Mechanism of Aquaporin 4 in Alzheimer's Disease

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Abstract

Alzheimer's disease (AD) is a neurodegenerative disease characterized by progressive cognitive impairment, which seriously endangers human health. AD is caused by the imbalance of production and clearance of β -amyloid ($A\beta$). AQP4 is a member of the aquaporins family, which maintains water homeostasis in the brain and plays the role of transporters. In recent years, the mechanism of AQP4 in developing various neurological diseases has attracted much attention. This paper studies the role of AQP4 in the pathogenesis of Alzheimer's disease and provides new ideas and methods for the diagnosis and treatment of Alzheimer's disease.

Keywords: Alzheimer's disease; aquaporin 4; astrocytes; glutamic acid; neuroinflammation; brain-derived neurotrophic factor

Alzheimer's disease (AD) is a degenerative disease of the central nervous system that is highly correlated with age and is mainly characterized by progressive cognitive impairment and memory impairment. AD accounts for about 70 % of the total number of patients with Alzheimer's disease. The most characteristic pathological changes in AD patients are senile plaques (SP) formed by deposition of β -amyloid protein ($A\beta$), neurofibrillary tangles (NFTs) formed by aggregation of abnormally phosphorylated tau protein, loss of neuronal synapses, and neuronal apoptosis. Astrocytes play a protective role in the clearance and degradation of $A\beta$. The lack of AQP4 in cultured astrocytes will lead to the decrease of $A\beta$ -induced activation of astrocytes. AQP4 in astrocytes is considered to be a molecular target for the treatment of AD.

As an essential water transport protein in the central nervous system, AQP4 is highly expressed in the foot processes of astrocytes around the blood vessels to maintain brain water balance. AQP4 has the characteristics of no dependence on membrane potential and no saturation for the transport of water molecules so that it can increase the permeability of cell membrane to water by several times to tens of times[1]. AQP4 is a part of the lymphatic system, and the lack of AQP4 aggravates the accumulation of $A\beta$, the decrease of glutamate transport, the intensification of neuroinflammation, and the loss of brain-derived neurotrophic factors in the hippocampus and cortex. This paper summarizes the function of AQP4 and its possible mechanism in the pathogenesis and progress of Alzheimer's disease to provide a new direction for the diagnosis and treatment of Alzheimer's disease.

1. Relationship between AQP4 and AD

1.1 AQP4 and clearance of $A\beta$

It is well known that senile plaques formed by $A\beta$ deposition can induce reactive proliferation and activation of astrocytes and microglia, affecting disease progression. $A\beta$ may reduce the drainage of the lymphatic-like system by causing the change of AQP4 polarity distribution in astrocytes around the plaque, and the decrease in the clearance function of the lymphatic-like system may be one of the reasons for the extensive deposition of $A\beta$. In recent years, it has been found that there is a lymphatic-like system around the cerebral vessels, and its primary role is to remove interstitial

proteins such as A β and tau. Burfeind et al.[2] found in the autopsy of AD patients that the loss of AQP4 distributed around the blood vessels could predict the progression of AD and was related to the density of large A β plaques. Iliff et al. [3]observed that AQP4 expression decreased the clearance rate of A β in the brain of mice, leading to increased deposition, indicating that AQP4 plays a vital role in the drainage function of the lymphoid system. The above studies show that AQP4 participates in the A β clearance process and further participates in the progress of cognitive decline in AD patients.

1.2 AQP4 and glutamate transport

Under physiological conditions, glutamate-activated N-Methyl-D-aspartate (NMDA) receptors in the extracellular space lead to an increase in Ca²⁺ influx, which leads to changes in neural metabolism and gene expression necessary to maintain normal brain function. After the role of glutamate, glutamate is rapidly removed, thereby preserving the expected level of glutamate in the extracellular space. Studies have found that A β stimulation can inhibit the uptake of glutamate by astrocytes. When the extracellular space glutamate is excessive, it can cause the over-activation of NMDA receptors, leading to excitotoxicity and oxidative stress, leading to cell death, thereby causing neurofibrillary tangles and AD. In the AQP4 knockout mouse model[4], it was proved that AQP4 in astrocytes interacted with glutamate transporters (GLT-1). The synergistic effect of AQP4 and GLT-1 in astrocytes had a protective effect on glutamate-induced neuronal damage caused by A β , which played a crucial role in regulating the neuroprotective response of different cells in AD. Therefore, maintaining extracellular glutamate homeostasis is vital for AD.

1.3 AQP4 and neuroinflammation

The glial inflammatory response is one of the necessary pathological features of AD, which is closely related to the pathological process of AD. The deposition of A β in the brain induces the activation of glial cells. At the same time, the activated glial cells secrete neurotoxic media and inflammatory factors, which aggravate the apoptosis of nerve cells. In the inflammatory state of the brain, the reactive proliferation of astrocytes will damage the polar distribution of AQP4 around the blood vessels, which leads to the damage of the clearance function of the glial lymph system and the abnormal accumulation of metabolic wastes in the brain-the experimental results of Li et al. [5]. Showed that after endotoxin induction, the inflammatory response of the central nervous system in AQP4 knockout mice was lighter, the swelling degree of astrocytes in vitro was more delicate, and the release of proinflammatory cytokines such as TNF- α and IL-6 was minor, suggesting that these two pathological processes may be AQP4. In summary, inflammatory response plays an essential role in the pathogenesis of AD, and AQP4 is involved in the inflammatory reaction of the central nervous system.

1.4 AQP4 and brain-derived neurotrophic factor

Brain-derived neurotrophic factor (BDNF), the most critical neurotrophic factor in the brain, plays a vital role in regulating the development of the nervous system and synaptic plasticity. AQP4 plays a crucial role in synaptic plasticity and memory formation. The regulation of synapses in the central nervous system depends partly on the balance of BDNF precursor and mature body. Inhibition of AQP4 expression can lead to NMDA receptor disorder, damage long-term potentiation (LTP), and specifically depend on the BDNF-TrkB receptor, resulting in cognitive impairment. Studies have shown that AQP4 knockout aggravates cognitive impairment and the loss of BDNF in APP / PS1

mice. A transcription factor regulating BDNF expression, the accumulation of A β is related to the decrease of BDNF level [6]. Therefore AQP4 may be involved in the pathogenesis of AD by affecting the production of neurotrophic factors.

2. Conclusion

AQP4 is essential for the functioning of the lymphoid system and participates in multiple processes of onset and progression of Alzheimer's disease. AQP4 can affect the occurrence and development of AD by participating in pathophysiological processes such as A β clearance, glutamate homeostasis, neuroinflammation, and neurotrophic factors. However, the specific mechanism still needs further study to clarify the precise role in each link, deepen the understanding of the disease and promote the research and development of new therapies.

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Analysis of the laws of acupoints selection in the treatment of peptic ulcer based on data mining

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Abstract

Objective To guide the clinic, this paper analyzes the relevant research on acupuncture and moxibustion in the treatment of peptic ulcers based on the data mining method and discusses the law of acupoint selection. **Methods** The relevant literature on acupuncture and moxibustion treatment of peptic ulcers in recent 20 years was retrieved by computer in three databases: CNKI, VIP, and Wanfang Data. After literature screening through NoteExpress3.0, input the data into Microsoft Excel 2019 software to establish a database. The IBM SPSS Modeler 18.0 was used to analyze the association rules of high-frequency acupoints. Cluster analysis was performed on acupoints using IBM SPSS statistics 22.0. **Results** 166 works of literature were included, 284 acupuncture prescriptions were extracted, involving 77 acupoints, and all acupoints were used 1780 times. The high-frequency acupoints involved Zhongwan (259 times), Zusanli (257 times), Neiguan (159 times), Weishu (155 times), and Pishu (149 times). The meridians with the highest frequency are Ren Meridian (467 times), Stomach Meridian (442 times), and Bladder Meridian (412 times). The specific acupoints with the highest frequency are Mu acupoint, Jiaohui acupoint, and Beishu acupoint. Seven groups were obtained by cluster analysis. Combined with correlation analysis, high-frequency acupoints were "Zhongwan-Neiguan-Zusanli" and "Pishu-Weishu." **Conclusion** Acupuncture and moxibustion in the treatment of peptic ulcer mainly focuses on regulating the Qi mechanism of the spleen and stomach and mostly follows the principle of "meridians pass through, indications reach." The main meridians are the Ren meridian, Stomach meridian, and Spleen meridian. Take Mu acupoint as the primary specific acupoint selection and pay attention to the regulation of viscera function. The core prescriptions are Zhongwan, Neiguan, Zusanli, Pishu and Weishu.

Keywords: Acupuncture; peptic ulcer; data mining; law of acupoint selection

Peptic ulcer (PU) can occur in many parts of the gastrointestinal tract, most commonly in the stomach and duodenal bulb^[1]. PU has a slow onset and migratory course, with intermittent epigastric pain as the primary clinical manifestation, often accompanied by acid reflux and belching^[2-3]. The symptoms of PU can be classified as "stomachache" and "gastric discomfort" in Chinese medicine, and Chinese medicine is effective in treating this disease^[4], and acupuncture, as a characteristic therapy of Chinese medicine, is effective in treating PU. Some Meta-analysis results showed^[5] that acupuncture was more effective than conventional drugs in treating peptic ulcer patients, and there were no adverse effects. In this paper, we collated and analyzed the literature on the treatment of PU with acupuncture in the past 20 years through data mining technology and summarized its clinical selection pattern, aiming to provide a reference for the clinical diagnosis and treatment of PU in TCM.

Literature and methodology

The search strategy was computerized and was conducted in three Chinese databases: China Journal

Full Text Database (CNKI), Vipers Journal Full Text Database (VIP), and Wanfang Data Knowledge Service Platform (WF). The search fields were a free combination of subject terms and keywords, with the search terms "acupuncture," "head acupuncture," "electroacupuncture," "auricular acupuncture," "moxibustion," "duodenal ulcer," "gastric ulcer," "upper peptic ulcer" and "peptic ulcer."

Statistical methods

The frequency of each acupoint in the database, the characteristics of the acupoints attributed to the meridians, and specific acupoints were described and analyzed using Microsoft Excel 2019 software. The association rules for high-frequency acupoints were analyzed using IBM SPSS Modeler 18.0 software, with the Apriori algorithm and visual network mapping. Clustering analysis and mapping of acupoints were performed using IBM SPSS Statistics 22.0 software.

Result and discussion

The five acupoints most frequently used in acupuncture to treat PU are Zhongwan, Zusanli, Neiguan, Weishu, and Pishu. Zhongwan is a Ren Vessel member and is located on the umbilicus, which is close to the site of PU and has a proximal treatment effect, tonifying the Qi flow and relieving pain. Zusanli is a crucial clinical point for treating gastrointestinal disorders, tonifying the spleen and strengthening the stomach, nourishing the Qi of the latter, and regulating the functions of the digestive and nervous system. Neiguan is also commonly used to treat abdominal disorders, relieve digestive symptoms, and improve prognosis by eliminating patient anxiety. The spleen and stomach points are also part of the bladder meridian and are shared by the spleen and stomach dorsal points, respectively, which regulate the qi flow and tonify the spleen and stomach, while the five high-frequency acupuncture points can tonify the root of the disease, in line with the principle of "treating the symptoms when it is urgent, and treating the root when it is slow." The combined use of the acupuncture points has the effect of nourishing Qi and blood, suggesting that the pathogenesis of PU is predominantly deficiency, with weakness of the spleen and stomach being the most common.

The Ren meridian is the most frequently used and runs through the middle of the abdomen, regulating the functions of the abdominal organs. The Spleen, Stomach, and Pericardium meridians, which are also high-frequency meridians, also travel through the abdomen, and PU is located in the abdomen and is related to the abdominal organs such as the liver and spleen. In addition, the bladder meridian is also frequently used in acupuncture treatment for PU, and all the back points are located in this meridian, tonifying the internal organs. The analysis of specific points showed that the recruitment point was the most frequently used specific point type, with a frequency of 30.69%. These points can be combined to harmonise yin and yang and treat the internal organs.

The combinations of acupuncture points with high support for the PU rule in acupuncture treatment were derived from correlation analysis and included Zhongwan-Neiguan-Zusanli and Pishu-WeiShu. Zhongwan-Neiguan-Zusanli is one of the most frequently occurring combinations in the clinical treatment of gastric disorders with acupuncture^[6]. Some experimental results showed that electroacupuncture stimulation of the above three points significantly reduced gastric mucosal injury in rats. The cluster analysis results yielded a total of six acupuncture point taxa, suggesting a pattern of acupuncture point combinations under different evidence types of PU. The primary acupuncture points used were Zhongwan, Neiguan, Zusanli, and Gongsun. For weakness of the

spleen and stomach, the back acupuncture point was often used in combination with Qihai. For Yang deficiency, Tianshu, Guanyuan, and Shenque are often used; for liver and stomach disharmony, Qimen, Yanglingquan and Taichong are often used; for the stagnation of the stomach ligaments, GeShu and Sanyinjiao are used.

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Sino-Russian cooperation opens up a new situation of health care under the background of big health industry

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Abstract: With the gradual enhancement of people's awareness of health care, the great health industry has developed rapidly, and the world has entered the "era of health care". Under the background of this era, Sino-Russian health care cooperation presents a new situation. This article will explain the new changes from the main members, cooperation contents and cooperation methods of Sino-Russian health care industry cooperation, and put forward some suggestions for the future cooperation and innovation between China and Russia.

Key words: Big health industry; Health care era; Sino Russian cooperation

The big health industry is an industry and service field based on medical and health products, health care products, nutritional food, health management, health consulting, etc. As an emerging industry, the great health industry has great international market potential. With the vigorous development of the great health industry, the world has entered a new era after the "electrification era" and the "information network era", namely the "health care era"¹.

Under such a background, the international cooperation between China and Russia in the field of large-scale health industry continues to deepen. With the deepening of the aging process, the continuous enhancement of people's self-care awareness and the continuous progress of scientific and technological innovation², the Sino Russian health industry cooperation has entered a stage of rapid development, presenting a new situation.

First of all, there are new changes in the major cooperative members of China-Russian health industry.

In the initial Sino Russian health care cooperation, the participating members were mainly Chinese and Russian governments and scientific research universities. 2020 -2021 is the year of Sino-Russian scientific and technological innovation, with the rapid development of scientific and technological innovation cooperation between China and Russia³. At this time, a large number of biomedical innovation companies, medical and health care innovation companies and related science and technology parks have emerged, and they have entered the domestic markets of both sides for exchanges and docking. The change of the cooperative members between China and Russia shows that the cooperation in the development of large-scale health industry between China and Russia is more active and closer than ever before.

Secondly, the content of Sino Russian cooperation in health industry is diversified.

In the early stage of the development of the big health industry, the two countries mainly focused on the cooperation and exchange of traditional Chinese medicine, among which several representative Chinese medicine universities in China took the lead. Through academic exchanges, the enthusiasm of studying Chinese medicine in Russia was promoted, and the rapid development of the integration of traditional Chinese and western medicine in Russia was promoted. With the rapid development of big health industry and the deepening of Sino-Russian cooperation, the current Sino-Russian

cooperation is not only limited to traditional Chinese medicine, but also includes medical devices, rehabilitation and health care, plant medicine and other fields. This made the Russian people feel the magic of Chinese traditional medicine and health care, and opened up their health care ideas. At the same time, Russia's advanced medical physics technology has also promoted the integration of Chinese traditional medicine and modern science and technology. The diversification of cooperation content has prompted China and Russia to gradually form a complete scientific research theoretical system in various fields of the great health industry.

In addition, the mode of cooperation between China and Russia has changed.

Gradually move towards telemedicine, upstream and downstream industrial chain cooperation, talent training, big data medical management and cloud academic sharing. During the COVID-19 epidemic, the two sides also carried out strategic cooperation in international epidemic prevention and control and vaccine research and development, which contributed to the development of human health⁴.

The great health industry is the inevitable trend of the development of the times. The friendly and mutually beneficial cooperation mode between China and Russia has promoted the development of the great health industry, brought tangible health benefits to the people of the two countries, and opened up a new situation for the development of the great health industry in China and Russia. In the future development, China-Russia cooperation in big health industry should strengthen technical capacity building and big data management, improve the standardization of industrial development, and further promote the development of big health industry by technology and big data governance!

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Effects of calcium supplements from different calcium sources on growth characteristics of mice

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Abstract Objective: To study the absorption of calcium from different calcium sources. **Methods:** Four-week weaned mice were randomly divided into four groups, a blank control group, a calcium carbonate D3 tablets (II) group (CC group), a calcium gluconate D2 chewable tablets (II) group (CG group), and a vitamin D2 calcium lactate chewable tablets group (CL group). After continuous intragastric administration for 30 days, the weight gain and feed consumption of mice were measured. The length and weight of the femur of mice were determined. The serum concentration of 1, 25-dihydroxyvitamin D₃, calcium and the activity of alkaline phosphatase (AKP) were determined, and the calcium contents of the intestinal supernatant were also analyzed. **Results:** Compared with the control group, the weight gain and feed consumption of CC group, CG group and CL group were no significant difference. The length and weight of the femur were increased significantly ($P < 0.01$), the serum concentration of the 1, 25-dihydroxyvitamin D₃ of CC group, CG group and CL group were increased significantly ($P < 0.05$). There were also significant increase in blood calcium content ($P < 0.01$) for CL group. In CG group, the calcium content of small intestine increased significantly ($P < 0.01$). There were also significant increases in blood AKP activity ($P < 0.05$) for CC group and CG group. **Conclusions:** All three calcium supplements can promote the growth of mice. The CL group has a more obvious promoting effect on the growth of mice.

Keyword: Calcium supplements; calcium carbonate; Calcium gluconate; Vitamin D2 calcium lactate; Calcium absorption

Calcium is one of the most abundant mineral nutrients in the body [1-3]. It is also one of the important components of bone tissue and teeth in human body, acting as one of the key factors affecting bone strength. The lack of calcium will lead to a series of diseases, and e.g. osteoporosis is caused by a massive loss of calcium in bone [4]. Adequate calcium intake is essential to maintain the normal bone mineral content and bone mineral density of children and adolescents, reach the peak of high bone mass, and reduce fractures. If the intake of calcium for children are short for a long time, symptoms such as night crying, convulsion of limbs, constipation, anorexia, night sweats, irritability would appear, and slow growth, rickets, "O" legs and other symptoms are also considered to be associated with the lack of calcium [5,6].

The absorption rate of calcium is affected by many factors, such as the age. In this study, three commercially available calcium supplements with common sources, including calcium carbonate, calcium lactate, and calcium gluconate were used as the research objects, and four-week old weaned mice were continuously gavaged to evaluate the effect of calcium supplementation in mice, to clarify the effects of different calcium sources on the growth of mice.

1 Experimental materials and methods

DNM-9602 Microplate reader was purchased from Beijing Plano New Technology Co., Ltd. Calcium, and alkaline phosphatase (AKP) test kits (batch numbers: c004-2, and a059-2) were purchased from Nanjing Jiancheng Bioengineering Institute. Four-week old weaned ICR mice, weight 18-22g, were purchased from Shanghai xipur-bikai experimental animal Co., Ltd (license number: SCXK (Shanghai) 2018-0006).

After a week of adaptive feeding, animals were randomly divided into four groups with ten animals in each group, half male and half female. The food consumptions were recorded once a day, and the body weights were measured every three days. 30 days later, at the end of the experiment, the related analyses were conducted.

SPSS 22.0 software was used for statistical analysis, and one-way ANOVA was used to test the significance of differences. The data were expressed in the form of mean \pm SD.

2 Results

The results of weight gain, feed consumption, and the length and weight of the femur of mice are shown in Table 1.

Table1 Effects of body weight gain, feed consumption, femur length and weight of mice

Group	weight change (g)	feed consumption (g)	femur length (mm)	femur weight X100 (g)
Control group	5.00 \pm 3.66	40.18 \pm 6.07	14.68 \pm 0.84 ^a	9.42 \pm 2.61
CC group	5.51 \pm 2.07	38.73 \pm 5.96	15.98 \pm 0.63 ^b	11.39 \pm 0.66 ^a
CG group	5.34 \pm 2.96	39.06 \pm 6.93	15.67 \pm 0.83 ^b	11.74 \pm 0.86 ^b
CL group	5.46 \pm 1.70	38.91 \pm 5.80	15.71 \pm 0.73 ^b	11.84 \pm 0.86 ^b

Note: compared with the control group, ^a P<0.05, ^b P<0.01.

The results of the effects of calcium supplements from different calcium sources on the index in the serum of mice are listed in Table 2.

Table 2 Serum indicators and calcium content in small intestine of mice

Group	small intestine Calcium content (mmol/L)	1,25-dihydroxyvit amin D3(ng /ml)	Calcium content (mmol/L)	AKP/ (U/1L)
Control group	3.82 \pm 0.74	3.91 \pm 0.85	0.79 \pm 0.05	19.96 \pm 1.94
CC group	5.09 \pm 1.25	4.23 \pm 0.87 ^a	0.88 \pm 0.09	14.02 \pm 1.64 ^b
C G group	6.67 \pm 1.40 ^b	4.07 \pm 0.71 ^a	0.87 \pm 0.15	15.28 \pm 2.36 ^b
CL group	4.50 \pm 1.29	4.21 \pm 0.95 ^a	1.04 \pm 0.13 ^b	18.89 \pm 1.29

Note: compared with the control group, ^a P<0.05, ^b P<0.01.

3 Discussion

The three groups of calcium supplements can all increase the weight of mice, although there is no significant difference compared with the control group. The addition of three calcium supplements can promote the growth of mice.

1, 25-dihydroxyvitamin D3 is the main form of active vitamin D in the body. Clinical studies have shown that it can improve bone metabolism and bone mineral density. Phosphorus can form bones together with calcium and maintain its structural integrity. Phosphorus in plasma is mainly in ionic

state.

Serum calcium content is affected by both intestinal calcium absorption and bone calcium dissolution. In this experiment, the length and weight of the femur, the serum concentration of the 1, 25-dihydroxyvitamin D3 were increased significantly for CC group, CG group and CL group. There was significant increase of the calcium content of small intestine in CG group. There were also significant increases in serum calcium content for CL group.

In this experiment, all the three calcium supplements have certain curative effects. The calcium lactate group has a more obvious promoting effect on the growth of mice.

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Effects of Harvest Time and Drying Methods on The Quality of Schisandra Chinensis in Heilongjiang

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Abstract

The HPLC was used to detect the content of lignans in *Schisandra chinensis* to investigate the best harvest time and processing method of *Schisandra chinensis* in Qinghe Forestry Bureau of Tonghe County in Xiaoxing'anling area of Heilongjiang Province. The Conclusion of this study is that the best harvest time of *Schisandra chinensis* in Qinghe Forestry Bureau of Tonghe County in Xiaoxing'anling area of Heilongjiang Province is October 2, and the best drying method is freeze-drying method. These results can provide a reliable basis for improving the utilization of *Schisandra chinensis*, making rational use of plant resources, and providing a guarantee for improving the quality and comprehensive benefits of *Schisandra chinensis*. It is also of great significance in production and in ensuring the clinical efficacy of traditional Chinese medicine.

Key words: Heilongjiang province; *Schisandra chinensis*; Harvest time; Drying method; Lignans

Schisandra chinensis, a perennial deciduous woody vine, also known as *Zanthoxylum bungeanum*, *Prunus chinensis*, Xuanji, etc., is the dry and mature fruit of *Schisandra chinensis* [*Schisandra chinensis* (Turcz.) Baill.] of Magnoliaceae^[1-2]. *Schisandra chinensis* is a commonly used traditional Chinese medicine in clinic, which has the effects of astringent and astringent, tonifying qi and generating fluid, tonifying the kidney and calming the heart. It can be used in clinic to treat palpitations, insomnia, spontaneous sweating and night sweating, internal heat and thirst, Tianjin injury thirst, chronic cough and asthenia, frequent urination, nocturnal ejaculation, persistent diarrhea and other diseases. Its medicinal value and application are widely^[1-2].

Schisandra chinensis, as a traditional and genuine medicinal material in Northeast China, is mainly produced in Heilongjiang, Jilin, Liaoning and other provinces. At present, the planting area of *Schisandra chinensis* in China is about 30000 hm². Due to its geographical location and environmental advantages, Heilongjiang accounts for 50% of its planting area^[3]. The quality and efficacy of North *Schisandra chinensis* is better than that of South *Schisandra chinensis*. Its market demand is large, and the wild resources are decreasing day by day, resulting in large-scale artificial cultivation of *Schisandra chinensis* in Northeast China in recent years, and the phenomenon of green picking is serious, resulting in the quality of medicinal materials being affected^[4]. The harvest time of *Schisandra chinensis* is from the end of August to October every year^[5]. The ripening time of *Schisandra chinensis* in different regions is not exactly the same, which makes the best harvest time of *Schisandra chinensis* slightly different according to different regions, and the content of effective components of medicinal plants in different growth and development stages is also different. It can be seen that the proper harvest of traditional Chinese medicine can have an important impact on the quality of medicinal materials; At the same time, the tissue of fresh Chinese medicinal materials is still undergoing active metabolism and respiration after harvest. The

medicinal part of *Schisandra chinensis* is berries, which has high water content. If it is not dried in time after harvest, it is easy to mildew and rot, which is not conducive to storage, and its effective components will also change, which will also affect the quality of medicinal materials. In order to facilitate transportation and storage, it is dried into dry fruits that are easy to preserve^[6]. Compared with traditional sun drying and drying methods, freeze-drying technology has the advantages of reducing the decomposition of active ingredients, maintaining the activity of active ingredients to the greatest extent, good appearance, color and smell, so as to ensure the quality of medicinal materials. It can be seen from the above that the harvest time and processing method are important factors affecting the quality of medicinal materials, and the curative effect can be guaranteed only with quality. The best harvest time and processing method of *Schisandra chinensis* should be studied in combination with production practice.

Objective

To determine the best harvesting time and drying method of *Schisandra chinensis* in Qinghe Forestry Bureau of Tonghe County in Xiaoxing'anling area of Heilongjiang Province.

Materials and methods

The fruits of *Schisandra chinensis* from September to October were collected and processed by three different drying methods: freeze-drying, 50 °C drying and air drying; The contents of schisandrin a (SCA), schisandrin B (SCB), schisandrin A (Sch A) and schizandrin B (Sch B) in *Schisandra chinensis* were determined by HPLC; The different harvest times, drying methods and markers were analyzed to explore the effects of different harvest times and drying methods on the quality of *Schisandra chinensis*.

Results and Conclusion

The contents of SCA, SCB, Sch A, Sch B and mixed lignans in *Schisandra chinensis* samples treated by freeze-drying method are significantly higher than those in drying group and air drying group; The content of target components in *Schisandra chinensis* treated by sun drying was the lowest; There were significant differences in the content of target components among the three drying treatment groups ($p < 0.05$); According to the quality standard that the content of SCA in Chinese Pharmacopoeia should not be less than 0.40%, the three drying methods meet the requirements, and the content of SCA in the air drying group is the least. Taking SCA as a reference, the content of SCA in freeze-drying group increased by 4.48% and 13.95% respectively compared with drying group and air drying group. Therefore, the best drying method in this study is freeze-drying.

The content of mixed lignans in *Schisandra chinensis* samples collected by Qinghe Forestry Bureau in Qinghe town, Tonghe County, Xiaoxing'an Mountain area, Heilongjiang Province, was the highest on October 2, showing a gentle upward and downward trend with the passage of the harvest period. The content of SCA, SCB and Sch A was the highest on October 2; The content of Sch B was the highest on September 25. The statistical results showed that there were significant differences in the contents of four lignans at different harvest times ($p < 0.05$). Combined with the provisions of Chinese Pharmacopoeia on SCA, the best harvest time of *Schisandra chinensis* was determined to be around October 2.

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Observation and Analysis of Clinical Characteristics and Vaginal Microecological Characteristics of 422 Women with Aerobic Vaginitis

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Abstract:

The patients with aerobic vaginitis who attended at gynecological clinic from January to December in 2018 were collected and medical information about age, onset solar term, clinical characteristics and vaginal microecological characteristics were analyzed. Most of them were 18~48 years old (79.62%), and most were attacked in summer (44.79%) and autumn (54.74%). The patients often had abnormal amount, color, quality and taste of vaginal discharge, and were mostly accompanied by vulva or vaginal pruritus (62.56%), sexual intercourse pain (19.67%), or vaginal burning (24.88%). This vaginitis was easy to be mixed infection with vulvovaginal candidiasis (44.62%) or bacterial vaginosis (38.02%). Vaginal microecological of them were made up of vaginal flora density +++ (63.03%), vaginal flora diversity ++ (73.93%), and dominant bacteria including gram-positive bacilli G+b (88.63%) and gram-positive cocci G+c (11.37%). By observing and analyzing the clinical characteristics and vaginal microecological characteristics of the patients, we can improve understanding of the disease and provide a strong basis for clinical treatment and prevention.

Key words: Aerobic vaginitis; Vaginal microecology; Clinical characteristics;

Aerobic vaginitis (AV) is a kind of vaginitis proposed by Donders in 2002, which is characterized by the proliferation of aerobic bacteria and the reduction of lactobacillus [1]. It tends to occur in women of childbearing age, adolescence or old age and often be mixed infection with Bacterial vaginosis (BV), Vulvovaginal candidiasis (VVC) and Trichomonas vaginitis (TV) [2-4]. Clinical manifestations include increased, yellow or yellow green, thin purulent or foam, smelly but not fishy smell vaginal secretions, often accompanied by vulva or vaginal pruritus, sexual intercourse pain or vaginal burning, even vaginal mucosa or cervical congestion and edema, bleeding points, ulcers or other inflammatory changes [5]. AV is relatively common with a high relapse rate, which seriously affects women's reproductive health. Therefore, it is of great significance to improve the cure rate of AV and prevent recurrence. There is an interdependent and mutually restrictive vaginal microecological dynamic balance system in the female vagina. Once affected by internal or external factors, the vaginal microecological will be imbalance and lead to the occurrence of vaginitis. Consequently, observing the changes of female vaginal microecology is meaningful to diagnose vaginitis, improve the diagnosis rate and guide treatment.

Objective

To improve the understanding of AV by observing and analyzing the clinical characteristics and vaginal microecological characteristics of AV patients, as well as providing basis for clinical diagnosis and treatment.

Materials and methods

A total of 422 patients with aerobic vaginitis were collected from the gynecological clinics from

January to December in 2018, and their age, onset solar term and clinical characteristics were analyzed. Also took the vaginal secretions of patients for vaginal microecological characteristics analysis (including vaginal pH value and vaginal secretions microscopic detection [6,7]). AV diagnostic criteria: 1) symptoms: increased, yellow or yellow green, thin purulent or foam, smelly but not fishy smell vaginal secretions, or accompanied by vulvovaginal pruritus, burning sensation, or sexual intercourse pain. Signs: vaginal mucosa is red and swollen, with bleeding points or ulcers; 2) Donders wet film microscopy: AV score ≥ 3 [1,8,9].

Results and discussion

422 patients with AV: 336 cases (79.62%) aged 18-48 years, 60 cases (14.22%) aged 49-60 years, and 26 cases (6.16%) aged 61-84 years. Onset solar terms: 2 cases (0.47%) in spring including 2 cases at Grain Rain (6th solar term), 189 cases (44.79%) in summer among which 13 cases at the Beginning of Summer (7th solar term), 16 cases at Lesser Fullness (8th solar term), 6 cases at Grain in Ear (9th solar term), 38 cases at the Summer Solstice (10th solar term), 71 cases at Slight Heat (11th solar term) and 45 cases at Great Heat (12th solar term); 231 cases (54.74%) in autumn among which 87 cases at the Beginning of Autumn (13th solar term), 64 cases at the Limit of Heat (14th solar term), 47 cases at White Dew (15th solar term), 15 cases at the Autumnal Equinox (16th solar term), 11 cases at Cold Dew (17th solar term) and 7 cases at Frost's Descent (18th solar term). Clinical features: 176 cases (41.71%), 229 cases (54.27%), 325 cases (77.01%) and 164 cases (38.86%) had abnormal amount, color, quality and taste of vaginal discharge respectively. There were 264 cases (62.56%) of vulvar or vaginal itching, 83 cases (19.67%) of sexual intercourse pain and 105 cases (24.88%) of vaginal burning. There were 301 cases of simple AV (71.32%), 54 cases (12.80%) of AV combined with VVC, 46 cases (10.90%) of AV combined with BV, 16 cases (3.80%) of AV combined with TV, and 5 cases (1.18%) of AV combined with VVC and BV. Vaginal microecological characteristics: Vaginal flora density of +~+++ accounted for 21 cases (4.98%), 135 cases (31.99%) and 266 cases (63.03%) respectively. The diversity of vaginal flora was +~+++ in 23 cases (5.45%), 312 cases (73.93%) and 87 cases (20.62%) respectively. Vaginal dominant bacteria: gram-positive bacilli G+b in 374 cases (88.63%) and gram-positive cocci G+c in 48 cases (11.37%). Vaginal leukocyte count: $<10/HPF$ in 278 cases (5.45%) and $>10/HPF$ in 144 cases (73.93%). Vaginal pH: pH 3.8~4.5 in 237 cases (56.16%) and pH > 4.5 in 185 cases (43.84%).

The investigation of this study shows that the incidence of AV is high, mostly in women of childbearing age, and more frequently in summer and autumn. It can be manifested as abnormal changes in the amount, color, quality and taste of vaginal discharge, and pruritus, sexual intercourse pain or burning sensation in the vulva or vagina. AV is easily infected with BV or VVC. The density and diversity of vaginal flora was increased, and the vaginal flora was dominated by gram-positive bacilli or gram-positive cocci. Through the observation and analysis of the clinical characteristics and vaginal microecological characteristics of AV patients, we hope to improve the understanding of AV and provide strong evidence for clinical prevention and treatment.

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Role and mechanism of oxidative stress in type 2 diabetes mellitus

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Abstract:

Type 2 diabetes mellitus (T2DM) has long been categorized as a complex and multifactorial metabolic syndrome. Oxidative stress has been considered as a major hallmark for the pathogenesis and development of T2DM, the latest studies have shown the increasing trends for the involvement of oxidative stress in the pathogenesis and development of T2DM. This article discusses the role of oxidative stress in T2DM and focuses on the potential therapeutic methods of oxidative stress in T2DM.

Keywords: type 2 diabetes mellitus, oxidative stress, mechanism, targeted treatment

Oxidative stress has long been considered as one of the main damaging factor responsible to induce various causative factors that are responsible for the development of insulin resistance, impaired insulin secretion from the β -cells of pancreatic islets and pathogenesis of T2DM. Though, how oxidative stress is produced is still debatable, it has been proposed that various mechanisms are involved in the generation of oxidative stress.

1. Oxidative stress and inflammatory responses

It has been evidenced that chronic exposure of elevated levels of glucose, TGs and FFAs increase the oxidative stress through the activation of NADPH oxidase. Once oxidative stress is produced, it potentiates the generation of various pro-inflammatory mediators notably, IL- β , IL-6, TNF- α , and IL-1 β -dependent numerous other cytokines and chemokines.

2. Oxidative stress and insulin resistance

Insulin resistance of T2DM is strongly associated with development of systemic oxidative stress as measured by the increased concentrations of urinary11-dehydro-thromboxane B2 (TXM) and 8-epi-prostaglandin F2a (8-epi-PGF2a).

3. Oxidative stress and β -cells dysfunction

β -cells of pancreatic islets are more vulnerable and susceptible to the generation of oxidative stress and the levels of anti-oxidant enzyme capacity in β -cells is found to be very low as compared with other metabolic tissues. And hyperglycemia can increase cellular stress in β -cells (as measured by the increased level of heme oxygenase-1 protein), but the activities of anti-oxidant enzyme capacity was not increased which supports the notion that pancreatic islets are the most vulnerable tissues to the generation of oxidative stress. Oxidative stress in pancreatic islets is induced by number of stimuli notably hyperglycemia, hyperlipidemia and inflammation. Once oxidative stress is produced, it potentiates various molecular and transcriptional pathways that are responsible to induce inflammation in pancreatic islets that ultimately leads suppress the normal functioning of IRS-1 that is responsible for the production of insulin from β -cells of pancreatic islets.

4. Oxidative stress and medicinal plants

It has been reported by several scientific studies that medicinal plants contain variety of phytochemical constituents that have diverse anti-oxidant properties against variety of diseases. These medicinal plants have been used since ancient times for the treatment of oxidative

stress-induced diseases. As far as the use of medicinal plants for the treatment of oxidative stress-induced T2DM is concerned, nigella sativa, coffee, ginger and onion are full of naturally occurring anti-oxidants against oxidative stress-induced T2DM. Recent studies have also reported that among various types of pharmaceutical constituents present in medicinal plants, flavonoids and polyphenols are the most important one that have been reported for their anti-oxidant properties against oxidative stress-induced diseases.

Conclusion

From the findings mentioned in the aforementioned sections, we bring to an end that oxidative stress play their decisive role in the development of T2DM whereas the use of anti-oxidant treatment approach is one of the best choice to ameliorate the deleterious effects of oxidative stress. At the same time, it is necessary to pay attention to the use of plant-based anti-oxidants for their mechanism of action for the prevention and treatment of T2DM.

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Construction of health industry innovation and development based on the idea of "Knowing how to receive because of happening, Heilongjiang cold region regimen"

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Abstract

Through the collection and collation of literature, to provide theoretical and practical experience support for the prevention and treatment of diseases and longevity for the residents of cold areas, and to provide a solid theoretical basis for the study of the path to building a healthy Heilongjiang. Standardize the existing industry standards for health care thus further promoting the healthy development of health in our province. Heilongjiang is located in the cold temperate zone, with an aging population and gradually lagging economic development. Heilongjiang region can apply the theoretical doctrine of Chinese medicine to explain the natural environment, social environment and life activities combined with the internal laws, for the human body's birth, old age, disease and death, disease prevention and treatment, life extension and put forward the corresponding health theory and methods, to guide the health of people with time, climate change and appropriate adjustment of diet, living, exercise and other life activities.

Key words: Knowing how to receive because of happening; health; regimen

The Qing dynasty doctor Huang Qian first mentioned "Knowing how to receive because of happening". "Knowing how to receive because of happening" is the manifestation of symptoms that the body should reflect when the disease occurs. The manifested phenomenon is not a judgment based on climate change, but on the state of the patient's body. After all kinds of external evil acts on the human body, whether or not the disease develops depends on the result of the struggle between evil and positive. The concept of "knowing how to receive because of happening" is to infer the type of attack on the body based on its manifestations and to diagnose and treat it. Modern cold land health science is guided by the principles of Chinese medicine health cultivation, refining the content of regimen, combining with the natural environment and lifestyle habits of the modern cold region, improving it, and proposing a more suitable for modern cold region residents of health cultivation methods. According to the law of changes in human life activities, ultimately, people can achieve the results of less disease, later disease, no disease, and no recurrence. Changes in the spectrum of modern diseases and changes in the living environment have led to changes in regimens from ancient times to the present, resulting in new research content.

Objective

Through the collection and collation of relevant literature, we provide theoretical and practical experience support for preventing and treating diseases and prolonging life for the residents of cold regions.

By studying the theory of cold region health cultivation, highlighting the characteristics of the cold region, forming a cold region health cultivation method for the water, soil and customs of Heilongjiang Province and the physical constitution of residents, filling the gaps of regional health

cultivation, making the cold land a livable and nurturing health cultivation area, helping to retain and attract talents, and promoting regional development.

Standardize the existing industry standards of health cultivation, improve the quality of life, improve the state of existence, extend the length of life, and enrich the system of cold region health cultivation and Chinese medicine theory and method, thus further promoting the healthy development of health in Heilongjiang Province.

Materials and methods

Through literature research, we summarized and analyzed the research results, explored their guiding significance for building a healthy province, and formed research on the path of building a healthy province based on the academic thought of "knowing how to receive because of happening, Heilongjiang cold region regimen".

Results and discussion

Geography: Heilongjiang Province is the province with the highest latitude in China and the only cold-temperate region in China. The concept of cold place health care originates from the famous "Treatment In Accordance With Three Categories Of Etiologic Factors" in the ancestral medicine "Taking Actions Suiting Local Circumstances ". Cold can reduce the body's metabolism, slowing down cell apoptosis, thus extending life expectancy.

Population: 15.61% of the population in our province is over 65 years old, which shows that our province has entered the stage of population aging. With the economic development and the deepening of the public health concept, the TCM health industry relies on the holistic concept of TCM, the diagnosis and treatment, and emphasizes the characteristics of prevention over treatment.

Economy: The economy of Heilongjiang Province as a whole is on a downward trend, and Harbin's GDP in 2021 is ranked 48th among mainland cities in the country, with slow economic development.

The " Heilongjiang cold region regimen" is generated by the special geographical location and climate change of this province, using Chinese medicine Taking Actions Suiting Local Circumstances theory to explain the natural environment, Taking Actions Suiting Local Circumstances social environment and life activities combined with the internal laws, from the dynamic concept of health cultivation, for the human body's birth, old age, disease and death, disease prevention and treatment, life prolongation and put forward the corresponding health care theory and methods to guide the life activities of health care, so that health care is more relevant and effective.

Cold region health cultivation is rooted in traditional Chinese medicine regimen, which has been accumulated through long-term experience, theoretical sublimation, and practical verification, and has comprehensive, practical, and extensive characteristics, and combines rich humanistic and philosophical ideas. At the same time, it has enriched the independence and targeting characteristics based on traditional Chinese health science and is a more specific and imaginative form of embodiment than traditional Chinese health science.

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The innovation and development of the Traditional Chinese Medicine comprehensive healthcare industry under the background of the new era

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Abstract

In the context of the era of comprehensive healthcare, combined with the fact that is currently in the stage of rapid development of population aging and people's increasing demand for health in China. Analyze the current situation of the development of the Traditional Chinese Medicine (TCM) comprehensive healthcare industry, explain the importance of the innovation and development of the TCM comprehensive healthcare industry, and find the problems existing in the development of the TCM comprehensive healthcare industry in China. To boost the development of the TCM health industry.

Key words: Traditional Chinese Medicine (TCM), comprehensive healthcare industry

With the enhancement of China's comprehensive national strength, people's health consciousness is also increasing. The continuous development of social economy and the transformation of people's life style lead to the change of disease spectrum. The increasing proportion of aging population in China, including the increasing demand for health, will bring unprecedented development and opportunities for the health service industry. TCM resources are important resources with Chinese characteristics, including health preservation, health care, medical treatment and so on. The medical field with TCM related products as the core has spawned the comprehensive healthcare industry of TCM. It is also an economic resource with great development potential. However, compared with developed countries, China's comprehensive healthcare industry is still in its primary stage. How to better promote the development of China's TCM comprehensive healthcare industry has become an important subject of the current research on the industrialization of TCM ^[1].

Opportunities for the development of TCM comprehensive healthcare industry

Due to the influence of our country large population base, a large number of elderly people, the COVID-19 epidemic and other factors, in addition, with the promotion of the construction of Healthy China and the building of a moderately prosperous society in an all-round way, the general public's health awareness is constantly enhanced, which objectively promotes the development of TCM health industry. Then, the Chinese medicine industry has attracted attention at home and abroad. First, Researcher Tu Youyou won the Prize of Physiology or Medicine for artemisinin in 2015, which made Chinese medicine stand out on the international stage. Second, TCM has also played a decisive role in the prevention and treatment of COVID-19, including Qingfei Jiedu Decoction and Baduanjin. At the same time, the development of TCM health industry is also strongly supported by the CPC Central Committee. These documents include the development Plan for TCM Health Services (2015-2020), The Protection and Development Plan for Chinese Medicinal Materials (2015-2020), and the Outline of the Strategic Plan for the Development of TCM (2016-2030). Considering China's national conditions, international recognition of TCM, national attention and public demand for health jointly promote the development of TCM health industry ^[2].

Problems faced by the development of TCM health industry

At the same time, there are many problems in TCM health industry. First of all, the industrial chain of TCM is not complete and cannot highlight regional characteristics. At present, the TCM health industry is in its infancy, and many places are in the trial stage, without forming a complete industrial chain, highlighting local characteristics and giving play to regional advantages, and the policy support system of the local government is not perfect. In addition, research and development efforts are weak. At present, there are relatively insufficient professionals engaged in the research and development of TCM big health industry in China, and the investment of scientific research funds is too little. Most TCM health products in China are characterized by short speed and low added value, and there are problems such as low technology content and large waste of raw materials. As well as, the international competitiveness of TCM health products is weak. Due to the differences between Chinese and Western cultural backgrounds, foreign consumers have a vague understanding of TCM theories and other basic knowledge. And due to the lack of organic integration between the western medicine research system and the theoretical system of TCM, it is difficult for traditional Chinese medicine therapy to pass the standards set by the international pharmaceutical market, so the standardization and modernization of traditional Chinese medicine is an urgent problem to be solved. In addition, Japan, South Korea, the United States and other similar products competition. To sum up, it is the top priority to accelerate the development of TCM comprehensive healthcare industry to improve the industrial chain of TCM, increase the investment in professional personnel training and scientific research, and improve the competitiveness of TCM comprehensive healthcare products [3].

Conclusion

In a word, the development of TCM comprehensive healthcare industry is the inexhaustible driving force for the innovative development of TCM in China. It is necessary to keep pace with The Times and gradually improve the TCM comprehensive healthcare industry chain, so as to bring the development of TCM big health industry into the fast lane as soon as possible and boost the development of TCM comprehensive healthcare industry in China.

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Cognitive dysfunction after chronic fatigue syndrome treated with transcranial magnetic stimulation: a potential therapeutic approach?

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Abstract

With the continuous development of science and technology, transcranial magnetic stimulation (TMS) is widely used in neurological diseases. In the treatment of cognitive impairment patients after chronic fatigue syndrome (CFS), whether the use of TMS can provide a potential therapeutic effect for it deserves our in-depth study. This paper reviews the application and development of TMS, assumes that TMS has a potential therapeutic effect on cognitive impairment after chronic fatigue syndrome, and discusses its specific application and efficacy in the treatment of CFS and cognitive impairment.

Keywords: transcranial magnetic stimulation, chronic fatigue syndrome, cognitive impairment
Chronic fatigue syndrome (CFS) is a disease with unknown etiology and disabling fatigue as well as a series of symptoms clinically defined. Cognitive disorders, including poor memory, impaired attention, difficulty in finding words and reasoning, are common in CFS patients.^[1] Transcranial magnetic stimulation (TMS) has been used since 1985 by Anthony Baker's team^[2] Since it was first proposed and studied, it has attracted the keen attention of researchers in the field of neuroscience. With the development of clinical research and technology, TMS technology has been used to treat some neurological diseases (such as chronic fatigue syndrome^[3], depression, stroke^[4], epilepsy^[5] etc.) has achieved significant results. In this study, we hypothesized that TMS has a potential therapeutic effect on cognitive impairment after chronic fatigue syndrome, and explored the specific application and efficacy of TMS in the treatment of CFS and cognitive impairment.

Objective

This paper aims to explore the specific application and efficacy of TMS in the treatment of CFS and cognitive impairment. Assuming that TMS has a potential therapeutic effect on cognitive impairment after chronic fatigue syndrome, we want to consider the role and innovation of TMS technology in the field of cognitive impairment after CFS.

Materials and methods

In this paper, the literature analysis method was used to summarize and analyze the high-quality literature about the application of transcranial stimulation in chronic fatigue syndrome at home and abroad. Research methods: In the core journal database of CNKI, PubMed, and Web of Science citation database, using "transcranial magnetic stimulation", "chronic fatigue syndrome" and "cognitive impairment" as the keywords, we retrieved the relevant literature on TMS technology in China and abroad in the past decade, and collected, organized and screened the literature related to chronic fatigue syndrome and cognitive impairment, summarized the related results by classification, and summarized the potential therapeutic effects of TMS on cognitive impairment after chronic fatigue syndrome.

Results and conclusions

TMS is widely used for the clinical treatment of neurological diseases, and it is the most common treatment mode in TMS treatment of cognitive impairment, with significant results. The dorsolateral prefrontal cortex plays an important role in controlling cognition and working memory^[6], the results of a study showed that 20 Hz TMS treatment in the dorsolateral prefrontal cortex can cause significant improvement in cognitive ability^[7]. Bersani et al.^[8]four of the five studies that evaluated the effects of deep transcranial magnetic stimulation applied to the dorsolateral prefrontal cortex on the cognitive ability of psychotic patients and healthy participants reported improvements in cognitive function. The results of one study provide key evidence for the role of the left dorsolateral prefrontal cortex in long-term memory, suggest that the application of deep transcranial magnetic stimulation to the left dorsolateral prefrontal cortex can improve subsequent recognition memory, and prove the beneficial effects of deep transcranial magnetic stimulation in enhancing cognitive function^[9]. When applied to the dorsolateral prefrontal cortex, it can improve the fatigue symptoms of CFS patients, and the results of research on cognitive impairment have shown that it can also improve the cognitive level. Therefore, we speculate that TMS, when applied to the dorsolateral prefrontal cortex, may play a beneficial role in the cognitive impairment after CFS.

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Application and discussion of transcranial magnetic stimulation on depression after chronic fatigue syndrome

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Abstract

Transcranial magnetic stimulation (TMS) is a new type of physical therapy technology. Because of its non-invasive and safe advantages, it has increasingly shown potential application prospects in the treatment of chronic fatigue syndrome and depression. Although clinical studies have confirmed the therapeutic effectiveness of this technology, the research on whether TMS can treat depression after chronic fatigue syndrome is still under discussion, and there are still many uncertainties about its mechanism and research. In this paper, the therapeutic mechanism of TMS technology in the treatment of depression after chronic fatigue is analyzed, and its existing problems are summarized, and the possible future development prospect is prospected, so as to promote the in-depth research of TMS technology in the treatment of depression after chronic fatigue syndrome.

Key words: transcranial magnetic stimulation, chronic fatigue syndrome, depression

Chronic fatigue syndrome (CFS) is characterized by persistent or repeated debilitating fatigue for 6 months or more^[1]. Besides physical symptoms such as fatigue, it is often accompanied by mental symptoms such as depression, anxiety and cognitive impairment. At present, the pathogenesis of CFS is still unclear, and the exact cause of pathophysiology of CFS is uncertain. However, studies have shown that nerve, immunity, autonomic nerve, endocrine and metabolic disorders are related to the damage of energy metabolism^[2]. Many studies at home and abroad show that the onset of CFS is related to psychological and social factors^[3]. Chronic fatigue patients have a higher incidence of depression than ordinary people^[4].

Transcranial magnetic stimulation (TMS) therapy, as one of the physical means to treat depression in clinic, can alleviate the symptoms of depression after chronic fatigue syndrome, and is widely used in clinic. It is safe, painless, patient compliance is high, and the curative effect is not limited to people^[5].

Objective: Through the application of transcranial magnetic stimulation in depression, this article analyzes the factors of clinical effect of transcranial magnetic stimulation in patients with depression after chronic fatigue syndrome.

Materials and methods: In this paper, literature analysis is used to summarize and analyze the high-quality literature on the application of transcranial stimulation in nervous system diseases at home and abroad. Methods: In PubMed, Wanfang database, CNKI core journal database, and Web of Science citation database, this paper searched the related literatures about transcranial magnetic stimulation at home and abroad in recent ten years with the key words of "transcranial magnetic stimulation", "chronic fatigue syndrome" and "depression", collected, sorted and screened the literatures related to chronic fatigue syndrome and depression, and inquired the representative related literatures. The related achievements were classified and summarized, and the clinical

effects of TMS on the pathogenesis of depression after chronic fatigue syndrome were summarized.

Results and discussions: The clinical role of TMS in the pathogenesis of depression after chronic fatigue syndrome is summarized as follows: (1) Regulating nerve excitability: high-frequency rTMS or intermittent explosive θ -wave stimulation (iTBS) can increase nerve excitability, while low-frequency stimulation or cTBS has the opposite effect. After TMS acts on the human body, it not only stimulates the local nerves, but also triggers the neural network in the stimulated area to produce a series of long-term biological effects. (2) Regulation of neurotransmitters and receptors: Stimulating cerebral cortex by TMS can regulate dopamine (DA), 5-hydroxytryptamine (5-HT), glutamate, etc., and modulate the sensitivity of receptors. (3) Effect on gene expression: TMS can regulate the expression of c-FOS gene, CREB phosphorylation and mRNA in cortex^[6]. Long-term rTMS can induce gene expression changes, and it can regulate the expression of immediate early genes (IEG)^[7]. The effect of a TMS sequence can increase the mRNA of proto-oncogene c-FOS in paraventricular nucleus of thalamus^[8]. (4) Promoting the production of brain-derived neurotrophic factor: High-frequency rTMS and iTBS can promote the production of brain-derived neurotrophic factor (BDNF) and play an important role in the repair of nerve injury^[9,10]. BDNF is a major member of neurotrophic factor family, which plays an important role in the growth, differentiation, survival, regeneration and proliferation of neurons^[11]. (5) Regulation of cerebral blood flow, metabolism and endocrine function: TMS can increase the brain's emergency response ability by affecting the function of pituitary-adrenal axis^[9]. BDNF is an important regulator of hypothalamic-pituitary-adrenal axis (HPA) stress adaptive response^[12]. BDNF regulates HPA, and is highly expressed in the brain regions that control emotions and responses to stress.

With the aggravation of physical fatigue, the emotional state of patients will be changed, which will inevitably affect patients' subjective feelings and judgments, and then negative emotions characterized by anxiety and depression will accompany chronic fatigue symptoms, and the relationship between them. TMS, as one of the physical means to treat post-chronic fatigue syndrome depression clinically, can alleviate the symptoms of post-chronic fatigue syndrome depression, and is widely used in clinic. It can induce nerve depolarization in specific areas of cerebral cortex, and generate cascade activation in the internet, thus improving patients' symptoms. Although TMS is a safe, reliable and effective treatment technique, it can be used in many areas.

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Mechanism of Hua Qi Ze Ren for the treatment of insulin resistance based on the levels of CaSR expression and phospho-AKT in the adipose tissues of the rats Abstract

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Abstract

Methods: The insulin resistance (IR) model of type 2 diabetes mellitus was replicated by intragastric administration of fat emulsion. After 4 weeks, the insulin sensitivity index (ISI) was calculated. qRT-PCR and Western blot methods were used to detect the expression levels of calcium-sensing receptor (CaSR) mRNA, CaSR protein and phospho-AKT (Ser473 and Thr308) proteins. **Results:** Compared with the control group, the ISI was significantly decreased, and the expressions of CaSR mRNA, CaSR protein and phospho-AKT (Ser473 and Thr308) protein in the adipose tissues were significantly decreased in the model group. Compared with the model group, the ISI was significantly increased, the CaSR mRNA, protein and phospho-AKT (Ser473 and Thr308) were significantly increased in the adipose tissues of the Hua Qi Ze Ren (HQZR) group, and they have no effect in the positive group. **Conclusion:** HQZR may regulate AKT activity in PI3K/AKT signaling pathway by reducing the expression of CaSR, to improve IR of type 2 diabetes mellitus.

Key words: Hua Qi Ze Ren, Type 2 diabetes mellitus, Insulin resistance, Calcium-sensing receptor, AKT activity.

Diabetes mellitus is a metabolic disorder characterized by hyperglycemia, hyperlipidemia, and hypertension (1). Insulin resistance (IR) is the main mechanism of the pathogenesis of type 2 diabetes mellitus. IR refers to the inability of insulin to activate glucose transport, promote lipid uptake, and inhibit lipolysis (2). The phosphatidylinositol 3-kinase/protein kinase B (PI3K/AKT) signaling pathway plays a crucial role in insulin signaling. Calcium-sensing receptor (CaSR) is an extracellular Ca²⁺ sensor which is a regulator of Ca²⁺ secretion and circulation (3). CaSR is a G protein-coupled receptor which can significantly enhance AKT activity. Its inhibitors can inhibit AKT activity (4), suggesting that CaSR is closely related to the PI3K/AKT signaling pathway. As an empirical prescription for the treatment of type 2 diabetes mellitus, the study mainly explores whether the AKT activity in the PI3K/AKT signaling pathway is affected by the regulation of CaSR in the IR of type 2 diabetes mellitus.

Objective

Based on the expression of CaSR gene, CaSR protein, and phospho-AKT (Ser473 and Thr308) proteins, to explore the molecular mechanism of HQZR in the IR of type 2 diabetes mellitus.

Materials and methods

The procedures involving the use of Wistar rats were approved by the Animal Experimental Ethical Committee of Heilongjiang University of Chinese Medicine (Harbin, China), RNAiso Plus, PrimeScript™ RT reagent Kit with gDNA Eraser and TB Green® Premix Ex Taq™ II (TaKaRa,

Japan); CaSR antibody (Abcam, USA); β -actin antibody (ZSGB-BIO, China); AKT, phosphor-AKT(S473 and T308) antibody (CST, USA).

The IR of type 2 diabetes mellitus model were replicated by gavage of fat emulsion and intraperitoneal injection of streptozotocin. Rats were given HQZR at a dose of 4.5g/kg by intragastric administration in the HQZR group. Rats were given rosiglitazone at a dose of 0.4 mg/kg by intragastric administration in the positive control group. Rats were given an equal volume of distilled water 10 ml/kg in the control group and the model group. Dosing for 4 weeks. Insulin sensitivity index (ISI) was calculated according to fasting blood glucose and fasting insulin levels. CaSR mRNA was detected by qRT-PCR, and the operation was performed according to the kit instructions. Western blot method was used to detect the expression levels of CaSR protein and phosphor-AKT (Ser473 and Thr308) proteins.

Results and discussion

The ISI of the control group was -4.35 ± 0.42 , it was -6.24 ± 0.26 in the model group, it was -4.96 ± 0.29 in the HQZR group, it was -5.18 ± 0.38 in the positive group. Compared with the control group, the ISI was significantly decreased in the model. Compared with the model group, the ISI of the HQZR and the positive groups were significantly increased ($P < 0.05$).

In adipose tissues, the expression level of CaSR mRNA was 0.97 ± 0.06 in the control group, it was 0.53 ± 0.05 in the model group, it was 0.82 ± 0.07 in the HQZR group, it was 0.62 ± 0.07 in the positive group. Compared with the control group, the CaSR mRNA expression level in the model group was significant decreased. Compared with the model group, the CaSR mRNA expression level was significantly increased in the HQZR group ($P < 0.05$), while was not statistically significant in the positive control group.

In adipose tissues, the protein expression level of CaSR and phospho-AKT (Thr308 and Ser473) were 0.56 ± 0.03 , 0.62 ± 0.04 and 0.57 ± 0.03 in the control group, they were 0.24 ± 0.04 , 0.20 ± 0.04 and 0.17 ± 0.03 in the model control group, they were 0.42 ± 0.05 , 0.48 ± 0.04 and 0.28 ± 0.05 in the HQZR group, and they were 0.31 ± 0.04 , 0.35 ± 0.03 and 0.19 ± 0.02 in positive control group. Compared with the model control group, the protein expression level of CaSR and phospho-AKT (Thr308 and Ser473) were significantly increased in the HQZR group ($P < 0.05$). They were increased in the positive control group, which were not statistically significant.

PI3K/AKT signaling pathway is a classic pathway of IR. PI3K/AKT signaling pathway regulates metabolism by promoting glycogen synthesis (5), promoting glucose transport, and inhibiting gluconeogenesis (6). Glucose transport is regulated by insulin, when insulin binds to the insulin receptor (IR), insulin receptor substrate 1 (IRS1) is phosphorylated and binds to PI3K to activate its downstream AKT.

As a member of the transmembrane G protein-coupled receptor family, CaSR is activated by binding to extracellular calcium, followed by cleavage of phosphatidylinositol diphosphate (PIP2) to the secondary messenger diacylglycerol via the phospholipase C (PLC) pathway (DAG) and inositol 1,4,5-triphosphate (IP3). CaSR plays an important role in maintaining calcium and cell homeostasis, as well as regulating gene expression and hormone secretion of various cell proliferation, differentiation, apoptosis (7)

Conclusion

The present study shows that HQZR has improved ISI in the IR of the type 2 diabetes mellitus. It can increase the expression of CaSR mRNA, CaSR protein, and phospho-AKT (Ser473 and Thr308) proteins, suggesting that HQZR may regulate AKT activity in PI3K/AKT by reducing the expression of CaSR, to improve IR of type 2 diabetes mellitus.

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Network Pharmacology Combined with GEO Database to Explore the Mechanism of *Panax ginseng* in the Treatment of Gastric Cancer

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Abstract

Gastric cancer (GC) is one of the most common cancers in the world and one of the cancers with high mortality. The research on its therapeutic drugs has become a hotspot. One promising candidate with cancer-preventive effects that are not specific to any organ is *Panax ginseng*, a herb with a long medicinal history. In this paper, through the combination of network pharmacology and Gene Expression Omnibus (GEO) database, we found the potential active ingredients and targets of ginseng in the treatment of gastric cancer, which provided a theoretical basis for *Panax ginseng* anti-gastric cancer and laid the foundation for clinical treatment of the disease.

Key words: Network Pharmacology, GEO Database, *Panax ginseng*, anti-gastric cancer

GC is one of the main causes of global cancer morbidity and mortality. Risk factors included helicobacter pylori infection, age, high salt intake and low fruit and vegetable diet. However, since the specific symptoms of early GC are not obvious, most patients with GC have been diagnosed as advanced at the time of discovery. In the past few decades, GC has made great progress in treatment and tried many effective treatment strategies. However, the incidence and mortality of GC remain high. Therefore, the development of efficient drugs for gastric cancer has become a hot spot *Panax Ginseng*.

Panax Ginseng has been one of the most valuable natural supplements in the East for many years. *Panax ginseng* has been extensively used in Chinese medicine for the treatment of gastric diseases, especially GC and gastric precancerous lesions. In this study, the potential active components and targets of *Panax ginseng* against GC were screened by network pharmacology combined with GEO database, providing a theoretical basis for *Panax ginseng* treatment.

Objective

Therefore, this study combined with network pharmacology and GEO database to explore the molecular mechanism of *Panax ginseng* against GC, and lay the foundation for the subsequent development of anti-gastric cancer Chinese medicine.

Materials and methods

This work selected the effective components and targets of *Panax Ginseng* the Traditional Chinese Medicine Systems Pharmacology (TCMSP) database. The bioactive ingredients of *Panax Ginseng* were selected by drug-likeness (DL) > 0.18 and oral bioavailability (OB) > 30%. Targets related to lung cancer were searched for in the GEO database (accession number GSE118916). The volcanic and thermal maps of differential expression genes (DEGs) were produced using the software R. Then, the target genes were analyzed by Gene Ontology (GO) and Kyoto Encyclopedia of Genes and Genomes (KEGG) analysis using the software R.

Results and discussion

This study discovered a total of 22 main components along with 12 possible anti-gastric cancer targets. The results of show that Stigmasterol was potential active components, while PTGS2 and

PLAU were key targets. We observed that the therapeutic effect of *Panax Ginseng* was a synergy of multi-component, multi-pathway, and multi-target. GO functional annotation revealed 20 biological processes (BPs), the most significant BPs were associated with to the response to nutrient levels, response to hypoxia and cellular response to external stimulus etc. According to the molecular functions (MFs) analysis, the targets were related to the monooxygenase activity, NAD-retinol dehydrogenase activity and heme binding etc. Regarding cellular components (CCs), the targets were associated with 8 CCs, the targets were associated with caveola, membrane raft, membrane microdomain and so on.

Based on the KEGG analysis, 22 pathways were enriched. The pathways were associated with NF-kappa B signaling pathway and TNF signaling pathway, among others. The results revealed that the therapeutic effect of *Panax Ginseng* on gastric cancer might be achieved in different ways.

This study explained the main candidate components, targets, and pathways involved in the action of *Panax Ginseng* against GC, and further provided a theoretical basis for clinical use.

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Study on the mechanism of Huaqizeren intervening KDSR gene expression in insulin resistant mice to improve skeletal muscle insulin resistance

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Abstract

From the perspective of *kdsr* gene, to explore whether Huaqizeren(HQZR) can improve mouse skeletal muscle IR by interfering with the expression of KDSR. The insulin resistance model of C57BL/6 mice was established, and HQZR Decoction and positive drug rosiglitazone were administered for 28 days. The changes of body weight, insulin sensitivity index (ISI), *kdsr* gene and protein expression level, CaSR protein expression, PI3K, Akt protein expression and phosphorylation level in skeletal muscle tissue were observed before and after administration. The results showed that compared with the control group, the body weight, aucgtt and aucitt levels of the model mice were increased; FBG and fins levels increased; ISI level decreases; The expression of KDSR gene and protein in skeletal muscle increased significantly; The expression of CaSR protein decreased significantly, and the expression and phosphorylation levels of PI3K and Akt protein decreased significantly. The body weight, aucgtt and aucitt levels of mice decreased after administration; The levels of FBG and fins decreased; ISI level increased; KDSR gene and protein expression in skeletal muscle decreased significantly; The expression of CaSR protein was significantly increased, and the expression and phosphorylation levels of PI3K and Akt protein were significantly increased. In conclusion, one of the mechanisms of HQZR to improve insulin resistance may be to up regulate the expression of CaSR by inhibiting the expression of KDSR gene and protein in mouse skeletal muscle tissue, so as to improve the activity of PI3kK/Akt signaling pathway and improve IR.

Key words: Insulin resistance, KDSR, Huaqizeren, CaSR, PI3K/Akt.

Type 2 diabetes (T2DM) is a metabolic disease with multiple etiologies, which is characterized by chronic hyperglycemia caused by insulin release disorder, insulin dysfunction, or both [1]. Insulin resistance (IR) is one of the characteristics of type 2 diabetes, which means that the metabolic response of target cells to insulin is reduced, or at the whole biological level, the lowering effect of circulating or injecting insulin on blood glucose is impaired [2,3]. Skeletal muscle is an organ closely related to insulin resistance. Ectopic lipid accumulation in skeletal muscle and other peripheral tissues caused by obesity leads to IR, which is an important risk factor for type 2 diabetes [4].

KDSR gene is one of the genes that affect IR found by our research group, which can affect IR by participating in lipid synthesis. Calcium sensitive receptor (CaSR) is a G protein coupled receptor [5]. The down-regulation of the expression of CaSR can reduce the activity of PI3K/Akt signaling pathway and cause IR. HQZR is an empirical prescription for the clinical treatment of IR in type 2 diabetes, which has a good therapeutic effect on IR, and it has been previously confirmed that HQZR can significantly improve IR symptoms in mice. This study will explore the mechanism of HQZR in improving IR in mouse skeletal muscle from the perspective of KDSR and cCaSR/PI3K/Akt signaling pathways.

Objective

From the perspective of KDSR gene, to explore whether HQZR can improve mouse skeletal muscle IR by interfering with the expression of kdsr, and to explore the mechanism of HQZR to improve skeletal muscle IR from this perspective.

Materials and methods

The procedures involving the use of C57BL/6 mice were approved by the Animal Experimental Ethical Committee of Heilongjiang University of Chinese Medicine (Harbin, China), RNAiso Plus, PrimeScript™ RT reagent Kit with gDNA Eraser and TB Green® Premix Ex Taq™ II (TaKaRa, Japan); KDSR, CaSR antibody (Abcam, USA); β -actin antibody (ZSGB-BIO, China); PI3K, phosphor-PI3K(P85), AKT, phosphor-AKT(S473) antibody (CST, USA).

Eight week old male C57BL/6 mice were selected. After one week of adaptive feeding, the insulin resistance model was established by high-fat diet feeding combined with low-dose intraperitoneal injection of streptozotocin (STZ). The successful mice were randomly divided into model control group, HQZR group and positive control group; Normal C57BL/6 mice were the blank control group. HQZR group was perfused with HQZR Decoction at a dose of 5.4g/kg, the mice in the positive control group were perfused with rosiglitazone at a dose of 0.3 mg/kg, and the blank control group and the model control group were perfused with the same amount of normal saline 10ml/kg. After 28 days of administration, observe the weight changes of each group before and after administration; Draw the curves of glucose tolerance test (GTT) and insulin tolerance test (ITT) in mice, and calculate the area under the curve; Insulin sensitivity index (ISI) was calculated according to fasting blood glucose (FBG) value and fasting insulin (FINS) level; QRT PCR and Western blot were used to detect the gene and protein expression level of KDSR in skeletal muscle tissue of each group according to the instructions; Western blot was used to detect the expression of CaSR protein in each group, and the protein expression and phosphorylation level of PI3K (p85) and Akt (s473) were detected at the same time.

Results and discussion

Compared with the blank control group, the body weight, AUC_{gtt} (area under GTT curve) and AUC_{itt} (area under ITT curve) levels of the model control group were significantly increased ($p < 0.05$ or $p < 0.01$); The levels of FBG and fins increased significantly ($p < 0.01$); ISI level decreased significantly ($p < 0.01$); The expression of KDSR gene and protein in skeletal muscle increased significantly ($p < 0.01$); The expression of CaSR protein decreased significantly ($p < 0.01$), and the expression and phosphorylation levels of PI3K and Akt protein decreased significantly ($p < 0.01$). Compared with the model control group, the body weight, AUC_{gtt} and AUC_{itt} levels of mice in HQZR group and positive control group were significantly reduced ($p < 0.05$); The levels of FBG and fins decreased significantly ($p < 0.05$); ISI level increased significantly ($p < 0.05$); This shows that rosiglitazone and HQZR can improve insulin resistance in mice. Compared with the model control group, the expression of KDSR gene and protein in skeletal muscle tissue of HQZR group and rosiglitazone group decreased significantly ($p < 0.05$); The expression of CaSR protein increased significantly ($p < 0.05$), and the expression and phosphorylation levels of PI3K and Akt protein increased significantly ($p < 0.05$).

The above results suggest that HQZR may up regulate the expression of CaSR by down regulating the expression of KDSR in mouse skeletal muscle tissue, and then improve the activity of PI3k/Akt signal pathway, and finally improve IR.

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Molecular mechanism of Corn silk in the treatment of type 2 diabetes based on network pharmacology and molecular docking

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Abstract

Type 2 diabetes mellitus (T2DM) is a metabolic disease with multiple etiologies. It is characterized by disorders of glucose, lipid, and protein metabolism, and its etiology is chronic hyperglycemia caused by insulin secretion disorders or insulin resistance. Corn silk is the style and stigma of the grass maize, it has the effect of diuresis and swelling, clearing liver and gallbladder. At present, reports on the application of corn silk in diseases of glucose metabolism are increasing day by day, but most of the studies stay at the level of pharmacodynamics, and the research on its active ingredients for diabetes intervention is still blank, and the research on its mechanism of action has not been in-depth. The purpose of this study is to use the network pharmacology method and molecular docking technology to discover the potential active ingredients and targets of corn silk in the treatment of T2DM, provide a theoretical basis for the treatment of T2DM by corn silk, and lay a foundation for clinical treatment of T2DM.

Keywords: Corn silk; Type 2 diabetes; Network pharmacology; Active ingredients; molecular mechanism

At present, studies have shown that corn silk and its active ingredients have obvious regulatory effects on blood sugar, but the current mechanism of corn silk in the treatment of T2DM is difficult to scientifically, effectively and comprehensively explain. Network pharmacology is a powerful analytical tool emerging in recent years, which is good at systematically exploring the relationship between drugs and diseases from a holistic perspective. Molecular docking technology uses application tools such as molecular simulation, protein structure analysis, small molecule data processing, and protein-small molecule docking research to conduct virtual screening of conventional drugs, which can help drugs find their target and predict the mechanism of drug action. The purpose of this study was to use the network pharmacology method and molecular docking technology to explore the effective components and targets of corn silk in the treatment of T2DM, and to screen the key components and key signaling pathways. To provide a theoretical basis for further research and application of corn silk in the treatment of T2DM.

Objective

To explore the potential effective components, related action targets and signal pathways of corn silk in the intervention of T2DM by using network pharmacological methods and molecular docking technology, and to speculate the potential mechanism of its intervention in T2DM.

Materials and methods

The effective components and corresponding molecular targets of *Panax quinquefolium* were obtained from tcmsp database; Collect the disease targets of T2DM in GENECARD, OMIM, PharmGKB, TTD and grugbank databases; Take the intersection of the two to get the drug disease protein target gene, and draw the drug disease Venn map; Construct the "drug component target" visual network diagram and protein interaction network diagram through Cytoscape 3.9.1 software,

and use the cytonca plug-in to screen the core target genes; Go function and KEGG enrichment analysis of target proteins were carried out by using R language data package; Conduct molecular docking operation on the structural formula of drugs and gene targets through MOE2019.01 software.

Results and discussion

In this study, a total of 85 effective components of corn silk were found, 11,055 molecular targets of T2DM, and 83 common targets of corn silk and T2DM. A total of 7 core genes in the protein interaction network were obtained through CytoNCA plug-in screening, namely AKT1, MMP9, JUN, PTGS2, CASP3, TP53, and BCL2L1, which may be the main targets of corn silk for prevention and treatment of type 2 diabetes. The enrichment analysis obtained 30 main biological signals of GO. The predicted corn silk was mainly involved in regulating biological processes such as the response to oxygen and the response of cells to oxygenated compounds, and was closely related to the intervention of diabetes. Participates in 30 major signaling pathways of KEGG, mainly distributed in 4 categories including diabetes, circulatory system, cancer, and inflammation, including PI3K-Akt signaling pathway related to T2DM, Lipid and atherosclerosis, Endocrine resistance, and other pathways. It is observed that the therapeutic effect of corn silk is a synergistic effect of multiple components, multiple pathways and multiple targets. It provides a theoretical basis for clinical application.

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Research Progress of Calcium Sensitive Receptor (CaSR) in Pancreatic Islet B Cells

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Abstract

Calcium sensing receptor (CaSR) is a G protein-coupled receptor, also known as a polycation sensor. Because of its unique ligand binding site, CaSR has multiple positive and variable binding sites. Several different G proteins are subject to bias signals and have many pathological and physiological effects. It is currently a recognized therapeutic target for diabetes, asthma, cardiovascular disease and cancer. Pancreatic islet B cells are endocrine cells that secrete insulin in the pancreas. They play an important role in regulating glucose homeostasis. Unbalanced glucose homeostasis or damage to pancreatic islet B cells can lead to diabetes. Calcium-sensitive receptors participate in and regulate a series of physiological activities. This review summarizes recent studies that provide insights into the relationship between calcium-sensitive receptors and pancreatic islet B cells, which are expected to provide further theoretical reference for related research.

Key words: Calcium sensing receptor ; pancreatic islet B cells ; research progress

Pancreatic Islets are secretory functional units, which are irregular cell populations dispersed in the pancreas composed of at least three types of cells (A, B, D). Pancreatic islets are regulated by blood glucose levels, gastrointestinal hormones, and nerves, and secrete glucagon, insulin, ghrelin, and gastrin. Among them, islet B cells account for about 70% of islets as important cells that secrete insulin. Calcium-sensing receptors (CaSRs) can be found in a variety of cell types unrelated to controlling plasma calcium. Pancreatic islets are one such tissue, and this receptor plays a rather important role in regulating islet B cell function. Studies have shown that CaSR can affect insulin secretion by mediating signal propagation in pancreatic islets, and insulin secreted through this pathway can be without accompanying glucose stimulation [1].

Mechanisms of CaSR-mediated signaling through islet B cells

After glucose enters islet B cells and is taken up by glucose transporter (GLUT), glucose metabolism is controlled by low-affinity glucokinase (GK), so that the increase of ATP/ADP ratio closes the ATP-sensitive potassium ion channel K^{+}_{ATP} , resulting in the removal of cell membrane. polarized, and opened the L-type voltage-dependent Ca^{2+} channel (VDCC). Extracellular calcium enters cells with a steep concentration gradient to stimulate islets to secrete free Ca^{2+} and other divalent cations to co-release with insulin, thereby increasing the local concentration of extracellular calcium (Ca^{2+}_e) in the intraislet space.

These local changes generate high concentrations of extracellular calcium (Ca^{2+}_e) in the space surrounding adjacent islet B cells and activate CaSR on adjacent cells in a paracrine manner. The CaSR-mediated increase in intracellular calcium (Ca^{2+}_i) propagates the signal throughout the islet, coordinating islet-wide activity and enhancing glucose-induced insulin secretion.

The effect of CaSR on insulin secretion

It is highly unusual for the receptor to be able to initiate an insulin secretion response in the absence

of glucose stimulation. However, activation of CaSR initiates insulin secretion from human and rodent islet B cells without concomitant nutritional stimulation [2].

Changes in plasma glucose concentration are the major regulators of insulin release. Metabolism of glucose in B cells alters the ATP/ADP ratio and closes the ATP-dependent K⁺ channel K⁺ATP, thereby depolarizing the cell membrane and opening L-type voltage-dependent Ca²⁺ channels (VDCCs), thereby increasing intracellular calcium Ca²⁺_i, and cause a pulse of insulin release [3].

Multiple signal transduction pathways of CaSR in pancreatic islet B cells

CaSR-coupled Gq/11 is generally considered a major signaling pathway, as mentioned above: activation of phospholipase C (PLC)-β, hydrolysis of phosphatidylinositol 4,5-bisphosphate to IP₃ and diacylglycerol. IP₃ triggers the release of intracellular Ca²⁺, such as in the endoplasmic reticulum, while diacylglycerol (DAG) alone or in combination with Ca²⁺ activates protein kinase C (PKC). Cytoplasmic phospholipase A₂, a fast-digesting enzyme in arachidonic acid metabolism, is also activated by the CaSR-mediated Gq/11 pathway via calmodulin and calcium/calmodulin-dependent protein kinase II [4].

CaSR activates multiple mitogen-activated protein kinase (MAPK) cascades, including extracellular signal-regulated kinase (ERK) 1/2, p38 MAPK, and c-Jun N-terminal kinase (JNK) (also known as stress-activated protein Kinase (SAPK)) to regulate the release, proliferation and other functions of PTHrP [5]. Several signal transduction pathways including c-Jun N-terminal kinase (JNK), p38 mitogen-activated protein kinase and protein kinase C (PKC) are known to be affected by oxidative stress, endoplasmic reticulum stress in several cell types. Oxidative stress and endoplasmic reticulum stress are important causes of islet B cell damage. Therefore, it is necessary to explore the signaling pathway of CaSR in islet B cells. Recent studies have shown that the JNK pathway is activated by oxidative stress in islet B cells, and the activation of the JNK pathway is involved in the reduction of insulin gene expression by oxidative stress, and inhibition of the JNK pathway can protect islet cells from oxidative stress [6].

Conclusion and discussion

In this paper, the mechanism and multiple transduction pathways of CaSR's signal transduction in pancreatic islet B cells are expounded. The current research focus has also been on finding the relationship between CaSR's related target genes or signaling pathways in pancreatic islets, in order to find Diseases, especially diabetes, are possible treatments. At present, the mechanism of action of CaSR needs to be discussed more deeply and comprehensively, and the target of action is also of great significance for treatment.

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Research progress on the role of microRNAs in T2DM insulin resistance

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Abstract

MicroRNAs (miRNAs) are RNA molecules present in eukaryotes that regulate the expression of other genes. They are derived from RNA transcribed from DNA but cannot be further translated into proteins. Studies have shown that miRNA is involved in the pathogenesis of type 2 diabetes and plays an important role. This paper reviews the regulatory role of miRNA in the occurrence and development of insulin resistance, aims to provide a reference for safe and efficient new miRNA treatment methods.

Key words: T2DM; insulin resistance; miRNAs

Type 2 diabetes mellitus (T2DM) is associated with increased health expenditures and poor quality of life due to progressive loss of insulin secretion from beta cells associated with insulin resistance. These small non-coding RNAs play a key role not only in the regulation of growth, differentiation and organ function, but also in glucose homeostasis. Dysregulated miRNAs affect various metabolic and signal transduction pathways associated with T2DM, and play an important role in the occurrence and development of T2DM.

Objective

To investigate the role and mechanism of miRNAs in T2DM, provide new ideas for further treatment of T2DM.

Materials and methods

To search for miRNA-related research contents in studies on the related mechanisms of insulin resistance in T2DM.

Results and discussion

1.miRNA

The main function of miRNAs is to inhibit the synthesis of proteins (such as enzymes, receptors, structural proteins, hormones, and other inherent biological substances). Some miRNAs may also activate gene expression, which may enhance the stability of mRNA through direct activation or indirect inhibition. So far, about 2,000 forms of miRNAs have been synthesized in humans, potentially affecting the expression of almost a third of human genes (including those involved in glucose metabolism, beta cell function and insulin secretion).

1.miRNA regulates insulin resistance

MiRNA can act on a variety of key target genes that regulate insulin resistance, and its maladjustment can induce insulin resistance in different target tissues. The related miRNA and its target genes and tissues are shown in Table 1. It induces insulin resistance by regulating INSR,

IRS-1, GLUT4 and other downstream effector factors, and participates in the regulation of glucose and lipid metabolism, insulin secretion, oxidative stress and other physiological and pathological processes, and then participates in the occurrence and development of insulin resistance in type 2 diabetes.

Tab 1. miRNAs involved in insulin resistance in T2DM

miRNA	Target	Tissue/cell line used
miR-375	Mtpn	Pancreatic cells
miR-143	ERK5	Adipose tissue
	Atg2b, HK2	Hepatocytes
miR-9	Granuphilin/Slp4	Pancreatic cells
miR-29	TRAF3	Pancreatic cells
miR-29a	GLUT4	Adipose tissue
	PPAR ^δ ,	Adipose tissue,
	PGC-1 ^α	skeletal muscles
miR-125a	Ptges2	Adipose tissue, Hepatocytes
miR-320	GLUT-4	Adipose tissue
miR-126	IRS-1	Hepatocytes Cardiac muscle cell
miR-103/ miR-107	Caveolin-1	Hepatocytes, Adipose tissues
miR-106b	mitofusin-2	myotube
miR-200	Ypel2	Pancreatic cells
miR-15b	INSR	Hepatocytes
miR-96	INSR, IRS-1	Hepatocytes
miR-128-3p	ISL1	Pancreatic cells
miR-27a	PPAR ^γ	skeletal muscles
miR-17	GLUT4	skeletal muscles
miR-222	IRS-1	Hepatocytes, skeletal muscles
miR-221		Hepatocytes

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Advances in pharmacology of calcium-sensing receptors in ossifying diseases

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Abstract

Calcium Sensitive Receptor (CaSR) is a dimeric family of C-G protein-coupled receptors, highly expressed in ossified tissues such as parathyroid glands and kidneys, and sends signals through G protein and β -arrestin. CaSR plays a key role in both bone and mineral metabolism, as it regulates parathyroid hormone secretion, urinary Ca^{2+} excretion, bone development and lactation. CaSR is very important for the process of calcification. This is reflected in familial hypocalciuric hypercalcemia caused by the loss of CaSR function and autosomal dominant hypocalcemia caused by the gain of CaSR function. In addition, the change of CaSR expression in parathyroid glands is one of the important pathogenesis of primary and secondary hyperparathyroidism. Therefore, CaSR is an important therapeutic target for hyperparathyroidism. This article summarizes the research progress of calcium-sensing receptors in ossification diseases in recent years, and provides a reference for improving calcium-sensing receptors and related factors in the future research on the treatment of ossification diseases.

Key words:CaSR ; Parathyroid glands ; Ossification ; Ca^{2+}

Structure of CaSR

CaSR belongs to the C-GPCRs family and plays a key role in neurotransmission, nutrient sensing and Ca^{2+} homeostasis [1]. These receptors are functionally active as homodimers or heterodimers. It is characterized by the presence of a large extracellular domain (ECD) [2] that contains a Venus flytrap (VFT) module that binds ligands and is structurally similar to the nutrient-scavenging bacterial periplasmin [3]. CaSR is thought to have emerged during vertebrate evolution and is functionally active in vertebrates ranging from cartilaginous fishes to terrestrial mammals [4]. X-ray crystallography studies have shown that human CaSR has a glycosylated ECD that binds extracellular Ca^{2+} (Ca^{2+}_e) at three distinct positions within the VFT module, and also in the VFT module and the cysteine-rich domain (positional binding between CRDs) [5]. CaSR also binds amino acids within the gap of the VFT module, and the binding of Ca^{2+} and amino acids may fully activate CaSR. Additional anion-binding sites, such as phosphate and sulfate, are contained within the CaSR VFT module, and these anions may keep CaSR in an inactive conformation [5]. Agonist-induced conformational changes in the CaSR ECD may lead to rearrangement of helices within the transmembrane domain (TMD), thereby promoting G protein binding and intracellular signaling.

CaSR is expressed in the parathyroid glands

The Ca^{2+} sensitive receptor (CaSR) is highly expressed in the parathyroid gland, which is located in the posterior and adjacent parts of the thyroid gland. CaSR in the parathyroid glands detects a

decrease in extracellular Ca^{2+} (Ca^{2+}_e), which leads to parathyroid hormone (PTH) release. PTH acts on the PTH1 receptor (PTH1R) in the bone, increases the absorption of Ca^{2+} in the bone, and promotes the reabsorption of Ca^{2+} in the urine. PTH acts on the PTH1 receptor (PTH1R) in the kidney to increase the 1- α -hydroxylase (1 α Ohase) in the kidney. The expression of 25-hydroxyvitamin D (25D) precursor metabolites is converted into active 1,25-dihydroxyvitamin D (1,25(OH)₂D). Elevated 1,25(OH)₂D increases dietary calcium absorption by acting on the vitamin D receptor (VDR) in the gut [6]. CaSR in the thick ascending limb of renal cortex regulates urinary Ca reabsorption independently of PTH [7]. The increase in 1,25(OH)₂D concentration leads to a negative feedback from the parathyroid gland, which inhibits further release of parathyroid hormone.

CaSR signaling

The calcium-sensing receptor (CaSR) is functionally active as a constitutive homodimer that can interact with other families of C-G protein-coupled receptors such as growth plate chondrocytes and metabolic glutamate receptors in the central nervous system. and GABA B receptors) to form heterodimers [2]. The CaSR ectodomain binds Ca^{2+} within multiple regions of the Venus flytrap (VFT) module and cysteine-rich domain (CRD). CaSR also binds amino acids in VFT cleavage. Synthetic phenylalkylamine positive allosteric modulators (PAMs) and aminoalcohol negative allosteric modulators (NAMs) bind to the CaSR transmembrane domain (TMD). Ca^{2+} binding leads to Gq/11-dependent activation of phospholipase C (PLC) and membrane-bound phosphatidylinositol 4,5-bisphosphate (PIP2) to generate diacylglycerol (DAG) and inositol 1,4,5 - Activation of triphosphate (IP3). Increased intracellular IP3 levels promote intracellular Ca^{2+} storage (eg, release from the endoplasmic reticulum), DAG activates protein kinase C (PKC), which in turn activates the mitogen-activated protein kinase (MAPK) pathway to phosphorylate extracellular signaling Regulates the kinase 1 (pERK1) and/or pERK2 pathways. CaSR also activates Gi/o proteins, thereby inhibiting adenylate cyclase (AC)-mediated cyclic adenosine monophosphate (cAMP) production. These signaling events result in decreased parathyroid hormone (PTH) secretion and increased urinary Ca^{2+} excretion. The CaSR cell surface is regulated by agonist-driven internalization signaling, which mediates anterograde trafficking of the receptor [8]. Retrograde receptor trafficking is mediated through an endocytic complex composed of clathrin, β -arrestin, and the heterotetrameric adapter-associated protein complex 2 (AP2) .

Conclusion and discussion

CaSR is a pharmacological therapeutic target in ossifying diseases; calcimimetic drugs are an established drug for the treatment of hyperparathyroidism and are effective in FHH and some forms of non-hyperparathyroidism. Calcifying agents may be targeted therapy for vasopressin and may also have potential in other treatments for hypoparathyroidism. Nonetheless, CaSR drug discovery remains limited by limited tools. For example, commercially available radioligands or fluorescently labeled ligands and lack of drug discovery based on the 7TM and full-length CaSR structures.

Given that calcium-sensing receptors and calcium homeostasis are critical to human health, understanding the structure, activity, and signaling, function, and physiology of CaSR, and closely linking the relationship between CaSR and disease, can further strengthen and update the study of CaSR, stimulate the potential future pharmacological research progress of CaSR in ossified tissues and the whole body, and lay the foundation for the clinical treatment of CaSR in ossification diseases.^[9]

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Research progress of *Schisandra chinensis* in the treatment of type 2 diabetes

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Abstract

Schisandra Chinensis (Turcz.) Baill. (SCE) is one of the most common Chinese medicinal materials and can also be used as food and medicine. Modern pharmacological studies have confirmed that SCE has a variety of active components, such as lignan, polysaccharide and so on, which can effectively improve insulin resistance (IR) and reduce blood glucose. This paper reviews the recent researches on SCE in the treatment of type 2 diabetes mellitus (T2DM) by reviewing the literatures in recent years. In order to provide reference for further study of SCE in the treatment of T2DM.

Key words: *Schisandra Chinensis* (Turcz.) Baill.; active ingredients; type 2 diabetes mellitus

SCE is a dried and mature fruit of magnoliaceae plant SCE, which has the functions of hemostasis and detoxification, lung consolidation, antiperspirant, essence fixation and qi benefiting. In addition, schisandra has no side effects. Diabetes mellitus (DM) is a metabolic disease caused by defects in insulin secretion and (or) action. At least 171 million people worldwide have DM, according to the World Health Organization (WHO). By 2030, that number could double to 366 million. Then, T2DM is characterized by IR and islet β -cell dysfunction. SCE can lower blood sugar and has anti-diabetes potential. It can improve pancreatic function, increase insulin secretion and reduce diabetes complications.

Objective

To study the effect of SCE on T2DM, provide new ideas for further treatment of T2DM.

Materials and methods

The effect of schisandra chinensis on T2DM was investigated in the latest study of SCE on T2DM.

Results and discussion

1. Hypoglycemic effect of *Schisandra chinensis* polysaccharide

Niu J et al showed that schisandra chinensis water-soluble polysaccharide (SSPW1) can improve glucose tolerance, reduce fasting blood glucose (FBG), improve fasting insulin (FINS) and Insulin sensitivity index (ISI) in T2DM model rats. It can reduce malonaldehyde (MDA) content and increase glutathione peroxidase (GSH-PX) enzyme system, catalase (CAT) and superoxide dismutase (SOD) activity. These results suggest that SSPW1 reduces blood glucose through antioxidant action.

Some researchers induced T2DM model in rats by high-fat diet (HFD) combined with low-dose Streptozotocin (STZ) intraperitoneal injection. *Schisandra chinensis* acidic polysaccharide (SCAP) was found to reduce FBG, the levels of Triglyceride (TG), Total cholesterol (TC), low-density lipoprotein cholesterol (LDL-C) and MDA, respectively. The levels of insulin, high-density lipoprotein cholesterol (HDL-C) and SOD were increased, and the pathological changes of pancreas were improved. In addition, SCAP also inhibited the up-regulation of c-Jun N-terminal kinase (P-JNK), B-cell lymphoma 2-associated X protein (BAX) and Cleaved caspase-3 proteins. Increased protein expression of B-cell lymphoma 2(Bcl-2), phosphorylated insulin receptor substrate-1 (p-IRS-1), phosphorylated phosphatidylinositol 3-kinase (P-PI3K), and phosphorylated

protein kinase B (p-AKT). The results showed that SCAP can improve IR of T2DM rats by inhibiting oxidative stress and inflammatory response.

2. Hypoglycemic effect of Schisandra chinensis lignans

Schisandra chinensis oil is extracted from the seeds of schisandra chinensis and obtained by low-temperature concentration with ethyl acetate. Its main component is lignan, which can reduce blood glucose and hyperlipidosis caused by HFD, improve insulin secretion, reduce glucagon secretion, and mitigate IR and inflammation. It was found that schisandra chinensis oil could significantly reduce the levels of FBG, TC, TG and MDA, and increase the activities of SOD and CAT. The expressions of Bcl-2, PDX-1, GLUT-2 and GCK were up-regulated in T2DM rats treated with Schisandra chinensis oil. Schisandra chinensis oil can improve the function of islet β cells by enhancing the antioxidant capacity of pancreas, up-regulating the expression of anti-apoptotic genes, increasing the expression of glucose metabolism and delaying the apoptosis of islet cells.

In summary, schisandra polysaccharide, lignan and schisandra oil can significantly reduce blood glucose level and improve the expression of related proteins, and play a good role in the prevention and treatment of T2DM.

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Research progress on chemical composition and pharmacological effects of patchouli

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Abstract

Patchouli is a widely used traditional Chinese medicine with complex chemical composition, including flavonoids, terpenes, phenylpropanoids, steroids, alkaloids, etc. It has rich pharmacological effects, mainly including antibacterial, antiviral, parasitic killing, gastrointestinal activities, digestion, intestinal barrier protection, anti-inflammatory and analgesic, anticancer cells and antioxidant, etc. This paper mainly explores and summarizes the chemical composition and pharmacological effects of patchouli for subsequent compatibility research.

Key words: Pogostemon cablin, chemical component, pharmacologic action

As a commonly used Taoist and southern medicine, patchouli has a history of cultivation in China for thousands of years, and it is an essential and important traditional Chinese medicine in the inheritance and development of traditional Chinese medicine in China. It not only has many pharmacological research value, widely used in clinical, but also has great commercial value, mainly used in cosmetics industry and incense industry. Its chemical composition is more complex, it is a kind of aromatic wet traditional Chinese medicine. Nowadays, there are many prescriptions with patchouli as the main ingredients in the pharmaceutical market.

Objective

Nowadays, patchouli has rich pharmacological effects and is widely used in clinical practice. This article summarizes the chemical composition and pharmacological effects of TCM patchouli for subsequent research.

Materials and methods

Literature collection method was used to review the literature on Pogostemon cablin and Atractylodes in recent 20 year, and summarize the chemical constituents, pharmacological action and clinical application of them.

Results and discussion

1 The main chemical components of patchouli

Patchouli has a more complex chemical composition. Since the end of the 19th century, researchers have isolated and extracted them and obtained antibacterial ingredients. Nowadays, with the development of science and technology, spectroscopy technology and mass spectrometry technology have made a qualitative leap, and the chemical composition of patchouli has been further studied. At present, more than 90 compounds have been extracted and isolated from patchouli, which can be roughly divided into two categories, volatile oils and other non-volatile components. Among them, volatile oil (that is, patchouli oil) is mostly used as the medicinal active ingredients of patchouli, which can roughly include flavonoids, terpenoids, phenylpropanoids, steroids, alkaloids, etc. At present, more than 20 kinds of flavonoids extracts have been found, including flavonoids, isoflavones, dihydroflavones, flavonols, chalcones and so on; Terpenoids are mainly sesquiterpenes, diterpenes, etc.; there are still a certain amount of large polar glycosides in

patchouli; All of the steroids are bean steroids. In addition, a small amount of fatty acid compounds were also isolated from patchouli. All of the above-mentioned compounds showed strong bioactivity.

2 Pharmacological effects of patchouli

Studies show that patchouli oil has strong antibacterial, antiviral and parasitic killing pharmacological effects. According to statistics, it can directly or indirectly inhibit the growth and reproduction of more than 20 species of fungi and more than 30 species of bacteria. As far as fungi are concerned, *Candida albicans* which causes vaginitis, *Cryptococcus neoformans* which causes pneumonia and meningitis in AIDS patients, and moss, which is easy to cause skin moss; In terms of bacteria, the intestinal bacteria such as *Staphylococcus aureus*, *Escherichia coli* and dysentery are inhibited, as well as the skin bacteria that cause armpit odor and beriberi^[7]. Patchouli oil also has a strong antiviral activity, which suppresses the proliferation of influenza A virus and adenovirus, and also has a strong antimalarial effect on *Plasmodium hei*.

Patchouli regulates the activity of the gastrointestinal tract. It protects the gastric mucosa and relieves the gastrointestinal spasm, which also increases the secretion of gastric acid and improves the activity of pepsin to promote digestion. It is found that patchouli oil can inhibit gastrointestinal smooth muscle spasm caused by acetylcholine and barium chloride, and can also relieve visceral colic caused by glacial acetic acid; and it can enhance the repair function of intestinal mucosal epithelial cells and protect the intestinal barrier function.

Patchouli oil has an anti-inflammatory and analgesic effect. Studies have shown that patchouli oil regulates the synthesis of cyclooxygenase-2 at inflammatory sites to inhibit the production of prostaglandin E, reduce the accumulation of peroxide and malondialdehyde, and combat the local vasoconstriction caused by exogenous substances, so as to achieve anti-inflammatory effects, swelling and pain relief.

Nowadays, some scholars have found that patchouli has great medical research value for anti-tumor cells and regulation of the immune system. It has been found that patchouli oil has an inhibitory effect on the differentiation of endometrial cancer cells, prostate cancer cells DU145, colon cancer cells, lung cancer cells A549, human skin melanoma cell A375 and other cancer cells, to promote their apoptosis, so as to achieve the anti-tumor effect. Patchouli volatile oil has a regulating effect on peripheral leukocytes, phagocytes in the abdominal cavity, and lymphocytes in the spleen, which can enhance humoral immunity and inhibit cellular immunity to a certain extent.

Patchouli oil can remove free radicals in the body, achieve antioxidant effect, and is used to treat the brain apoptosis caused by reactive oxygen species, so as to protect human brain cells from their damage. Patchouli can also restore the skin damage caused by UV irradiation and prevent photoaging. Patchouli still has some other pharmacological effects, which can relieve cough, relieve asthma, stop vomiting and so on.

With the in-depth research on the pharmacological effect of patchouli, single-flavor patchouli is less used to treat diseases clinically, and various prescriptions associated with patchouli are more widely used. At present, the compatibility research of patchouli has been relatively standardized, but there are still problems such as incomplete synergy between drugs and toxic effects, so it is necessary to deeply study the compatibility between patchouli and other traditional Chinese medicines.

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Effects of Tianxingjianyikang Granule on brain of D-GAL induced aging rats

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Abstract

This paper introduces the effect of Tianxingjianyikang Granule on the brain of D-GAL induced aging rats. Male SD rats were selected for the experiment, and the aging model was established by intraperitoneal injection of D-GAL. Vitamin E was used as a positive control drug to observe the general state of Tianxingjianyikang Granule at high, middle and low doses respectively on aging rats. The activity of superoxide dismutase (SOD), glutathione peroxidase (GSH-Px) and malondialdehyde (MDA) in brain and the morphological structure of hippocampus. According to the analysis, high dose Tianxingjianyikang Granule can improve the general state and brain atrophy of rats, increase SOD and GSH-Px in brain, reduce MDA content, and improve the morphology of hippocampal area.

Key words: Tianxingjianyikang Granule, D-GAL, Aging, Brain

At present, the aging of population has become an important issue concerned by the international community. With the growth of age, various physiological functions of the human body will slowly deteriorate, which will lead to increased susceptibility to age-related diseases. At the same time, the aging population has led to increasing demand for medical care, which has added to the economic burden. Therefore, the concept of great health is deeply rooted in people's minds, the development of anti-aging drugs and health care products has become a hot research direction. Traditional Chinese medicine has a unique understanding and outstanding effect on the prevention and treatment of aging, and has received wide attention in the field of anti-aging research. Health care products Tianxingjianyikang Granule is based on the theory of traditional Chinese medicine and consists of 10 traditional Chinese medicines.

Objective

To evaluate the effects of Tianxingjianyikang Granule on D-GAL induced aging rat brain tissue, and reveal its mechanism and efficacy, which will lay a foundation for the development of anti-aging health care products.

Materials and methods

60 male SD rats were randomly divided into blank group, model group, vitamin E positive control group, Tianxingjianyikang Granule low dose, middle dose and high dose groups, with 10 rats in each group. The aging model was established by intraperitoneal injection of D-GAL, except for the blank group, and the other 5 groups of rats were intraperitoneal injection of D-GAL solution according to the standard 0.5g/kg for a total of 42 days of modeling. From the 15th day of modeling, vitamin E positive control group was given vitamin E solution at the standard of 27mg/kg, Tianxingjianyikang Granule low dose, middle dose and high dose groups were given vitamin E solution at the standard of 1.35g/kg, 2.7g/kg and 5.4g/kg, respectively, blank group and model group were given normal saline at the same volume once a day. A total of 28 days of intragastric administration. During the experiment, the changes of general state of rats in each group were observed. After the experiment, the body weight of 60 rats was measured last time. The brain tissue

of rats was taken out quickly and completely in the ice box, its mass was weighed, and the organ index was calculated. The contents of SOD, GSH-Px and MDA in brain tissue were determined. HE staining sections of rat brain tissue were made to observe the changes of hippocampal morphology.

Results and discussion

According to the experimental results, compared with blank group, the general state of model group was poor, including rough, dry and loose skin, decreased exercise and depressed mental state, etc. Compared with model group, the general state of rats in each administration group was improved to varying degrees; Compared with blank group, organ index, SOD and GSH-Px activities in brain of model group were significantly decreased ($P < 0.01$), MDA content was significantly increased ($P < 0.01$); Compared with model group, Tianxingjianyikang Granule could increase the organ index and the activities of SOD and GSH-Px in brain of rats in each group ($P < 0.05$ or $P < 0.01$), decreased the content of MDA ($P < 0.05$ or $P < 0.01$); in the blank group, the hippocampal tissue structure was compact, the cytoplasm and nucleus were clearly stained. No hyperemia or edema was observed. In the model group, the tissue structure of the hippocampus was loose, the nucleus was obviously pyknotic, the number of apoptotic bodies, microglia and inflammatory cells was significantly increased. Compared with model group, hippocampal tissue morphology of rats in all drug administration groups was improved to varying degrees, among which vitamin E group and Tianxingjianyikang Granule high dose group had the most obvious improvement.

Tab. Effects on the brains of aging rats induced by D-GAL ($\bar{x} \pm s$, $n = 10$)

Group	index of the brain(%)	SOD(U/mgprot)	GSH-Px(umol/L)	MDA(nmol/mgprot)
Blank group	0.61±0.03**	464.36±54.41**	41.09±4.81**	3.54±0.62**
Model group	0.47±0.03###	326.14±47.53###	28.54±3.19###	6.54±0.64###
Vitamin E group	0.58±0.03**	422.94±47.22**	37.15±3.49**	4.12±0.62**
Low dose group	0.50±0.02*	342.41±37.14	32.01±3.02*	5.82±0.78*
Middle dose group	0.54±0.03**	371.18±35.83*	33.13±3.40**	5.85±0.87*
High dose group	0.58±0.03**	410.22±42.16**	38.16±2.84**	4.18±0.53**

Note: compared with model group, * $P < 0.05$, ** $P < 0.01$; compared with blank group, ### $P < 0.01$.

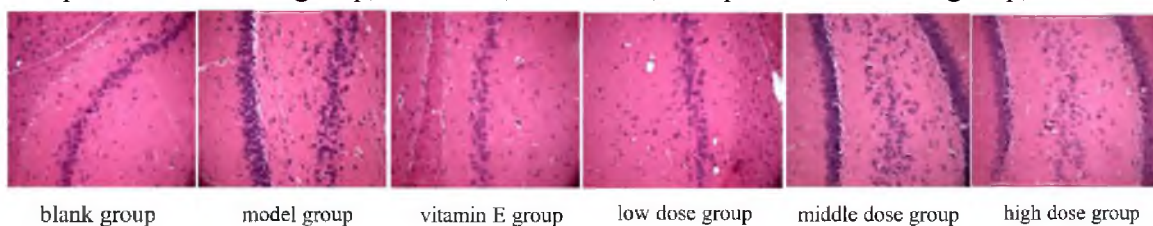


Fig. morphological observation results of hippocampal area in each group of rats

Thus, Tianxingjianyikang Granules can improve the general state and brain atrophy of aging rats, increase the activities of SOD and GSH-Px in the brain tissue of aging rats, and reduce the content of MDA, so as to resist the oxidation of brain, and improve the tissue morphology of hippocampus in the brain of aging rats. It has certain effect on delaying brain aging.

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Experimental study on antioxidative effect of Shenwei Granule on D-GAL induced aging rats

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Abstract

Objective: To evaluate the antioxidant capacity of Shenwei Granule on D-GAL induced aging rats, and to lay a foundation for the development of anti-aging health care products. **Methods:** The model was established by intraperitoneal injection of D-GAL. Blank group, model group, VE group (positive control group), Shenwei Granule low dose, middle dose and high dose groups were set up. Modeling lasted for 42 days. On the 15th day, gavage was started simultaneously. After the last administration, blood was taken from abdominal aorta. Liver, spleen and thymus were taken to calculate the organ index, and superoxide dismutase (SOD), malondialdehyde (MDA) and glutathione peroxidase (GSH-Px) in serum and liver were measured concurrently. **Results:** After giving different doses of Shenwei Granule, the organ index of D-GAL induced aging rats increased markedly, the levels of SOD and GSH-Px in serum and liver were significantly increased, while the level of MDA was decreased. **Conclusion:** Shenwei Granule can improve the organ atrophy state of aging rats, improve antioxidant capacity, and has a certain effect on delaying aging.

Key words: Shenwei Granule, D-GAL, Aging, Antioxidant

Aging is a stage that everyone has to go through. Modern medical studies on anti-aging mainly focus on anti-oxidation, scavenging free radicals and other contents. As the concept of great health has gained popularity, traditional Chinese medicine (TCM) is prominent in the field of anti-aging research, and the application of TCM to delay aging has attracted more attention. Shenwei Granule is made of Ginseng, Poria cocos, Rhizoma Atractylodis Macrocephalae, Black plum, Schisandra chinensis and other traditional Chinese medicines, which plays an important pharmacological role in delaying natural aging and has certain clinical research value.

Objective

This experiment investigated the effects of Shenwei Granule on organ index and SOD, MDA and GSH-Px in serum and liver of aging model rats, in order to provide experimental basis for the efficacy study of Shenwei Granule.

Materials and methods

Sixty healthy male SD rats with body weight of 180-220g were randomly divided into blank group, model group, VE group (positive control group), Shenwei Granule low dose, middle dose and high dose groups, with 10 rats in each group. Except the blank group, the aging model of rats was established by intraperitoneal injection of 0.5g/kg D-GAL, and the blank group was intraperitoneal injection of 0.9% sodium chloride with the same volume, once a day. From the 15th day, VE group (27mg/kg) and Shenwei Granule low dose, middle dose and high dose groups (1.35g/kg, 2.7g/kg, 5.4g/kg) were given intragastric administration, the other groups were given the same amount of normal saline, once a day. The body weight of 60 rats was weighed after the last administration, and blood was taken from abdominal aorta after chloral hydrate anesthesia. The tissues of liver, spleen and thymus were collected and weighed to calculate the organ index. SOD, MDA and GSH-Px in

serum and liver tissues of rats were determined according to corresponding ELISA kit instructions.

Results and discussion

The results showed that compared with the blank group, organ indexes of liver, spleen and thymus in model group were significantly decreased ($P<0.01$), suggesting that organ atrophy might occur in D-GAL induced aging model rats. The levels of SOD and GSH-Px in serum and liver were significantly decreased ($P<0.01$), and the level of MDA was significantly increased ($P<0.01$). Compared with model group, organ indexes of liver, spleen and thymus of aging rats in VE group and Shenwei Granule low dose, middle dose and high dose groups were increased to varying degrees ($P<0.05$; $P<0.01$); The levels of SOD and GSH-Px in serum and liver were significantly increased ($P<0.01$ or $P<0.05$), while the level of MDA was significantly decreased ($P<0.01$ or $P<0.05$). (See Table 1-2 for details).

Tab1. Determination of SOD, MDA and GSH-Px in serum of D-GAL induced aging rats
($\bar{X}\pm S$, n=10)

Group	SOD(U/ml)	MDA(nmol/ml)	GSH-Px(umol/L)
Blank group	647.04±44.52**	2.19±0.46**	1939.28±200.77**
Model group	544.38±55.64###	4.75±0.69###	1604.97±197.79###
VE group	622.69±47.28**	2.74±0.40**	1900.40±170.32**
Low dose group	586.28±35.32*	3.38±0.43**	1704.13±270.57
Middle dose group	592.29±49.99*	3.01±0.40**	1806.23±187.13*
High dose group	618.45±33.07**	2.68±0.66**	1884.79±141.19**

Note: Compared with model group, * $P<0.05$, ** $P<0.01$; Compared with blank group, ### $P<0.01$.

Tab2. Determination of SOD, MDA and GSH-Px in liver of D-GAL induced aging rats
($\bar{X}\pm S$, n=10)

Group	SOD(U/mgprot)	MDA(nmol/mgprot)	GSH-Px(umol/L)
Blank group	504.31±48.72**	0.60±0.13**	171.92±25.22**
Model group	345.33±32.37###	1.08±0.22###	108.49±18.44###
VE group	465.28±38.71**	0.59±0.17**	153.54±21.18**
Low dose group	388.87±46.31*	0.93±0.17*	128.22±25.36*
Middle dose group	418.97±48.08**	0.88±0.17**	130.12±16.95*
High dose group	452.63±42.47**	0.71±0.13**	140.03±19.63**

Note: Compared with model group, * $P<0.05$, ** $P<0.01$; Compared with blank group, ### $P<0.01$.

In conclusion, Shenwei Granule can improve the organ atrophy state of D-GAL induced aging rats to a certain extent. At the same time, the levels of SOD and GSH-Px in serum and liver of aging rats were increased and the level of MDA was decreased in the three dose groups of Shenwei Granule, which improved the antioxidant capacity of rats and delayed the aging of rats.

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The new development of the Sino-Russian health industry based on traditional Chinese medicine

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Abstract:

With the gradual deepening of Sino-Russian strategic cooperation, the exchange and cooperation of the medical and health industry has also entered a new process. The development of the big health industry is required by the trend, and the Sino-Russian health industry cooperation can better improve the development of the health industry of the two countries one step closer, thereby improving the development level of the health industry of the two countries and promoting the in-depth cooperation between the two countries. Based on traditional Chinese medicine, this paper briefly discusses the application and development of traditional Chinese medicine in the Russian health industry through a summary and analysis of the overall geography and living customs of Russia. At the same time, it can also promote further exchanges and development of the health industry between China and Russia.

Keywords: big health industry; Traditional Chinese Medicine; Exchange and cooperation; Healthcare

The vast territory of Russia has complex climatic characteristics, but because most of the land is above 60 degrees north latitude, only a small part of the region belongs to the oceanic and monsoon climate, and most of the regions are obvious continental climates, so the overall climate is cold and long, the winter experience is long, and the rest of the seasons are short. What kind of climate also determines what kind of living habits, because of its cold climate, in order to adapt to the living environment, so only the intake of its high-calorie food can resist the cold, so their diet is based on high oil and high fat, and the taste is dominated by high salt, high sugar, and high oil. Therefore, in Russia, its cardiovascular and cerebrovascular diseases, obesity, diabetes and other diseases are multiple diseases, endangering the health of the Russian people. Medicine is part of the big health industry, the innovation of the pharmaceutical part is also the innovation of the big health industry, so through traditional Chinese medicine as the base point, improve the medical exchanges between China and Russia, use the theory of traditional Chinese medicine to provide new methods and theories for the great health of Russia, improve the level of the big health industry of the two countries, and promote the development of the health industry of the two countries.

Great health under the guidance of Chinese medicine

As one of the most important parts of the cause of traditional Chinese medicine, the development process of traditional Chinese medicine dominates, according to the four flavors of traditional Chinese medicine, functional indications, and through modern pharmacological methods, summarize the composition of drugs suitable for the Russian people, and then through the method of dialectical treatment, through the comprehensive analysis of the overall health status to achieve the overall concept of traditional Chinese medicine, summarize the appropriate prescription drugs for the people. Finally, through traditional Chinese medicine forms, pastes, pills, soup recipes and other traditional Chinese medicines or other modern dosage forms such as injections, the best

method suitable for its people is summarized. Thus the development of medicine, to further promote the development of the health industry.

Great health under the guidance of acupuncture

Acupuncture is the most influential part of traditional Chinese medicine in the world, is also the most indispensable part of traditional Chinese medicine, acupuncture as a green therapy, has the advantage of side effects, can be well applied to the big health industry, but also can promote the exchange of talents, improve the development of technical talents, not only promote the development of the pharmaceutical industry, but also promote the progress, and finally promote the combined development of the entire big health industry, from medicine and talent development have achieved the real progress and development of the big health industry.

Great health under the guidance of TCM exercises

Traditional Chinese medicine has a long history and is one of the treasures of traditional Chinese culture, promoting the development of Chinese health care. As an indoor exercise, TCM gongfa can first avoid Russia's cold climatic conditions, and TCM gongfa has the characteristics of softness, avoiding strenuous exercise, which is suitable for various groups of people, and there is obvious prevention and improvement of disease.

Through the combination of the above three, it can better promote the development of traditional Chinese medicine in the health industry, and at the same time, it can also spread the culture of traditional Chinese medicine, improve the influence of the traditional Chinese medicine industry, and finally further promote the exchange and innovation of the great health cause between the two countries

Summary and outlook

The big health industry is the future trend needs, the exchange and development of the health industry is indispensable, through traditional Chinese medicine as the base point, to promote the development of the big health industry between China and Russia is not only to promote the development of the health industry, but also to promote the deepening of strategic cooperation between the two countries, so as to make the exchanges between China and Russia more frequent, but also to promote the progress between the two countries.

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China's TCM Comprehensive Health Industry Development Status and Innovation Thinking

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Abstract: With the rapid development of economy and people's growing health needs, the comprehensive health industry has emerged and gradually developed and grown. In order to promote the new development of comprehensive health industry, it is an important element to build a platform for comprehensive health industry by giving full play to the characteristic advantages of Chinese medicine. The paper summarizes the background, development status and prospect of comprehensive health industry in China, and the development mode of TCM in comprehensive health industry. And it proposes the innovative ideas and practice models that have the possibility to realize the development of TCM in comprehensive health. It is hoped that the development of comprehensive health industry will be considered in many aspects of digitalization, economization and socialization, and the advantageous characteristics of ethnic medicine will be brought into play.

Key words: China's comprehensive health industry; development status; industry innovation; TCM development model

Objective: The purpose of this article is to analyze the current situation of the development of the TCM comprehensive health industry, to explore the possibilities for the sustainable development of TCM, and to promote innovation in the internationalization of TCM.

Due to the rapid development of the economy and the growing health needs of the people, the comprehensive health industry has emerged and gradually developed. In China, the comprehensive health industry covers medical equipment manufacturing, Chinese medicine health system, high-end medical and health services, precision medicine, digital medical and other aspects, the industry runs through the whole process of people's clothing, food, housing, transportation and birth, old age, sickness and death. The comprehensive health industry of TCM is a new concept of the whole picture, and its development revolves around various types of health needs such as mental, physical, social, environmental and moral standards^[1]. Since 2015, when the Chinese government first proposed the concept of "Healthy China" in its work report, the importance of "Healthy China" as a long-term national policy has been continuously highlighted. In the "14th Five-Year Plan" issued by the State Council in April 2022, we can see that the promotion of the new state and new mode of the health industry has become one of the national initiatives to protect the health of the nation, and the advantages of Chinese medicine is an important part of the construction of the health industry platform.

1. Background, development status and prospect of comprehensive health industry in China

In *The outline of the health China strategy for the new era*, it is pointed out that the people's pursuit of health and a better life, economic and social transformation and upgrading, and the establishment of a national governance system are the important purposes and significance of building a "Healthy China"^[2]. At present, the developed countries have formed a complete industrial chain in the comprehensive health industry, in the scale and system has been perfected, forming a model of mutual assistance and reciprocity between the health industry and economic growth. In contrast,

China's health industry has only recently started, far below the level of developed countries in Europe and the United States. With the increasing intention of the state to support the health industry, policies such as the "Health China 2030 Planning Outline" have been introduced one after another. No matter from the macroeconomic or microeconomic point of view, the development prospect of comprehensive health industry has unlimited power.

2. TCM health concept and comprehensive health industry

The health concept of TCM is characterized by "prevention before illness" and "prevention and control of aggravation of illness". As the traditional medical model "disease - cure - recovery" changes to the modern health model "prevention - treatment - health". The health industry, based on the concept of Chinese medicine, is considered a strategic new industry with great economic and social value. First of all, due to the COVID-19 epidemic, the online medical model is quietly emerging, and technological means such as remote consultation and medical data are driving the transformation of medical resource allocation. Chinese medicine has played an important role in the fight against COVID-19 epidemic, especially in the prevention and rehabilitation phases. At the same time, people's awareness of TCM has been increased because of the increased publicity channels^[3]. Secondly, Chinese medicine has the characteristics of low cost, stable nature, real efficacy, and relatively low toxic side effects, and plays a role in the treatment of chronic diseases that is unmatched by Western medicine. These advantages are in line with the virtuous cycle model of combining medical treatment and health care pursued by the comprehensive health industry. The third point is that TCM is one of the key industries protected by the state, and China clearly encourages the development of TCM. Premier Li Keqiang had said at the government work report meeting, "We will support the inheritance, innovation and development of traditional Chinese medicine, we will promote the integration of traditional Chinese and western medicine."

3. The development mode and innovative thinking of Chinese medicine in comprehensive health industry

The development mode of Chinese medicine in the comprehensive health industry in China is mostly focused on the research and development of medicinal herbs, medicine and food, rehabilitation medicine and health care for the elderly. China's Chinese herbal medicines amount to 12,807 kinds of herbs and 600 kinds of commonly used herbs, providing resources for the development of Chinese medicine's comprehensive health industry. The development mode of Chinese medicine in the comprehensive health industry in China is mostly focused on the research and development of medicinal herbs, medicine and food, rehabilitation medicine and health care for the elderly. China's Chinese herbal medicines amount to 12,807 kinds of herbs, and 600 kinds of commonly used herbs, which provide resources for the development of Chinese medicine's comprehensive health industry^[4]. In the health care market and herbal cosmetics market, the market demand size was RMB 400 billion and RMB 110 billion respectively in 2014 alone. In many of the production areas of the local herbs, because of the Belt and Road policy to ride on the economic express of the comprehensive health industry^[5]. At present, China is in the normalization stage of epidemic prevention and control, restoring economic and social development, promoting high-quality economic development of the key period. Therefore, TCM should rely on the continuous development of the comprehensive health industry and help the domestic industry to expand the international pharmaceutical and health field. Increase the integration with the Internet,

policies and regulations to bring into play the comprehensive health industry with the unique advantages of TCM, and tap the potential of TCM modernization and digital development. Cultivate TCM innovation and entrepreneurial talents in the comprehensive health industry, and develop curriculum based on the division of labor system in the comprehensive health industry.

Conclusion and Discussion

The development of TCM health industry has unlimited prospects, but it is a long way to go. We should analyze the current situation of the industry from the perspective of internationalization of TCM industry and seek innovative development strategies from the perspective of health for Chinese people. Consider the development from digitalization, economization and socialization in many aspects while giving full play to the advantageous characteristics of ethnic medicine.

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Clinical study on the treatment of stroke hemiplegia by staged acupuncture combined with transcranial repetitive acupuncture

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Abstract

Objective: To explore the clinical efficacy of staged acupuncture combined with transcranial repetitive acupuncture on stroke hemiplegia. **Methods:** Sixty cases of stroke hemiplegia patients were selected randomly divided into observation group and control group, with 30 cases in each group. The control group was given traditional acupuncture combined with transcranial repetitive acupuncture, while the observation group was given staged acupuncture combined with transcranial repetitive acupuncture. After the same courses of treatments, evaluating the clinical efficacy, the neurological function, motor function and quality of life of the two groups. **Results:** Comparing the clinical efficacy after treatment, the total clinical efficiency of the observation group was higher than that of the control group (90.26% vs 73.87%, $P < 0.05$). After treatment, the scores of FMA and MBI in both groups were higher than before, and the observation group's was higher than the control group's ($p < 0.05$). While, the scores of the NIHSS and CSS in both groups were lower than before, and the observation group's was lower than the control group's ($P < 0.05$). **Conclusion:** Both treatments are effective in improving the neurological function, motor function and quality of life in stroke hemiplegia patients. Staged acupuncture combined with transcranial repetitive acupuncture has better efficacy.

Keywords: Stroke hemiplegia, Staged acupuncture combined with transcranial repetitive acupuncture, Clinical study

Stroke is characterised by a high incidence, high mortality and high disability rate worldwide. Hemiplegia after stroke, which is mainly a motor impairment of the limbs, is most common and places a great burden on patients' themselves, their families and society¹.

Acupuncture is widely used in the treatment of stroke hemiplegia, and its efficacy is confirmed. Under the guidance of concept of "The Great Health", staged acupuncture is used according to Brunnstrom's different stages in the treatment of stroke hemiplegia, due to the theory of considering body constitution in treating disease and treatment based on pattern differentiation, which can restore limb functions in a more targeted manner.

Objective

To explore the clinical efficacy of staged acupuncture combined with transcranial repetitive acupuncture on stroke hemiplegia.

Materials and methods

Sixty patients with stroke hemiplegia who were hospitalized in the Five Department of Acupuncture in the Second Hospital of Heilongjiang University of TCM from May 2021 to May 2022 were selected and divided into observation group and control group by random number table method, and there were 30 patients in each group, the two groups were comparable with no statistical difference ($P > 0.05$).

Transcranial repetitive acupuncture: The selected acupoints are the motor area, Baihui, Shuang

Shencong, Shenting and Shuaigu, each acupoint is performed with a rapid twisting technique at 200 r/min for 3 to 5min.

Control group: On the basis of transcranial repetitive acupuncture combined with conventional body acupuncture, the selected points were Hegu, Waiguan, Shousanli, Quchi, Jiquan, Liangqiu, Xue hai, Fenglong, Yinlingquan, Yanglingquan, Zusanli, Sanyinjiao, Xuanzhong and Taichong, applying 0.30 mm x 40 mm acupuncture needles to pierce 13~25 mm directly.

Observation group: Based on the transcranial repetitive acupuncture, and due to Brunnstrom's theory² (stage I: flaccid phase; stage II: mild spasticity; stage III: increased spasticity; stage IV: reduced spasticity; stage V: establishment of voluntary movement; stage VI: movement close to normal), divide stroke hemiplegia into the soft paralysis period (Brunnstrom I~II), the spasticity period (Brunnstrom II~III), the recovery period (Brunnstrom IV~V) and the sequelae period (continuous Brunnstrom III), and different acupuncture techniques are used according to the characteristics of each period³. (1) Soft paralysis period: In this period, the patient's muscle strength and tone are low. Selecting the acupoints of healthy side like Binao, Quchi through Shousanli, Yangchi through Waiguan, Biguan through Futu and Yanglingquan through Xuanzhong, while 0.30 mm x 75 mm acupuncture needles were used for the upper limb acupoints and 0.30 x 125 mm needles were used for the lower limb. The needles were left in place for 30 minutes, once a day. In addition, Binao and Waiguan can be selected from the upper limbs, while Zusanli and Fenglong from the lower limb, using a 1ml syringe to draw methylcobalamin injection for acupoint injection therapy, once every other day. (2)The spasticity period and the recovery period: The patient had increased muscle tone and muscle spasm in these periods. Jianqian, Sanjian through Houxi, Biguan, Taibai through Shugu were selected acupoints used 0.30 mm x 75 mm acupuncture needles. Furthermore, the wrist and ankle needles using 0.30 mm x 40 mm acupuncture needles were applied on the affected side for antagonistic movements. The patient was instructed to perform flexion and extension and rotation movements of the wrist and ankle joints, and the needles were retained for 30 minutes once a day. (3)The sequelae period: 0.30 mm x 40 mm needles were used to Hegu, Waiguan, Shousanli, Quchi, Jiquan, Liangqiu, Xuehai, Fenglong, Yinlingquan, Yanglingquan, Zusanli, Sanyinjiao, Xuanzhong and Taichong of the affected side which were pierced 13~25 mm. While Guanyuan and Qihai were pierced 30~35 mm.

The treatment was 1 time per day, and 6 days constituted a course, with a total of 4 courses for both of the two groups. Refer to Fugl ~ Meyer Motor Function Assessment Scale (FMA), Modified Barthel Index (MBI), National Institutes of Health Stroke Scale (NIHSS) and Chinese Stroke Clinical Neurological Deficit Scale (CSS) to evaluate the effectiveness of treatments.

Results and discussion

Comparing the clinical efficacy after treatment, the total clinical efficiency of the observation group was higher than that of the control group (90.26% vs 73.87%, $P < 0.05$), which was statistically significant. Before treatments, the FMA and MBI in the control group were 33.83 ± 3.77 and 48.66 ± 7.13 respectively, while 34.65 ± 4.28 and 48.09 ± 6.89 in the observation group respectively. After treatments, the FMA and MBI in the control group were 71.85 ± 6.07 and 68.45 ± 6.58 respectively, while 81.03 ± 6.58 and 82.51 ± 7.89 in the observation group respectively. The scores of FMA and MBI in both groups were higher than before, and the observation group's was higher

than the control group's ($p < 0.05$). Before treatments, the NIHSS and CSS in the control group were 17.87 ± 2.73 and 37.26 ± 3.98 respectively, while 17.38 ± 2.66 and 36.96 ± 3.57 in the observation group respectively. After treatments, the NIHSS and CSS in the control group were 10.88 ± 1.57 and 18.65 ± 1.89 respectively, while 5.74 ± 1.02 and 9.51 ± 1.52 in the observation group respectively. The scores of the NIHSS and CSS in both groups were lower than before, and the observation group's was lower than the control group's ($P < 0.05$).

Therefore, staged acupuncture combined with transcranial repetitive acupuncture is effective and worthy of clinical application.

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Application of Liuwei Dihuang Pill in senile diseases

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Abstract

Liuwei Dihuang pill is the holy agent of nourishing kidney essence. It has the function of filling marrow, nourishing yin and tonifying kidney. It is widely used in senile diseases, involving nervous, respiratory, digestive, endocrine and other systems. This paper summarizes the clinical research of Liuwei Dihuang Pill in senile diseases in recent 20 years, in order to provide theoretical basis for the application and development of Liuwei Dihuang pill.

Key words: Liuwei Dihuang pill, Geriatric diseases, Application, Clinical research

Liuwei Dihuang Pill (formerly known as Dihuang pill) was cut from the kidney qi pill in the synopsis of the golden chamber by song Qianyi. The whole prescription is composed of prepared Dihuang, Cornus, dried yam, Alisma orientalis, peony bark and poria cocos. It can fill the essence, nourish yin and tonify the kidney, and mainly treat the deficiency of kidney yin and essence. It can be used for the treatment of soreness of waist and knees, night sweats, nocturnal emission, blurred vision, tinnitus and deafness, dizziness, and thirst-quenching, etc. It is regarded by later generations as the holy agent for nourishing kidney essence, and is also the representative formula of "three tonics" and "three purges". The kidney is the congenital foundation, and the deficiency of kidney yin and essence is closely related to the occurrence of senile diseases. Modern pharmacological studies have found that Liuwei Dihuang pill has significant effects in delaying aging, anti-tumor, improving immunity, improving cardiovascular and cerebrovascular systems, etc. Suggesting that Liuwei Dihuang pill can be widely used in the prevention and treatment of senile diseases.

Objective

This paper summarizes the clinical research of Liuwei Dihuang Pill in senile diseases in the past 20 years, In order to provide theoretical basis for the application and development of Liuwei Dihuang pills.

Materials and methods

Retrieve China hownet, ten thousand China academic journals database, d PuZhongWen science and technology periodical database, the Chinese biomedical literature database and PubMed database in both English and Chinese, in search of Liuwei Dihuang pill in diseases of aging related literature, the publication time for January 1, 2002 - January 1, 2022, filtering and sorting of literature.

Results and discussion

1.Treatment of hypertension

Taking Liuwei Dihuang pill with standard western medicine can improve the quality of life of elderly patients with hypertension to a certain extent, improve the symptoms of TRADITIONAL Chinese medicine, stabilize the condition, and improve the overall curative effect of traditional Chinese medicine.

2.Treatment of coronary heart disease complicated with hyperlipidemia

Liuwei Dihuang Pill has a synergistic effect with rosuvastatin, which can effectively regulate the

blood lipid level of patients with coronary heart disease complicated with hyperlipidemia, reduce inflammation, improve vascular endothelial function, and reduce the incidence of adverse reactions.

3.Treatment of insomnia

In the treatment of elderly patients with primary insomnia (liver and kidney Yin deficiency), Liuwei Dihuang Pill and Huanglian Ejiao Decoction can significantly improve sleep quality, prolong sleep time, relieve depression and anxiety, regulate neurotransmitters, fewer side effects and high safety.

4.Treatment of Alzheimer's disease

The addition of Liuwei Dihuang Pill on the basis of conventional Western medicine can significantly enhance the efficacy of mild and moderate AD, improve the TCM syndrome, and improve the living ability and intelligence of patients.

5.Treatment of schizophrenia

Conventional western medicine combined with Liuwei Dihuang Pill can significantly improve the cognitive function and schizophrenia symptoms of patients, and can increase the levels of serum nerve growth factor (NGF), brain-derived neurotrophic factor (BDNF), interleukin (IL-2), IL-6, tumor necrosis factor (TNF $-\alpha$). Significantly reduced the level of glial fibrillary acidic protein factor (GFAP) and serum Hcy in elderly schizophrenia patients.

6.Treatment of recurrent oral ulcer

In the treatment of senile recurrent oral ulcer, adding Liuwei Dihuang pill can significantly enhance the curative effect, relieve oral pain and reduce the recurrence rate.

7.Treatment of oral candida

Liuwei Dihuang Pill combined with Western medicine has a better effect on the treatment of oral candidiasis in the elderly, which can improve the overall clinical efficacy and promote the rehabilitation of patients.

8.Treatment of diabetes

Liuwei Dihuang pill combined with metformin can significantly improve the levels of blood glucose and blood lipid in diabetic patients and improve the curative effect. In addition, studies have found that acupuncture combined with Liuwei Dihuang Pill can significantly reduce insulin resistance in elderly patients with type 2 diabetes (kidney-yin deficiency), reduce blood glucose level and improve clinical symptoms and signs of TRADITIONAL Chinese medicine.

9.Treatment of herpes zoster

The addition and reduction of Liuwei Dihuang Pill can improve the clinical symptoms of herpes zoster and improve the quality of life by enhancing immunity .

10.Treatment of chronic bronchitis

Liuwei Dihuang Pill has a preventive and therapeutic effect on chronic bronchitis in the elderly, which can regulate the immune function and reduce the recurrence rate.

11.Treatment of knee arthritis

Liuwei Dihuang Pill has a synergistic effect with sodium hyaluronate, which can reduce the serum CRP level and inflammatory response of patients, with definite curative effect.

12.Treatment of osteoporosis

Liu Wei Dihuang Pill can relieve the clinical symptoms of elderly male patients with osteoporosis, improve bone mineral density, and accelerate the synthesis of osteocalcin. Combination with conventional Western medicine can enhance the efficacy.

13. Treatment of chronic gastritis

Liuwei Dihuang pill is effective in treating chronic gastritis with little side effect.

14. Treatment of sexual dysfunction

Liuwei Dihuang pill combined with low dose of testosterone can promote the release of sex hormone and improve the sexual dysfunction of elderly men.

15. Treatment of urinary tract infections

Liuwei Dihuang Pill can also prevent and cure recurrent urinary tract infection, which can reduce the recurrence rate.

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To investigate the effect of rhizoma *Dioscoreae nipponicae* extract on hyperuricemia rats based on gut microbiome under the concept of big health

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Abstract

The article introduces the effect of rhizoma *Dioscoreae nipponicae* extract on gut microbiota in rats with hyperuricemia(HUA). The content of serum uric acid, and creatinine blood urea nitrogen was analyzed by a fully automated biochemical analyzer, and the changes in the gut microbiome were detected by 16S rRNA sequencing. The analysis results showed that the rhizoma *Dioscoreae nipponicae* extract significantly improved uric acid levels in HUA rats, reduced uric acid levels, had a protective effect on the kidney, significantly adjust the abundance and uniformity of the corresponding flora, improve the species richness of beneficial flora in the intestine of HUA, and reduce the abundance of harmful flora. It is speculated that the mechanism may be related to the regulation of intestinal flora structure.

Key words: rhizoma *Dioscoreae nipponicae* extract, hyperuricemia, gut microbiome, 16S rRNA

Hyperuricemia (HUA) is a metabolic disease caused by the imbalance of uric acid production and uric acid excretion due to the disorder of uric acid metabolism. In recent years, due to the obvious changes in dietary structure, the intake of purine has increased significantly, and the prevalence of HUA has increased sharply. The prevalence of HUA in China is between 10-35%, close to the level of western developed countries. HUA is an independent risk factor for metabolic diseases (diabetes, metabolic syndrome, hyperlipidemia, etc.), chronic kidney disease, and cardiovascular and cerebrovascular diseases. It is located in the alpine zone adjacent to Russia and has similar characteristics to HUA in northeast China. Therefore, it is of great significance to study the prevention and treatment of HUA. The popularization of the concept of great health also promotes the development of traditional Chinese medicine.

DIOSCOREAE NIPPONICAE RHIZOMA, a traditional Chinese medicine, has the main functions of dispelling wind and dampness, relaxing tendons and collaterals, promoting blood circulation, and relieving pain, and relieving cough and asthma. Its main active ingredient is rhizoma *Dioscoreae nipponicae* extract. Modern research has shown that *DIOSCOREAE NIPPONICAE* RHIZOMA has various pharmacological effects such as reducing uric acid levels, anti-inflammatory, anti-tumor, and hypoglycemic. Insufficient excretion of uric acid (SUA) plays a core role in the pathogenesis of HUA. Our previous study found that *DIOSCOREAE NIPPONICAE* RHIZOMA can reduce serum uric acid levels and promote uric acid excretion in HUA rats and mice by inhibiting URAT-1 and promoting ABCG2. Gut microbiota plays an important role in maintaining human health, and intestinal microecological therapy has become a new treatment strategy for HUA. HUA can lead to intestinal flora imbalance, resulting in intestinal mucosal damage, changes in intestinal permeability, reduction of probiotics, and an increase of pathogenic bacteria. Therefore, we speculate that *DIOSCOREAE NIPPONICAE* RHIZOMA can interfere with the development of HUA by regulating intestinal flora and body metabolism. The research on the intervention of *DIOSCOREAE NIPPONICAE* RHIZOMA on the intestinal flora is of great significance for the continuous

improvement of disease prevention, diagnosis, treatment, and rehabilitation.

Objective

To study the effect of rhizoma *Dioscoreae nipponicae* extract on the intestinal flora of HUA rats, and analyze the blood and intestinal flora of the rats to provide a basis for clinical treatment of HUA.

Materials and methods

SD male rats were fed with 10% yeast diet and molded with potassium oxyzincate solution by gavage for 4 weeks to establish a hyperuricemic rat model, and were randomly divided into model group, rhizoma *Dioscoreae nipponicae* extract group, allopurinol group and blank control group. On the 15th day of modeling, the rhizoma *Dioscoreae nipponicae* extract group was given rhizoma *Dioscoreae nipponicae* extract (400 mg·kg⁻¹), allopurinol group was given allopurinol (25mg·kg⁻¹), and the other two groups were given the same volume of distilled water for 14 consecutive days. The levels of uric acid, creatinine, and blood urea nitrogen were measured by an automatic biochemical analyzer to detect the changes in blood biochemical indexes in rats. The contents of the terminal cecum of 4 rats in each group were randomly extracted. It is used for high-throughput sequencing of 16S rRNA intestinal flora. The Illumina platform is used to perform paired-end sequencing of the community DNA fragments, and the Alpha and Beta diversity of the intestinal flora of each group of rats and the intestinal flora of each group of rats are analyzed. Analysis of differences in species composition, etc., to study the effect and mechanism of rhizoma *Dioscoreae nipponicae* extract on the HUA rat model.

Results and discussion

In this experiment, we successfully established an HUA model by combining yeast feed with Interacial potassium and evaluated the therapeutic effect and intestinal flora of rhizoma *Dioscoreae nipponicae* extract on HUA rats based on pharmacodynamic studies and 16S rRNA technology. Compared with the blank group, the contents of uric acid and creatinine in the type group were significantly higher ($P<0.01$), and with renal pathological changes. Compared with the model group, the serum uric acid content in the rhizoma *Dioscoreae nipponicae* extract group was significantly lower ($P<0.01$). Intestinal flora 16S rRNA gene sequencing analysis showed that compared with the blank control group, the species richness and evenness of intestinal flora in the model group were decreased; Compared with the model group,pielou-E index, Shannon index and Simpson index in the rhizoma *Dioscoreae nipponicae* extract group were significantly increased ($P<0.05,0.01$), and the species richness and evenness of intestinal flora were significantly increased. The results of species composition and difference analysis of intestinal flora in each group showed that, at the phylum level, the abundance of Proteobacteria in the rhizoma *Dioscoreae nipponicae* extract group was significantly reduced ($P<0.01$) and the ratio of Firmicutes to Bacteroides was increased ($P<0.05,0.01$). At the genus level, the rhizoma *Dioscoreae nipponicae* extract group could significantly down-regulation the abundance of Parabacteroides and Bacteroidetes, and increase the abundance of Lactobacillus and Ruminococcaceae_Ruminococcus ($P<0.05$).

In addition, this study also found that rhizoma *Dioscoreae nipponicae* extract can up-regulate the abundance of Acinetobacter, Turicibacter, Pseudomonas, down-regulate the abundance of Fecal bacteria, Parabacteroides and Bacteroides. Promote the restoration of normal structural levels of intestinal flora in HUA rats. To sum up, rhizoma *Dioscoreae nipponicae* extract can play a

therapeutic effect by improving the structure and abundance of intestinal flora and thus reducing the level of uric acid. To sum up, rhizoma *Dioscoreae nipponicae* extract can play a therapeutic effect by improving the structure and abundance of intestinal flora and thus reducing the level of uric acid.

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Based on the protective effect of *Dioscorea Nipponica* Makino extract on hyperuricemia in the context of big health

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Abstract:

This article describes the potential biomarkers and mechanisms of action of *Dioscorea Nipponica* Makino (DNM) in the treatment of hyperuricemia. Metabolomics methods using ultra-high liquid chromatography mass spectrometry (UPLC-MS) screened for potential biomarkers and combined with pharmacodynamic indicators demonstrated the therapeutic effect of DNM in hyperuricemia. Based on the results of the analysis, we noticed that DNM extract can reduce uric acid and inhibit the inflammatory response. In addition, a total of 31 potential markers associated with HUA were identified in rat urine. It provides a theoretical basis for finding the target of DNM in the treatment of hyperuricemia.

Key words: *Dioscorea Nipponica* Makino ; Hyperuricemia; Metabolomics; Biomarkers

Hyperuricemia (HUA) is a metabolic disease in which purine metabolism disorders or decreased uric acid excretion lead to excessive accumulation of uric acid in the body, which is the basis for gouty arthritis (GA) and various metabolic syndromes. According to the survey, the number of patients with hyperuricemia in China has reached 170 million, and it is increasing rapidly at an annual growth rate of 9.7%. Hyperuricemia has become the second largest metabolic disease in human beings after diabetes, and the subsequent development of gouty arthritis has seriously affected people's lives and health. With the implementation of the "13th Five-Year Plan" proposals, Healthy China was officially upgraded to the "National Strategy". The health industry has become a global hotspot. Chinese medicine as a green, natural medicine has become the focus of research. The pharmacopoeia records that the DNM *Qufengchushi*, *Shujinhuoluo* and *Huoxuezhitong*, and has anti-inflammatory, hypoglycemic uric acid, anti-tumor, hypoglycemic and other pharmacological effects. DNM is applied to rheumatic paralysis, joint swelling, pain numbness and so on. In previous experiments, we found that it has anti-inflammatory and uric acid-lowering effects. Therefore, this study aims to use metabolomics techniques to explore the mechanism of action of DNM in the treatment of HUA, and to compare the changes of metabolites in vivo and find regulatory pathways related to these products, It is of great significance for the interpretation of the scientific connotation of the treatment of HUA by DNM.

Objective

To establish a HUA rat model induced by potassium oxonate acid, conduct metabolomics analysis of urine, look for relevant potential targets, mechanisms of action and metabolic pathways, and explore the protective effect of DNM on hyperuricemia.

Materials and methods

30 SPF-grade SD rats were randomly divided into blank control group, model group, and DNM extract group (RDN group), with 10 rats in each group. A rat model of hyperuricemia was induced by gavage potassium oxonate and 10% yeast feed. Starting at 15 days, the dosing group was given RDN (0.4 g/kg). After 14 consecutive days of administration, after the last administration, serum

uric acid (UA), xanthine oxidase (XOD), creatinine (Cr), tumor necrosis factor (TNF)- α , interleukin (IL)-1 β and IL-6 levels were detected in the serum; Collect rat urine and analyze urine samples using ultra-high performance liquid chromatography tandem time-of-flight mass spectrometry UPLC-Q-TOF/MS. Principal components analysis (PCA) and partial least squares-discriminant analysis (PLS-DA) were used to compare urine metabolism profiles of different groups of rats to observe the effect of RDN on the content of potential biomarkers in the urine of treated RAT HUA rats. Plot THE VIP-plot plot to screen out potential biomarkers for VIP>1. By retrieving metabolic pathway databases such as the Human Metabolome Database (HMDB), the Kyoto Encyclopedia of Genes and Genomes (KEGG) and MetaboAnalyst, the mechanism of RDN intervention in the treatment of HUA was analyzed and discussed from the perspective of differential metabolites and metabolic pathways.

Results and discussions

The results of the pharmacodynamic study showed that compared with the normal control group, the serum levels of UA, XOD, Cr, IL-6, TNF- α , and IL-1 β in the model group were significantly increased ($P<0.05$, $P<0.01$). The above indicators of animals in the RDN group were obviously improved compared with those in the model group ($P<0.05$, $P<0.01$). The results of the urine metabolomics analysis showed significant differences in the metabolic profiles between the blank, the model and the RDN groups, we screened for 31 potential biomarkers from urine. These potential biomarkers are enriched in metabolic pathways such as tryptophan metabolism, phenylalanine metabolism, tyrosine metabolism, methionine circulation, and cysteine conversion ($P>0.10$).

Traditional Chinese medicine has obvious advantages in the treatment of chronic diseases, but due to the existence of multi-component, multi-target characteristics of traditional Chinese medicine, it is difficult to study the acting ingredients and pharmacological mechanisms of traditional Chinese medicines by traditional means, and the method of obtaining urine samples is simple, does not damage organisms, and can be sampled for dynamic analysis many times in a row, so this paper uses metabolomics and combines traditional theories to explore the mechanism of action of DNM extract in the treatment of HUA. RDN can affect the urine metabolism profile of HUA rats and alleviate the deviation of HUA production. The comprehensive analysis of related biological metabolites and metabolic pathways provides data and theoretical support for the in-depth study of the mechanism of action of hua, lays the foundation for clinical application, and contributes to the great health industry.

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Literature research on moxibustion to prevent stroke

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Abstract

To summarize the clinical application of moxibustion preventing stroke among general population with potential cardiovascular risk factors in literature from ancient to the present. Terms include “moxibustion”, “prevention”, “prevent”, “stroke”, “stroke signs”, “transient ischemic attack”, “TIA”, “high blood pressure” were searched as “title”, “keywords” or in “abstract” in CNKI and Pubmed from January 1st, 2000 till July 1st, 2022. We found 34 relevant articles and summarized 5 representative clinical methods of moxibustion to prevent stroke from Tang Dynasty to the present, compare different practices ranging from symptoms, acupoints, details of procedures, aims to sources of moxibustion as a preventive therapy.

Keywords: stroke, moxibustion, prevention, acupoints

According to *European Heart Journal* and *Circulation*, cardiovascular diseases (CVD) has become the leading cause of death in both China(36%)^[1] and Russia(46%)^[2]. Stroke is one of the main CVD that happens widely across the world in middle-aged and elders. Although once stroke could be an acute incidence, what indeed cause trouble are the sequelae after a stroke happened, involving physical and language disabilities、sensory disturbance、dysphagia and even inability to control bowel movements, which undermine one’s dignity and bring great pain to the patient’s family, while weighting financial burden to the country. Fortunately, before an actual stroke happens, “stroke signs” always appear first, taking transient ischemic attack (TIA) and high blood pressure for examples^[1]. Based on traditional Chinese medicine theory, moxibustion is a harmless and cost-effective health care measure to prevent most population from stroke. In general, moxibustion refers to use the heat generated by burning herbal preparations containing *Artemisia vulgaris* to stimulate acupuncture points on human body for positive effects^[3]. Herein we go through several papers regarding the clinical application of moxibustion in the prevention of stroke, attempt to find out some patterns of this promising therapy.

Objective

To summarize the clinical application of moxibustion preventing stroke among general population (mainly adults) with potential cardiovascular risk factors in literature from ancient to the present.

Materials and methods

Literature exploring the clinical usage of moxibustion preventing stroke from ancient to the present, terms include “moxibustion”, “prevention”, “prevent”, “stroke”, “stroke signs”, “transient ischemic attack”, “TIA”, “high blood pressure” were searched as “title”, “keywords” or in “abstract” in CNKI and Pubmed from January 1st, 2000 till July 1st, 2022. We mostly focus on selections of particular acupoints、representative methods of moxibustion and the medical theories stand behind

them.

Results and discussion

We found 34 relevant articles and summarized 5 representative clinical methods of moxibustion to prevent stroke from Tang Dynasty to the present, compare different practices ranging from symptoms, acupoints, details of procedures, aims to sources of moxibustion as a preventive therapy (the table). Moxa cones or moxa bars used in moxibustion have dual characters, they are medicine as well as tools. The medical effect comes from the way *Artemisia vulgaris* has been processed. This plant needs to be stored properly at least 3 years to acquire mild fire nature to cure diseases. Ancient Chinese doctors reckon that moxa's nature suits exactly for stroke's pathogenesis. It's a process gradually caused by disharmony between Yin and Yang, leading to disturbance of Qi and Blood, invasion of an evil wind and further generate pathological products such as an excessive fire in the upper, phlegm and stagnated blood in meridian system, which moxibustion can eliminate by its mild fire^[4,5]. It has been proved that moxibustion with grain-size cones in TIA patients can help promote vertebrobasilar arterial insufficiency and reduce dizziness^[6]. Massive moxibustion on CV4, ST36 2 hours per day lasts for 2 weeks alters TIA patients' blood flow condition significantly^[7]. Overall, moxibustion is expected to be an ideal health care measure to prevent stroke nationwide since it's simple and effective.

Table. Summary of Methods on Moxibustion to Prevent Stroke

symptoms	acupoints	procedures	aims	sources
Feeling restless or numbness in limbs	GV20, GB20, GV14, GB21, LI11, PC5, ST36	Start moxibustion immediately from head to legs, each acupoint lights 3 grain-size moxa cones for 14 days	Descending kidney-Yang back to the lower abdomen	Tang Dynasty· Sun Simiao Thousand-Gold Complementary Formula· Stroke; Sun Jifei, 2020 ^[6]
Sudden sore feet and knees that take long time to relieve	ST36, GB39	Each acupoints light 3 moxa cones directly on the skin to make wounds, then shower it with decoction made from spring onions, mint, peach leaves and willow leaves	Wounds made by moxibustion will activate one's physical ability to cure and defend evil wind from nature and inside the body	Ming dynasty· Yang Jizhou A Complete Works on Acupuncture· Overview of Curing Diseases; Liu Yueyuan, Song Xin, Qu Jian, et al, 2016 ^[7]
Dizziness, numb limbs, temporal soft paralysis, clumsy tongue,	GB20, ST36	Enteric-coated aspirin and Heat-sensitive Moxibustion for	Using the heat from moxibustion to improve blood flow, eliminate	Tian Ning, 2011 ^[4]

syncope		40min/d, last for a month	wind-evil qi hidden in blood	
Transient numb toes, lopsided tongue or ache lingual root, dizziness, headache, temporal amaurosis, cyanotic tongue with ecchymosis	GV20	Moxibustion with emedicinal cake made by powder of Panax notoginseng, Sichuan pepper and cinnamon, then do He's head and facial massage, 15days as a session	moxibustion with warm Yang and activating blood herbs provide a positive stimulation to both nerves and brain blood vessels, massage will help stimulate Yang Qi either	Gou Wulin, Wang Peng, 2017 ^[8]
Anxious, headache, dizziness, palpitation, shaky hands, bitter taste in mouth, dry mouth, constipation, reddish urine, numb limbs	ST36, GB20, GB21, GV12, BL18, BL23, CV12, CV6, LI10	Moxibustion with moxa cone or moxa bar per day, lasting for at least one month	Benefitng Qi meanwhile subduing Yang to prevent stroke	Zhang Jianbin, Li Hao, Zhou Yin, et al, 2019 ^[5]

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Clinical Observation On The Treatment Of Chronic Insomnia With Penetrate Acupuncture

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Abstract

Objective: This clinical study observed and compared the therapeutic effect difference between the penetrate acupuncture method and the conventional acupuncture method in the treatment of chronic insomnia, to explore a better clinical treatment for chronic insomnia.

Methods: The 60 patients with chronic insomnia selected in this clinical practice were randomly divided into two groups according to the sequence of visiting, namely the control group (conventional acupuncture group) and the treatment group (penetrate acupuncture group). There were 30 cases in each group, and 3 cases in the two groups fell off during the study. Finally, the clinical study was completed with 29 cases in the control group and 28 cases in the treatment group. In the control group, acupoints Baihui, Sanyinjiao, Anmian, Shenmen, Zhaohai and Shenmai were selected. The treatment group selected acupoints Yintang, Shenting to Baihui, Shendao to Lingtai, left and right Shencong, Anmian, Taiyang, Fengchi, Shenmen and Neiguan. The needles retaining was kept for 50 minutes in both groups, once a day, and the efficacy was evaluated after 4 weeks of continuous treatment. By observing and comparing the Pittsburgh Sleep Quality Index (PSQI) total score and individual scores before and after treatment between the two groups, the degree of symptom improvement and differences in clinical efficacy were evaluated.

Results: There were no significant differences in the basic conditions and observation indicators before treatment between the two groups ($P>0.05$). The comparisons of PSQI total score and individual scores before and after treatment in the two groups were significantly different ($P<0.01$). The comparisons of PSQI total score and PSQI difference before and after treatment between the two groups were highly significant ($P<0.01$), and the decrease of PSQI score of the treatment group was more obvious. Comparing individual PSQI scores between the two groups after treatment, the treatment group was significantly better than the control group in improving sleep quality ($P<0.01$), and better in improving time before falling asleep, time of sleep duration, sleep disorders, and daytime function ($P<0.05$); there is no difference between the two groups in terms of sleep efficiency ($P>0.05$). Comparing clinical efficacy between the two groups, the control group had a total effective rate of 82.76%, and the treatment group had a total effective rate of 92.86%, indicating the difference was highly significant ($P<0.01$), and the treatment group was better than the control group.

Conclusion: Penetrate acupuncture method can improve various related symptoms of patients with chronic insomnia, especially the aspect of sleep quality; the method was better than conventional acupuncture in the treatment of chronic insomnia.

Keywords

Chronic insomnia, Penetrate acupuncture, Clinical observation

Pain Relief For Tendinopathy In Sham-acupuncture Controlled Clinical Trials

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Abstract

Tendinopathy is a common soft tissue disease caused mainly by repeated mild tendon injuries or tendon degeneration for overuse. During excessive exercise, the frequency and speed of loads increase dramatically, which repeatedly puts heavy pressure on muscle tendons. Accordingly, the disease is more common in athletes and the elderly, generally manifested as pain in and surround tendons, anthorisma or local swelling, or joint dysfunction. This kind of pain is very harmful to human health. Acupuncture is widely applied to soothe pain in clinical practice.

In recent years, the effectiveness of acupuncture in clinical pain relief has been a research hot spot worldwide, involving over 31 countries and regions. Among 8 multi-centered, blind, and large control trials initiated in Germany, 6 clinical trials^[1,2] reported that there was no difference in the effectiveness between the acupuncture trial group and the sham acupuncture plus placebo group. While both groups had a better effectiveness than the drug therapy group, this finding brought tremendous impacts and challenges to traditional acupuncture theory. Conversely, several systematic reviews^[3-5] indicated that the acupuncture group had a better performance in relieving chronic pain than the control group. However, their effectiveness was limited as their control group adopted such sham acupuncture treatments as drugs, exercises or physical treatments. Thus, the systematic review and meta-analysis, with tendinopathy patients as research subjects and sham acupuncture treatments adopted in the control group, evaluated the analgesic effect of acupuncture in tendinopathy using an evidence-based medicine method.

Key words: tendinopathy; acupuncture; sham acupuncture; pain; meta-analysis

Objective

The analgesic effect of acupuncture remains a hot dispute according to foreign studies. This systematic review analyzed the analgesic effect of acupuncture in tendinopathy and compared it with that of sham acupuncture, primarily exploring whether the pain relief of acupuncture in tendinopathy is a kind of “placebo” effect.

Materials and methods

Based on the Cochrane Handbook for Systematic Reviews of Interventions, randomized controlled trials on the acupuncture treatment for tendinopathy published until April 2022 were searched not only from foreign and domestic databases but also from American Clinical Trial Registry Platform (<https://clinicaltrials.gov>) and Chinese Clinical Trial Registry Platform (www.chictr.org.cn). Included trials adopted acupuncture treatment in the trial group and sham acupuncture (non-acupoint, non-penetrating and subcutaneous penetration) in the control group. Statistical analysis was performed based on the data extracted from these trials using RevMan5.3 and Stata15.0.

Results and discussion

A total of 21 trials were included, with 836 patients in total, 426 cases in the acupuncture group and

410 cases in the sham-acupuncture group, respectively. The present study analyzed the visual analogue scale (VAS), pressure pain threshold (PPT) and motor function of limbs after treatment and during follow-up. In terms of these analyses, the acupuncture group showed better results than the sham acupuncture group, with VAS (MD = -1.67, 95% CI [-2.27, -1.07], P<0.01), follow-up VAS (MD = -1.05, 95% CI[-2.07], -0.02], P = 0.05), PPT (MD = 1.17, 95% CI[0.93, 1.42], P<0.01), and function score (MD = 1.07, 95% CI[0.32, 1.82], P<0.01).

The mechanical theory of tendon injury indicates that “overload” of the tendon tissue is considered to be fundamental to the pathologic process. During this process, microscopic failure may occur within tendons, especially with reperable to vascular complications in specific areas^[6]. At an acupuncture research conference in 1997, the National Institutes of Health (NIH) in America proposed the concept of sham acupuncture and encouraged us to take it as a control when researching the efficacy of acupuncture. This proposal was a milestone in sham acupuncture research. There are many reasons for the international controversy: acupuncture has the same efficacy as placebos. First, current Western medicine differs from traditional Chinese medicine in the main paradigm basis for treatment. Western medical adopts the mechanical cytopathology paradigm, which requires to take intervention measures for well-studied or virtualized pathological changes at the level of our cells.^[7] Nevertheless, it is not ideal for chronic diseases. That's because most chronic diseases are closely associated with immune system imbalance, disorders of the immune-neuro-endocrine system, and related mental disorders. On the other hand, as foreign studies tend to take sham acupuncture as a general standard to judge the analgesic effect of acupuncture when designing control trials, they ignore that the whole process of acupuncture treatment involves patients' psychological and psychoactive effect. That resonates with the concept of regulating mental activities proposed in the Inner Canon of Huangdi, one of the earliest medical classics in China. This kind of doctor-patient bodily contacts and affective communications is essential for nonspecific therapy, but it is hard to quantify and standardize in clinical trials.^[8]

In reference to Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) statement and also in compliance with related guidance, the present systematic review performed literature search and statistical analysis of data, so as to comprehensively analyze VAS before and after treatment, follow-up VAS, PPT as well as limbs motor functions before and after treatment. Existing evidence indicated that acupuncture had a better performance in the immediate pain relief for tendinopathy than sham acupuncture. Specifically, in the acupuncture group, patients' pain was relieved and the pain threshold increased; VAS score in mid- and long-term prognosis was lower than the immediate continuing score; and the functions of tendons and joints were also improved. Despite high quality of the included clinical trials, the present study had a limited sample size. In the future, we will continue to keep a close eye on this theme in order to further study the long-term analgesic effect of acupuncture with a larger sample size.

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Application of metabolomics in the treatment of type 2 diabetes mellitus with traditional Chinese medicine

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Abstract:

Type 2 diabetes mellitus (T2DM) is a kind of endocrine disease with chronic hyperglycemia caused by insulin resistance (IR) and/or deficiency of insulin secretion. The incidence of T2DM and its complications is increasing year by year. In the world, traditional Chinese medicine (TCM) is often used to assist the treatment of T2DM. The TCM has obvious effects and is widely accepted, but its mechanism is still largely unknown. Metabolomics is a new research method, which provides an opportunity to clarify the theory of TCM and the mechanism of Chinese herbal medicine treatment. In recent years, metabolomics has been widely used to elucidate the mechanism of TCM in the treatment of T2DM. This paper reviews the application of metabolomics in the treatment of TCM in T2DM.

Keywords: T2DM, TCM, metabolomics, biomarker, metabolic pathway, treatment

1 Background

Diabetes is a metabolic disease characterized by hyperglycemia, which is due to the decrease of insulin secretion and the action of insulin resistance (IR). Once the onset of diabetes, the body metabolism is easy to be in disorder. The incidence of diabetes is increasing year by year, and more than 90% of cases belong to type 2 diabetes (T2DM). T2DM can lead to serious microvascular and macrovascular complications. The traditional Chinese medicine (TCM) has been treating T2DM for thousands of years. There are a lot of records about diabetes in *Huangdi Neijing*. Meanwhile, the TCM has great potential in the treatment of metabolic diseases, which plays an important role in reducing blood glucose, delaying or alleviating diabetic complications.

At the end of the 20th century, the concept of metabolomics was put forward by Nicholson, which was specifically defined as the quantitative measurement of dynamic multi parameter metabolic response of biological system caused by the stimulation of pathophysiology or gene change [1]. Metabolomics will become a new and reliable technology in the future, which will bring great benefits to patients in diagnosis and treatment. It regards organisms as a dynamic whole and studies the metabolic changes of the organism caused by internal and external factors. Metabolomics is consistent with the overall concept of TCM. Therefore, metabolomics can explain and explore the essence of TCM in treating diseases. The purpose of this article is to review and summarize the application of metabolomics in the treatment of T2DM with TCM.

2 Application of metabolomics in the treatment of T2DM with TCM

Up to now, metabolomics has been widely used to explore the principle of TCM treatment of T2DM. TCM treatment of T2DM is multi-channel and multi-target. It can be concluded that TCM mainly treats T2DM by acting on glucose metabolism, fatty acid metabolism, amino acid metabolism and so on. These findings can be summarized as follows.

2.1 Glucose metabolism

Abnormal glucose metabolism is an important mechanism of T2DM. The abilities of glycogen synthesis and gluconeogenesis in T2DM patient increase, while that of glycolysis decreases. Gegen Qinlian Decoction (GQD) also regulates the balance between glucose catabolism and anabolism by reducing gluconeogenesis and increasing glycolysis, making the metabolic profile of T2DM rats close to that of healthy rats [2]. IR is mainly due to the disturbance of signal transduction such as ins R/IRS1/PI3K/Akt/GLUT4, which leads to the decrease of insulin-mediated glucose uptake and utilization in target insulin sensitive tissues. Yinlantiaozhi capsule (YLTZ) can enhance insulin sensitivity by influencing this insulin signaling pathway [3].

2.2 Fatty acids metabolism

Long term high level of free fatty acids can induce or aggravate IR, and lead to the development of T2DM. This may be related to the inhibition of peripheral glucose utilization and the promotion of gluconeogenesis by fatty acids. Under the condition of high fatty acid, the oxidation metabolism of fatty acid is enhanced, and the gluconeogenesis reaction is active. In addition, excessive fatty acids also interfere with insulin signaling by affecting protein kinase C (PKC) induced insulin receptor substrate 1 (IRS-1) phosphorylation. Berberine can down regulate the high level of free fatty acids in patients' serum, and thus mediate glucose and lipid metabolism.

2.3 Amino acid metabolism

The increase of branched chain amino acids level aggravates the damage of insulin sensitivity. The study [4] had shown that Qijian mixture can regulate the metabolism of amino acids by reducing the levels of leucine, isoleucine and valine. In vivo, most of phenylalanine are oxidized to tyrosine by phenylalanine hydroxylase, and then transformed into important neurotransmitters and hormones, which are involved in glucose metabolism and fat metabolism. The level of phenylalanine is higher in T2DM patients. *Potentilla discolor* can also reduce the level of phenylalanine.

3 Conclusion and future considerations

The development of T2DM involves many metabolic pathways, such as glucose, fatty acid, amino acid and so on. TCM can regulate these metabolic pathways to reduce plasma glucose levels or enhance insulin sensitivity. With the continuous development of metabonomics, a breakthrough will be made in the early diagnosis, prevention and treatment of T2DM. In the future, metabonomics will show great advantages in TCM syndrome differentiation and treatment and in clarifying the mechanism of TCM action (Figure 1).

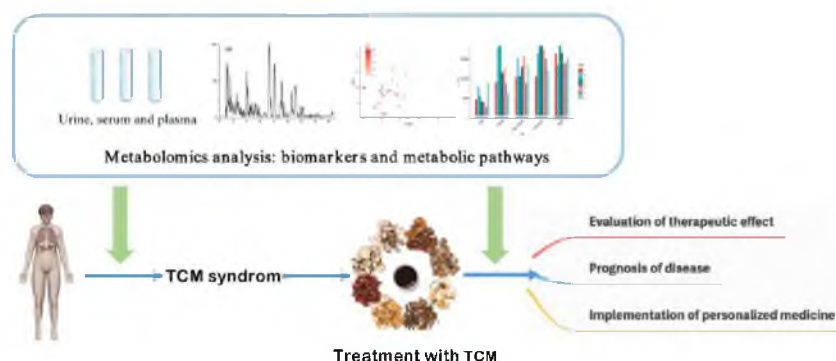


Fig. 1 The application of metabolomics in the treatment of T2DM with TCM in the future

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Analysis of the Application Value of Leech in Cardiovascular Diseases Based on a Large Health Background

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Abstract

"Great health" is a comprehensive concept based on human health based on the development of the times and social needs. At the same time, with the development of society and the intensification of the aging population, the prevalence of cardiovascular diseases in China has gradually increased. It is very necessary to use traditional Chinese medicine to prevent and treat cardiovascular diseases. Leech is a traditional Chinese medicinal herb. Its main active ingredient is polypeptide protein. It has anticoagulant, antithrombosis, anti-inflammatory, regulating blood lipids, etc. It has great potential in the prevention and treatment of cardiovascular diseases. Therefore, the promotion of the concept of "great health" may bring great opportunities and challenges to the traditional Chinese medicine-leech industry. This article aims to elaborate the clinical value of leech for the reference of relevant researchers and enterprises.

Key words: great health, leech, cardiovascular disease, anticoagulant

Leech, also known as locust, has a long history of medicinal use at home and abroad. It is a dry whole of leech, leech, willow leaf leech, European medical leech, lateral medical leech, etc. Modern pharmacological studies have found that ¹, the active components of leech are mainly polypeptide protein macromolecules, and the pharmacological effects are characterized by anticoagulant activity: ①anticoagulant polypeptide: thrombin inhibition peptide, Xa factor inhibition peptide, platelet aggregation inhibition peptide, anticoagulant peptide, ②protease activity inhibitor peptide: trypsin inhibition peptide, other protease Antibody peptides, ③ anti-inflammatory peptides, etc. Leech can be applied clinically to the treatment of cardiovascular diseases. The main mechanisms of action are: inhibiting platelet activation and accumulation, inhibiting and reducing anti-inflammatory response, regulating endothelial cell function, anticoagulation and promoting fibrinolysis, regulating blood lipids and stabilizing plaques, etc.².

Cardiovascular disease (CVD) is a type of disease involving the heart or blood vessels. It is ischemic or hemorrhagic diseases in the heart and blood vessels caused by hyperlipidemia, blood viscosity, atherosclerosis, hypertension, etc. Ageing, hypertension, smoking, diabetes and obesity are the main risk factors for CVD. CVD is a major public health problem that endangers the world and plagues cardiovascular doctors, and is also the main cause of premature human mortality. Relevant literature shows that³ by 2030, CVD will be the cause of 30.5% of human deaths worldwide. At the same time, the mortality rate of cardiovascular diseases in high-income areas has decreased in the past few decades, but 50% of cardiovascular mortality and 80% of the global burden of cardiovascular diseases occur in low- and middle-income. Equal-income countries (LMIC). The prevalence of CVD in China is closely related to population aging, CVD risk factors and medical level. Only in the context of population growth and aging, the annual growth rate of cardiovascular disease events is expected to exceed 50% between 2010 and 2030, and the current trend of risk factors will make

cardiovascular during this period. The growth rate of disease events increased by another 23%⁴. Therefore, with the intensification of aging and the transformation of social lifestyles, cardiovascular diseases will be a serious challenge facing our country and the world.

Objective

To explore the mechanism of leech active ingredients in the treatment of cardiovascular diseases, which can provide new ideas for the prevention and treatment of cardiovascular diseases.

Materials and methods

Search for leeches, cardiovascular diseases, atherosclerosis and other keywords from the database, select qualified papers, sort out the paper data and analyze them.

Results and discussion

The main pathological change of cardiovascular disease is atherosclerosis, which is formed by the accumulation of fat, cholesterol and inflammatory cells in the coronary vascular system, leading to plaque formation and limited blood flow⁵. Relevant research shows that thrombin can regulate the pathogenesis of atherosclerosis by enhancing the expression of adhesion molecules, chemokines, cytokines, etc., enhancing the proliferation of smooth muscle cells, and stimulating monocytes, T lymphocytes and fibroblasts in atherosclerosis⁶. Hirudin is a polypeptide molecule extracted from leech. It is the strongest natural specific thrombin inhibitor found so far, so it has an anti-atherosclerosis⁷. Guo and other scholars⁸ found that recombinant hirudin may play an anti-atherosclerosis by regulating blood lipid levels and inhibiting the p38 MAPK/NF- κ B signaling pathway, thus protecting the blood vessels and anti-apoptosis effects of AS rats and protecting the vascular endothelium.

Leech was first recorded in the Shennong Herbal Sutra. It is flat, salty, bitter, and slightly poisonous. It has the effect of breaking the meridian and removing blood stasis, and different processing methods will produce different levels of active ingredients⁹. Modern research shows that leech has extremely high medicinal value, containing at least 51 compounds, which can mediate various vascular regulation signaling pathways, such as antithrombosis, anticoagulation, anti-inflammatory and antiplatelet aggregation pathways. It can not only treat cardiovascular diseases, but also serve as an adjuvant treatment for diseases such as venous embolism, diabetic feet and tumors¹⁰. Therefore, under the concept of "great health", we should pay attention to the clinical value and scientific research value of leech, in order to find new ideas for the treatment of chronic diseases, and at the same time promote the improvement of the traditional Chinese medicine leech industry.

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Sarcopenia in Liver Cirrhosis: from Mechanism to Treatment Based on TCM Visceral Manifestation Theory

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Liver cirrhosis, due to its chronic wasting characteristics and frequent complications, seriously affect the patient's physical. Sarcopenia which is one of the complications of cirrhosis is a syndrome reduced mass and strength of skeletal muscle. Some problems exist in the pathogenesis, diagnosis and treatment of sarcopenia in Modern medicine. The traditional Chinese medicine theory and treatment have been to be effective by researches. This article explores the treatment strategies of sarcopenia in liver cirrhosis from the liver, spleen and kidney based on the visceral manifestation theory.

Key words: sarcopenia, liver cirrhosis, visceral manifestation theory

Cirrhosis is the chronic progressive liver structure and function disorder caused by multiple etiologies, which is the main factor in the death of liver-related diseases worldwide, making the nutritional status and function of patients bad. In China, cirrhosis of the liver is mainly based on hepatitis B, while alcoholic hepatitis is the main factor for it in Europe and the United States. Sarcopenia is a syndrome characterized by progressive and generalized reduction in skeletal muscle mass and strength. European Working Group on Sarcopenia in Older People defines it as a syndrome of progressive reduction in muscle mass, strength and function, which leads to the decrease in body function and quality of life. The incidence of sarcopenia in patients with cirrhosis is 40% to 70%, and sarcopenia is closely related to the survival rate and complications of patients with cirrhosis.

Objective

At present, sarcopenia in liver cirrhosis lacks standardized diagnosis and treatment worldwide. There are still some problems in the treatment of sarcopenia by modern medical. China and Russia have a high incidence of liver cirrhosis. This essay aims to explore the TCM mechanism and treatment strategy of sarcopenia in cirrhosis from the perspective of the visceral manifestation theory.

Materials and methods

The pathogenesis of sarcopenia in cirrhosis are not thoroughly understood, such as insufficient energy intake in patients, hunger response acceleration, activation of signaling pathways in hyperammonemia, growth hormone and testosterone content decrease, systemic inflammatory response caused by cirrhosis, activation of ubiquitin-proteasome system and autophagy increasing, resulting in protein homeostasis imbalance, hydrolysis increase, which decreases muscle mass. Interventions for sarcopenia are mainly to improve living habits, increase protein intake, avoid prolonged starvation, promote energy intake, and maintain a positive nitrogen balance. The transjugular intrahepatic portosystemic shunt (TIPS) and liver transplantation restore liver function and reduce complications. Some studies have demonstrated that testosterone, rifaximin and other drugs have certain improvement effect on sarcopenia, but the clinical data is less. Further research

in the future will benefit diagnosis and treatment of patients with sarcopenia in liver cirrhosis. The theory of TCM to identify and treat sarcopenia has achieved effect in many researches. According to the TCM theory, the sarcopenia can be classified as flaccidity syndrome or consumptive disease, or other categories. The etiology and disease mechanism treat from pattern differentiation with the visceral manifestation theory of liver, spleen and kidney. The combination of TCM and modern medicine will obtain a better treatment effect, which is the new research direction in the future.

In the perspective TCM theory, the etiology of cirrhosis can be summarized as liver depression and qi stagnation, blood stasis and obstructing collaterals, dampness-heat exuberance, yin deficiency and retention of water fluid, etc., which is the physiological functions disorder of the liver, spleen, stomach, kidneys and other organs. The liver demonstrates its splendor on the nails, nourishing the sinews and producing blood, which ensures the normal use of the tendons and claws. The spleen and stomach are the roots of granary, which transform food into nourishment with nutrient-qi to nourish the muscle. The kidney, the house of essence, coordinates with the bones, nourishing the marrow, which makes power for movements. After the liver cirrhosis, blood and yin deficiency in the liver cannot nourish the tendons, resulting in contracture of tendons. The spleen qi insufficiency with dampness encumbrance, resulting in muscle atrophy and limbs useless. The disharmony between liver and spleen makes disorder of qi movement, and blood stasis. Yin and yang in kidney cannot undertake the glory of qi and blood produced by the spleen and stomach. The vital qi from long-term liver cirrhosis patients has been damaged. The three viscera are damaged, with the bones, tendons and muscles losing the nourishment from qi, blood, liquid and humor, resulting dysfunction.

Results and discussion

The sarcopenia in cirrhosis can treat with nourishing liver yin and blood, strengthening spleen and harmonizing stomach to benefit qi, on the same time, with the treatment of soothing liver to regulate qi and eliminating dampness. Function of liver yang bases on yin and blood, so that the function of tendons and vein is normal without disease. Strengthening spleen, the root of acquired constitution, and benefiting qi make the muscle get the nourishment without dampness and phlegm in order that the limbs muscle function can recover. The *Yellow Emperor's Canon of Medicine* says that treatment for flaccidity aims at stomach meridian Foot-YangMing. In addition to strengthen spleen qi, the meridians of the spleen and stomach should be adjusted, so that the function can be restored, without being disturbed by evil. Kidney is the innate foundation, and filling the kidney essence is the key in the treatment of sarcopenia, which strengthen muscle and bones. The spleen and kidneys are co-main, the liver and kidneys are of the same origin. The qi, blood, fluid and essence are used for each other, and the musculoskeletal bones complement mutually. During the treatment of sarcopenia, it should not be the only method to treat the liver, while the viscera are systemic. The overall treatment to improve the efficacy of disease diagnosis and treatment, in TCM theory, calls Concept of Wholism.

Previous studies have shown that Chinese medicine with strengthening spleen and benefiting qi can exert anti-inflammatory effects through a variety of pathways, and ShenQi compound recipe can upregulate the expression level of GLUT4 protein in skeletal muscle, and improve skeletal muscle mass and function to a certain extent. A supplementing kidney compound can activate the signaling

pathway, improve the expression of protein in the bones and skeletal muscle of the corresponding pathway, promote osteogenesis differentiation, and increase bone density. Through the theory of TCM and clinical treatment effect, it can be concluded that TCM has a certain effect on sarcopenia. However, the existing researches were mostly a single experimental study, so there is still a lack of experimental studies. Furthermore research will benefit treatment and prevention of sarcopenia in liver cirrhosis.

TCM is the particular part of Chinese excellent traditional culture, but also the treasure of world medicine. Treating sarcopenia in liver cirrhosis with TCM theory from liver, spleen and kidney plays its therapeutic characteristics. China and Russia have a high incidence of cirrhosis. Exploring the mechanism of post-hepatitis cirrhosis and its complications with TCM theory promotes communication and cooperation in the biomedical industries of China and Russia, contributing to healthy function.

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Effect of TCM acupoint application on simple obesity

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Simple obesity is no obvious diseases of the nervous system, endocrine system, but because the body of the calories consumed more than the quantity of heat that use up, supernormal cause accumulation of visceral and subcutaneous fat and weight, the formation is given priority to with obesity and metabolic disorder diseases^[1], its incidence in developed countries and developing countries are rapidly rising, It has become an important global public health problem affecting human life quality and health.

Adipose tissue is a place to store energy and also plays a role as an endocrine organ. It synthesizes and releases various adipokines with specific biological functions in the form of autocrine and paracrine^[2]. Therefore, we find that the existence and disappearance of obesity are closely related to adipokines.

Traditional Chinese medicine has remarkable effect in the treatment of simple obesity. Among the acupoints on the human body, Shenque acupoint has the function of invigorating the spleen and benefiting qi, and can regulate lipid metabolism. Shenque acupoint (navel) is the one with the most special structure and the most definite location. Umbilical organs through the viscera, connected to the body meridians is the total meridian pivots, qi hui sea. Through relevant experiments, it has been proved that the application of Shenque point through the skin of *Wucornus officinalis* can treat obesity and regulate lipid metabolism. The sophomore College of Traditional Chinese Medicine in Heilongjiang province mixed the drugs of *atractylodes macrocephala*, *Atractylodes atractylodes*, *Poria cocho* and *Rhizoma ceratidis* into umbilicus patch, which can effectively improve obesity and slow down weight growth. Ear point sticking can also be used to treat childhood obesity, and animal experiments have further proved that acupoint sticking can improve the structure of fat cells and the level of inflammatory factors in cells in simple obesity rats, thus reducing the occurrence of obesity.

Key words: Simple Obesity, Acupoint Sticking Therapy

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Professor Cong Huifang's experience in treating threatened abortion by tonifying kidney and activating blood circulation

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Abstract

As a common disease in women's pregnancy, the causes of threatened abortion show a diversified trend. The progress of modern medicine and the improvement of patients' medical cultural literacy have made this disease more attention, so that more timely and accurate prevention and treatment can be carried out. Traditional Chinese medicine identifies this disease as threatened abortion and fetal movement uneasiness. At the same time, the main clinical features are lower abdominal pain, lumbosacral pain and bulge, and a small amount of vaginal bleeding. In clinical treatment, Sanqi, Angelica and Ziheche Sanwei are often used as the basis of prescription for treatment, which are used to invigorate the kidney and replenish the essence, invigorate qi and activate blood, and remove blood stasis and regenerate new ones. The usual dosage is 3g of Panax notoginseng, 10g of Angelica sinensis, and 2g of Ziheche fine powder.

Key words: threatened abortion; Benefit kidney; invigorate the circulation of blood

Objective

Threatened abortion is the occurrence of bloody vaginal discharge before 20 weeks of pregnancy, which may be accompanied by suprapubic discomfort or persistent low back pain, of which vaginal bleeding is the most predictive risk factor [1]. Western medicine believes that its etiology includes embryo, mother, father and environment [2]. Traditional Chinese medicine believes that the main pathogenesis is the imbalance of Chong Ren's Qi and blood and the lack of solid fetal yuan [3]. Chen su'an proposed that "pregnancy and fetal movement are uneasy, which will probably blunt the blood deficiency of the second meridian of Ren". Western Medicine suggests that the treatment of threatened abortion is mainly observation and bed rest, but it often does not improve the pregnancy outcome. Cong Shi, in line with the idea of "prevention before falling", prevented the pregnancy outcome of "death if blood runs out", and intervened against women with adverse pregnancy conditions, so as to achieve good fetal protection effect.

Materials and methods

According to the traditional dialectical thought of traditional Chinese medicine [4], relying on the diagnosis of modern medicine and following the dialectical thinking of traditional Chinese medicine, teacher Cong determined the classic prescriptions and medicines, and paid attention to the "antecedents" and "consequences" before and after the disease, so as to achieve the clinical effect of "treating the disease and stillbirth". This paper summarizes professor cong huifang's experience in the treatment of threatened abortion with the method of Tonifying the kidney and activating blood circulation.

1. The imbalance between impulse and responsibility is always the cause.

"New edition of pulse formula" points out that "the fate of those who leak blood from the husband and fetus is different". There are also many discussions on the causes and pathogenesis of medical

diseases in ancient literature, such as "there are seven causes..." recorded in the summary of Guangsi, According to the general record of Shengji, "you Chong Ren is weak and cannot maintain the fetus". However, the causes of this disease can be summarized into four categories: blood heat, weakness of Qi and blood, deficiency of spleen and kidney, and trauma. These four factors will lead to the failure of Chong Ren to reconcile, and eventually the fetus is unstable and threatened abortion. Therefore, only by "rushing to be Ronghe, like a fish in the abyss, can children and mothers be at peace."

2. Stasis and blockage of cellular veins are fruits.

Master Cong believes that a woman's womb is like a mulberry field, and a woman's pregnancy is like a field sowing seeds. Chinese traditional peasant thought believes that if you want to have a bumper harvest, you must need fertile land to provide nutrition for it, and if the soil is barren and hardened, it will not bloom and bear fruit. Wang Qingren said, "there is blood stasis in the uterus first... Blood does not enter the fetus, and the fetus has no blood to support." If there is blood stasis and internal obstruction, new blood will not be produced, and if the fetus is lost, the fetus will not be solid.

Results and discussion

Cong Shi believes that the disease of threatened abortion should start with the cause of the disease and the pathogenesis. Aiming at the fruit of adverse pregnancy outcomes, we should target Sanwei Xiaofang as the basis to achieve the state of both children and mothers. The method of Tonifying the kidney and activating blood circulation selects Panax notoginseng, Angelica sinensis and Ziheche to mix with stasis, blood circulation and regeneration.

Panax notoginseng, sweet, slightly bitter, warm, belongs to the liver and stomach meridian. Efficacy: remove blood stasis and stop bleeding, promote blood circulation and relieve pain. Cong Shi compared the pregnancy of the fetus in the womb to the "old farmer farming". If the land is barren, hardened and lack of nutrition, the crops will naturally grow unhappily; If the land is loose and fertile, a bumper harvest will surely be achieved, which is the so-called "muddy pond and marsh without grass". The menstrual pregnancy and childbirth of the uterus are all based on blood and used by blood. If Chong Ren is not adjusted, blood and Qi are disharmonious, blood and Qi stasis in the uterus, new blood is difficult to settle, and fetal yuan is not solid, abortion will be threatened. Panax notoginseng can stop bleeding, remove blood stasis and produce new ones. It has the characteristics of "stop bleeding without leaving blood stasis, remove blood stasis without hurting the right", and it can also replenish deficiency and strengthen ^[5]. Only when the blood stasis is removed, the vein is unblocked, the Chong Ren is smooth, and the fetus has new blood, the mother and fetus are at ease.

Angelica sinensis, sweet, pungent, warm, belongs to the liver, heart and spleen meridians. Efficacy: tonifying blood, activating blood circulation, regulating menstruation, relieving pain, moistening intestines. Angelica sinensis is a good medicine in blood because it has the advantages of tonic but not stagnation ^[6]. Both hemostasis and stasis removal should be taken into account, hemostasis and blood circulation should be promoted, and blood circulation should be promoted without blood circulation ^[7].

Ziheche, sweet, salty, warm, guixinjing. Efficacy: tonifying kidney and essence, nourishing blood and Qi. Zihe Che is the dry placenta of healthy people. It is the product of flesh and blood. It is born

of human essence and blood. It is a product that supplements both qi and blood, yin and Yang. Pharmacology believes that it contains a variety of hormones, immune factors, amino acids, trace elements, vitamins, etc^[8], to promote the development of uterus, vagina and mammary gland.

During the whole treatment process, the tutor firmly grasped the key to the pathogenesis of blood stasis caused by Chong Ren imbalance, and used the method of Tonifying the kidney and activating blood to increase or decrease clinically, so the curative effect was significant.

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Discussion on female "triple" syndrome based on the theory of underlying evil

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Abstract

The theory of Fu Xie originates from the Yellow Emperor's Internal Classic and is an important part of the theory of traditional Chinese medicine. Fu Xie has the pathogenic characteristics of Fu later and repeated attacks. With the continuous development of the research on the theory of pathogenic factors, its application scope has gone beyond the field of febrile diseases and has been widely used in the diagnosis and treatment of various diseases. Female "triple" syndrome is caused by liver depression, phlegm coagulation, blood stasis, qi stagnation, lying in the thyroid gland, breast, uterus, and lack of healthy qi, unable to drum evil out, resulting in the existence of evil Qi, lying down and then occurring, resulting in their successive or combined onset. In the treatment, the fundamental method is to support the right and eliminate the evil, and the main treatment principles are to eliminate phlegm and dampness, regulate qi and activate blood circulation. Based on the theory of pathogenic factors, this paper discusses the pathogenesis of female "triple syndrome", and draws on the experience of famous experts to provide guidance for traditional Chinese medicine to prevent and improve female "triple syndrome".

Key words: The theory of subduing evil; "Triple" syndrome; Stagnation of liver Qi

Objective

The liver Qi is not comfortable, and stagnates in the meridians, hindering the normal biochemical operation of Qi, blood and body fluid. It can be transformed into the evil of phlegm, blood stasis and Qi, gall disease in the thyroid gland, breast addiction in the breast, and fibroids in the uterus. The occurrence and development process of female "triple" disease is the evolution process of underlying pathogenic factors. Guided by the theory of pathogenic factors, this paper discusses the onset and clinical characteristics of female "triple" syndrome, and discusses and summarizes its treatment and transmission, so as to guide new ideas of clinical treatment.

Materials and methods

1. Connotation of evil theory.

The theory of latent evil is mainly applied to many diseases with complex etiology and pathogenesis, concealed early diagnosis, and poor prognosis. Most of them are due to the lack of healthy qi, which is not removed in time, or the deficiency of positive Qi is unable to remove evil, resulting in the insistence of evil Qi, resulting in qi depression, blood stasis, and phlegm congealing in the muscles. The Qi of subduing evil will wait for the opportunity, and it will be "visible outside" over time. Therefore, in the treatment, we should pay attention to the idea of preventing disease, and do not forget to support the right when dispelling evil.

2. Analyze the characteristics of female "triple" disease from the theory of underlying evil.

2.1 evil Qi is hidden and occurs after the opportunity

There is a step-by-step process for the disease to be caused by evil. In the early stage of feeling evil, the evil Qi often hides in the body and does not appear outside. As stated in "thin Yin medical superfluous": "if the disease does not happen, it will be easy to feel it". The evil of disease lies in

the human body, and it often happens at the right time. When the patient lies inside, there are no obvious clinical symptoms, like "ordinary people", no symptoms can be identified, with the characteristics of "hair is evidence-based, and Fu is inorganic to follow" [1].

The onset of female "triple" syndrome is a gradual and hidden process. In the early stage of onset, there are mostly no conscious symptoms, only thirst, astringent eyes, headache, migraine, neck discomfort and other symptoms, but there are no "triple" related discomfort symptoms, which is the characteristic of underlying evil and unconscious. Although "Sanlian" disease belongs to different categories such as "gall", "mastophilia" and "symptoms and pains" in traditional Chinese medicine, it is mostly due to poor emotions, stagnation of liver qi, blocking the movement of Qi, blood and body fluid, and the evil Qi of qi stagnation, blood stasis and phlegm condensation lies in the meridians and collaterals that "Sanlian" goes through. Its etiology has its common features.

2.2 stagnation of liver qi, stagnation of Qi and blood, phlegm and coagulation, and many evils.

"Liver depression" is a common pathogenesis of the "triple" disease. Stagnation of liver Qi leads to abnormal drainage function. Danxi heart method points out that "those who are depressed gather and cannot get over". Liver qi depression is not smooth, has been depressed for a long time, the opening and closing of the cardinal is unfavorable, and the blood and body fluid fall into evil; Or the liver Qi is not comfortable, resulting in emotional depression, which turns into emotional evil [2], and the resulting evil often hides in it, or lies in the body, or lies in the viscera, or lies in the meridians.

2.3 the course of disease is lingering and recurrent.

Modern medical research shows that the incidence of hystero myoma is positively correlated with thyroid nodules, breast fibroadenomas and other diseases [3], and the incidence rate of women's "triple" disease is much higher than that of men [4], in which estrogen and progesterone play a key role [5]. Western medicine believes that the "triple" diseases belong to the hypothalamus pituitary gland axis, with similar physiological and pathological basis; Traditional Chinese medicine believes that the "triple connection" of foot Jueyin liver meridian has common pathological products, which will be affected by liver depression. The incidence of thyroid, breast, uterus and other places are related [6]. Usually, one place is affected, and others are affected, so that the disease is tender and difficult to heal, and attacks repeatedly.

Results and discussion

All knot fetishism tumors belong to depression [7]. The visible solid evil caused by gall tumor, breast fetishism and syndrome is caused by stagnation of liver qi, accumulation of Qi, blood, phlegm and blood stasis in the local area, waiting for the time. As a common multiple disease of gynecology and endocrinology, the common cause of "triple" disease is still unknown. It often occurs in one place and many places, and there is still a lack of corresponding guidance plan in treatment. The theory of pathogenic factors is an important part of the theory of febrile diseases, which has important guiding significance for the diagnosis and treatment of various diseases. There is a close relationship between the "triple" disease and the pathogenic characteristics and treatment methods of Fu Xie. Therefore, the theory of Fu Xie is applied in the clinical treatment, aiming at the syndrome differentiation and treatment of "rhombic disease" in the "triple" part caused by the stagnation of liver qi and the Fu Qi, Fu Yu and Fu phlegm generated by Fu Xie entering the collaterals.

Explaining the pathogenesis and characteristics of "triple" disease based on the theory of pathogenic factors can broaden the thinking of clinical diagnosis and treatment, but it still needs a large sample of clinical and experimental to verify its effectiveness, which provides a new theoretical basis and clinical treatment ideas for the treatment of "triple" disease.

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Acupuncture For Spinal Cord Injury For Russian Guidance

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Abstract

Spinal cord injury (SCI) is a common traumatic neurological disease with a high disability rate, which brings serious economic and psychological burdens to patients and families around the world, including China and Russia. More and more clinical studies have proved the effectiveness of acupuncture in the treatment of SCI patients. This article summarizes and summarizes acupuncture in the treatment of SCI.

Key words: Neurogenic Bladder, Acupuncture ,Sino-Russian Health

SCI usually results from damage to the spinal cord structure caused by trauma such as car accidents and falls, resulting in functional impairment below the plane. For every 1 million people in China, 569 people are sick, mainly due to falls and car accidents. There are about 66,000 new cases in China each year, and about 759,000 existing cases^[1]. In St. Petersburg, the incidence of spinal cord injury is 17.6 per million people. Unemployment is an important factor, as well as outdoor activities on summer weekends, which may increase the risk of spinal cord injury^[2]. The manifestations of spinal cord injury mainly include motor and sensory disturbances, as well as a series of complications such as neurogenic bladder disorders, sexual dysfunction, autonomic disorders, and neurogenic bowel disorders. The main symptoms of neurogenic bladder are urinary incontinence, urinary retention and other urinary tract symptoms, etc. Because of the patient's privacy, the patient's psychological pressure is huge.

Objective

Targeted rehabilitation training is required for patients with severe spinal cord injury, which can effectively improve the quality of life of patients. However, there is currently no definite treatment for spinal cord injury in the world. Therefore, we advocate the use of acupuncture therapy to improve the neurological function of patients. Promote patient recovery more efficiently and safely.

Materials and methods

A literature search was conducted on CNKI to find the clinical observation literature about acupuncture treatment of neurogenic bladder after spinal cord injury in recent years, and high-quality literature was screened out according to the ranking of journal attributes, which were summarized and reported here.

Results and discussion

1 Acupuncture and moxibustion acupoint selection rules

1.1 Distant and near acupoints

Distant and near acupoint matching is a commonly used acupoint matching method in clinical acupuncture. It is widely used in a variety of diseases, and its therapeutic effect is good. The method can restore the nerve fibers in the inhibited state to a certain extent, so as to achieve the original nerve function. Luo Jing^[3] selected acupuncture at Zhongji, bilateral bladder Shu, Sanjiao Shu, Sanyinjiao, Yinlingquan, Ciliao, Xialiao and Guilai points on the basis of rehabilitation. Bladder

function was better after treatment.

1.2 Bailiao Point

Bailiao acupoints belong to the bladder meridian of Foot-Taiyang, and specifically refers to the upper, the second, the middle liao, and the lower liao. Difficulty urinating. Existing studies have shown that the total effective rate of using Bailiao as the main treatment for neurogenic bladder after spinal cord injury is 93.3% to 100.0%, which reflects the importance of Bailiao. Another study has shown^[4] that electro-acupuncture at Bliiao point combined with electrical stimulation of nerves in the projection area of the body surface can improve the contraction movement and coordination function between the detrusor and the internal bladder sphincter, which is conducive to the formation of urination reflex and improves patient control. Urinary function, improve the quality of life.

2 Acupuncture combined with other treatments

2.1 Electroacupuncture

Electro-acupuncture is based on piercing the acupuncture points with needles, connecting the acupuncture needles to the positive and negative electrodes of the electroacupuncture instrument, and applying current to match the appropriate stimulation waveform and frequency. The method has the advantages of simple operation and controllable stimulation. Cheng Xiankuan^[5] performed acupuncture on Bliiao and Huiyang, followed by lifting and inserting, and then connected to an electro-acupuncture apparatus. After 2 months of treatment, related scales such as catheterization volume, bladder residual urine volume, and urinary incontinence score were significantly improved. Studies have shown that electro-acupuncture of Bliiao and Huiyang can relieve and prevent urinary tract infections and reduce the pain of patients.

2.2 Acupuncture and medicine combination

The combination of acupuncture and medicine specifically refers to the application of external acupuncture and moxibustion to patients, and the use of traditional Chinese medicine orally. Wang Neng^[6] selected acupuncture as the control group for the treatment of neurogenic bladder with spinal cord injury. The treatment group was given Jinkuishenqi Pill on the basis of acupuncture. After 4 weeks, the clinical indicators and quality of life of the treatment group were significantly improved. The effective rate of the control group was 67.27%, while that of the treatment group was 92.73%. The acupuncture and medicine group achieved the effects of regulating Qi, warming and tonifying kidney-yang.

There has been some clinical progress in the research of spinal cord injury, but how to alleviate the clinical symptoms of patients and ensure the quality of life of patients after secondary injury of spinal cord injury is still the direction we need to work on. As a result, Acupuncture has definite curative effect on neurogenic bladder patients after spinal cord injury, and can effectively improve bladder function and urinary tract infection.

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Identification of genes associated with diagnosis and prognosis of ovarian cancer patients based on integrated bioinformatics analysis

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Abstract

Objective To use genetic analysis to identify the main ovarian cancer-related genes and to assess the prognosis. **Methods** The ovarian cancer chips GSE14407, GSE54388, and GSE16708 were downloaded from the gene expression omnibus database (GEO), and differential expressed genes (DEGs) were screened by R software. The key genes in DEGs were then examined by the String 11.0 database and Cytoscape 3.7.2 software, and the prognosis of the key genes was confirmed using the Kaplan Meier plotter online software. **Results** A total of 341 differentially expressed ovarian cancer-related genes were examined, including 205 up-regulated genes and 136 down-regulated genes. Five important genes were identified after screening and prognosis analysis, including the increasing genes CDCA7, UBE2C, PRAME, and the falling genes CXCL6, CACNA2D1. **Conclusions** Ovarian cancer may be associated with CDCA7, UBE2C, PRAME, CXCL6, and CACNA2D1, and these factors may also offer a possible therapeutic target.

Key words: GEO; Ovarian cancer; Differential expressed genes

In the world, ovarian cancer (OC) affects 290,000 women, and 180,000 of them pass away from the disease each year. More gravely, with a five-year survival rate below 45%, OC is the most fatal gynecological malignancy [1, 2]. Gene chip technology has become widely used in the study of cancer since the human genome project was completed. In 2000, the GEO database was created. It includes gene expression data that was provided by numerous international universities. It is a platform for public data retrieval, storage, and download. It offers a fresh and methodical approach to the study of tumor-related genes and is widely applied to molecular diagnostics, therapy, drug discovery, and other areas. In this study, bioinformatics analysis was conducted using the appropriate GEO database chips, and the differential genes and their related functions were investigated using the appropriate software. This provided a theoretical framework for the study of OC mechanism and provided guidance for the search for OC molecular markers and potential therapeutic targets.

Objective

Through the GEO database, the important genes for the occurrence and progression of OC were identified, and the survival and outlook of the genes were examined.

Materials and methods

Get OC chips from the GEO database. R software was used for data set processing and differential expression gene screening; import the string database with the key targets identified through dataset mapping; Utilize Cytoscape 3.7.2 to do visual processing and analysis on the PPI network; $P < 0.05$ was statistically significant when using Kaplan Meier to examine and confirm the survival status of differential gene expression.

Results and discussion

From the outcomes, choose the data set representing clinical samples with high-level serous OC, and then identify and download the data sets GSE14407^[3], GSE16708^[4], and GSE54388^[5]. Data from GEO14407, GEO16708, and GSE54388 all contain 12 OC samples and 12 normal ovarian epithelial samples. GEO14407 data also contains 18 OC samples and 9 normal ovarian epithelial samples. The up-regulated gene count was 205 and the down-regulated gene count was 136 after Wayne diagram analysis of the differential genes identified by the three data (Fig.1).

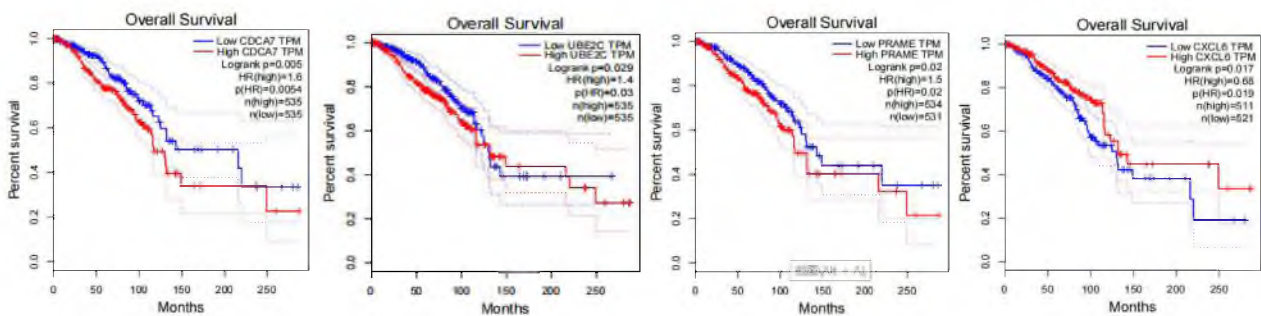


Fig.1 The key genes in DEGs After eliminating isolated and loosely connected nodes, string database PPI network was used to construct differential gene expression products in OC (Fig.2).



Fig.2 PPI network

Five important genes—CDCA7, UBE2C, PRAME, CXCL6, and CACNA2D1—were confirmed through survival analysis of differentially expressed genes, as illustrated in Figure 3.



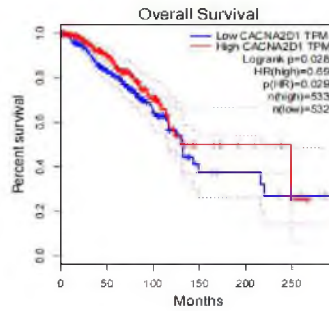


Fig.3 Survival analysis of DEGs

Overall, 341 differentially expressed genes associated with OC were examined, including 205 up-regulated genes and 136 down-regulated genes. Five important genes, including CDCA7, UBE2C, PRAME, CXCL6 and CACNA2D1, were discovered after screening and prognostic analysis. These genes may be connected to the onset and progression of OC and may represent prospective therapeutic targets for the disease.

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The role of biological agents in psoriasis

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Abstract: An immune-mediated polygenic hereditary skin condition called psoriasis has a negative impact on sufferers' physical and mental health as well as their quality of life. Psoriasis is treated using biological medicines, a new therapeutic approach. In order to offer fresh perspectives and references for the clinical treatment of psoriasis, the literature on the treatment of psoriasis with biologic drugs over the previous three years was searched, arranged, and described in this article.

Key words: Psoriasis; Biologics; Progress

Lesions from psoriasis, a T-cell-mediated chronic inflammatory skin disease, are typically confined to the scalp, knees, and elbows^[1-2]. It can be classified into a number of subgroups depending on how it manifests clinically, including common psoriasis, plaque psoriasis, and pustular psoriasis^[3]. It primarily affects people in the 20–30 and 50–60 age ranges and has a prevalence of 2%-4% worldwide^[4-5]. Psoriasis has several different root causes, and its development is primarily influenced by immunological, genetic, and environmental abnormalities^[1]. TNF inhibitors, IL-17 inhibitors, IL-12/23 inhibitors, and IL-23 inhibitors are the main biologic medications used to treat psoriasis^[6]. In order to serve as a reference for readers, the article reviews and summarizes the biologic therapies used to treat psoriasis over the last three years.

1. TNF inhibitors

TNF inhibitors are a class of biologic therapies that target the pro-inflammatory cytokine TNF, including etanercept (E), infliximab (I), adalimumab (A), certolizumab pegol (C), and golimumab (G), and are first or second-line treatments for a variety of immune-mediated inflammatory diseases^[7-9]. TNF- α plays an important role in the pathogenesis of psoriasis, and studies have shown that TNF- α inhibitors can neutralise and bind to its activity, thereby blocking TNF- α binding to receptors and producing anti-inflammatory effects, such as Etanercept, Infliximab, Adalimumab, etc^[10-11].

2. IL-17 inhibitors

IL-17 inhibitors are among the most advanced biologics that play an important role in the IL-23/Th17 signalling pathway in psoriasis^[12]. They mainly include secukinumab, ixekizumab and brodalumab, among which secukinumab and ixekizumab can specifically inhibit IL-17A and brodalumab can selectively bind to IL-17A and IL-17F and prevent both from binding to the receptor, thus inhibiting IL-17 pathway activation of the IL-17 pathway^[13-14]. Current studies show good efficacy of secukinumab in moderate-to-severe psoriasis, ixekizumab in paediatric patients with psoriasis and brodalumab is FDA approved for use in adults with moderate-to-severe psoriasis who do not respond to systemic therapy or phototherapy, but its safety needs further confirmation^[15].

3. IL -12/23 inhibitors

Ustekinumab, a human IgG1 monoclonal antibody that inhibits IL-12/23, is approved for the treatment of psoriasis^[16-17]. A retrospective study has indicated that long-term use of ustekinumab is effective and safe in moderate-to-severe chronic psoriasis^[18].

4. IL -23 inhibitors

IL-23 inhibitors exhibited good efficacy and safety in the treatment of persistent plaque psoriasis and showed greater PASI 75 and PASI 90 response rates compared to conventional TNF- and IL-12/23 inhibitors^[19].

5. Discussion

More and more biological agents are being produced for the treatment of psoriasis as contemporary medicine continues to advance. Despite their effectiveness, a variety of issues have arisen, including their relatively high cost and the negative side effects that come along with their use. Following therapy with TNF inhibitors, the literature indicates that about 25% of patients develop cutaneous side effects, such as skin infections and tumors^[20-21]. Biologics need to be further validated as an emerging therapeutic modality on the basis of evidence-based medicine, for instance, by increasing sample numbers to guarantee safety, in order to be better employed in the future to aid more patients in recovering.

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Regulatory effect of electroacupuncture preconditioning on autophagy in isolated rat myocardial ischemia-reperfusion myocardium

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Abstract:

Objective: to observe the regulatory effect of electroacupuncture at "Xinshu" (Bl-15) and "Shenmen" (HT-7) on autophagy of isolated myocardial ischemia-reperfusion in rats.

Methods: 36 rats were randomly divided into three groups: control group (Con group), model group (IR group) and electroacupuncture pretreatment group (EA group). The isolated myocardial ischemia / reperfusion model of rats was made by using Langendorff device. Rats in IR group received balanced perfusion of 20min, ischemia 40min, and no ischemia-reperfusion operation in 2 h reperfusion group. EA group received electroacupuncture intervention 3 weeks before model establishment, electroacupuncture at "Xinshu" point and "Shenmen" point respectively, once a day, 6 days a week, and IR group was replicated 3 weeks after balanced perfusion. The rats in the EA group received electroacupuncture at "Xinshu" point and "Shenmen" point respectively, once a day, 6 days a week, and 3 weeks later. The contents of cardiac creatine kinase (creatinekinase,CK), myocardial kinase isoenzyme [creatinekinase,MB (CK-MB)] and lactate dehydrogenase (lactatedehydrogenase,LDH) in perfusate were measured; the pathological changes of autophagy in myocardial cells of rats with ischemia-reperfusion were observed by hematoxylin-eosin (HE) staining; and the ultrastructural changes of myocardial cells of rats with ischemia-reperfusion were observed by transmission electron microscope. The expression of autophagy marker protein Beclin-1,LC3 in myocardial tissue of rats in each group was detected by Westernblotting.

Results: compared with Con group, the contents of CK, CK-MB and LDH in perfusion fluid of IR group were significantly higher than those of IR group, while the contents of CK, CK-MB and LDH in EA group were lower than those of Con group. The results of HE staining showed that compared with Con group, myocardial fiber in IR group showed lysis, fracture and even necrosis, and swelling was obvious. In EA group, the myocardial fiber space was slightly widened, the necrotic focus was alleviated, and the cardiomyocytes were slightly swollen. The results of transmission electron microscope showed that compared with the Con group, the myocardial muscle fibers of the IR group were lysed, broken or even necrotic, and the crest was arranged irregularly and broken. Compared with Con group, the ratio of autophagy marker protein Beclin-1, LC3II increased significantly in EA group, and the expression level of autophagy marker protein in EA group was lower than that in IR group ($P < 0.05$). The structure of nucleus and mitochondria were slightly broadened in EA group, and the ratio of autophagy marker protein Beclin-1, LC3II in EA group was significantly higher than that in IR group ($P < 0.05$). Conclusion: electroacupuncture at Neiguan acupoint can reduce the expression of autophagy marker protein Beclin-1,LC3 and protect myocardium from myocardial ischemia-reperfusion injury in rats.

Key words: ischemic preconditioning, electroacupuncture, myocardial ischemia-reperfusion, autophagy, Beclin-1,LC3

Bushen huatan formula improves early-stage low-grade inflammations in obese polycystic ovary syndrome

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Abstract

Based on Traditional Chinese Medicine theory, Bushen HuaTan Formula (BHF) are used to ameliorate obesity Polycystic ovary syndrome (PCOS) in clinic. It is also effective in improving PCOS patients' ovarian ovulation function. Studies reported that PCOS was an inflammatory condition, and numerous inflammatory markers were observed in PCOS patients.

Key words: BuShen HuaTan Formula, obese, polycystic ovary syndrome, inflammation

Objective

This study is aimed to explore the effect of BHF on the inflammatory regulation among obese PCOS, and its underlying mechanisms in ovarian granular cells (GCs).

Materials and methods

40 PCOS subjects ($24 \text{ kg/m}^2 \leq \text{body mass index (BMI)} < 30 \text{ kg/m}^2$) and 40 healthy subjects ($24 \text{ kg/m}^2 \leq \text{BMI} < 30 \text{ kg/m}^2$) were recruited. All 40 PCOS subjects were treated with BHF twice a day for 6 consecutive months. The 40 healthy subjects did not receive any intervention. The blood samples were collected before, 3 months and 6 months after BHF interventions respectively to detect the level of inflammatory cytokines. In vitro study, we isolated GCs from PCOS rats induced by Letrozole (LET) intervention for 6 (LET6W) and 12 weeks (LET12W). The levels of inflammatory cytokines in GCs of each group were compared, and the regulatory effect of BHF containing serum on them was also observed.

Results and discussion

Subjects with PCOS and obesity had higher levels of IL-1 β , IL-6, IL-8, and TNF α compared with healthy subjects, which were significantly reduced after 3 and 6 months of BHF intervention. There were higher levels of TNF α , IL-1 β , IL-6, IL-8, LBP, LPS, CD14, hsCRP and the protein of TGF- β 1 in rats with LET6W and LET12W. Moreover, the levels of these inflammatory cytokines in LET12W were higher than those in LET6W. At the same time, BHF reversed the increase of the above eight cytokines and TGF- β 1 protein in both LET6W and LET12W, and showed better modulation in LET6W.

This study confirmed that there was hyper-reactive inflammatory response in GCs of PCOS and during the development of PCOS. However, BHF can effectively ameliorate this pathology process, and early treatment with BHF may lead to better therapeutic results.

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The prevention and staged treatment of female salpingitis infertility from the perspective of "stasis"

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Abstract

In recent years, a variety of factors have led to the increasing incidence of salpingitis infertility, which has a potential impact on the overall population birth rate in society. Therefore, prevention and effective treatment of salpingitis infertility is significant. Our hospital has always been at the leading level in the treatment of infertility. This article summarizes the clinical diagnosis and treatment experience of our hospital in order to bring the gospel to more infertile women. At the same time, combining the idea of treating pre-disease with the academic theory of Longjiang Han's gynecology, comprehensively discusses disease prevention, staged treatment and post-treatment methods, emphasizing the selection and medication rules of staged treatment and auxiliary treatment methods. It is of great practical significance to improve quality and restore female reproductive function.

Key words: salpingitis infertility, staged treatment

Methods

1."Prevent disease before disease"

Regulate the emotions to recharge the spirit: The functions, mental states and emotional activities of the human body are all governed by the divine machine. We must maintain a positive and optimistic attitude towards life, it is necessary to have a good emotion as an internal response, and it should be "beautiful food, let it be served, be happy with the customs, and do not admire each other", it is important to prevent the occurrence of this disease. Adapt to the changing seasons to maintain the righteousness: It is of great significance to adapt to the changes of the four seasons and adjust the daily routine. Moderate exercise to maintain muscle strength: Appropriate exercise is particularly important for nourishing the body and strengthening qi, this can promote qi and blood circulation. Through moderate exercise, the body can be moved to adjust the organs. This is the way to cultivate and nourish our body, and strengthen the blood. Adjust daily diet to protect your stomach: Food, water and grain enter the stomach from the mouth, they were decomposed, transported and transformed, producing subtle qi, filling the viscera, which is the so-called "flavor returns to shape, shape returns to qi, qi returns to essence, essence returns to transformation, essence eats qi, shape eats taste, transforms and generates essence" [1].

2."Prevent the disease from becoming a disease"--the concept of staged treatment

2.1 Early stage: clearing heat, dispelling cold and clearing blood: Han believes that if the blood stasis is not removed and new blood is not produced, the evil should be given a way out, and the products of promoting blood circulation and promoting qi should be given. If the damp stasis is prolonged, the yin and yang are out of balance, and the symptoms are irritable and irritable, add

Maidong, lotus heart, Zhuru and other yin nourishing products, or use the Chinese patent medicine Yankening Granule to clear dampness and heat. At the same time, external application of traditional Chinese medicine should be given, and the medicine bag or medicine is applied to acupoints. Through the penetration of medicine and warm stimulation, it can reduce inflammation and relieve pain, promote blood circulation and remove blood stasis, warm the meridians and collaterals, release the adhesion of fibrous tissue and promote the absorption of inflammation. Mild disease, equivalent to simple salpingitis, tubal stenosis or tubal rigidity, the combination of drugs played a total of activating blood circulation and stagnation, and Tongli blood vessels, and the effect was remarkable.

2.2 Mid-term: The disease initially damages the uterus, and if it persists for a long time, it will cause blood stasis and qi blockage. It can be known that blood stasis caused by various reasons is not only a pathological product formed by the disease process, but also a new etiology with pathogenic effect. Compared with hydrosalpinx, empyema, obstruction, severe adhesion and closure of the umbrella end in modern medicine, this period is an important turning point for the disease. It is a great significance of proposing the treatment methods of "activating blood circulation and removing blood stasis, promoting qi and relieving pain", attaching importance to "internal and external treatment" and "comprehensive conditioning". According to the severity of the patient's condition, clinicians use dual therapy (oral Chinese medicine + rectal administration), triple therapy (dual therapy + physiotherapy) and quadruple therapy (triple therapy + characteristic therapy) as appropriate. This can improve the state of oviduct lumen stasis.

2.3 Late stage: nourishing the kidney and soothing the liver, regulating and replenishing Chongren: Han established a unique academic system "the theory of liver and kidney", emphasizing that the normal function of liver and kidney plays an important role in the prognosis of this disease. The focus of this period of treatment is based on the evaluation of the comprehensive treatment effect and systemic condition of the patient. We promote the recovery of reproductive function of patients by regulating the liver and kidney. In the stage, according to the patient's condition, the doctor can instruct the patient to take Bailingtiaogan decoction, Bushenhuoxue tiaochong decoction and other drugs to promote the recovery of oviduct peristaltic function.

3. "Prevent relapse after recovering" - the concept of recuperation

After cure, if we not pay attention and nursed back to health, the disease is easy to relapse. In daily life, we should avoid wind and rain, keep warm, soothe our emotions, exercise in moderation, restrain our selfish desires, combine work with rest, eat light foods, supplement crude fiber and high-quality protein, adjust diet in time and so on. At the same time, with foot bath, medicated bath, acupoint massage and other methods to enhance righteousness and regulate qi and blood.

Discussion

Traditional Chinese medicine emphasizes the holistic medical concept represented by the correspondence between man and nature and the idea of treating disease before it [2]. The etiology and pathogenesis of female salpingitis infertility is complex, usually caused by a combination of multiple factors. The occurrence, development and severity of the disease are related to women's daily physiological activities and physical factors [3]. Based on years of clinical experience and academic research, Longjiang Han's Gynecology has summed up theories such as prevention and treatment principles, staged treatment and liver and kidney theory. Professor Liu Li is a

representative descendant of Longjiang Han's Gynecology, and innovatively proposed "activating blood circulation and removing blood stasis" for this disease. She emphasizes the importance of disease prevention and treatment from "stasis". The clinical effect is remarkable, and it is of great significance to improve the clinical cure rate and restore female reproductive function. This article focuses on reconciliation, regulation, and recuperation[4], combined with the idea of "prevention before disease, prevention of degeneration after disease, prevention of relapse after recovery", and discusses the preventive measures and staged treatment ideas for female salpingitis infertility. In order to provide a certain theoretical basis for the prevention and treatment of this disease.

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The mechanism of pyroptosis in the pathogenesis of mild cognitive impairment

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Abstract

Mild cognitive impairment (MCI) is a transitional state between normal cognitive function and dementia. Alzheimer's disease (AD) is the most common type of dementia. It has been suggested that the ultra-early stage of AD can be characterized by MCI. Therefore, early intervention in the MCI stage contributes to the prevention and diagnosis of AD, thereby slowing down the progression of AD. In recent years, many scholars have proposed that hippocampal pyroptosis induced by a chronic inflammatory cascade can affect the pathogenesis of MCI, which provides a new idea for the treatment of MCI. This article describes how inflammation leads to pyroptosis, which further affects the pathogenesis of MCI.

Keywords: Pyroptosis; Mild cognitive impairment; pathogenesis

At present, modern medicine has carried out research on the pathogenesis of MCI from multiple angles, mainly including: senile plaques caused by the excessive deposition of β -amyloid ($A\beta$); Hyperphosphorylation of Tau leads to neurofibrillary tangles; Autophagy; Synaptic dysfunction; Oxidative stress injury; Imbalance of intestinal flora; Chronic inflammatory cascade, etc. Among them, the chronic inflammatory cascade is mainly involved in the deposition of $A\beta$, which may be related to the release of large amounts of pro-inflammatory cytokines by activated microglia, leading to neuroinflammation.

Objective

With the rapid aging of the global population and the increasing proportion of dementia patients year by year, Alzheimer's Disease International predicts that the number of people with dementia will reach nearly 82 million in 2030 and more than 152 million in 2050. This not only brings great pain to patients, but also brings heavy mental pressure and economic, medical and care burdens to families and society. This article describes the specific process of inflammatory pyroptosis aggravating MCI.

Materials and methods

First, articles on the pathogenesis of MCI in recent years were retrieved and collected from websites such as CNKI and PubMed on the Internet, and inflammation and pyroptosis were selected. After careful reading, these articles found and summarized the conclusions of how inflammation and pyroptosis contribute to the pathogenesis of MCI.

Results and discussion

The chronic inflammatory cascade involving activated microglia is closely related to pyroptosis. Microglia activation releases a large number of pro-inflammatory cytokines, which promote the activation of NLRP3 inflammasome, which is composed of NLRP3 protein, apoptosis-associated dot-like protein and cysteine protease caspase-1. The N-terminal pyridine domain of NLRP3 allows for homotypic interaction with dimer-linked apoptosis-associated dot-like proteins, which subsequently recruit procaspase-1 through CARD-CARD interaction. Procaspase-1 recruitment results in adjacently induced caspase-1 oligomerization and autocatalysis, leading to the release of

interleukin -1 β (IL-1 β) from the active caspase-1 fragment. IL-1 β is secreted and activated in a biologically inactive form by caspase-1, whose activity is controlled by NLRP3 signaling. As the main medium of innate immunity, caspase-1 initiates a new type of pro-inflammatory cell death pattern, called pyroptosis. This pyroptosis is morphologically different from apoptosis. During pyroptosis, the cells expand continuously until the membrane breaks down, resulting in the release of highly pro-inflammatory cell contents.

The classical pyroptosis pathway is mainly dependent on caspase-1. Intracellular pattern recognition receptors can act as receptors in response to danger signals, connecting the receptor protein NLR to the adaptor protein ASC to form a multi-protein complex that activates caspase-1. This kind of danger signals mainly include exogenous danger signals such as bacteria and viruses and endogenous risk signals of stress factors released when the body is damaged. After caspase-1 is activated, Gasdermin protein and form peptide segments with GSDMD N-terminal active domain, which can make cell membrane perforation and change the osmotic pressure inside and outside of the cell. Extracellular substances enter the cells in large amounts to rupture and necrosis the cells, and release a large number of inflammatory factors, thus inducing or aggravating the inflammatory response of the body. In addition, activated caspase-1 can also cut the precursors of interleukin -18(IL-18) and IL-1 β , and release them into the extracellular system after activation. Moderate release of IL-1 β and IL-18 active inflammatory factors can combine with the surrounding immune cells to eliminate pathogens. On the contrary, the excessive use causes the accumulation of a large number of inflammatory cells to deteriorate the inflammatory response of the body, leading to the occurrence of MCI.

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Modern medical exploration of hepatocellular carcinoma with depression

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Abstract

Patients with hepatocellular carcinoma are mostly accompanied by emotional abnormalities, with anxiety and depression being the most common. The pathogenesis of hepatocellular carcinoma with depression is complex, and it interact and promote each other through neuroendocrine, inflammatory immune, metabolic abnormalities and neurotransmitters. In this paper, we review the pathogenesis of depression associated with hepatocellular carcinoma in order to provide reference for related studies.

Keywords: Hepatocellular carcinoma; depression; pathogenesis

Hepatocellular carcinoma is one of the five most common malignant tumors, and its mortality rate ranks 4th in cancer deaths worldwide^[1]. Due to factors such as painful disease process, high treatment cost, and large adverse reactions to radiotherapy and other treatments, patients suffer from both physical and mental pain, which often lead to anxiety and depression easily, and there is a positive correlation between the occurrence of liver cancer and depression, and the incidence of liver cancer with depression is as high as 68.42%^[2].

Objective

Depression in cancer patients is not only a concomitant condition, but also may be the cause of cancer development. Hepatocellular carcinoma with depression has a complex pathology. In this paper, we systematically explored the mechanisms by which liver cancer and psychosomatic diseases affect each other and exacerbate each other's disease progression, in order to provide a theoretical basis for the prevention and treatment of liver cancer with emotional abnormalities.

Materials and methods

Firstly, articles about the pathogenesis of Hepatocellular carcinoma and Depression in recent years were collected, and pathogenesis was selected. After careful reading, the conclusion the pathogenesis of liver cancer with depression and summarized by these articles. The above articles were retrieved from the Internet CNKI, PubMed, etc.

Results and discussion

The hypothalamic-pituitary-adrenal axis (HPAA) is an important component of the neuroendocrine system, serving as a hub of brain regions, glands, and hormones that can participate in and regulate a variety of organismal activities and stress translation^[3]. Abnormal expression of inflammatory factors is closely associated with tumor-associated depression, and liver cancer and mood disorders such as depression can interact via inflammatory factors^[4]. There is a close and complex relationship between chronic inflammation and anti-cancer immunity in the liver, and chronically high levels of pro-inflammatory chemokines can alter immune cell subsets, affecting the anti-cancer function and immune clearance of T lymphocytes and NK cells, leading to a diminished ability to monitor and kill tumor cells^[5].

Most of the current studies have explored the pathogenesis of hepatocellular carcinoma and depression from the aspects of neural signals, endocrine system, immunity, inflammation, etc. In

general, these causes affect the growth and value-added of hepatocellular carcinoma cells and metastasis on the one hand, and promote the progression of tumor, and affect the neural prominence and transmitters in the brain on the other hand to trigger depression, which in turn affects the development of tumor with depression.

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Industrial innovation and new development of comprehensive healthcare between China and Russia in the new era based on the model of traditional Chinese medicine¹

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Abstract:

As the one of the central countries along *the Belt and Road*, China and Russia have always maintained friendly relations and close cooperation. Under the background of the comprehensive healthcare era, the global communication of traditional Chinese medicine (TCM) has gained unprecedented opportunities and challenges. At the same time, international exchange of TCM culture has also encountered many problems, such as the cultural difference between TCM and western medicine, the lack of international exchange platform of TCM and the limited trade logistics. Therefore, the innovation and new development of China and Russia's comprehensive healthcare industry under the background of TCM mode in the new era is of great significance.

Key words: comprehensive healthcare, TCM, China, Russia

Comprehensive healthcare is an emerging health management concept proposed according to the developmental requirements of the times, the changes of human disease spectrum and the needs of human society, which is aiming at promoting human beings to pursue a healthier lifestyle from physiological, psychological, social and moral aspects¹. Traditional Chinese medicine (TCM), a unique and advantageous health resource in China, has been tempered and tested for thousands of years and has made great contributions to the healthy reproduction of the nation. With the gradual elevation of international status of TCM, the internationalization of TCM has soundlessly become a mainstream trend. On the one hand, internationalized TCM caters to the current alternations in people's health concepts and medical models, and on the other hand, it reflects the needs of its own development. At the same time, it is also an important strategic path to enhance China's soft power and export Chinese culture².

In recent years, with the promotion of *the Belt and Road Initiative*, cooperation between China and Russia in various fields has been continuously strengthened. The epidemic of COVID-19 in 2019 has further accelerated the development of China-Russia medical trade, reflecting the strong complementarity of the medical industries and markets between China and Russia, and also brought new challenges and opportunities for TCM in Russia. Therefore, it is of cross-era significance to discuss the innovation and development of China and Russia's comprehensive healthcare based on the model of TCM.

Objective

To explore the current situation, innovation and new development of comprehensive healthcare industry in the new era under the model of TCM.

Materials and methods

Search PubMed, Web of Science and other databases as well as the related news websites. The limitation of time is set ranging from the establishment of the database to present and the searching keywords include comprehensive healthcare, China and Russia relations, traditional Chinese medicine, etc.

Results and discussion

1. Current status of comprehensive healthcare industry between China and Russia based on TCM

Due to the influence of regional, historical, cultural, environmental and other differences between China and Russia, as well as the fact that China's TCM of comprehensive healthcare industry is still in developing stage, the international competitiveness of comprehensive healthcare industry is relatively weak. Additionally, on account of the harsh legal environment, the legal status of TCM has not yet been achieved and the registration of TCM herbs is difficult, which means that the industry competition is fierce and the quality of TCM clinics is worrying.

Meanwhile, western sanctions in recent years have had a considerable impact on the Russian pharmaceutical industry market, which is highly dependent on imports, and have monopolized the Russian market for many years. This kind of sanctions provide opportunities for China to compete in high-end medical apparatus and instruments as well, which also offer a lot of space for cooperation in key technologies and core components apart from the product itself. Although TCM has been amazingly effective in the treatment of COVID-19 since 2019, which has greatly promoted the development of comprehensive healthcare industry to a certain extent, its core competitiveness is still insufficient.

2. New thinking on the innovation and development strategy of TCM of comprehensive healthcare between China and Russia

Russia, as a large country rich in herbal resources, has more than 4,000 herbal varieties³, which supplies the possibility to the development of TCM of comprehensive healthcare between China and Russia. Firstly, China and Russia need to further deepen and broaden international exchanges and cooperation in TCM. With the help of bilateral and multilateral international relations, China has conducted numerous meetings and activities with Russia and other countries concerning the field of traditional medicine, greatly promoting the booming of TCM among countries.

Secondly, avoid cutthroat competition and seek local cooperation. By 2035, Russia expects to receive \$100 billion a year for exporting herbal raw materials to China and occupy 25 percent of the Chinese market, RIA Novosti reported. We should take this express train of TCM herbs and accelerate bilateral cooperation in cultivating Chinese herbs so as to stimulate the innovation and development of TCM of comprehensive healthcare.

In addition, our strategic focus should be placed in standardized plantations, research and development of new varieties, exploitation of trade logistics and the development of Internet+ TCM e-commerce platform⁴ in order to establish and perfect the TCM of comprehensive healthcare products of modern logistics system, to support a number of herbs with high-marketed advantages and high qualities between Chinese and Russian markets.

In a word, China and Russia are closely linked both geographically and in international relations. We should tread on the heels of the relevant instructions of *the belt and Road Initiative* and utilize TCM culture as a bridge to vigorously promote the industrial innovation and new development of China and Russia's comprehensive healthcare.

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Clinical research progress of needle knife loosening therapy for painful heel syndrome

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Abstract

Objective

Painful Heel Syndrome, (PHS) is defined as a clinical syndrome caused by lesions in the heel bone and its surrounding soft tissue, most of which are induced by chronic strain, long-standing obesity, more women than men. The clinical manifestation is heel pain or soreness. In order to understand the progress of needle knife loosening treatment with pain, this paper through consulting and research nearly five years needle knife loosening therapy or needle knife loose solution with traditional Chinese medicine external fumigation, shock wave, autologous platelet rich plasma treatment with pain clinical progress research, summarizes the needle knife loosening for pain innovative development and efficacy advantages, can better with pain patients, provide better choices for patients to solve disease problems.

Calcaneus is an important part to maintain the stability and load-bearing of the arch of the foot. Multiple articular surfaces and talus maintain subtalar joint complex, which guarantees the stability of subtalar joint motion and mechanics. The joint with the largest area is the posterior articular surface, which bears most of the body weight^[1]. In terms of anatomical morphology, calcaneal fat pad disease, plantar aponeurosis, nerve entrapment, calcaneal spur, plantar aponeurosis, calcaneal hypertension, etc. are caused by excessive weight, long-term exercise, fatigue and other factors^[2], these pathological changes are the causes of heel pain. At present, the general treatment includes avoiding barefoot walking, changing the cushion, not wearing high heels, avoiding violent exercise that affects the blood supply of the heel, etc. From the history and development of Chinese medicine, traditional Chinese medicine has very rich clinical experience in the treatment of heel pain.

Materials and methods

1. Clinical application of simple acupotomy the treatment method of acupotomy for heel pain is generally to stab the acupotomy into the pain point of the foot, and the acupotomy is perpendicular to the deformation direction of the plantar fascia of the foot, enter the lesion, cut, release and peel off^[3].

2. Clinical application of needle knife lysis combined with traditional Chinese medicine fumigating and washing. First, thermotherapy can expand local blood vessels through thermal effect, so that blood circulation and drug absorption become faster; Secondly, the medicinal power of traditional Chinese medicine acts directly on the local lesion, which can effectively improve the local medicinal power. At the same time, it can also form a drug ion pile to enhance the drug stimulation on the lesion, so as to achieve a better fumigation effect. Therefore, drug fumigation can effectively treat heel pain and alleviate local pain^[4].

3. Clinical application of acupotomy combined with shock wave the effect of shock wave combined

with Acupotomy in the treatment of plantar aponeurosis heel pain is significantly better than that of acupotomy alone or shock wave alone. Shock wave combined with needle knife can significantly reduce the high stress state of plantar aponeurosis, relieve the tension and contracture of fascia and soft tissue, and effectively restore the biomechanical balance.

4. Clinical application of needle knife lysis combined with autologous platelet rich plasma (PRP) autologous platelet rich plasma (PRP) is a substance with strong regeneration ability and can promote the repair of musculoskeletal injury in musculoskeletal medicine. In the treatment of heel pain patients, the pain score of needle knife combined with autologous platelet rich plasma is better than that of needle knife alone, and it can improve the foot function of patients.

5. Acupotomy combined with other therapies, Acupotomy can cut soft tissue and increase the absorption of inflammatory factors^[5]. At the same time, moxibustion has an anti-inflammatory mechanism, which can reduce the content of local inflammatory factors, which has a good anti-inflammatory effect on the complex pathogenesis of heel pain soft tissue or bone inflammation. Needle knife can relieve the high stress performance of heel pain, and cooperate with local pain point closure at the same time^[6], the injected drugs anesthetize nerve endings to reduce pain, eliminate soft tissue spasm, relieve vasoconstriction, and improve local blood circulation. The combination of the two can enhance the therapeutic effect. The cutting effect of the needle knife increases the blood circulation of the lesion. Combined with the long-acting glucocorticoid triamcinolone acetonide acetate, its strong anti-inflammatory effect can reduce the permeability of capillaries, reduce congestion, and inhibit the migration of inflammatory cells to the inflammatory site^[7]. The combination of needle knife activating blood circulation and removing blood stasis, anti-inflammatory and analgesic effects and the detumescence and anti-inflammatory effects of manual treatment makes the diseased parts more fully treated, and the manual treatment is economical and convenient, which is worthy of clinical promotion.

Results and discussion

Acupotomy or acupotomy combined with other therapies in the treatment of calcaneodynia has the advantages of significant, lasting, rapid, small trauma, low cost and reducing the psychological burden of patients. As can be seen from the treatment results, this treatment method has a high cure rate, obvious pain relief effect, simple operation, suitable for most areas, worthy of widespread investment in clinical treatment.

Key words: Knife loosening therapy; Painful Heel Syndrome; Traditional Chinese medicine External fumigation; Shock wave; Autologous platelet-rich plasma

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Clinical study of Yuanluo Tiaoshen Acupuncture in the treatment of Cognitive dysfunction

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Cognitive dysfunction refers to a pathological state in which the human brain accepts external information, processing and other abnormalities, and is unable to acquire and apply knowledge^[1]. Cognitive impairment is the manifestation of brain dysfunction, including perceptual disorders, memory disorders, thinking disorders, etc., the most common in elderly patients, there are obvious nervous system damage, these disorders significantly reduce the living ability and social ability of patients. Western medicine treats the disease by improving cerebral blood flow, cerebral oxygen supply, improving learning and memory, using pyrrolidine drugs, antioxidants-ginkgo biloba extract and other therapeutic drugs, but the clinical effect is not very satisfactory. therefore, there is an urgent need for a new way of treatment. TCM acupuncture is effective in the treatment of this disease, among which the original collateral and mind-regulating acupuncture is the best, which can improve the excitability of the cerebral cortex. Enhance the energy metabolism of brain cells and activate neurons, which is helpful to improve cognitive ability. This article will introduce the clinical efficacy of Yuanluo Tiaoshen acupuncture in the treatment of trigeminal neuralgia for reference.

1. Case Data

Cheng, male, 55, went to see a doctor on May 21, 2019. The chief complaint was memory loss, poor computing power and poor sense of direction for 2 months. Two months ago, the patient had a short-term memory loss, could not recall his recent behavioral activities, and bought nut food to tonify the brain, but there was no effect. The later family found that the patient's computing power decreased, and the calculation was slow with internal addition and subtraction. Direction deviation and even errors. Now the patient's face is Shaohua, enters the ward, the body is fat, the mind is indifferent, the reaction is slow. Memory loss, ask about breakfast recipes, the patient can not recall. Occasionally head vertigo and heavy feeling such as wrapping, wrist abdominal distension discomfort, dry mouth do not want to drink, reduced diet, sticky stools, drowsiness easy to sleep. Physical examination: blood pressure: 150/90mmHg. The score of MMSE scale was 17. Poor computing power, spatial orientation obstacle. The tongue is fat with big tooth marks and white and greasy fur. The pulse string is slippery and the ulnar part is weak. Cranial MRI examination showed multiple lacunar infarction and mild brain atrophy. Color Doppler ultrasound examination of carotid artery showed that vascular plaque was formed, echo was uneven, and blood flow velocity slowed down. Triglyceride test showed that 6.65mmol/L. It was diagnosed as cognitive dysfunction (amnesia-phlegm-dampness blocking collaterals) and cerebral infarction (stroke). The acupuncture method adopts the acupuncture method of original collaterals and mind-regulating acupuncture for the treatment of cognitive dysfunction, and adopts the method of original collaterals and mind-regulating acupoints and the routine acupoints that should be adopted for cerebral infarction. Prescription: bilateral Ben Shen, Shenting, Baihui, Shenmen, Zhizheng, Daling, Waiguan, Taibai, Fenglong, Taixi, Feiyang. Operation: both sides of the god and the god court quickly lift, insert and

twist, piercing to Baihui direction. Shenmen, Taibai, Daling tonifying method, Fenglong acupoint catharsis method, other acupoints flat tonifying and purging. After 20 times of acupuncture treatment, the reaction speed of the patients was significantly improved, the eyes were alive, and the memory and calculation ability were improved. The score of MMSE is 24, which can distinguish the direction clearly. The feeling of dizziness and depression in the head was relieved, and after 2 months of consolidation treatment, the patient was significantly improved.

2. Discussion

Cognitive dysfunction still belongs to the category of "forgetfulness" in traditional Chinese medicine, which is more common in the elderly. The patient in this case is caused by old kidney deficiency, wind and phlegm disturbance, medullary deficiency and brain failure. "Nei Jing" cloud: "the heart governs the spirit, the main blood pulse", "the kidney dominates the bone to produce marrow, which passes through the brain". "the spleen is the acquired foundation and the source of phlegm." It can be seen that the patient in this case should be blamed on the heart, spleen and kidney. According to the special therapeutic effect of the method of regulating mind, combined with the acupuncture method of original collaterals and collaterals, Shenting, bilateral Benshen and Heart Meridian original acupoints Shenmen, small intestinal meridian acupoints are selected, pericardium meridian original acupoints Daling, Sanjiao meridian acupoints Waiguan, spleen meridian original acupoints are too white, stomach meridian acupoints Fenglong, kidney meridian original acupoints Taixi, bladder meridian acupoints flying, plus Baihui acupoints of Zhuyang, total regulation of qi and blood of fourteen meridians to achieve invigorating spleen and resolving phlegm. The effect of awakening and enlightening. Baihui, Shenting, and both sides of this god select acupoints for the proximal part, which can benefit the mind and awaken the mind. Because the area of the acupoint of the mind-regulating method is in the frontal pole, which belongs to the emotional area of Jiao's scalp acupuncture, which specializes in the treatment of mental diseases, acupuncture manipulation is applied with rapid lifting and twirling, 200 revolutions per minute, in order to pierce the needle into the sublayer of the cap aponeurosis through high-intensity resistance, so as to better treat the disease and achieve the maximum effect of treatment. In addition, modern medicine believes that the mind-regulating method is located in the projection area of the cerebral cortex with a large area and a large number of neurons, and continuous stimulation in a small range of rapid lifting and twirling can improve the excitability of the cerebral cortex and enhance the metabolic number of brain cells. activating neurons helps to improve cognition. The disease belongs to the deficiency and the real, and the course of the disease is longer, the treatment is more difficult, longer time, so in the treatment should be both symptoms and root causes, make up the deficiency, diarrhea in fact, and finally achieve the role of regulating mind and dredging collaterals, tonifying essence and filling pulp, calming the mind and calming the mind. In the treatment of this disease, first of all, we identified the pathogenesis and defined the location of the disease, adopted the method of original collaterals and mind-regulating acupuncture to treat cognitive dysfunction, and screened out the areas of regulating emotion, plus heart, pericardium, spleen, Shenyuan acupoints and small intestine, Sanjiao, stomach and bladder collaterals combined with Baihui of du meridians, regulating Zhuyang meridian, Yang qi was restored, positive qi was stored, and evil could not be done. In the treatment of this disease, we should pay attention to emotional regulation, give full play to the preventive role of acupuncture in the treatment of non-disease, pay attention to the importance of regulating mind

and the role of original collaterals and acupoints in the disease, the treatment should not be interrupted, we should continue to consolidate the treatment after remission, and carry out brain functional exercise to help it recover. the effect of this disease is good in the early stage and poor in the late stage. This method is effective for the disease. I hope all colleagues will actively explore the treatment of the late stage of the disease. In order to provide more powerful evidence for clinic.

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Clinical study on acupuncture treatment of trigeminal neuralgia

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Trigeminal neuralgia refers to the symptoms of paroxysmal pain in the distribution area of facial trigeminal nerve without damage to trigeminal nerve function. Clinically, the second and third branches are the most common. Most of the patients with this disease are middle-aged women, which are often induced by touching a certain point of the face, which may be related to cold, ischemia, etc., and the pain often shows paroxysmal lightning-like pain, such as knife cutting, burning, etc., so that the patients do not dare to wash their face, gargle and eat, seriously affecting their social life and life. There is no unified conclusion on the pathogenesis of this disease. Modern medicine thinks that it is related to the nerve "short circuit" caused by nerve demyelination caused by trigeminal microvascular compression, and the treatment is mainly painkillers, sealing needles and surgeries. Although the short-term curative effect is remarkable, but it can not eradicate pain, the curative effect is poor, and the cost is high, which is easy to increase the patient's sense of social pressure and is disadvantageous to the recovery of the disease. Traditional Chinese medicine is characterized by holistic concept, syndrome differentiation and treatment, in which acupuncture therapy is effective in the treatment of this disease, which has the advantages of simple, low, effective, wide and safe, and the cost and long-term effect are considerable. This article will introduce the clinical efficacy of acupuncture along meridians in the treatment of trigeminal neuralgia for reference.

1. Case Data

The patient, female, 79 years old, saw a doctor on March 19, 2021. Chief complaint: paroxysmal pain in the left cheek for more than 20 years, aggravated for 4 months. Current medical history: the patient had an involuntary beating of the left lower eyelid after a quarrel 20 years ago, which extended to the left cheek, followed by pain in the left cheek, which was dispersed like an electric shock along the zygomatic arch with the second molar of the upper tooth as the center, which could be induced by a little stimulation and slightly relieved in the local community. In March 2021, there was a sudden pain in the left cheek. Eating, talking, brushing teeth and gargling were all affected. The pain aggravated at night and could not fall asleep. Carbamazepine tablets were taken orally. The curative effect was significant in a short time, but relapsed after withdrawal. Engraved disease: the patient enters the hospital with his hand covering his left cheek, with a slightly fat figure, Shaohua complexion, abnormal expression, low voice, mournful desire to cry, dry eyes, mouth afraid to open, dry mouth, eating only with small spoons to test the entrance, sleepless at night, defecate 2-3 days once, quality dry. Physical examination: Zygomatic acupoints and Yingxiang acupoints on the left cheek induce severe pain like electric shock, accompanied by distension and discomfort of the mandibular joint. The body of the tongue is thin, the tip of the tongue is red, there are ecchymosis on the edge of the tongue, the coating is thin and white, and the pulse is thin. Western medicine diagnosis: trigeminal neuralgia; TCM diagnosis: facial pain (syndrome of blood

stasis blocking collaterals). Treatment principles: promoting blood circulation and removing blood stasis, dredging collaterals and relieving pain. Selection of acupoints: main points: facial acupoints (affected side Sibai, Xifeng, zygomatic, Yingxiang, Xiaguan, Jiaicheng paste), distal acupoints (Hegu, Zhongzhu, Taichong, Neiting, chivalrous brook); matching acupoints: Baihui, Xuehai. Operation: patients take supine position, tell them not to be nervous, acupoint skin routine disinfection, use 0.35mm × 40mm filiform needle, take far along meridians, first needle Hegu, Zhongzhu, Taichong, atrium, chivalrous brook, directly into the skin, after getting gas under the needle, twist, lift, insert and catharsis method, to acid distension as the degree, at the same time tell patients to try to do buckle teeth, masticatory movements, twirling once every 10min, twirling again tell patients to move the affected part. Then needling other acupoints, tonifying and relieving diarrhea. When needling the cheek acupoints such as zygomatic acupoint and Xiaguan acupoint, the needle depth should be up to 2.0 inch, and the local discharge-like nerve stimulation is the best. Fengfeng-Yingxiang, zygomatic-Xiaguan, electroacupuncture is used to connect the dense waves. Efficacy: after 7 days of acupuncture, the patient felt that the pain was relieved, he could lie down slightly at night, ate slightly better, but still felt the pain aggravated at night; after 14 days of acupuncture, the pain was obviously relieved, and the pain disappeared at night, but deep sleep and diet were available. Easy to chew food such as steamed bread and rice; after 21 days of acupuncture, the pain basically disappeared, there was only slight dull pain in the upper teeth, and the diet was basically normal. After 28 days of acupuncture, the condition was completely controlled, sleeping peacefully at night, normal diet and defecation, good spirit, fluent language, and the range of mouth opening and closing was close to normal physiology. The complexion was ruddy and the pain did not occur. Follow-up for half a year showed no recurrence.

2. Discussion

Trigeminal neuralgia refers to the symptoms of paroxysmal severe pain in the distribution area of facial trigeminal nerve without damage to the function of trigeminal nerve. This disease belongs to the category of "facial pain" in traditional Chinese medicine, mainly because of wind, fire, phlegm and blood stasis, which invades the facial venation of hand and foot three yang. This patient due to the course of the disease for a long time, coupled with old age, afraid of its deficiency of vital qi, essence and blood deficiency, long-term disease into collaterals, blood stasis, deficiency and excess mixed treatment to remove pathogens, dredge collaterals and relieve pain. According to the dialectical circulation of meridians and collaterals, the patient's pain should belong to Yangming and Shaoyang meridians. The course of the disease is prolonged for a long time, with a mixture of deficiency and reality. Acupuncture can relieve pain by affecting the level of plasma β -endorphin, through its own analgesia and inhibiting pain signals [1]. According to the comprehensive analysis, if it is urgent, the standard should be treated, and the principle of distal movement along meridian and disease should be taken under the principle of selecting the distal acupoints of hand and foot with the same name, such as Xiashi, Neiting, Zhongzhu and so on. In the selection of Blood Sea, Taichong, Hegu, so that the qi and blood bar unobstructed. Wu Zhuyang Baihui, through the fourteen meridians of qi and blood, exorcise evil spirits to go out. At the same time, select the local acupoints of the lesions, (Yifeng, Xiaguan, zygomatic, Yingxiang, Jiaicheng paste), this group is commonly used in the treatment of facial pain, acupuncture should be deep stimulation, the appearance of electric shock-like feeling is better. The patient's condition is repeated and delayed

for a long time, which brings certain difficulty to clinical treatment, but it is analyzed dialectically from the aspects of "deficiency and excess" and "meridian circulation", and good results have been achieved in the treatment of this disease by remote movement along meridians.

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Clinical observation of conventional acupuncture combined with SUN's abdominal Moxibustion in the treatment of subacute insomnia

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Abstract

Subacute insomnia refers to patients' dissatisfaction with sleep time and/or quality, including difficulty in falling asleep, difficulty in maintaining sleep or early waking in the morning, etc., the course of disease ≥ 1 month, < 6 months. Insomnia symptoms are diverse, mainly manifested as difficulty in sleep initiation (difficulty falling asleep), difficulty in sleep maintenance, early awakening, and impairment of daytime functions, such as fatigue, attention impairment, and decreased social ability [1,2], which seriously affect the quality of life of patients. Its prevalence rate can reach 10% to 15% [3], and it is an important factor for the persistence of various mental diseases [4,5]. At present, drug therapy is mainly used in clinic, but long-term drug intervention may lead to drug-related adverse reactions, addiction and other side effects. Acupuncture is a green, safe treatment with few side effects, which plays a huge advantage in the treatment of insomnia [6, 7]. Sun Shentian, a master of Traditional Chinese medicine, took the ventral brain theory as the theoretical core and put forward "Sun's abdominal region", which regarded the abdomen of human body as the projection area of cerebral cortex function positioning, patients with insomnia using abdominal zone I and zone VIII for treatment. The purpose of this study was to observe the clinical efficacy of conventional acupuncture combined with Sun's abdominal moxibustion in the treatment of subacute insomnia.

Key words: subacute insomnia; Moxibustion; Sun's abdominal region;

Objective:

To observe the clinical efficacy of conventional acupuncture combined with Sun's abdominal moxibustion in the treatment of subacute insomnia.

Materials and methods:

A total of 60 patients diagnosed with subacute insomnia in the Outpatient department of acupuncture and Moxibustion of the Second Affiliated Hospital of Heilongjiang University of Traditional Chinese Medicine from January 2020 to January 2022 were selected. The patients were randomly divided into treatment group and control group by random number table method, with 30 patients in each group. The control group was given conventional acupuncture, and the points were selected from the "acupuncture therapeutics" of "facial paralysis" in the "13th five year plan" general higher education planning textbook: "Zhaohai", "Shenmai", "Shenmen", "Sanyinjiao", "Anmian", "Sishencong". On the basis of the control group, the observation group was given moxibustion in the abdominal zone I and zone VIII. The location of the abdominal zone I was as follows: 0.5 inch under xiphoid process and its left and right sides open 1 inch, a total of three acupoints; the zone VIII of abdomen: 0.5 inches above and below the navel, 0.5 inches left and right

the navel, a total of four acupoints. Operation and technique: acupuncture point skin is routinely disinfected with ethanol, and disposable stainless steel needle of Huatuo brand is selected. Acupoints are located according to the national standard of the People's Republic of China "meridian location". In Zhaohai straight thorn 0.5 inch, Shenmai straight thorn 0.3 inch, Shenmen straight thorn 0.3 inch, Sanyinjiao straight thorn 1.0 inch, Anmian straight thorn 1.0 inch, Si Shencong flat thorn 1.0 inch, all acupoints are applied with smooth reinforcing and reducing, the needle retention time was 25 minutes. Moxibustion treatment was performed in the zone I and zone VIII of abdomen, once a day, and each treatment time was 25min. Continuous treatment for 5 days, rest for 2 days, 7 days as a course, a total of 4 courses. Efficacy evaluation criteria: Both groups were evaluated according to Pittsburgh Sleep Quality Index (PSQI), Insomnia Severity Index (ISI) score and guidelines for Clinical Research of Traditional Chinese Medicine drugs before and after treatment. The efficacy of the two groups was compared.

Results and discussion:

After treatment, PSQI and ISI scale scores in both groups were lower than those before treatment, the difference was statistically significant ($P < 0.05$), and the decrease was greater in the treatment group than in the control group ($P < 0.05$). The total effective rate of the treatment group was 86.67% (26/30), higher than that of the control group 60.00% (18/30), the difference between the two groups was statistically significant ($P < 0.05$). The results showed that the therapeutic effect of the two groups was improved obviously, and the clinical effect of the treatment group was better than that of the control group.

Therefore, conventional acupuncture combined with moxibustion in the abdominal area of Sun's for the treatment of subacute insomnia can significantly improve the sleep quality of patients, improve the clinical efficacy, and is worthy of clinical application.

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Research Progress of Acupuncture and Moxibustion Treatment of Spinal Cord Injury Based on the Regulation of MAPK Signaling Pathway

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Abstract: Spinal cord injury is a high incidence of disease in the world, has the characteristics of high morbidity, and it's more common seen in the young adults. Its clinical manifestation is damage more plane disappeared following spinal cord function, movement, sensory disturbance, and often accompanied by neurogenic bladder, neurogenic bowel dysfunction, complications such as neuropathy pain, seriously affect the patients quality of life. In recent years, acupuncture therapy has been widely used in the treatment of spinal cord injury and has a relatively definite effect. MAPK (mitogen-activated protein kinase), as an important signal transduction pathway in biological body, participates in the mediation of various cellular physiological processes and plays a key role in the pathophysiology of spinal cord injury. In this paper, based on MAPK pathway, the mechanism of acupuncture treatment of spinal cord injury in recent years was reviewed, in order to provide new ideas and methods for future scientific research and clinical research.

Keywords: acupuncture; spinal cord injury; MAPK; review

Spinal cord injury (SCI) is one of the most common diseases in the world. In recent years, due to the popularity of tourism, transportation and other reasons, the incidence of SCI has increased. Spinal cord injury is a serious disabling disease, which will cause varying degrees of disturbance in patients' movement, sensation and defecation, and seriously threaten patients' quality of life, and even affect their life expectancy.

Mitogen-activated protein kinase (MAPK) cascade is an important pathway of intracellular and intracellular signal transduction, which can respond to various extracellular stimuli and regulate a variety of basic cellular physiological and pathological processes. The MAPK family consists of four subgroups, Extracellular signal-regulated kinase 1/2(ERK1/2), C-Jun n-terminal kinase (JNK), P38 and ERK5.

1. 1 ERK1/2 signaling pathway

ERK1/2, or extracellular signal-regulated kinases, include ERK1 and ERK2^[1]. This pathway is involved in the regulation of many cellular processes, including apoptosis, cell proliferation, immune response, nervous system function, and RNA synthesis and processing^[2], and is also the key to signal transmission from cell membrane surface to nucleus

Dai Ni ^[3] used electroacupuncture to acupuncture the bilateral Sanyi acupoints and Zusanli acupoints of SCI model mice, and found that the expression of P-ERK1/2 increased significantly. She believed that electroacupuncture could improve the oxidative stress response after SCI, activate the ERK1/2 pathway, and activate the transcription of Nrf2 and HO-1 downstream genes to play an anti-oxidative stress role. Then promote the repair of spinal cord function; Shi Suhua ^[4] received electroacupuncture treatment at dazhui and Mingmen acupuncture points, and found that the expressions of MEK2 and P-ERK1 proteins increased significantly after 7 days of treatment (P<

0.05), it is speculated that electroacupuncture can promote the recovery of motor function in SCI rats, because electroacupuncture can up-regulate the expression of MEK2 and P-ERK1 protein in SCI rats, thus promoting the repair and regeneration of neurons;

1.2 JNK signaling pathway

JNK, or C-Jun amino terminal kinase, has three family members, namely, JNK1, JNK2 and JNK3^[5]. Lu Wei et al.^[6] found that electroacupuncture at Dazhui point and Mingmen point in SCI rats reduced the expression of P-C-Jun in spinal cord tissues of the Du acupuncture group compared with the model group, with statistically significant difference ($P < 0.05$), indicating that electroacupuncture treatment can inhibit the activation of JNK pathway and effectively reduce the apoptosis phenomenon caused by the mass aggregation of P-C-Jun

1.3 P38MAPK pathway

P38 is the main protein of the P38 pathway (P38 mitogen-activated protein kinase), with a molecular weight of 38000^[7]. The mammalian p38MAPK family consists of four members: P38 α , P38 β , P38 γ and P38 δ . Chen Wei^[8] treated SCI rats with jiji electroacupuncture at the modeling segment, and found that the positive expression of P38 MAPK in the electroacupuncture group was significantly lower than that in the model group, and the BBB score was significantly higher. It was speculated that the improvement of motor function of rats by electroacupuncture was related to the inhibition of P38 MAPK pathway by electroacupuncture and the reduction of nerve cell apoptosis at the injury site

1.4 ERK5 signaling pathway

The ERK5 signaling pathway is a newly discovered member of the MAPK family and can be activated by many extracellular stimuli, such as hypertonic pressure, hypoxia, oxidizer and fluid shear stress^[9]. Wang Di^[10] found through experimental studies that clip-spine electroacupuncture treatment in rats with spinal cord injury can up-regulate the expression of ERK5 and P-ERK5, and this regulation can be blocked by ERK5 specific inhibitor XMD8-92, indicating that ERK5 signaling pathway is involved in the process of spinal cord injury repair and has an inhibitory effect on apoptosis. It is one of the mechanisms of treatment of spinal cord injury by jia-ji electroacupuncture.

2. Discussion

MAPK pathway is one of the important signal transduction pathways in biological body. Acupuncture and moxibustion intervention on the four pathways of MAPK family can inhibit cell apoptosis in the injured site and promote nerve function repair and regeneration. There are many literatures on the mechanism of acupuncture and moxibustion in the treatment of spinal cord injury based on this pathway, but there are still some deficiencies: Acupuncture and moxibustion in the treatment of SCI is a multi-target, multi-level and multi-pathway process, which is the result of the joint participation of multiple pathways. Most of the current studies focus on one pathway, which is relatively one-sided; (2) Various acupuncture methods, acupoints and manipulations were used in the experiment. Future research should be standardized and unified as far as possible on the basis of being close to clinical practice to reduce the influence on experimental results.

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STUDY ON THE MECHANISM OF ELECTRO ACUPUNCTURE PROMOTING THE RECOVERY OF MOTOR FUNCTION AFTER SPINAL CORD INJURY

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Abstract: Spinal cord injury belongs to central nervous system disease, and its disability rate is high. Motor dysfunction after spinal cord injury has a great impact on the life of patients. The study found that electroacupuncture was helpful to the recovery of motor function after spinal cord injury, without obvious adverse reactions. This paper reviews the mechanism of electroacupuncture treatment, in order to provide reference for the study of electroacupuncture promoting the recovery of motor function after spinal cord injury.

Key words: Electroacupuncture; Spinal cord injury; Motor function; Mechanism research

Spinal cord injury (SCI) is a traumatic disease of the central nervous system with a high disability rate, which often leads to the death of spinal cord neurons and the loss of sensory, motor and autonomic nerve functions. According to the cause of the disease, it is divided into primary SCI and secondary SCI^[1-2]. At present, the incidence rate of SCI in China shows an obvious upward trend. Those with serious conditions often have serious complications, even paraplegia^[3-4]. Therefore, the effective treatment of SCI is very important. A large number of studies have shown that electroacupuncture has a significant effect on the recovery of motor function after SCI, and its clinical effect is accurate. It is a research hotspot in the treatment of SCI in recent years.

1.Electroacupuncture Therapy

Electroacupuncture therapy refers to that after the filiform needle is inserted into the acupoints to get Qi, a small amount of biological pulse current is connected at the end of the needle handle. Through the stimulation of acupuncture and current at the same time, the Qi of the meridians of the human body is stimulated to prevent and treat diseases. Electroacupuncture has been widely used in clinical and scientific research because of its simple operation, controllable stimulation intensity and long duration.

2.Study on the mechanism of electroacupuncture in the treatment of motor dysfunction after spinal cord injury

Electroacupuncture treatment of SCI is a complex process involving many factors, which may promote the recovery of motor function through the following mechanisms.

2.1 Increase the expression of neurotrophic factors

Neurotrophic factors, a widely existing protein in the central nervous system, play an important role in the protection of nerve cells and the growth of axons. Xu HY et al^[5]. took 25 adult male SD rats as the research object. The experiment found that Du pulse electroacupuncture intervention could

increase the opening time and frequency of calcium channel l-vgcc and activate the downstream α CaMK II pathway, thereby promoting the synthesis of nerve growth factor NT-3, has a positive effect on the survival and regeneration of axonal neurons at the injured site after spinal cord injury.

2.2 Genes related to apoptosis

Neuronal apoptosis is a kind of programmed cell death, which is characterized by cell contraction, genome disruption, chromatin aggregation, and nuclear pyknosis. It is the main cause of delayed cell death at the injury site after SCI, and often aggravates the injury of the spinal cord [6].

2.3 Improve the microenvironment of damaged parts

Secondary spinal cord injury has appeared within a few minutes of primary spinal cord injury, causing inflammation, ischemia, hypoxia and other microenvironments at the injured site, hindering the recovery of neural function. Liu Yingying et al^[7]. established a spinal cord injury model with 50 male Wistar rats as experimental objects. The results showed that the motor function of rats recovered significantly compared with that of the model group. It may be that electroacupuncture promoted the flow of blood and cerebrospinal fluid and the recovery of neural function by improving the microenvironment in rats, so as to gradually restore the motor function of rats.

2.4 Promote axonal regeneration and functional recovery

The regeneration length of axons can be observed 6 hours after SCI, but the scar tissue formed at the injured site inhibits the growth of axons. At 48 hours after injury, axons stop growing and lose contact with distal axons. Xiao WP et al^[8]. used electroacupuncture to treat SD rats with spinal cord injury. The results showed that electroacupuncture could inhibit nogo/ng2 and rho/rock signal pathways after spinal cord injury and reduce the adverse effects on axon growth, which may be an important mechanism for electroacupuncture to promote the recovery of motor function after SCI.

3 Discussion and Prospects

In recent years, the extensive application of electroacupuncture combined with other therapies in the field of SCI has effectively promoted the recovery of patients' motor dysfunction. Although researchers have revealed some mechanisms of electroacupuncture in the treatment of SCI, the more comprehensive and in-depth mechanism is not clear. In the future, we should continue to explore the mechanism of electroacupuncture in treating SCI and clarify the target of electroacupuncture; At the same time, it can also conduct interdisciplinary research, based on the traditional acupuncture theory and the combination of software and hardware, so as to promote the development of electroacupuncture in the direction of intelligence, further improve the pertinence and accuracy of treatment, and benefit patients.

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Research progress of traditional Chinese medicine rehabilitation therapy in the treatment of neurogenic bladder after spinal cord injury

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Abstract: Neurogenic bladder is the most common complication after spinal cord injury. Although its clinical treatment has made some progress, there is still no effective treatment for the recovery of nervous system diseases and the regeneration of nerve injury. By collecting the relevant literature of neurogenic bladder in recent ten years, this paper summarizes the traditional Chinese medicine rehabilitation treatment of neurogenic bladder after spinal cord injury, and puts forward the deficiencies, hoping to provide reference for future clinical treatment.

Key words: Rehabilitation therapy of traditional Chinese Medicine; Spinal cord injury; Neurogenic bladder; Research progress

Neurogenic bladder (NB) is the most common complication after spinal cord injury (SCI), which is often caused by damage to the central nervous system or peripheral nervous system that controls urination function. Urinary incontinence or urinary retention are the most common symptoms^[1]. At present, western medicine mostly adopts rehabilitation treatment technologies such as intermittent catheterization, reinnervation, surgery and drug therapy for the treatment of NB after SCI, but there are problems such as long treatment cycle, large toxic and side effects, poor remote curative effect and so on. This paper summarizes the literature on the traditional Chinese medicine rehabilitation treatment of neurogenic bladder after spinal cord injury in recent ten years, hoping to provide help to improve the treatment of the disease. The review is as follows:

1 Rehabilitation therapy of Traditional Chinese Medicine

Traditional Chinese medicine rehabilitation therapy is a traditional rehabilitation treatment method under the guidance of the basic theory of traditional Chinese medicine and guided by the holistic view and syndrome differentiation and treatment. It has unique advantages in the treatment of this disease.

1.1 Acupuncture

Acupuncture therapy for neurogenic bladder after spinal cord injury mainly includes electroacupuncture, warm acupuncture, fire acupuncture so on.

At present, electroacupuncture is the most widely used in clinical application. Research shows that electroacupuncture can effectively promote the recovery of nerve function of injured cells and accelerate the cell electrical conduction of injured nerves through the dual stimulation of physical stimulation and low-frequency electrical stimulation of acupoints^[2]. At the same time, the density wave provided by electroacupuncture to the body can also promote the blood circulation and metabolism of the damaged parts and reduce inflammatory edema^[3]. Warm acupuncture combines acupuncture and moxibustion to form a high-temperature conduction area in the injured part and conduct along the meridians, promote vascular dilatation on the formed high-temperature conduction wire, and accelerate the energy metabolism of the tissue^[4]. Fire acupuncture is a kind of traditional acupuncture and moxibustion therapy, which is also often used in the treatment of this

disease. Relevant literature shows that fire needle can not only inhibit cell apoptosis, but also promote the proliferation of neural stem cells in SCI rat model, thus promoting the recovery of nerve function at the injured site and improving the functional state of bladder^[5].

1.2 Moxibustion

"Introduction to medicine · acupuncture and Moxibustion" says: "if the medicine is not as good as the needle, it must be moxibustion." It shows that moxibustion has a unique therapeutic effect different from acupuncture, which can make up for the deficiency of acupuncture. Because moxibustion has the functions of warming, dredging and medicine, it can dredge the meridians, help the bladder to gasify and improve the bladder function when moxibustion is applied^[6].

1.3 External use of traditional Chinese Medicine

The external use of traditional Chinese medicine includes traditional Chinese medicine fumigation, acupoint application, traditional Chinese medicine ironing, etc. it is safe and effective in clinical use, which can reduce the adverse reactions of drugs and the stimulation to the gastrointestinal tract, and its local warming effect also has the function of warming the meridians and regulating the bladder. However, its absorption is not as good as oral drugs and its bioavailability is high. Therefore, it is often used in combination with other treatment methods in clinic.

1.4 Massage therapy

Massage therapy is common in the rehabilitation of traditional Chinese medicine, which has the functions of dredging the meridians, adjusting the functions of viscera, promoting qi and activating blood circulation. Its operation is simple, safe and effective, with wide indications and no obvious side effects. There are many manipulations of massage. Patients with neurogenic bladder after spinal cord injury often use kneading or palm rubbing to act on local parts of the body to produce heat sensation.

2 Discussion and Prospect

In recent years, the rehabilitation treatment of neurogenic bladder after spinal cord injury has shown a diversified trend. Whether it is the combination of a variety of traditional Chinese medicine or the combination of traditional Chinese and Western medicine, it has a certain effect on the rehabilitation of the disease. However, compared with the complications of drug resistance, liver and kidney function damage and urinary tract infection caused by long-term use of Western medicine, traditional Chinese medicine rehabilitation treatment shows unique advantages. Acupuncture and moxibustion have been widely used in clinic, and some special acupuncture and moxibustion therapies have also provided unique ideas for clinic and made outstanding contributions to the treatment of NB because of their unique theories. It is expected that the following large samples, big data, evidence-based medicine evidence, as well as the use of neurogenic bladder animal model after spinal cord injury, will fully explore the therapeutic effect of traditional Chinese medicine rehabilitation therapy, and explore its therapeutic mechanism, so as to formulate a standardized, safe and scientific comprehensive treatment plan for the rehabilitation of NB patients after SCI, and promote its application.

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Clinical observation on the treatment of peripheral facial paralysis by electroacupuncture at the fourth point of mastoid process

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Abstract

Objective: To observe and analyze the clinical efficacy of electroacupuncture at four points of mastoid process in the treatment of peripheral facial paralysis. **Methods:** 60 patients with peripheral facial paralysis were randomly divided into observation group and control group, with 30 cases in each group. The control group was given routine acupuncture treatment, and the observation group was given acupuncture at the four points of the mastoid process on the affected side on the basis of the control group; Observe and evaluate its clinical efficacy and safety. **Results:** house brackmann (H-B) facial nerve function rating scale and facial disability index scale (FDI) were used as the efficacy criteria. The cure rate of the observation group was 90% (27/30), and that of the control group was 76.67% (23/30). **Conclusion:** Electroacupuncture at the four points of mastoid process can effectively improve the clinical symptoms of peripheral facial paralysis, which is worthy of further promotion.

Keywords: peripheral facial paralysis; Four points of mastoid process; Acupuncture;

Peripheral facial paralysis, known as facial paralysis or bell paralysis in western medicine, is usually an acute unilateral disease with an onset time of less than 72 hours [1], which is a common and frequently occurring disease in clinic. The treatment program of Western medicine has a relatively long course of treatment, and the curative effect on the improvement of symptoms and sequelae is relatively poor. Acupuncture and moxibustion therapy is a green, safe and less side-effect treatment method, which has played a great advantage in many methods of treating facial paralysis [2, 3]. The continuous exploration of the treatment scheme of facial paralysis by doctors of all dynasties through a large number of clinical practice has further enriched the theory and method of acupuncture and moxibustion in the treatment of peripheral facial paralysis.

Professor gaoweibin is a national famous and old expert of traditional Chinese medicine, and the instructor of inheriting the academic experience of the national old expert of traditional Chinese medicine. Based on neuroanatomy, Professor Gao founded the four mastoid points and put forward the theory of "electroacupuncture bone conduction". Dense wave electric pulse transmits through bone, Qi reaches the place of disease, and cures diseases and dispels pathogens. Therefore, electroacupuncture at the four points of mastoid process was mainly used to treat peripheral facial paralysis, and compared with traditional acupuncture to observe its clinical effect.

Objective

To observe and analyze the clinical efficacy of electroacupuncture at four points of mastoid process in the treatment of peripheral facial paralysis.

Materials and methods

A total of 60 patients with peripheral facial paralysis were selected from the Department of acupuncture and moxibustion, the Second Affiliated Hospital of Heilongjiang University of

traditional Chinese medicine from January 2019 to January 2021. The patients were randomly divided into observation group and control group, with 30 cases in each group. The control group was given routine acupuncture, and the acupoints were selected from the "acupuncture therapeutics" of "facial paralysis" in the "13th five year plan" general higher education planning textbook: "Yangbai"(GB14), "Sibai"(ST2), "Quanliao"(SI18), "Dicang"(ST4), Yifeng(TE-17), Qianzheng, Taiyang(EX-HN5) of the sicken side were selected, and the healthy side Hegu(L14) were selected. On the basis of the control group, the observation group was given acupuncture at the four points of the ipsilateral mastoid process. The location of the four points of the mastoid process: mastoid 1: 1cm behind the posterior sulcus of the auricle, flat the upper edge of the external auditory canal; mastoid 2: 1cm behind the posterior sulcus of auricle, flat the lower edge of external auditory canal; mastoid 3: 2cm behind the posterior sulcus of auricle, flat the upper edge of external auditory canal; mastoid 4: 2cm behind the posterior sulcus of auricle, flat the lower edge of external auditory canal. Acupuncture angle: 15-30 degrees along the direction of the external auditory canal, with the tip of the needle against the mastoid process as the degree; Reinforcing and reducing method: smooth reinforcing and reducing. Operation: the patient is in a sitting or lateral position, and the skin is routinely disinfected with 0.30 × 40mm Andy brand filiform needle, after acupuncture, choose Great Wall brand kwd-808 I electroacupuncture instrument, mastoid 1 and mastoid 3 as a group; mastoid 2 and mastoid 4 are a group; Pulse current was applied, dense wave was used, and the amount of current was to the extent that the subjects could tolerate it. The needle retention time was 30 minutes. The treatment was once a day, 6 days a week, and 1 day of rest, a total of four weeks of treatment. Evaluation criteria of curative effect: the curative effects of the two groups were compared according to the scores of house brackmann (H-B) facial nerve function rating scale and facial disability index scale (FDI).

Results and conclusion

After treatment, the H-B facial nerve function grades of the two groups were better than those before treatment ($P < 0.01$). There was no significant difference between the two groups after treatment ($P > 0.05$); The scores of facial disability index (FDI) in the two groups were better than those before treatment ($P < 0.01$). There was no significant difference between the two groups after treatment ($P > 0.05$); House brackmann (H-B) facial nerve function rating scale and facial disability index scale (FDI) were used as the efficacy criteria. The cure rate of the observation group was 90% (27/30), and that of the control group was 76.67% (23/30).

Acupuncture at the four points of mastoid process participates in the regulation of facial nerve, which has a significant effect on improving facial nerve circulation and facial nerve excitability.

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A preliminary exploration of the application and promotion possibilities of TCM composition in the field of comprehensive healthcare

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Abstract

Under the background of the development of the times, and based on the development of Comprehensive Healthcare industries to a new stage, Comprehensive Healthcare is a global health concept based on social needs. The key point of prevention is to have evidence to follow, and the theory of Traditional Chinese medicine(TCM) provides the basis for treating the disease before it occurs. Physical constitution is the basis for the occurrence of diseases, and it determines the susceptibility of people with different physical constitutions to diseases. The research progress and feasibility of further application of TCM body constitution and comprehensive healthcare in this article.

Key words:TCM constitution; comprehensive healthcare

In the process of understanding the nature of disease, a new field of health has been discovered in which the previous disease-centered model cannot be effectively applied to human health, and therefore a new cognitive framework has to be constructed to explain the health phenomenon. This new cognitive framework is called the concept of comprehensive healthcare. The concept of macrohealth is the logical starting point for human exploration and practice in the field of health, and its emergence is a major trend. In recent years, the definition of health by the World Health Organization has been generally accepted: a person is healthy when he or she is in good condition not only physically but also mentally and socially. Health is a holistic and comprehensive health, that is, physical, mental, behavioral, social, intellectual, spiritual, moral, and environmental health, and gradually the understanding of "comprehensive healthcare" has been formed . The concept of "comprehensive healthcare" is to change the focus on the treatment of diseases into the focus on people's health, to focus on the sum of the health level and state of different groups and individuals, and the relationship between the environment and health, including the "three whole" life cycle, life in all aspects, health process, covering life, production, life "three life "[1].

The TCM constitution is an objective life phenomenon, which is a comprehensive and relatively stable trait of morphological structure, physiological function and psychological state of an individual based on heredity and acquisition during the life process [2]. The influence of life cycle, mental health, environmental factors, and genetic factors on the formation of physique in the basic principles of TCM constitution system is similar to the concept of "three holistic" in the concept of comprehensive healthcare. Moreover, it has been found that the application of body constitution identification in community health management is highly operable, easy to understand and accept, and easy to promote [3], therefore, the traditional TCM body constitution can be applied and promoted as an important tool of the comprehensive healthcare.

Objective

A preliminary exploration of the application and promotion possibilities of TCM composition in the field of comprehensive healthcare.

Materials and methods

Based on TCM theory, research and his own experience, Professor Wang Qi has classified the Chinese population into nine basic types of physical constitution, namely gentleness, qi deficiency, yang deficiency, yin deficiency, phlegm-damp, damp-heat, blood stasis, qi yu, and special endowment, and his team has conducted several studies on the distribution pattern of TCM body constitution types in the general population, which confirmed the objective existence of the nine types of physical constitution and clarified their distribution pattern [4]. The distribution of TCM constitution in the Chinese population was studied based on Wang Qi's 9 basic TCM body constitution classification, and it was found that the TCM constitution types have obvious gender differences, and the TCM constitution based on the data suggest that more attention should be paid to women's physical health, and the focus of intervention should be different for different genders. The distribution of physique type is related to age, which shows that in the transition stage between middle age and old age, people's physique is prone to more obvious changes, and when they enter old age, they start to show their own trend characteristics, so people in this age should be given special attention. Therefore, special attention should be paid to this age group. The geographical differences of body mass distribution are obvious in different regions, meanwhile, the elderly population shows more geographical differences and has its own characteristics. Long-term studies on the distribution characteristics of body mass can clarify the trends of body mass distribution and provide data support for the application of TCM constitution mass typing in health maintenance, treatment of diseases and health management, which is of great significance for the intervention of body mass and prevention of related diseases in groups. Using clinical epidemiological methods, the integration of TCM constitution system and disease risk assessment system, forming a new model of longitudinal and horizontal integration of body disease correlation, is expected to remedy the shortcomings of the current TCM system of prospective trend warning .

Results and discussion

Studies have been conducted on the application of TCM constitution in the context of comprehensive healthcare. Some researchers have applied TCM constitution theory to the prevention and treatment of malignant tumors in the context of general health, which not only helps to monitor the population prone to malignant tumors, but also realizes early health guidance for the population prone to malignant tumors and thus reduces the incidence of malignant tumors. By studying the distribution of malignant tumors in Chinese medicine and applying body constitution identification to the epidemiological survey of malignant tumors, we can realize the initial screening of people with high risk of malignant tumors and provide individualized guidance on body conditioning interventions to prevent malignant tumors to individuals, which is expected to reduce the incidence of malignant tumors. Healthy residents can improve their biased physique early through targeted TMC body conditioning not only to keep them healthy, but also to prevent the biased physique from further developing into a high-risk physique for malignant tumors. The early warning of people with risky physique for malignant tumor can be achieved by identifying the physique of the population [5]. Another researcher investigated the distribution of TCM constitution of chefs to provide guidance for targeted prevention of occupational diseases, etc. Using the cross-sectional survey method, 137 chefs were randomly selected from some hotels in Dongcheng District, Dongguan City to conduct a questionnaire survey on TCM physique. The purpose of the

survey is to improve the health awareness of the chef population and to analyze the distribution of the chef's TCM constitution, , to provide basic information for improving the chef's constitution to prevent and treat related occupational diseases[6]. The application of TCM constitution in the field of comprehensive healthcare is promising because it can be used as a screening tool for the general public and for a specific occupational group to see the potential occurrence of diseases in their occupations.

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The development of TCM in China-Russia medical cooperation

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Abstract

Objective

With the deepening of the "Belt and Road" strategy, the proportion of TCM in China-Russia medical cooperation has gradually increased. Based on this, the difficulties and development prospects encountered in the development of TCM are briefly discussed.

Materials and methods

Traditional Chinese medicine is a treasure constantly explored and summarized by ancient Chinese people after long-term clinical practice. With its systematic theoretical system, the purpose is to adjust the balance of Yin and Yang to achieve the state of "Yin and Pingyang secret, spirit and even". Professor Tu Youyou has proved the value of Chinese medicine to the world by extracting artemisinin to treat malaria. With the continuous development and innovation of medicine and health care, ancient France has also provided more scientists with ideas in the development of new drugs and promoted the development of modern medicine.

With its magical efficacy, TCM has attracted more and more attention from people of all ethnic groups around the world. In its 2018 government report, the government clearly pointed out the strong support for the development of traditional Chinese medicine and ethnic minority medicine. With the continuous development of the global entrepreneurial structure, China has put forward the new idea of "Belt and Road" to promote the development of multilateral economy. As an important partner of the countries along the "Belt and Road" route, Russia has gained a deep understanding in the economic, political and cultural aspects. With the deepening of the international cooperation in medicine, the speed of the internationalization process of pharmaceutical products is also gradually accelerating. The prospect of TCM trade cooperation in China-Russia pharmaceutical products has also become more and more broad.

Development status of pharmaceutical product trade

According to statistics^[1], the total drug trade of shows a whole development trend of expansion. The trade^[2] of pharmaceutical products between China and Russia is mainly in the category of western medicine, traditional Chinese medicine and medical devices, but traditional Chinese medicine does not have an advantage. The main reason is that it is difficult to register and approve traditional Chinese medicine products in Russia, and the understanding of the clinical effect of TCM is insufficient. Therefore, under the strategic background of "Belt and Road", the innovative development of TCM culture will help to better promote the development of Sino-Russian pharmaceutical product exchanges. By 2017^[3], 50 TCM manufacturers, TCM diagnosis and treatment equipment manufacturers and integrated Chinese and Western medicine cooperative hospitals have settled in Russia, which is conducive to the promotion of TCM in Russia.

China and Russia have deepened medical cooperation

China-russia relations is gradually on track, traditional Chinese medicine with its efficacy is more and more popular with the Russian public, the demand for Chinese medicine is more and more big,

more and more Russian students came to Chinese medicine culture, strengthen the cooperation and exchanges of scientific research institutions, build a good policy environment and provide appropriate learning environment to promote china-Russia medicine exchanges ^[4].With its own geographical advantages^[5], in Heilongjiang Province plays an important role in this process, and makes positive contributions in strengthening the medical personnel and technical exchanges between China and Russia, and improving the service level of medical cooperation at home and abroad. In 2020, COVID-19 swept the whole world. The Chinese government controlled the development of COVID-19 in the shortest time. TCM played a pivotal role in this campaign, showing the world the effective effect of TCM and promoting the development of TCM in the world. According to the task of the Chinese government, Heilongjiang Province has appointed a traditional Chinese and western medicine assistance team to Russia to provide epidemic assistance and guidance, which has promoted the development of TCM in Russia to a certain extent.

Results and discussion

With the help of the strategic support of the Internet and "Belt and Road", TCM has gained a solid platform, and the dissemination of TCM culture also has a persistent mass base ^[6].The author believes that the development prospect of traditional Chinese medicine culture in China-Russia medical cooperation is very broad.

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Therapeutic effect of Cyperi Rhizoma on Mammary gland hyperplasia in rats

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Abstract

Mammary gland hyperplasia is one of the most common breast diseases. In recent years, with the acceleration of people's pace of life and the increase of work pressure, the incidence rate increases year by year, and the onset age tends to be younger. For this disease, the treatment of western medicine has great side effects, easy to cause damage to other endocrine organs. Therefore, the use of traditional Chinese medicine to treat the disease has become a hot topic. Cyperi Rhizoma has the pharmacological activity of soothing liver and relieving depression, which is the key traditional Chinese medicine in clinical treatment of mammary gland hyperplasia. In this study, the mammary gland hyperplasia model of rats was established by injection of exogenous hormone and treated by intragastric administration of rhizoma cyperus extract. The therapeutic effects of Cyperi Rhizoma were studied by western blot and immunohistochemistry, and its mechanism was preliminarily discussed. The results showed that intramuscular injection of estradiol combined with progesterone was a simple and effective method to replicate rat mammary hyperplasia model. Cyperi Rhizoma can significantly reduce the diameter of the nipple in the hyperplasia rats, so that the number of acinar in the hyperplasia mammary tissue is reduced, the acinar atrophy, the ductal lumen becomes smaller, and the hyperplasia is effectively improved.

Key words: Cyperi Rhizoma, Hyperplasia of mammary gland

The occurrence of mammary gland hyperplasia is affected by a variety of factors, such as mental factors, living habits, dietary structure and factors of marriage and breeding. With the progress of social concepts, women have more and more space to play in the workplace. They are in a state of high mental tension for a long time, which is easy to cause endocrine disorders in the body. With the gradual improvement of living standards, people's diet structure has also undergone some changes. Excessive intake of high-fat and high-protein food and unreasonable diet structure will also cause changes in the human body environment, resulting in endocrine and metabolic disorders. In addition, the incidence of induced abortion is increasing, induced abortion will lead to serious imbalance of hormones in the body, with the increase of the number of abortions, the risk of breast hyperplasia also increases.

Traditional Chinese medicine can regulate endocrine metabolism, fundamentally improve endocrine disorders, so as to play a therapeutic role. The toxic side effects of traditional Chinese medicine is small, will not cause damage to the body, therefore, for the treatment of breast hyperplasia, the most common choice, easy to accept the treatment method is oral Chinese medicine. As a traditional

Chinese medicine, Cyperi Rhizoma also has a unique effect in the treatment of mammary gland hyperplasia.

Objective

To study the therapeutic mechanism of Cyperi Rhizoma on mammary hyperplasia, and to separate the chemical components of Cyperi Rhizoma, and further study the material basis of Cyperi Rhizoma treatment on mammary hyperplasia.

Materials and methods

In this study, a large amount of estradiol and a small amount of progesterone were injected to replicate the rat mammary gland hyperplasia model. This method can simulate the endocrine environment with high estrogen level and imbalance of estrogen progesterone. From the perspective of a nipple diameter measurement and pathological results, stop hormone injections a month later, model control group of mammary gland hyperplasia in rats and no obvious improvement, from the serological index analysis, compared with normal control group, model control group rats still remain at high levels of estrogen, progesterone remains at a low level, estrogen progestin ratio imbalance still. So directly caused the continuous progress of mammary hyperplasia. It's a continuous progression of mammary hyperplasia. Cyperi Rhizoma medicinal materials are purchased in heilongjiang medicinal materials market.

Results and discussion

Mammary gland hyperplasia is the most common mammary gland disease, and its incidence is increasing year by year, and the onset age tends to be younger. The pathogenesis of this disease is still unclear and there is no unified and effective treatment. TCM scholars generally believe that the disease is caused by liver stagnation, qi stagnation, liver and kidney deficiency. Western medicine mainly uses endocrine therapy to treat the disease, and the drugs used have large side effects, which can easily cause excessive endocrine disorder and damage to other endocrine organs of the body. TCM therapy has few side effects and can effectively regulate endocrine disorders, so it is more acceptable to patients.

In the rat model of mammary hyperplasia induced by combined injection of exogenous hormones, various endocrine hormones appeared disorder in serum, mainly reflected in the imbalance of estrogen and progesterone ratio. From the perspective of a nipple diameter measurement and pathological results, stop hormone injections a month later, model control group of mammary gland hyperplasia in rats and no obvious improvement, from the serological index analysis, compared with normal control group, model control group rats still remain at high levels of estrogen, progesterone remains at a low level, estrogen progestin ratio imbalance.

Serum estrogen level was significantly decreased and progesterone level was significantly increased in the treatment group, and the imbalance of estrogen progesterone ratio was also improved. These results indicate that Rhizome rhizome can improve the condition of mammary hyperplasia and has good clinical application value in the treatment of mammary hyperplasia.

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Arisaema Cum Bile Aqueous Extracts alleviates epilepsy-induced neuronal damage by improving oxidative stress and inflammation

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Abstract: Epilepsy is regarded as a disorder of brain, characterized by an enduring predisposition for the generation of epileptic seizures because of hyperexcitability and hypersynchrony of brain neurons¹⁻². Traditional Chinese medicine (TCM) has a long history in the treatment of epilepsy and has definite curative effect. According to traditional Chinese medicine and a previous literature, Arisaema Cum Bile (BA) has been used for clearing heat and reducing phlegm and stop wind and spasm. Based on modern pharmacological studies, BA has sedative, analgesic, anticonvulsant, anti-inflammatory, and antioxidant effects. A previous study reported that BA (Cattle Bile) aqueous extract has obvious anticonvulsant effect. However, there are few studies about the anti-epileptic effect of the aqueous extract of BA (Cattle Bile) in PTZ-induced epileptic rats. Therefore, this study aimed to investigate the protective effect of aqueous extract of BA on PTZ-induced epileptic rats, and preliminarily explore mechanism³⁻⁴. A rat model of epileptic was established by intraperitoneal injection of PTZ. Histopathological studies were carried out in the hippocampus of the rat brain by HE and Nissl staining; ELISA assays to detecte antioxidant enzymes and inflammatory responses cytokines; the expression levels of several key proteins involved in apoptosis and autophagy in hippocampus were detected by qRT-PCR, western blot and immunohistochemistry to clarified the underlying mechanisms.

Key words: Epilepsy; Arisaema Cum Bile; autophagy; apoptosis; inflammatory responses; oxidative stress.

Objective: This study aimed to investigate the protective effect of aqueous extract of Arisaema Cum Bile on PTZ-induced epileptic rats, and preliminarily explore mechanism.

Materials and methods: A total of 80 rats were recruited in this study. After being weighed, 68 rats were intraperitoneally injected with PTZ (50 mg/kg), every 24 h till to 7 d, to establish acute epilepsy models. Rats in the control group (n = 12) were injected with anequal amount of physiological saline. Epilepsy was graded according to Racine's scale (Racine, 1975), when the rats reached stages 4 and seizure lasted 30 minutes or longer, it was regarded as successful construction of epilepsy. The Control group and PTZ group were daily orally administered with normal saline for 21 days. PTZ + VPA group were orally administered with VPA (200 mg/kg). Rat in PTZ + BA groups were simultaneously given the aqueous extract of BA at 0.3, 0.6 or 1.2 g/kg for 21 days.

Results: Observation of HE and Nissl staining. The results of HE and Nissl staining showed that in the PTZ group, obvious neuron loss was observed in the CA1 and CA3 regions of the hippocampus; the neurons of rats were disordered, with abnormal structures and unclear boundaries; decreased Nissl bodies in cytoplasm chromatin margination and blocking and cell enlargement (Fig. 1a). When compared to the PTZ group, BA at 0.3 and 0.6 g/kg mildly improved the neuronal damage in the CA1 and CA3 regions of the hippocampus, and BA at 1.2 g/kg obviously reduced neuronal damage

in the CA1 and CA3 regions of the hippocampus. BA Attenuated Inflammatory Responses and Oxidative Stress in Rat. As shown in Fig.2, compared to the PTZ group, BA at all three doses groups decreased the levels of MDA, IL-1 β , IL-6, TNF- α and iNOS and increased the levels of SOD, GSH, CAT. In general, the above data indicated that compared with the PTZ group, BA has significant difference at the dose of 1.2 g/kg ($p < 0.01$), which can significantly improve epilepsy. LC3 I , LC3 II , p62, Beclin 1 and COX IV mRNA expression levels of the epilepsy-related gene We performed qRT-PCR to explore the effect of BA on the gene levels of LC3 I , LC3 II , Beclin 1, p62 and COX IV in epileptic rats. When compared with PTZ group, expressions of LC3 II , COX IV, Beclin 1 were substantially decreased in PTZ + BA group, while LC3 I and p62 was increased ($p < 0.01$) (Fig.3). BA group decreased the expression of Caspase-3 and increased the expression of p62 in the hippocampus of epileptic rats Compared to the PTZ group, PTZ + BA group significantly decreased the expression levels of caspase-3 in the hippocampus of the PTZ group ($p < 0.05$), and the expression levels of p62 was significantly increased ($p < 0.01$) (Fig.1b). Effect of BA on the Expression of apoptosis and autophagy pathway related-proteins in the hippocampus of epileptic rats. When compared with PTZ group, expressions of LC3II/I, Beclin 1, Atg5, Atg7, Atg12 and caspase-3 were substantially decreased in PTZ + BA group, while p62 was increased ($p < 0.05$) (Fig.4).

Conclusion: In summary, our study demonstrated that Arisaema Cum Bile (Cattle Bile) treatment protected neurons against PTZ-induced neuronal damage in epileptic rat models. Treatment with BA significantly alleviated oxidative stress and the inflammatory response, protecting neurons against autophagy and apoptosis in hippocampal of epileptic rats.

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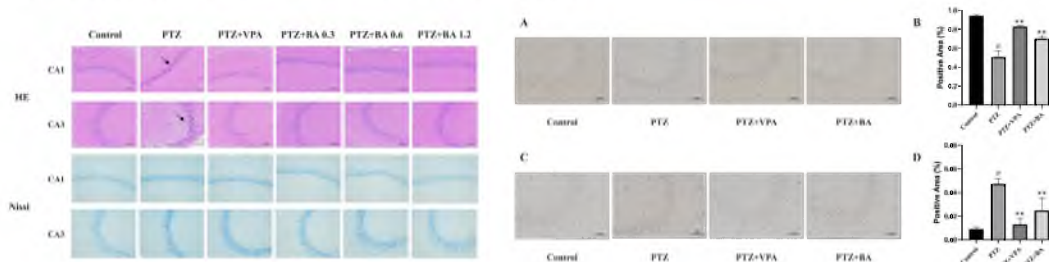


Fig.1. a) Observation of HE staining and Nissl staining for the hippocampus morphological changes in each group ($\times 200$). b) The expression of p62 and caspase-3 in hippocampus was detected by

immunohistochemistry (ICH) ($\times 200$). #, $p < 0.05$ vs. Control group; *, $p < 0.05$ vs. PTZ group; **, $p < 0.01$ vs. PTZ group.

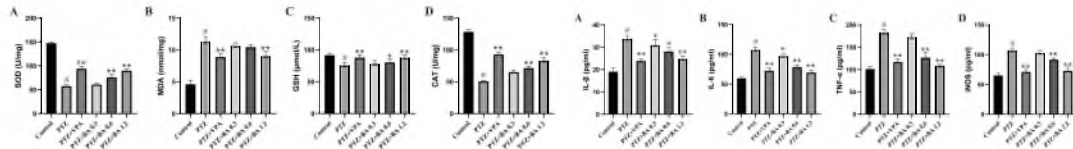


Fig.2. The levels of SOD, MDA, GSH, CAT, IL-1 β , IL-6, TNF- α , and iNOS in hippocampus of rats were detected by chromatometry (n = 8). #, $p < 0.05$ vs. Control group; *, $p < 0.05$ vs. PTZ group; **, $p < 0.01$ vs. PTZ group.

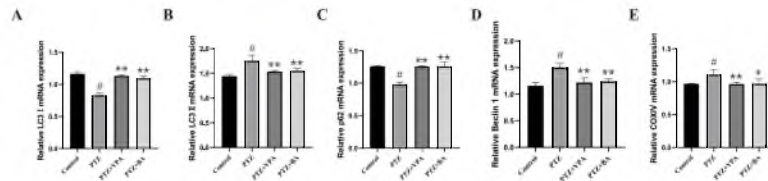


Fig.3. The expression of LC3 I , LC3 II , p62, beclin1 and COX IV in hippocampus detected by quantitative real-time PCR (qRT-PCR). #, $p < 0.05$ vs. Control group; *, $p < 0.05$ vs. PTZ group; **, $p < 0.01$ vs. PTZ group.

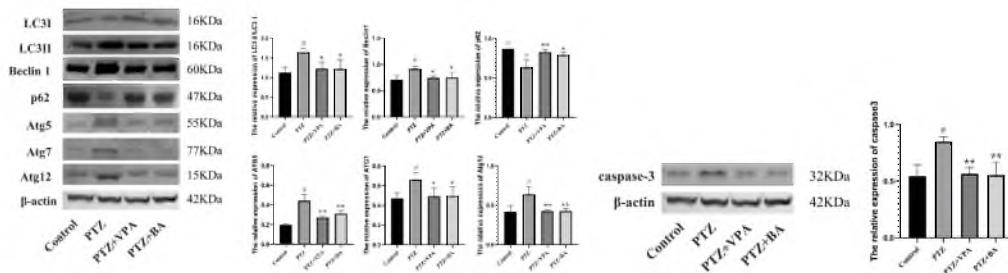


Fig.4. The expression of LC3 II/I , Beclin 1, p62, Atg5, Atg7, Atg12 and caspase-3 in hippocampus detected by western blot. #, $p < 0.05$ vs. Control group; *, $p < 0.05$ vs. PTZ group; **, $p < 0.01$ vs. PTZ group.

Cattle bile *Arisaema* ethanol extracts protect against febrile seizures in rats through regulating neurotransmitters

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Abstract

Cattle bile *Arisaema* is a traditional Chinese medicine used for the treatment of febrile seizures for thousands of years in China. However, its application is greatly limited due to cost reasons, and pig bile *Arisaema* is the main commercial product instead. Additionally, the underlying mechanism of cattle bile *Arisaema* for the treatment of febrile seizures still remains unknown. In this study, we investigated the anti-convulsant effect and potential mechanism of the cattle bile *Arisaema* ethanol extract for the first time through a hot-water bath-induced febrile seizures rat model. Our results showed that pre-treatment with cattle bile *Arisaema* dramatically lowered the incidence rate and generation times and prolonged the latency of febrile seizures. In addition, cattle bile *Arisaema* effectively ameliorated neuronal damage and regulated neurotransmitter disorder induced by febrile seizures in the rat hippocampus. The enzyme-linked immunosorbent assay, western blotting, immunohistochemical, qRT-PCR results exhibited that cattle bile *Arisaema* suppressed the expression of GFAP, HMGB1, IL-1 β and BDNF. These findings indicate that cattle bile *Arisaema* exerts a protective effect on febrile seizures through regulating neurotransmitter disorder.

Key words: cattle bile *Arisaema*, febrile seizures, neuronal damage, neurotransmitter, anti-convulsant

Febrile seizure is an epileptic convulsion defined by the International Alliance for the Prevention and Treatment of Epilepsy. It is frequently encountered in infants aged from 6 months to 5 years with a prevalence rate of 2-5%. It is often accompanied by fever and hippocampal injury, but there is no obvious evidence of central nervous system infection. Clinical guidelines recommend the employment of antipyretic drugs combined with antiepileptic drugs to alleviate febrile seizure, such as diazepam, phenobarbital, and valproate. Unfortunately, the potential toxicity of these antiepileptic drugs to children is frequently greater than their therapeutic effects. They are not suitable for long-term use due to their serious side effects. Therefore, it is imperious to discover a drug with better effect and fewer side effects to fight febrile seizures.

Bile *Arisaema* is a traditional common medicine to treat infant febrile convulsion clinically, it is the fermented product made of *Arisaema* rhizome and different biles including pig, cattle and sheep, as documented in China Pharmacopoeia Committee. Bile *Arisaema* possesses bitter and cold properties, which can clear heat, dissipate phlegm, dispel wind, and relieve convulsions. Studies have shown that cattle bile *Arisaema* exhibited a better effect on febrile seizure than that of pig bile *Arisaema*. The records of cattle bile *Arisaema* can be traced back to the Song Dynasty, and ancient Chinese people usually adopted cattle bile as raw material for fermentation. But as time went by, the processing raw materials of bile *Arisaema* were gradually replaced by pig bile. Therefore, it is meaningful to identify a processed product of bile *Arisaema* with the best effect on febrile seizure and explore the underlying mechanism.

Objective

To investigate the anti-convulsant effect and underlying mechanism of cattle bile *Arisaema* ethanol extracts through hot-water bath-induced febrile seizure rat model.

Materials and methods

Raw *Arisaema* samples (Batch No. 2005001) were supplied by Sichuan Neijiang Lianghui Pharmaceutical Co., Ltd. The fresh cattle bile was collected from Yingtan Qiaokang traditional Chinese medicine Co., Ltd.

Three-week-old young rats were selected as the research objective as previously recorded. 45 °C was determined as the best modeling temperature, as it had the advantages of a high modeling success rate and low mortality compared with the other conditions. Exposure to hyperthermia was conducted by maintaining the water in a glass jar at a temperature of 45 °C by placing it in a temperature-controlled water bath. The depth of the water in the glass jar was based on the fact that the rats could stand up against the side of the bath with only their head above water. The rats were immediately removed from the water after 5 min or once seizures occurred. After modeling and treatment, all unbroken brain tissues and serum of rats were collected for the following analysis.

Results and discussion

In our experiment, there appeared various types of severe seizure-like symptoms, and progressed to tonic-clonic convulsions with a high core temperature. In addition, the rats in the model group were inactive and needed longer time to recover. In contrast, the rats treated with a high dose of cattle bile *Arisaema* had a shorter duration of convulsion, longer seizure latency, and a lower core temperature. In addition, after hot water bath modeling, the amount and cellular morphology of the hippocampal neurons in the rats showed severe changes compared with those in the control group. In the hippocampal CA1 and CA3 areas of the rats in the model group, more neurons were shrunk, the cell staining was deepened, and the boundary between the nucleus and cytoplasm was unclear. The rats treated with a high dose of cattle bile *Arisaema* displayed near total restoration, their hippocampal neurons were abundant and closely arranged, with a normal morphological structure, clear nuclear cytoplasmic boundary, and an obvious nucleolus.

Besides, we measured the contents of two neurotransmitters (GABA and Glu) to explore whether the mechanism of cattle bile *Arisaema* in the treatment of febrile seizure is related to regulating the balance of excitatory and inhibitory neurotransmitters. The results showed that the onset of febrile seizure reduced the content of GABA and increased the content of Glu in rat hippocampus. In contrast, when treated with cattle bile *Arisaema*, the content of neurotransmitters in the rat hippocampus exhibited an opposite trend to that in the febrile seizure group. It is worth noting that the ability of high-dose cattle bile *Arisaema* to regulate neurotransmitter disorders in rat hippocampus is the best. To sum up, these data suggested that cattle bile *Arisaema* may inhibit the development of febrile seizure by regulating the neurotransmitters in the hippocampus.

An ELISA assay was conducted to determine the HMGB1 and IL-1 β expression levels in the hippocampus. The results showed that the expression levels were dramatically increased in model rats and decreased after an oral high-dose cattle bile *Arisaema* pre-treatment. The western blotting analysis exhibited the increasing expression level and down-regulating expression level of HMGB1. The immunohistochemical and qRT-PCR analysis revealed that the BDNF and GFAP expression levels in model rats were up-regulated while down-regulated after cattle bile *Arisaema*

pre-treatment.

To sum up, the report of this study on the mechanism of oral administration of cattle bile *Arisaema* ethanol extract in the treatment of febrile seizures, supplements the existing literature on the ameliorative effect of bile *Arisaema* of FS. We confirm that the mechanism of cattle bile *Arisaema* combating febrile seizure may involve the regulation of neurotransmitters and remission of neuronal damage in the hippocampus.

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Urine metabolomics to reveal the ameliorate effect of *Coptidis Rhizoma* on hyperthyroidism rats

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Abstract

Purpose: This study is aiming to probe the activities of the *Coptidis Rhizoma* (HL) on hyperthyroidism. **Methods:** Firstly, the physical sign, thyroid function and metabolism profile (multivariate statistical analysis) were assessing for HL. A metabolomics approach was explored the mechanism of the HL effected on hyperthyroidism. **Results:** It is proved that the HL could effectively ameliorate the physical sign, thyroid function and metabolism profile in hyperthyroidism rats. Moreover, HL could regulate energy metabolism, glutathione metabolism, taurine hypotaurine metabolism, thyroid hormone synthesis, arachidonic acid metabolism and linoleic acid metabolism and the inflammation mediated by inflammatory factor (IL6, IL17), Ca²⁺ and MAPK signaling pathway. **Conclusion:** In a word, HL could alleviate hyperthyroidism by ameliorate thyroid hormone synthesis, restraining inflammation and oxidative stress via regulating energy metabolism, glutathione metabolism, taurine hypotaurine metabolism, arachidonic acid metabolism and linoleic acid metabolism and Ca²⁺ / MAPK signaling pathway, which might be a useful strategy for treating hyperthyroidism.

Key words: *Coptidis Rhizoma* (HL), Metabolomics, Hyperthyroidism, Target prediction

Hyperthyroidism is the most common thyroid disease in clinical and effect all populations worldwide, particularly in pregnancy and childhood¹. The prevalence of hyperthyroidism is 0.3% in Australia², 1.2 % (0.5 % overt and 0.7 % subclinical) in the United States³. Its most essential clinical manifestation is decreased cognitive function, depression, anxiety, irritability, and weight loss. It's diagnosed and treatment are simple, mainly include antithyroid drug, iodine radiotherapy and surgery, but the yardstick of treatment is difficult to grasp, especially for the management of subclinical hyperthyroidism has been controversial. Therefore, the development of new and simple controllable approaches for the hyperthyroidism administration is warranted. Particularly, the complex pathophysiology of hyperthyroidism may necessitate combination treatments. An information from WTO reported that approximately 80 % individual is administrating medicinal herbs for treatment of several disease, owing to their cost effectiveness and negligible side effects. The theory of 'cold and heat' property of TCM play the key role in clinical practice, and is widely used and confirmed. Generally, the occurrence of diseases is attributed to the imbalance of Yin (cold) and Yang (heat) in the body. The hyperthyroidism was belonged to the classic heat syndrome category in Chinese medicine⁵. Previous researches have explored the 'cold / heat' property nature of herbs from the chemical composition⁶, the energy and substance metabolism, endocrine system and central nervous system. The overall effect and the underlying mechanisms of the 'cold' property herbs on hyperthyroidism is still poorly understood.

Materials and methods

Coptidis Rhizoma (HL) was purchased from Beijing Tongrentang Co., Ltd (Beijing, China). 6-propyl-2-thiouracil (PTU) was purchased from Sigma-Aldrich (Merck KGaA, Darmstadt,

Germany, batch Number: BCBR87087), L-thyroxine was purchased from Aladdin Biochemical Technology Co., Ltd., (Shanghai, China, batch Number: H2014187).

After adaptive breeding for 1 week, all rats were randomly divided into 4 groups: control group (control, n=7), hyperthyroidism model group (Hyper, n=8), positive drug group (PTU, n=8), and treatment group (HL, n=8). With the exception of the rats in the control group, the hyperthyroidism model was established in all rats by intraperitoneal injection L-thyroxine (0.3 mg / kg / d) for 28 days consecutively. Positive drug group was intra-gastrically administered PTU (10 mg / kg / d) from days 14 to the end. Treatment group was continuous intra-gastrically administered HL (2.4 g / kg / d) for 28 days.

On the day 28, The urine sample was collected for 12 h after the last administration, which was centrifuged 10 min, at 12000 rpm. The supernatant was stored at - 80 °C until analysis. Serum was collected by centrifugation at 3000 rpm for 10 min, and stored at - 80 °C until further analyses.

Results and discussion

In this study, the increased phenotypical index, including body weight, level of food /water intake and rectal temperature in hyperthyroidism rate were observed. And this high metabolite status was improved by HL. The increased levels of T3 and T4 and the declined concentration of TSH in serum were ameliorated after administration with HL. Meanwhile, a severe thyroid glands pathological damages, including oedema, atrophy and some follicles showed luminal obliteration or devoid of colloid, follicular epithelial cell nucleus pyknosis and shedding, was observed in the Hyper group. However, these T4 induced pathological changes were improved by HL.

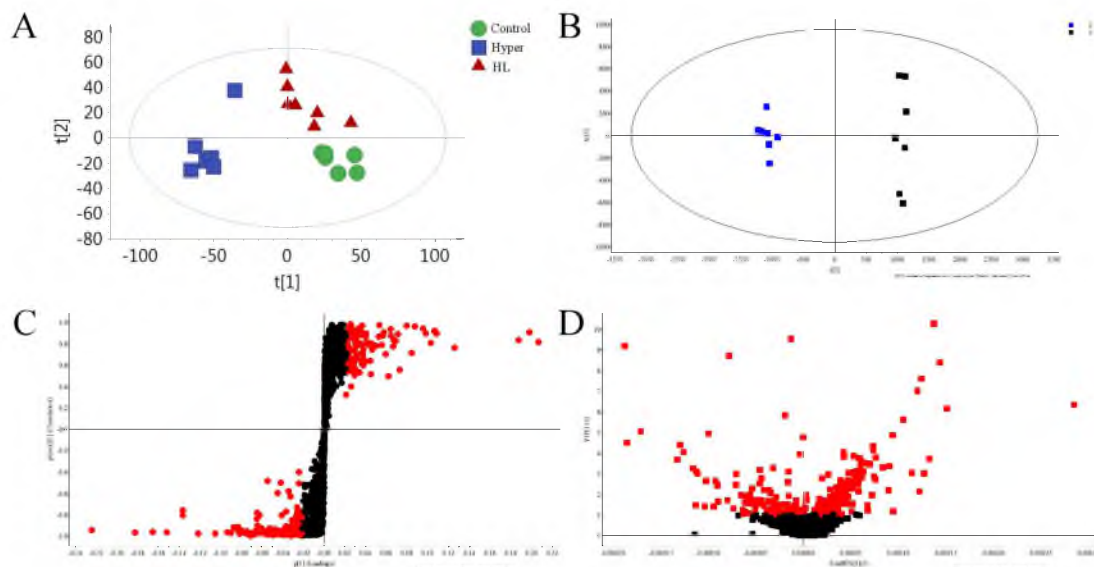


Figure 1. The PCA (A), OPLS-DA (B), S-plot (C) and VIP value (D) analysis after administrate HL on hyperthyroidism rate

Urine metabolomics reveal that HL mainly through the energy metabolism, thermogenic to improvement the exosyndrome of hyperthyroidism; the glutathione metabolism and taurine hypotaurine metabolism to adjusted thyroid hormone synthesis and the Ca²⁺ influx mediated by oxidative stress; regulate arachidonic acid metabolism and linoleic acid metabolism to reduce the inflammation mediated by inflammatory factor (IL6, IL17), Ca²⁺ signaling pathway and MAPK signaling pathway.

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The Effect of Aqueous Extract of Seeds of *Pharbitis purpurea* on Hyperlipidemia Rats

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Abstract

High-fat diet (HFD) induced hyperlipidemia rat model was used to explore the anti-hyperlipidemia effect of aqueous extract of seeds of *Pharbitis purpurea* (PSAE). A total of 36 healthy male SD rats were divided into control group and model group. The control group were fed with basal diet, while the model group was fed with HFD. The model rats were divided into model control group, positive control (simvastatin group, 7.5 mg • kg⁻¹), PSAE low-dose group (203 mg • kg⁻¹), PSAE medium dose group (406 mg • kg⁻¹) and PSAE high-dose group (812 mg • kg⁻¹). The control group and model group were given normal saline, and other treatment groups were given corresponding drugs by gavage. After four weeks, the contents of serum total cholesterol (TC), triglycerides (TG), low density lipoprotein cholesterol (LDL-C), high density lipoprotein cholesterol (HDL-C), alanine aminotransferase (ALT), and aspartate aminotransferase (AST) levels in rats were determined. Rats liver histopathology was observed. Compared with the model group, PSAE can increase the content of HDL-C, reduce the level of TG, TC and LDL-C in serum of hyperlipidemic rats, improve the pathological morphology of liver, and reduce the content of ALT and AST in liver. In conclusion, PSAE has the effect of reducing blood lipid and protecting liver, laying foundation for further study on the lipid-lowering effect of PSAE.

Key words: *Pharbitis purpurea* seeds Hyperlipidemia, Lipid-lowering effect

Hyperlipidemia is a kind of disorder of lipid metabolism. The main indexes in serum are cholesterol (TC), triglyceride (TG), low density lipoprotein cholesterol (LDL-C) and high density lipoprotein cholesterol (HDL-C). According to the epidemiological survey, 15-20% of the adult population in the world is suffering from hyperlipidemia. At present, there are 160 million hyperlipidemic patients in China, with an incidence of 18.6%. Hyperlipidemia is associated with obesity, diabetes and fatty liver, and its greatest risk is cardiovascular disease (ASCVD) that leads to arteriosclerosis [1,2].

So far, exercise therapy and drug therapy are effective measures for the treatment of hyperlipidemia. However, there are great differences in the efficacy of different exercise therapy in patients with hyperlipidemia, mainly drug therapy at present. Statins are the priority drugs used in patients with hyperlipidemia. But some of these drugs are expensive and have serious side effects [3].

Therefore, the most important thing at present is to find a lipid-lowering drug that has no toxic side effects and is in line with human physique. As we all know, the efficacy of traditional Chinese medicine is usually mild. It is accompanied by mild or even negligible side effects. *Pharbitis purpurea* seeds in traditional Chinese medicine with the effect of purging water and defecating, eliminating phlegm and washing drink, killing insects and attacking accumulation, were repeatedly used in prescription that have the effects of reducing weight and reducing blood lipids [4,5].

Objective

To assess the effects of PSAE on body weight, liver index and serum biochemical index of model animals, the lipid-lowering effect of PSAE were studied, and its hypolipidemic effect was further discussed.

Materials and methods

SPF-grade male SD rats, aged from 6 to 8 weeks and weighing 180.0-200.0 g. During the experiments, the rats were fed with a free access to water and food, and acclimated to the environment in the laboratory for 7 days. The temperature of the animal room was 20.0°C–22.0°C, and the relative humidity was 50%–60%.

The hyperlipidemia model was established by feeding rats with HFD for 2 weeks. The experimental group was randomly divided into basal diet control group, high-fat diet induced hyperlipidemia model group (HFD group), positive control group, PSAE-L[low-dose PSAE: 203 mg kg⁻¹ (body weight per day)] group, PSAE-M [medium-dose PSAE: 406 mg kg⁻¹ (body weight per day)] group and PSAE-H [high-dose PSAE: 812 mg kg⁻¹ (body weight per day)] group.

All rats were weighed every 7 days. At the end of the experiment, the rats were anesthetized with chloral hydrate. The blood of abdominal aorta and the tissues of liver, spleen and kidney were collected and stored at –80°C for further analysis.

Results and discussion

Compared with the control group, the body weight of the model group increased ($p<0.05$), the rats liver index extremely significantly increased ($p<0.01$) in the model group. The levels of rats serum TC, TG, LDL-C, ALT and AST significantly elevated and HDL-C extremely significantly reduced ($p<0.01$), the hyperlipidemia model group was established successfully. Compared with the HFD model group of experimental animals, PSAE-H group could reduce the body weight of rats ($p<0.05$), PSAE-L group could significantly reduce the body weight of rats ($p<0.01$).

Compared with the liver index of HFD model group, The TC index of PSAE-M group decreased significantly ($p<0.05$). HDL-C index of PSAE-H group increased ($p<0.05$). compared with the serum index of HFD model group, The TG index of different doses groups of PSAE decreased ($p<0.05$). LDL-C index of PSAE-L and PSAE-H groups decreased significantly ($p<0.001$).

The liver injury index ALT and AST in the model group increased significantly, compared with the HFD model group of experimental animals, ALT index of PSAE-L decreased significantly ($p<0.01$), PSAE-M group reduced the AST index of experimental animals ($p<0.05$)

Conclusions

This study demonstrates that PSAE significantly suppress the development of hyperlipidemia in HFD-induced rats, can reduce the level index of TC, TG and LDL-C, increase the index of HDL-C in hyperlipidemic rats, and reduce the liver damage caused by reducing the liver injury index such as ALT and AST. In order to lay a foundation for further research on the treatment of hyperlipidemia by PSAE, the therapeutic mechanism of hyperlipidemia can be further discussed.

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Study on Pharmacokinetic changes of Panax Notoginseng saponins in Hyperlipidemia Animal Model

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Abstract

The effects of hyperlipidemia on the pharmacokinetics and distribution of Panax notoginseng saponins (PNS) in liver, kidney, heart and brain were observed. Determination of Serum Lipid level and biochemical Indexes of liver function in Hyperlipidemic Rats treated with PNS, determination of PNS in rat plasma and mouse tissues by HPLC. PNS can significantly reduce the levels of blood lipid TC, TG and LDL-C in hyperlipidemic rats, and significantly reduce the values of ALT, AST and AKP in serum of hyperlipidemic rats. Under the condition of hyperlipidemia, the half-life of PNS in vivo is prolonged and the tissue distribution is increased, which is beneficial to the long-term retention in vivo to exert the curative effect.

Key words: Panax notoginseng, Hyperlipidemia, tissue distribution

Hyperlipidemia (HL) means that one or more levels of total cholesterol, triglyceride and low density lipoprotein cholesterol in serum are too high or high density lipoprotein cholesterol too low. HL is an invisible killer of human health and its seriousness can not be ignored. With regard to the epidemiological survey of HL, the results showed the sick population gradually tended to be younger^[1]. Panax notoginseng comes from *the Compendium of Materia Medica*, which can promote blood circulation and remove blood stasis. Modern pharmacology shows that Panax notoginseng can significantly reduce the levels of serum triglyceride and total cholesterol, increase the ratio of high density lipoprotein to cholesterol, reduce aortic intimal lipid plaque and reduce arterial wall damage^[2,3]. The process of drugs changes in vivo under the condition of hyperlipidemia. Therefore, the evaluation of the pharmacokinetic behavior of active components of traditional Chinese medicine in model experimental animals is more objective, accurate and of practical significance than the experiments based on healthy experimental animals.

Objective

In this study, the pharmacokinetics of PNS was studied from normal animals and hyperlipidemic model animals, to determine the changes of PNS in normal and hyperlipidemic model animals, in order to provide more credible guidance information for clinical drug use.

Materials and methods

1 Materials

Xuesaitong for injection (freeze-dried); Simvastatin tablets; Ginsenoside R_{g1} standard; ginsenoside R_{b1} standard; notoginsenoside R₁ standard; daidzein standard. The methanol, acetonitrile and glacial acetic acid were of HPLC grade.

2 Methods

In this study, the pharmacokinetics of PNS was studied from normal animals and hyperlipidemic model animals. Determination of Serum Lipid level and biochemical Indexes of liver function in Hyperlipidemic Rats treated with PNS, determination of PNS in rat plasma and mouse tissues by HPLC, in order to provide more credible guidance information for clinical drug use.

Results and discussion

1.1 Pharmacodynamic effects of PNS on Hyperlipidemia Rats

After giving PNS, The body weight of rats in all groups decreased after administration, but the decrease in the high dose group of PNS was particularly significant. the values of TC, TG and LDL-C in each treatment group were significantly lower than those in the model group, and there were significant differences in TC and LDL-C indexes between the high-dose PNS group and the model group. The contents of AST, ALT and AKP in serum in the model group were significantly higher than those in the blank group, and the above-mentioned indexes decreased in all groups after administration. Figure 1 pathomorphological examination of the liver showed that the structure of hepatocytes in the model group was abnormal and there were local inflammatory necrotic foci, while only the hepatic sinusoid dilated and the inflammation disappeared in the treatment group. It can be concluded that PNS is effective in the treatment of hyperlipidemia.

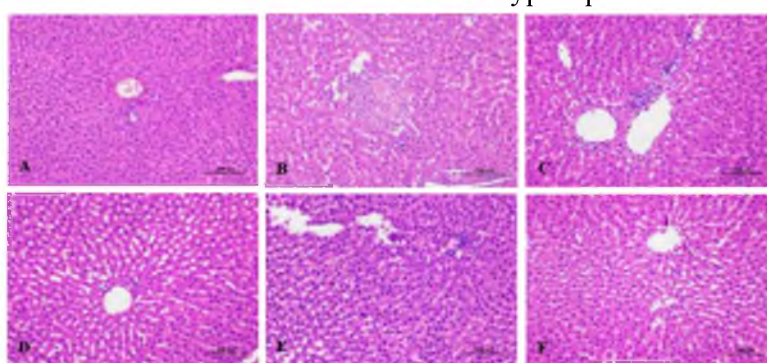


Fig.1 HE-stained sections of livers from each group after Drug Administration ($\times 200$)

(A: Blank group; B: model group; C: Positive control group; D: PNS low-dose group; E: PNS medium dose group; F: PNS high-dose group)

1.2 Effect of Hyperlipidemia on Pharmacokinetics of PNS in Rats

After administration of PNS, the blood concentration-time curve and pharmacokinetic parameters of each group were analyzed. Figure 2 shows compared with the normal group, the half-life of each index component of PNS in the model group was prolonged, the clearance rate decreased, and the area under the curve increased, and the ginsenoside Rb₁ components were significantly different, indicating that the retention time of PNS in hyperlipidemia rats was prolonged, and the drug action time was also prolonged.

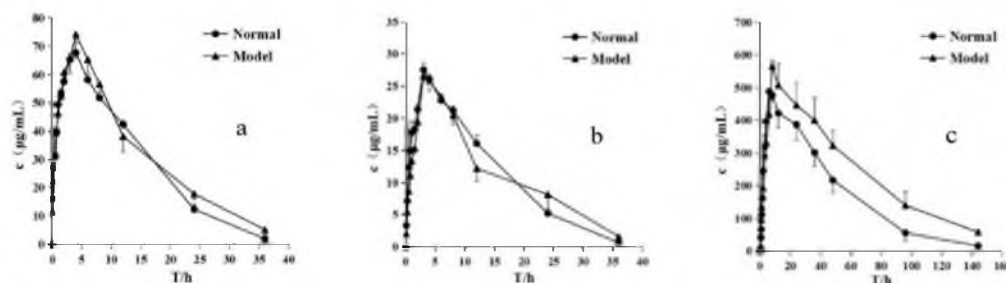


Fig.2 Plasma drug time profiles of Notoginsenoside R₁、Ginsenoside Rg₁、Ginsenoside Rb₁ in normal versus model rats (a: Notoginsenoside R₁; b: Ginsenoside Rg₁; c: Ginsenoside Rb₁)

1.3 Effect of Hyperlipidemia on tissue Distribution of Total saponins of Panax Notoginseng in mice
Notoginsenoside R₁ and ginsenoside Rg₁ in kidney and heart were lower than those in normal group, but the content in liver was higher than that in normal group, while the content of ginsenoside Rb₁

in kidney, liver and heart was lower than that in normal group, while that in brain tissue was higher than that in normal group. PNS R₁ may regulate lipid metabolism by increasing the content of CYP7 α and decreasing the levels of HMG-CoAR and SREBP-2 in steatosis L02 hepatocytes. Ginsenoside Rg₁ may induce Keap1-Nrf2-ARE signal pathway to reduce liver injury and achieve hepatoprotective effect^[4]. Therefore, the increase in the content of both in the liver may be related to its efficacy in the treatment of hyperlipidemia. Ginsenoside Rb₁ can inhibit the production of TNF- α and IL-6, and protect the integrity of blood-brain barrier by inhibiting the activity of MMP-9 and NOX induced by inflammation^[5]. It is speculated that this may be related to the increase of ginsenoside Rb₁ in the brain tissue of hyperlipidemia.

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A brief analysis of the law of medicine in distinguishing classics and Treating - taking Jiuwei Qianghuo Decoction as an example

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Abstract: Syndrome differentiation of meridians is one of the classical dialectical theories of traditional Chinese medicine, which is based on the distribution of meridians to determine the specific location of the lesion and the viscera associated with it, so as to take corresponding treatment methods. This paper will explore the medication characteristics and prescription formation rules of ancient prescriptions from the aspects of the formulation rules of Jiuwei Qianghuo Decoction, the representative prescription of meridian differentiation and treatment, and the new clinical application of meridian differentiation and treatment, so as to strengthen the understanding of ancient traditional prescriptions, and look forward to better use and dissemination of ancient methods and prescriptions to guide modern clinical application.

Keywords: The ancient; Drug characteristics; Distinguishing the differentiation; Jiuwei Qianghuo decoction

It is the core idea of acupuncture and moxibustion to judge the meridians of diseases according to the syndromes of the parts of meridians that go through^[1]. Meridian differentiation and treatment take meridian as the core, and judge the specific position of meridian lesions through the analysis of position differentiation and meridian return, and use meridian drugs to dredge the meridian and regulate Yin and Yang of the five zang organs. Differentiation of classics and treatment is the advantage and essence of TCM theory and one of the important principles guiding TCM diagnosis and treatment of diseases and syndromes. However, with the development of Traditional Chinese medicine, the current clinical application of traditional Chinese medicine prescription theory is mainly dialectical treatment, and the theory of meridian differentiation is gradually weakened, and even only applied in acupuncture point selection.

Objective

The representative prescription of the theory of differentiation of classics and treatment is Jiuwei Qianghuo Decoction, which, as a famous prescription through the ages, can be used to cure six classics and four periods. This article will start from the emergence of differentiation of classics and treatment, the analysis of its representative prescriptions and modern clinical application, to provide reference for the ancient prescriptions and the use of ancient methods today.

Methods

1. Medication characteristics and prescription rules of Jiuwei Qianghuo Decoction

Nine flavor Qianghuo Soup originated from the Yuan Dynasty doctor Wang Haogu's "It's Hard to know", which pioneered the use of the theory of classics differentiation to guide the treatment of diseases. The whole recipe is composed of nine herbs: qiang Huo, fangfeng, Atractylodes, Asarum, Ligusticum chuanxiong, Angelica dahurica, Shengdi, Scutellaria baicalensis and licorice. The passage of four times is a prescription for diverging, relieving typhoid fever and treating

miscellaneous diseases. The effect is sweating, removing dampness, and clearing heat. Indications external wind cold and damp evil, inside accumulate heat syndrome.

Qiang live, general manager sun, and into the jue Yin, and xinfeng bi pain relief. "Herbal Words": "The qiang living body is light but not heavy, the air is clear but not cloudy, the taste is spicy but can be scattered... Reach the body to clear up the evil and smooth the blood." The main entry in the table, outside, in the sun, shengfa Yang qi, up to the liver wood, purgation of liver qi, search liver wind, and wind-proof, atracylodes can be compatible with the spleen dehumidification solution table, tongli meridians.

Fangfeng, atracylodes introduced taiyin, embellish dryness degree. Wind-proof good dispelling the wind to solve the table, in addition to the vein of moisture evil, for the embellish agent in the wind; Attylodes walk and do not keep, fragrance dry strong, dedicated drainage open yu, spleen dispellant wind cold. Two drugs a run a dry, fill but not greasy, dry and not hurt, regulating qi, health transport spleen and stomach, dreading meridians phlegm wet.

Asarum leads the meridian to less Yin, disperses the kidney water cold. Into the shaoyin meridian blood points, through the heart and lung of the upper coke gas, warm coke cold drink, relieve the limbs pulse cramps pain, through the lower coke kidney and bladder, communication inside and outside. Treatment of pharyngeal pain, pharyngeal itching, nasal congestion runny nose, limb pain and other diseases.

Angelica yangming, evacuation of qi and blood, clear analgesia. Gas fragrance, through nine orifice, Yangming stomach by gas and blood, the main blood of the disease, angelica treatment yangming meridian pain syndrome and table demonstration. Compatible with hosh, puerariae, gypsum, etc., can treat sweat, fever and cold, pulse floating slow long real.

Chuanxiong leads through liver and gallbladder, supplementing Yin and collecting Yang. Taste spicy, warm, go to the liver meridian, gallbladder meridian, pericardium meridian, ligusticum chuanxiong is the only medicine that can enter Yin and Yang meridian, not only can shun jue Yin liver blood, the treatment of liver blood deficit, bitter mouth, dry pharynx, dizzy Yin cold, but also can discharge less Yang gallbladder, adverse, regulating Yin and Yang.

Raw rehmannia sweet, major cold, into the kidney Yin, blood tone. The taste of scutellaria is bitter and thin. Common prevention of other drugs xinwen dry strong injury Yin abuses. Licorice to make medicine, care in the coke spleen and stomach, harmonic medicine.

2. New modern clinical application of differentiation of classics and treatment

In the development of individual diagnosis and treatment in Traditional Chinese medicine, the thought of differentiation of classics and treatment shows great significance. Chuanxiong tea Powder can be used to treat headache by adding or subtracting medication^[2]. Ligustrazine and ferulic acid, the unique components of Chuanxiong tea, can improve microcirculation, inhibit platelet aggregation and relieve headache. Guizhi soup into the foot sun bladder meridian, muscle relief and regulating Yin and Yang, the treatment of neck shoulder waist leg pain bi^[3]; Small bupleurum soup double solution, treatment of shaoyang gallbladder meridian disease. Syndrome differentiation of channels and collaterals in the treatment of difficult and complicated diseases in clinical practice, direct meridian medicine, communication of Yin and Yang of the five organs of the human body, strong specificity, outstanding curative effect.

Results and Conclusions

By referring to the literature and clinical experience, the author found that the method of differentiation of classics and treatment has been spread for a long time. The representative prescription jiuwei Qianghuo Decoction has a detailed analytical theory of meridian differentiation, and its application of meridian differentiation is worthy of affirmation. However, in clinical practice, most of the prescriptions are limited to the meridian differentiation and treatment of a certain kind of medicine, and the idea of meridian differentiation and treatment of Jiuwei Qianghuo Decoction is not systematically reflected in clinical diagnosis and treatment, and the meridian differentiation and treatment method is more applied in the field of acupuncture and moxibustion. Differentiation of classics and treatment, syndrome differentiation and treatment, combination of acupuncture and medicine should not be neglected. Learning the ideas and compatibility rules of ancient prescriptions and digging into the core meanings, drug use and prescription compatibility of such prescriptions will certainly play a more important role in promoting TCM clinical diagnosis and treatment to a new stage.

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Rapid characterization and identification of the chemical constituents and rat metabolites in the calyx of *Physalis alkekengi* L. var. *franchetii* (Mast.) Makino using UHPLC-Orbitrap-MS

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Abstract

The calyx of *Physalis alkekengi* L. var. *franchetii* (*P. alkekengi*) is a traditional Chinese medicine (TCM) with remarkable clinical effect in the treatment of antitumor, anti-inflammatory, and immunosuppressive effects. In this work, there is efficient approach based on UHPLC-Orbitrap-MS in both positive and negative ion modes was developed to profile and characterize *P. alkekengi* calyx metabolites in rat plasma, urine and feces. 63 components were tentatively characterized from the crude extracts of *P. alkekengi* calyx. Major metabolic reactions of *P. alkekengi* calyx were methylation, hydroxylation, dehydroxylation, hydrogenation, deglycosylation, glycosylation, and their complicated reactions. This study firstly developed a valid analytical strategy for characterization of the chemical compounds and metabolites of *P. alkekengi* calyx using UHPLC-Orbitrap-MS and could provide a feasible and effective data screening technique for the analysis of herbal constituents and metabolites *in vivo*.

Keywords: *P. alkekengi* calyx; Chemical constituents; Metabolites; UHPLC-Orbitrap-MS

Physalis Calyx seu Fructus (Jin denglong), the calyxes and fruits of *Physalis alkekengi* L. var. *franchetii* (Mast.) Makino, has a long history of the treatment of human diseases, and are widely cultivated species, especially in northeastern China [1]. It has long been grown throughout China, Japan, and Europe. Physalins, flavonoids, alkaloids and phenylpropanoid have been identified in the calyx of *P. alkekengi* [2].

Systematic chemical composition characterization and metabolic studies of the calyx of *P. alkekengi* have been limited to a few studies. Feng et al [3] have identified and tentatively characterized 24 compounds in the calyx of *P. alkekengi* extract and detected 24 metabolites in urine and plasma by ultrahigh-pressure liquid chromatography quadrupole time-of-flight mass spectrometry (UPLC/Q-TOF-MS/MS). The defect was that the conventional method searching manually and intuitively the differences between the control and dosed chromatograms may lose artificially some components, which hindered the full display of the constituents in the calyx of *P. alkekengi* and the information on the prototype constituents and metabolites, which hindered interpreting the more valuable potential bioactive constituents and studying the pharmacology and mechanism of action of *P. alkekengi* calyx.

Objective

To explore the components of *P. alkekengi* calyx and detecting the absorbed prototype constituents and metabolites, which are of great significance to clarify the effective substances of this herbal medicines.

Materials and methods

Mass spectrometry grade acetonitrile, methanol and formic acid (Fisher Scientific, USA). Ultrapure

water was purified by a Milli-Q system (Millipore, Bedford, MA, USA). Other chemicals were analytical-grade. The calyx of *P. alkekengi* was purchased from Shiyitang Pharmaceutical Factory of Harbin Pharmaceutical Group.

Dried calyx of *P. alkekengi* (100 g) were extracted with distilled water (1 L× 3, 2 heach) under reflux. Then, the extract was collected and evaporated to obtain dried powder under vacuum, which was dissolved in methanol-water (1:1, v/v) and filtered through 0.22 μm membranes (pore size) prior to use, and 5 μL of the final supernatant were used for UPLC/Q-TOF-MS/MS (Thermo Fisher, Waltham, MA, USA).

Male Sprague-Dawley rats (200±20 g) were obtained from the Laboratory Animal Center of Heilongjiang University of Chinese Medicine (Beijing, China, license No. SCXK(JING)2016-0006) and housed in an animal room (24±2°C, 60%±5% relative humidity, 12 h light/12 h dark cycle). They were given water and fed normal food ad libitum for 1 week before the experiment. Twenty rats were randomly divided into four groups with five rats per group. The rats in the Group I and II were orally administrated with the extract of calyx of *P. alkekengi* at the dosage of 0.5 g/kg and used for collecting blood, urine and feces samples.

200 μL plasma at each time point and 600 μL methanol were mixed for 3 min and centrifuged at 13,000 rpm for 15 min to precipitate the protein. The supernatants were evaporated to dryness under vacuum at 40°C, and then 200 μL of methanol-water (1:1, v/v) was used to dissolve the residue. The urine biosamples were treated respectively with the same ways as the plasma. The feces were mixed with 15 times of methanol (v/w) and extracted in ultrasonic bath for 30 min. The clear methanol layers were evaporated to dryness under vacuum at 40°C. Methanol-water (1:1, v/v) used to dissolve the residue was 200 μL. After centrifuging at 13,000 rpm for 15 min each sample, 5 μL of sample was used to analysis by UHPLC-Orbitrap-MS.

Results and discussion

This study systematically analyzed the chemical constituents of the calyx of *P. alkekengi* and its prototypes and metabolites in vivo using UHPLC-Orbitrap-MS (Figure 1). A total of 63 constituents of the calyx of *P. alkekengi* in vitro mainly including 46 physalins and 8 flavonoids, 25 prototypes and 45 metabolites in vivo were tentatively characterized and identified. The compounds of *P. alkekengi* main undergo glucuronidation and sulfation conjugation metabolic pathways. This identification and structural elucidation of the chemical compounds provided essential data for further pharmacological studies of *P. alkekengi*.

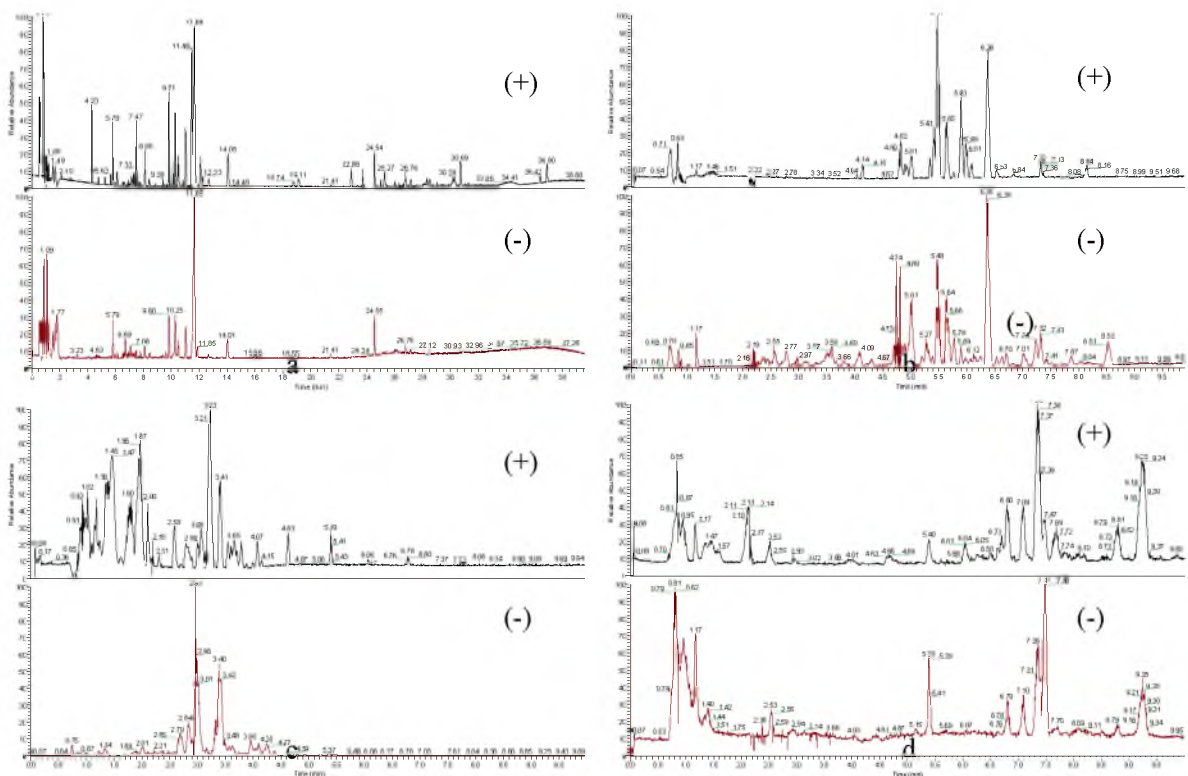


Figure 1. Total ion maps (a) Crude extracts of *P. alkekengi* calyx (b) Plasma (c) Urine (d) Feces

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Advances in the application of traditional Chinese medicine in the treatment of osteoporosis

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Abstract

Osteoporosis (OP) is the most common bone disease. It is a systemic bone disease characterized by bone loss, bone tissue microstructure degradation, increased bone fragility, and prone to fracture^[1]. The incidence of OP is related to age, systemic metabolism, hormonal effects, genetic factors, etc. The prevalence rate of women over 50 years old is higher than that of men. In the treatment of OP, traditional Chinese medicine has gradually become the focus of clinical research because of its good overall treatment effect, less adverse reactions and suitable for long-term use. This paper reviews the research progress of traditional Chinese medicine in the treatment of osteoporosis.

Key words: Traditional Chinese medicine; review; Osteoporosis

Objective

This paper reviews the application and research progress of traditional Chinese medicine in the treatment of osteoporosis, and summarizes its clinical research. Provide better treatment for patients, improve the quality of life, and provide reference for promoting the development of related medical fields.

Materials and methods

Asperosaponin (ASA) is the main active ingredient of *Dipsacus asperatus*, a traditional Chinese medicine. Xu Yong and others found that ASA can promote the proliferation of rBMSCs in osteoporosis model, enhance ALP activity, and enhance the expression of ALP, OPN and Runx2^[2]. The results showed that ASA could promote the osteogenic differentiation of rBMSCs in the osteoporosis model through pi3k/vakt signaling pathway, promote bone formation and bone formation, and have the effect of anti osteoporosis.

Ligustrum lucidum is a commonly used drug for the treatment of osteoporosis. Modern pharmacological studies have shown that *Ligustrum lucidum* and its components *Ligustrum lucidum* glycosides, oleanolic acid and ursolic acid can activate Wnt/ β -Catenin/Irp6 pathway promotes the differentiation of bone marrow mesenchymal stem cells into osteoblasts and inhibits the differentiation of osteoclasts. By studying the effect of *Ligustrum lucidum* polysaccharides on osteoporosis in ovariectomized mice, Wei Qiu et al. Confirmed that *Ligustrum lucidum* polysaccharides can effectively inhibit the reduction of bone mineral density caused by ovariectomy, which may be related to the regulation of bone metabolic balance and calcium and phosphorus metabolism^[3].

Epimedium has the effects of Tonifying the kidney and Yang, strengthening tendons and bones, and the low glycoside from *Epimedium Folium flavonoids* (LG) is the main part into the blood. Maoyuzhi^[4] found that LG has an effect on both primary and secondary osteoporosis, which can increase the number and thickness of bone trabeculae, bone density and quality by adjusting the

content of relevant biochemical indicators in serum. Pharmacological studies have shown that LG can up regulate the expression of bone formation, promote bone formation, and improve bone mass and bone resistance to destruction.

Results and discussion

The characteristics of traditional Chinese medicine are multi-level, multi effect, multi-target, small adverse reactions, etc. In recent years, great progress has been made in the basic research of traditional Chinese medicine in the treatment of osteoporosis. On the basis of a large number of experiments, it was found that the effective components play a therapeutic role in osteoporosis by regulating osteoblast differentiation and inhibiting osteoclast differentiation. But so far, the research on the mechanism of traditional Chinese medicine in the treatment of osteoporosis is still incomplete, and there is a lack of large sample, multi center clinical controlled experimental research, which suggests that researchers should strengthen the continuous research on the pharmacological effects and pharmacokinetic characteristics of relevant traditional Chinese medicine and its extracts and effective components in the human body, so as to enrich the reliable basis for clinical practice and provide more safe and efficient drugs for the treatment of osteoporosis.

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Experimental study on the effect of traditional Chinese medicine prescription on Superoxide Dismutase

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Abstract

In this paper, the effects of 34 kinds of traditional Chinese medicine prescriptions on superoxide dismutase activity were introduced. The gastrocnemius muscle of mice was detected by BioVision hypersensitive superoxide dismutase activity analysis kit, and three prescriptions with the strongest promoting effect on SOD activity were obtained, namely Chaihu Guizhi decoction, Bupleurum plus Dragon Bone Oyster decoction and Banxia Xiexin decoction, which can be listed as the preferred drugs for the treatment of Sarcopenia and lay the foundation for follow-up research.

Key words: Prescription, Superoxide dismutase, Sarcopenia

Superoxide dismutase (SOD) is an important component of antioxidant enzymes in the biological system, widely distributed in microorganisms, plants, animals and other organisms, is a kind of antioxidant metalloenzyme^[1]. Under normal circumstances, the superoxide anion free radical (O_2^-) produced in the body is necessary to maintain life activities, and the O_2^- produced and cleared should be in relative balance^[2]. However, if the amount of O_2^- produced by the body is higher than the amount it can remove, it will accumulate excessively in the body, thus damaging the body and eventually leading to the aging of the organism. The action mechanism of superoxide dismutase is to disproportionate O_2^- to produce O_2 and H_2O_2 , and then decompose the product into H_2O and O_2 with the participation of catalase, in order to complete the task of eliminating O_2^- and maintain the young state of the body. Because of the unique function of SOD, the products that can promote it will develop rapidly in food, health products, medical and other health industries, and have great development potential and broad market prospects. Sarcopenia is a disease formed mainly by the degeneration of the muscle system function due to the aging of the organism, which is mainly manifested by the weakening of muscle strength and the loss of muscle mass in various parts of the body. Some studies have shown that the changes in the release of reactive oxygen species with age affect the level of oxidative stress in skeletal muscle^[3]. Therefore, the antioxidant stress activity of SOD is also one of the indicators for evaluating and screening drugs for the treatment of Sarcopenia.

Objective

To study the promotion degree of different traditional Chinese medicine prescriptions on the activity of superoxide dismutase, and then select the best traditional Chinese medicine components for the treatment of Sarcopenia.

Materials and methods

Materials: Longdan Xiegan Decoction, Xinyi Qingfei Decoction, Banxia Xiexin Decoction and other 34 kinds of prescription test samples; BioVision hypersensitive SOD superoxide dismutase activity analysis kit; Tris; HCl; sucrose, EDTA; NaCl.

Methods

The configuration of buffer solution: 1.21g Tris, 1g HCl solution with 1% concentration, 85.5g sucrose and 0.37g EDTA were weighed by electronic balance, dissolved in distilled water in turn, dissolved by ultrasound, fixed volume to 1000mL, and the buffer solution with pH 7.4 was prepared.

Configuration of physiological saline: 4.25g of 0.85% NaCl solution was weighed by electronic balance, water was added to 500mL, fully dissolved, and dissolved by ultrasound, and stored in the refrigerator where drugs were stored for use.

The management of experimental animals: The mice were divided into experimental group and control group, and all the mice in each group were fed basic diet. The mice in each group were intragastrically perfused according to the volume of 0.1mL/10g every day. The samples of different prescriptions were given to the experimental group, and the corresponding volume of normal saline was given to the control group. The pre-trial period was 7 days, during which the appearance and general state of the mice were observed, and the experiment was carried out after the mice were stable. During the experimental period of 21 days, the mice were free to eat and drink, and the bedding was changed every 2 days. The feeding temperature was 18-22°C and the humidity was 50%-60%.

Determination of SOD activity: Mouse gastrocnemius muscle was washed with normal saline, added to the buffer, mixed and treated with ultrasound. Centrifuge the sample for 5 minutes and collect the supernatant. The activity of SOD in the supernatant was measured by SOD analysis kit. According to the results, the amount of SOD activity contained in the daily intake was calculated. By processing the data of several parallel tests, the final data were obtained, and then the prescription with the best effect was selected.

Results and discussion

The effects of some typical prescriptions on SOD were listed as follows: Chaihu Guizhi decoction 4956 (kU/d), Bupleurum plus Dragon Bone Oyster decoction 3182 (kU/d), Banxia Xiexin decoction 3110 (kU/d), Chaihu Guizhi dry ginger decoction 3021 (kU/d), Da Chaihu decoction 2885 (kU/d), Fangfeng Tongsheng powder 1616 (kU/d), Longdan Xiegan decoction 1485 (kU/d), Xinyi Qingfei decoction 1242 (kU/ day), Qingxinlianzi decoction 1180 (kU/d), Wulin powder 1135 (kU/d) and Xiao Chaihu decoction 779 (kU/d).

Through the above experiments, among the 34 prescriptions, Chaihu Guizhi decoction, Bupleurum plus Dragon Bone Oyster decoction and Banxia Xiexin decoction had the most obvious promoting effect on SOD activity, making the SOD activity up to 4956 (kU/d), 3182 (kU/d) and 3110 (kU/d) respectively. These prescriptions can enhance the antioxidant stress activity of the body, thus relieving the disease.

Because there are four indicators to evaluate and screen drugs for the treatment of Sarcopenia (advanced glycation end products, SOD antioxidant stress activity, Sirt1 gene transcriptional activity, NO), but only one is evaluated in this experiment, so 34 prescriptions need further experiments, and finally comprehensive screening. Each prescription is composed of a variety of Chinese herbal medicines. In order to further analyze and screen the drugs, the herbs in the prescription will be decomposed in the future research process, hoping to enhance the promotion rate of the drug to the activity of SOD, so as to enhance the therapeutic effect.

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Progress of potato prevention and treatment in Stroke

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Abstract: Stroke has the characteristics of high incidence rate, high recurrence rate, high disability rate, high mortality rate, high consumption rate, high consumption rate and low awareness rate. It is the second largest cause of population death in the world, second only to heart disease. Therefore, the early and effective prevention and treatment of stroke is particularly important. Potato is rich in high quality protein, vitamins, minerals, dietary fiber and other nutrients, and low calories, low fat. Potato, as a staple food, can greatly improve the dietary nutrition level, effectively regulate blood pressure, blood sugar, blood lipid, protect cardiovascular, to prevent stroke and after stroke of constipation, depression and other related diseases have therapeutic effect. This paper mainly reviews the regulation of stroke risk factors by potato and the prevention and treatment of related diseases after stroke.

Keyword: Potato;stroke;prevention;treatment

Stroke refers to the neurological deficiency syndrome caused by the acute cerebral blood circulation disorder caused by the stenosis, occlusion or rupture of the internal cerebral artery caused by various causes. Hypertension, diabetes, hyperlipidemia, heart disease, and obesity are the main risk factors. In recent years, medical experts have said that eating five or six potatoes a week can reduce the chance of stroke by 40 percent. Potato is the third largest food crop in the world, with less restrictions on growth environment and wide planting area. Compared with other major grains, potato is less affected by the international market and rich in a variety of nutrients. Taking as a staple food can solve the problem of nutritional imbalance and prevent stroke and other related diseases.

1. Potato and Stroke prevention

1.1 Potato and hypertension

Hypertension is the most important independent risk factor for stroke, and blood pressure is positively correlated with its incidence, regardless of any cerebrovascular disease. Therefore, the effective control of blood pressure can significantly reduce the incidence of stroke. Potatoes are rich in potassium ions, containing up to 300mg per 100g of potatoes, providing 21% of your daily potassium requirement, and it is the most potassium-containing¹ among more than 20 regularly consumed vegetables and fruits. Potassium ion has a good role in promoting the balance of internal and external acids and avoiding the sudden rise in blood pressure. In addition, potatoes contain a substance like a converting enzyme that vasodates blood vessels and lowers blood pressure.

1.2 Potato and Diabetes

Hyperglycemia and brain tissue ischemia and hypoxia increase anaerobic glycolysis and accumulation of acid products, leading to acidosis and aggravating local brain tissue ischemia and edema necrosis. The green skin dry-like powder contained in potato tubers is mainly, a natural active substance such as saponins. Saponin is a kind of natural hypoglycemic substance that can prevent excessive postprandial blood glucose; as a natural substance with a strong glucosidase

inhibitor, its 50% inhibitory concentration of 10-40 mol/L can effectively improve glucose tolerance. Since saponin is extremely toxic, it will be possible to step into the ranks of oral hypoglycemic drugs as a high efficiency and low toxicity drug.

The glycemic index of potato starch is very related to the cooking method. The potato starch cooled after cooking is recycled into resistant starch, incorporating the resistant starch with low glycemic index into the daily diet, which can prevent and treat type 2 diabetes.

1.3 Potato and hyperlipidemia

Serum cholesterol levels were associated with ischemic cerebrovascular disease, especially when more than cholesterol exceeded 4.14 mmol/L. Potatoes are rich in dietary fiber, and cellulose promotes the rapid excretion of cholesterol, thus controlling cholesterol in the blood. Potato rich vitamin C participates in the synthesis of cellular interstitial collagen, strengthening the decomposition of blood cholesterol and excretion. Animal and human trials have found that regular consumption of potatoes improves blood lipids, reduces serum total cholesterol, LDL, and raises HDL. The crude fat content of all potato whole flour is only 1 / 3 of wheat flour, which is a low-fat food. Appropriate consumption can increase satiety, improve blood lipid and reduce blood cholesterol level.

1.4 Potato and heart disease

Heart disease includes coronary heart disease, rheumatic heart disease, cardiac myxoma, etc., that is recognized as an important risk factor for cerebrovascular disease. The arrhythmias that can easily lead to cerebral embolism are mainly atrial fibrillation and pathological sinus syndrome. Its pathogenesis is that the irregular beating of the heart causes blood flow stasis, and it is easy to produce thrombosis in the left atrial appendage. Brain embolism can occur after the thrombus is pushed into the human circulation. Potato is rich in mucus protein, a mixture of polysaccharide proteins that can maintain the elasticity of the arteries, prevent various diseases of the cardiovascular system caused by fat deposition, and reduce the risk of stroke².

2. Potato and the related diseases after stroke

2.1 Potato and poststroke constipation

Stroke causes central nerve injury, affects sympathetic and parasympathetic function, weakens gastrointestinal motor function, and defecation muscle group dysfunction. Moreover, The bed time increased, leading in weakened bowel peristalsis and difficulty in voluntary defecation. The dietary fiber in potato can absorb water and expand, which is conducive to the timely excretion of intestinal contents, so it can prevent constipation and hemorrhoids³. Potato contains a lot of high-quality cellulose, which can enhance gastrointestinal power and prevent constipation.

2.2 Potato and post-stroke depression

Post-stroke depression is one of the common and treatable complications after stroke, which is manifested as a series of depressive symptoms and corresponding somatic symptoms. Potatoes are rich in vitamin B6, which can promote, deepen sleep, improve depression, anxiety and other symptoms. Potatoes are rich in vitamin C, abundant minerals and nutritional elements, which can maintain acid-base balance and regulate and improve people's mental state. Potatoes are rich in protein and B vitamins to improve their physique, improve memory, and help patients keep thinking clear to prevent post-stroke depression.

3. Matters needing attention of eating potatoes

Germinated potato contains solanine, strong irritation to gastrointestinal mucosa, can hemolysis, anesthesia central nerve, acetic acid easy to decompose into non-toxic solanine, high temperature cooked can also be destroyed, but fire roast or fried is not easy to destroy. When the temperature exceeds 120°C, the potato will produce the carcinogenic substance acrylamide, its neurotoxic, it is best to avoid eating fried potatoes.

4.Expectation

The nutritional structure of potato is more comprehensive and reasonable, but the content of calcium, vitamin A and protein is slightly low⁴. At present, the research on potato mainly favors on nutritional value, while less research on its medicinal value, which can be filled by interdisciplinary combination in the future.

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On the Basis of the Liver Research Progress for the Treatment of Insomnia with Anxiety Depression

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Abstract

The general overview of pattern identification and therapeutic principle in the basis of liver treatment for insomnia associated with anxiety and depression was reviewed. The researchers are based on a large number of randomized controlled clinical trials, and using SPSS to analyze the data. They summarized suitable Chinese medicine formulas for treatment insomnia associated with anxiety and depression. According to the analysis, using Chinese medicine formulas to treatment insomnia associated with anxiety and depression has a significant therapeutic effect in clinical practice.

Key words: liver; Insomnia; The research progress; review

Insomnia generally refers to the difficulty sleeping, and difficult to maintain related symptoms such as sleep and early awakenings, accompanied by fatigue, memory loss and other daytime dysfunction^[1], the Internal Classic has described it as “inability to sleep”, Insomnia mainly in clinical syndrome associated with liver, caused by the disorder of modern insomnia patients can be treated from liver^[2]. Wu Bing-Cai^[3] believes that the treatment of insomnia should with liver as foothold. Negatively emotions, such as anxiety, depression, greatly influences the pathogenesis of liver function, qi and blood will deficiency, liver pathogenesis, and then the body blood, Yin and Yang lose cloth unusually, and cause insomnia. Western medicine treatment of insomnia at present is mainly oral sedative hypnotics, but the side effect is bigger, part of drug addiction, and with depression or anxiety tendency with the poor efficacy of the treatment of patients with insomnia^[4].

Objective

In evidence-based medicine of traditional Chinese medicine clinical advantages in an increasingly reflected, its low cost, small side effects, can be flexibly combined with dialectical, adjust patients with negative emotions. This paper has to provide Suitable Chinese medicine formulas to treatment insomnia associated with anxiety and depression, and provide theoretical basis for clinical research.

Materials and methods

Searching for nearly 5 years about using formulas to treatment insomnia associated with anxiety and depression literature in cnki to review.

Results and discussion

Dialectical classification of insomnia associated with anxiety and depression can be divided into two classes, one is classification of vis ceral function, the other one is classification of five vitality. The most common factors in hepatic syndrome in the classification of visceral function are hepatic depression and qi stagnation syndrome and hepatic qi withdrawal in fire syndrome^[5-6]. Five vitality classification will liver type of insomnia unified summary for liver without ethereal soul type^[7-9]. Treatment tonify liver deficiency, and resolve depression with discharge liver fire. Soothe and

tonify liver deficiency of the formulas including: Jiawei Huozhi Decoction^[10], Chaihu Shugan powder^[11]; esolve depression with discharge liver fire on behalf of the formulas including: Xieqing pill with Shengjiang powder^[12], Xiaochai Hu decoction^[13-14], Longdan Xiegan pill^[15], Shugan decoction^[16] and Chaihu Longgu Muli decoction^[17]. Treatment of Five vitality classification insomnia using compound formulas as follow: Shugan Jieyu capsule with Shuanghe Zaoren granule^[18].

Psychological problems have always been ashamed to be mentioned for Chinese, because they are not as easy to gain compassion as other specific and organic diseases, variety of reasons make it difficult for people with psychological problems to explain their situation to others. In the clinic, patients will selectively answer doctors' questions, and tend to deny that their insomnia is directly related to anxiety and depression.

The relationship between insomnia and anxiety and depression is not mutually causal, they often arise together. If either partner's condition is relieved or cured, the other's condition will also improve. The complex of avoiding medical treatment will lead to a vicious circle of insomnia and negative emotions, which is not conducive to the physical and mental health of patients. Traditional Chinese medicine treatment of insomnia with anxiety and depression patients can flexibly avoid such problems, based on the theory of liver master regulation of emotional drainage , it is easier to get the acceptance and cooperation of patients, so as to further combine acumoxa with formulas to achieve more ideal efficacy.

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Clinical observation of Shenyan Zhixue decoction on isolated hematuria after Henoch Schonlein purpura of hyperactivity of fire due to yin deficiency type in children

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ABSTRACT: Objective: This topic through the observation of Shenyan Zhixue decoction on the treatment of children with isolated hematuria after Henoch Schonlein purpura of Hyperactivity of fire due to yin deficiency type and urine sediment changes in the number of red blood cells, which was intended to analyze the probability and security of its efficacy.

Methods: 34 patients diagnosed with isolated hematuria after Henoch Schonlein purpura of Hyperactivity of fire due to yin deficiency type by the clinic of the First Affiliated Hospital, Heilongjiang University of Chinese Medicine and Department of Nephrology, Harbin Children's Hospital from 12, 2019 to 12, 2020 were selected as the study subjects, and these 34 patients were randomly divided into two groups. The test group took Shenyan Zhixue decoction orally, while the control group took Hematuresis capsule and Zhibai Dihuang pill orally. Both groups were treated for three months as a course. The clinical effects were observed 2 weeks, 1 month, 2 months and 3 months after taking medicine.

Results:

1. At the end of the treatment, 16 patients in the experimental group and 15 patients in the control group met the requirements and achieved the expected goal.
2. Analysis of the total efficacy: After 2 weeks, 1 month, 2 months and 3 months of treatment, the total effective rate of the experimental group (70.6%,76.5%,82.4%,87.5%) was significantly higher than that of the control group ($P<0.05$).
3. Comparison of TCM syndrome score: After treatment, the total effective rate was 87.5% in the experimental group and 73.3% in the control group, the difference was statistically significant ($P<0.05$). Among them, the improvement of dizziness symptom was the most significant than the control group ($P<0.01$); in the improvement of irritability symptoms, there are statistical differences ($P<0.05$); but for thirst, feverish feeling in palms and soles, night sweats, it was not significant ($P>0.05$).
4. Recurrence rate comparison: After 3 months of follow-up, the recurrence rate was 7.14% in the experimental group and 18.18% in the control group. There was no significant difference between the two groups ($P<0.05$).

Conclusion:

1. Shenyan Zhixue decoction has significant clinical effect in the treatment of isolated hematuria after Henoch Schonlein purpura of hyperactivity of fire due to yin deficiency type.
2. Shenyan Zhixue decoction can effectively improve the symptoms of thirst, dizziness, night sweat, irritability, feverish feeling in palms and soles in children with isolated hematuria after purpura,

especially for dizziness and irritability.

3. Shenyang Zhixue decoction can significantly reduce the urine sediment red blood cell count of children with isolated hematuria after Henoch Schonlein purpura of hyperactivity of fire due to yin deficiency type.

Keywords: Henoch Schonlein purpura; Isolated hematuria; Hyperactivity of fire due to yin deficiency

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Clinical efficacy observation of Yiyin Zhuanggu pill in the treatment of Postmenopausal osteoporosis of liver-kidney yin deficiency type

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Abstract

Postmenopausal osteoporosis (PMOP) is a type of primary osteoporosis (OP) that occurs 5 to 10 years after menopause in women. It is caused by an imbalance between bone resorption and bone formation due to estrogen deficiency, resulting in bone loss, damage to bone microstructure, increased brittleness and susceptibility to fracture, resulting in a systemic bone disease characterized by the above-mentioned manifestations, which greatly affects the quality of life of postmenopausal patients. The risk of osteoporosis in women is 6-8 times higher than that of men at the age of 60-70 years, and the risk of fracture is also 10% higher than that of men. With the increasing aging of the global population, osteoporosis has become an important public health issue that needs to be addressed. This study was conducted to observe and clarify the efficacy and safety of Yiyin Zhuanggu Pill through a randomized controlled clinical trial, to provide a reference for the clinical treatment of PMOP, and to provide theoretical support and detailed data information for its further clinical application.

Keywords: Yiyin Zhuanggu Pill, Postmenopausal osteoporosis, liver-kidney yin deficiency type, Clinical efficacy observation.

The current Western medical treatment and prevention of PMOP includes basic measures, pharmacotherapy, physiotherapy and rehabilitation [3], the main treatment aims to reduce bone loss and increase bone mineral density, and basic measures are mainly lifestyle modification and application of basic bone health supplements of calcium and vitamin D. Drugs that are widely used clinically include bisphosphonates, calcitonin (CT), estrogen replacement therapy (ERT), selective estrogen receptor modulators (SERMs) and other bone resorption inhibitors, parathyroid hormone analogs (PTHa) and other mechanism-based drugs. Current guidelines recommend the use of bisphosphonates as the first choice of treatment for anti-osteoporosis. These drugs have different mechanisms of action and all have certain efficacy in clinical application, but all have more or less side effects, which affect patient compliance and therefore have certain limitations. Chinese medicine treatment modalities have proven to be clinically effective.

Objective

By combining with clinical practice, evaluate the clinical efficacy of the self-formulated formula Yiyin Zhuanggu Pill on postmenopausal osteoporosis with liver-kidney yin deficiency type.

Methods

Seventy-two patients with postmenopausal osteoporosis who met the criteria of liver-kidney yin deficiency type were randomly divided into two groups: 36 patients in the treatment group and 36 patients in the control group. All patients in the group were given calcium carbonate D3 and osteotriol

pills, alendronate tablets in the control group and Yiyin Zhuanggu Pill in the treatment group; the treatment course was 24 weeks. The changes of hip bone mineral density (BMD), quantitative TCM syndrome score, TCM single syndrome score, and visual analogue scale (VAS) of low back pain were recorded before and after the study in the two groups respectively, and the clinical efficacy was evaluated by statistical analysis.

Results

1. Comparison of the hip BMD: After 24 weeks of continuous treatment, the hip BMD was significantly higher in both groups ($P < 0.01$), and the efficacy of both groups was comparable ($P > 0.05$).

2. Analysis of the efficacy of TCM symptoms: After 24 weeks of continuous treatment, comparing the total efficacy of TCM symptoms of the two groups, 67.65% in the control group and 87.50% in the treatment group, the efficacy of the treatment group was better than that of the control group ($P < 0.05$).

3. Comparison of TCM symptom scores: Comparing the total TCM symptom scores, there was significant improvement in both groups after treatment ($P < 0.01$), and the treatment group was significantly better than the control group after 12 weeks and 24 weeks of treatment ($P < 0.01$); comparing the individual symptom scores within the group, after 12 weeks of treatment, the treatment group was better than the control group in the symptoms of the five upset hot and dryness in the eyes ($P < 0.05$), after 24 weeks of treatment, the symptoms of low back pain, weakness of the knees, five upset hot, cramps in the lower limbs, difficulty in walking, difficulty in holding weight, dryness in the eyes, insomnia and dreaminess improved significantly in the treatment group ($P < 0.01$), and tinnitus symptoms also improved ($P < 0.05$), the control group only saw an improvement in the symptoms of low back pain, weakness of the knees, lower limb cramps, difficulty in walking and difficulty in holding weight ($P < 0.01$), while the symptoms of five upset hot, insomnia and dreaminess, dryness of the eyes and tinnitus did not improve significantly compared with those before treatment ($P > 0.05$); comparing the individual symptom scores between groups after 24 weeks of treatment, the efficacy of the treatment group was significantly better than the control group in improving the symptoms of the five upset hot, dryness in the eyes and tinnitus ($P < 0.01$), in terms of symptoms of insomnia and dreaminess, the treatment group was more effective than the control group ($P < 0.05$), the two groups were equally effective in improving the symptoms of low back pain, weakness of the knees, cramps in the lower limbs, difficulty in walking and difficulty in holding weight ($P > 0.05$).

4. Comparison of VAS scores: After 24 weeks of continuous treatment, there was a significant reduction in VAS scores in both groups compared to pre-treatment ($P < 0.01$), and the improvement in VAS scores was comparable between the two groups after 12 and 24 weeks of treatment ($P > 0.05$).

Conclusion

1. Yiyin Zhuanggu Pill can clearly improve the hip BMD in PMOP patients of liver-kidney yin deficiency type.

2. Yiyin Zhuanggu Pill can significantly improve the TCM symptom scores in PMOP patients of liver-kidney yin deficiency type.

3. Yiyin Zhuanggu Pill can effectively alleviate the symptoms of low back pain, weakness in the knees, five upset hot, cramps in the lower limbs, difficulty in walking, difficulty in weight holding, insomnia

and dreaminess, dryness in the eyes and tinnitus in PMOP patients of liver-kidney yin deficiency type.
4. Yiyin Zhuanggu Pill can significantly reduce the VAS score of low back pain in PMOP patients of liver-kidney yin deficiency type.

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Summary of recent studies on the treatment of diabetes mellitus by acanthopanax senticosus

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Abstract

The treatment of diabetes mellitus(DM) has always been a hot topic discussed by various generations of scientists. In conclusion, the treatment of DM with acanthopanax senticosus has certain academic research value and great development prospect, but it also has certain deficiencies. First, the evaluation standard of therapeutic efficacy is different, and the improved symptoms and signs are different. Second, the number of clinical reports is too small, and some experimental studies lack control group, so the related action pathways and dose-effect relationship of drugs still need to be further studied.

Key words: Acanthopanax senticosus; Diabetes; Diabetes treatment; Diabetes research progress;

Objective and significance

In recent years, the number of diabetes patients in China has increased much more than expected, with the incidence rate rising to 11.2% from 2015 to 2017. There are also great differences among ethnic groups and regions. It not only adds a heavy burden to the country, society and economy, but also makes diabetics suffer mental and physical torture. At present, in the treatment of DM, no matter type 1 DM or type 2 DM, only a few patients can be cured, and most of them are difficult to cure.

Acanthopanax as a traditional Chinese medicinal, have drawn the attention of the researchers nowadays, a large amount of experimental study confirmed that its curative effect is in the treatment of DM and related mechanism research has become increasingly clear, systematic, acanthopanax treat DM with good curative effect, less side effects, more and more get to go for the majority of physicians and patients. To sort out the relevant data of acanthopanax senticosus in the treatment of DM, in order to provide new ideas for the treatment of DM on this basis, so as to provide new possibilities for improving the cure rate of DM.

Materials and Methods

Retrieval method and strategy

Through the electronic retrieval of literature, known in China journal full text database, VIP database, ten thousand medical database, Chinese biomedical literature database, database such as the United States medical database, the Dutch medical database retrieval, and in strict accordance with the filtered into and exclusion criteria, electronic retrieval self-built database to June 31, 2022. A manual search was conducted for articles in relevant journals, newspapers, and conference papers published before 2022 that met the criteria.

Chinese search included "Acanthopanax senticosus", "diabetes", "diabetes treatment", "Diabetes research Progress"; English search words "Acanthopanax senticosus", "diabetes", "diabetes treatment", "diabetes research progress".

Results and Discussion

DM ^[1] is caused by a deficiency in insulin secretion, a relative or absolute insufficiency of insulin

secretion; And insulin function defect changes the body target tissue sensitivity caused by; It is characterized by elevated blood glucose level. It can also be accompanied by abnormal blood lipid, intestinal flora changes and other clinical manifestations of metabolic diseases. There is no clear name for DM in ancient Chinese medicine books, and modern medical studies classify it ^[2] as "DM" and "hate of spleen" in Traditional Chinese medicine. Due to its complicated etiology and pathogenesis, doctors in past dynasties have different cognition of the disease. It is believed that the pathogenesis of the disease mainly lies in the deficiency of Yin and jin, and the hot and dry Yin deficiency as its samples. The two are interactive relations and mutual cause and effect. The diseased organs are mainly in lung, stomach and kidney.

Acanthopanax ^[3] is also known as tiger fetters, as well as stick-stick. Taste hot, slightly bitter, warm, spleen, kidney, heart meridian. Effect dispelling wind and dehumidifying, tonifying kidney and tranquilizing, invigorating qi and strengthening spleen. Its main effective components are the rhizome and various glycosides contained in the roots. In addition, the active components of Acanthopanax senticosus also include chlorogenic acid, polysaccharide and stearic acid. Li shizhen^[4] in its writing compendium of materia medica, called acanthopanax "this summit", has the strong bones and muscles, strong will, to fill gas etc, and long suit can be "intellectual man fit the old resistance". Xing's etc. ^[5] at the beginning of the induced by alloxan DM treatment of acanthopanax injection, the related experimental results show that acanthopanax injection of pharmacological action of multiple channels, can not only to regulate and improve blood sugar and lipid levels, also can make the body's antioxidant capacity was further promoted, so as to improve the metabolism of free radicals to adjust the disorder. Liu ^[6] randomly divided 103 diabetic patients into acanthopanax acanthopanax combined with Traditional Chinese medicine group and oral Xiaoke pill treatment group (control group). In the group of acanthopanax acanthopanax combined with Traditional Chinese medicine, 0.9% normal saline 250ml and Acanthopanax acanthopanax injection 40-60ml were given intravenous infusion once a day for a total of 30 days. One dose of Chinese medicine a day, three courses of 45 days. Xiaoke pill was used as the reference control group, 10 pills were given 3 times a day for 2 months. The results showed that the total effective rate of the treatment group was better than the control group. Compared with the control group, the blood lipid, blood glucose and urine sugar in the treatment group decreased significantly.

Western medicine treats DM with "five-in-one" throughout the treatment of diabetes. The methods include oral hypoglycemic drugs, insulin injection, surgical treatment and insulin pump combined with sports, education, prevention and other three-level treatments, which cause a lot of unnecessary burden to the life and work of patients. In the treatment of DM, traditional Chinese medicine practitioners of all dynasties often use nourishing Yin, clearing heat, moistening dryness and tonifying liver and kidney. With the leap of science and technology and the development of modern pharmacological research, the experimental research on Acanthopanax senticosus has become more refined and specific. Although there are few reports on TCM prescriptions for treating DM with acanthopanax, the relevant preparations and effective ingredients of acanthopanax have also achieved certain results in experimental research and clinical observation of DM treatment. It opens up new possibilities for curing DM. Application of acanthopanax ^[6] in the clinical treatment of DM to observe the result of research shows that application of the active components of acanthopanax can make the hemodynamic status is improved significantly in the patients with DM, reduce

hyperglycemia in patients with blood indicators to health value, and help to hypoglycemia in patients with blood sugar levels back to normal levels. The research on the treatment of DM with acanthopanax has an optimistic prospect, but it also has some shortcomings. First, the evaluation standards of therapeutic efficacy are different, and the symptoms and signs improved are different. Secondly, the sample number of clinical observation reports is too small, some experimental studies lack control group, and the related action pathways and dose-effect relationship of drugs need to be further studied.

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To explore the characteristics of adolescent insomnia from the perspective of qi depression theory

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Abstract

The prevalence of insomnia in adolescents is increasing year by year, but western medicine treatment of this disease is mostly adverse reactions and drug dependence. Chinese medicine in the treatment of adult insomnia has achieved a relatively significant effect, mostly from the Yin and Yang imbalance, hyperactive heart fire and other aspects of syndrome differentiation treatment. However, adolescents have their unique physiological characteristics and living habits. This paper discusses the characteristics of adolescent insomnia from the perspective of qi depression.

Key words: adolescents; Insomnia; Qi depression

Insomnia is a sleep disorder characterized by frequent and persistent difficulty in falling asleep or maintaining sleep and resulting in insufficient sleep satisfaction. In recent years, the incidence of Insomnia has gradually increased, because it is often accompanied by impairment of academic, family or social functions, and even increases the risk of mental, psychological and physical diseases. Adolescents are the key period for the growth and development of human body and the perfection of social functions, and the adverse effects of insomnia are particularly prominent [1]. Epidemiological investigation suggests that the incidence of insomnia among adolescents is 4%~5% [2-3]. At present, clinical doctors recommended for the treatment of insomnia in drug mainly including short, effect of benzodiazepines agonists, melatonin receptor agonists, sedating antidepressants can, etc., but the patient easy appeared dizziness, headache, drowsiness, adverse reactions such as memory impairment, and drug dependence, cause it does not apply to teenagers [1]. This paper discusses the characteristics of adolescent insomnia from the perspective of traditional Chinese medicine.

1. Teenagers' insomnia under the guidance of TCM theory

1.1 Insomnia in TCM

Chinese medicine thinks, insomnia belongs to "not sleep" category, etiology is diverse, pathogenesis is mainly Yin and Yang, qi and blood loss, viscera function maladjusted, as a result mind is disturbed, mind uneasy give up. Mind is the dominant sleep, is also the overall pathogenesis of insomnia. "Jing Yue Quan Shu" establishes the view that consciousness dominates sleep, and gives great inspiration to the later research on sleep. Another example is "Wu Wen · Disease Energy Treatise" said: "People have to lie down and feel uneasy... The dirt hurts." Besides, "plain ask · counter tone discourse" said: "stomach disharmony lies restlessness." Explain the pathogenesis of insomnia viscera. The occurrence of insomnia is also related to the disorder of ying wei's rhythm,

the disorder of Yin and Yang's sleep-wake mechanism, whether the blood is enough to nourish the soul, and whether the emotion is smoothly adjusted. Any problems in this link will cause abnormal sleep and become the cause of insomnia.

2. Adolescent insomnia and qi depression

2.1 Qi depression theory

"Plain ask · lift pain discussion" said: "all diseases are born in qi", qi is the main material to maintain the physiological activities of the human body, whether external sensory six erotic or emotional internal injury, the first impact is qi, qi shun is all diseases. When the qi can not normally rise and fall in and out and coalesce in, it will form "qi depression", is a state of "suppression but impassability". Qi machine is not free, Yin and Yang of human body cannot intersect, Yang does not enter Yin and send not sleep. Qi depression is closely related to physical factors, exogenous six evil qi, emotional disorders, eating disorders and other factors ^[4-5]. Wang academicians think ^[6]. qi depression, its formation is related to genetic and acquired by modern injury and its features are: body slants thin, can also be found in other bodily form, characterized by introverted fragile, to the mental stimulation stress ability is poor, often melancholy, easy to find, insomnia, much dream, loss of appetite, and heave a deep sigh, or pharyngeal foreign body sensation, or threats to bilge painful. External sensory six erotic, internal emotional injury, and diet can all affect the lifting function of qi, resulting in qi depression ^[4].

2.2 Adolescent insomnia qi depression theory

Adolescent period of transition from child to adult, its significant physiological characteristic is "kidney, menstruation to" mature, reproductive endocrine system development, this phase of the neuroendocrine regulation is not stable, often cause psychological, behavior, mental health is not stable, at the same time, the physiological aspects of changing may cause uncomfortable or easy to impulse, Environmental changes and increased exposure will also bring psychological problems in adapting to society ^[7]. Teenagers' academic pressure is heavy, coupled with bad living habits, such as playing mobile phones, we chat circle of friends and other bad information continued stimulation, electronic devices blue light, white light influence, will lead to psychological anxiety and disrupt the sleep law. An Xiao xian believes that ^[8]. children are shaoyang body, viscera "whole but not strong", combined with the physiological characteristics of teenagers, still conform to this characteristic. In clinical practice, adolescent insomnia patients are often accompanied by anxiety and depression. Professor Yu Rui ^[9] believes that this disease is mainly caused by the stagnation of liver qi and the adverse effect of shaoyang key, resulting in the imbalance of Yin and Yang, and eventually causing palpitations and restlessness, and the difficulty in sleeping at night. Adolescents are under great academic pressure, like to eat fat and sweet taste, and have big mood fluctuations, which can easily cause the maladjustment of liver and spleen, the obstruction of qi mechanism, and the formation of qi depression, and then lead to the dysfunction of zang-fu organs, the obstruction of qi, blood and body fluid, the production of hot phlegm, dampness and other pathological

products, affecting the communication of Yin and Yang, and causing insomnia because Yang does not enter Yin ^[10].

3. Conclusion

To sum up, adolescent insomnia is more common with qi depression. In the treatment of this disease, the Professor Qie Rui often uses Bupleurum and keel oyster decoction to add or subtract smooth qi machine, which makes the patient feel comfortable and has a good curative effect. The disadvantages of western medicine treatment of this disease have become increasingly prominent, perhaps from the perspective of TCM reasonable use of the characteristics of syndrome differentiation and the advantages of TCM treatment of this disease will become a hot spot for teenagers.

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Discussion on the medication regularity of professor Wang Xiuxia in the treatment of ovarian chocolate cyst based on set visualization Analysis

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Abstract

Objective: The collection visualization analysis system was used to explore the academic idea and medication rule of Wang Xiuxia in the treatment of ovarian endometrial cyst.

Methods: The effective prescriptions of Professor Wang in the affiliated Hospital of Heilongjiang University of traditional Chinese Medicine from September 1, 2017 to December 31, 2018 were collected, and the prescription database was established, while related medication rule was analyzed.

Results: A total of 145 valid prescriptions were included, involving 115 kinds of Chinese medicine. The commonly used medicine pairs and combinations in the prescriptions were analyzed, and 1 new prescription was evolved.

Conclusion: Professor Wang adheres to the essence of "positive deficiency and evil excess" in the treatment of ovarian endometrial cyst. On the basis of tonifying the kidney and soothing the liver, it is supplemented by the products of removing blood stasis and eliminating stagnation. It fully embodies the academic idea of "Tonifying the kidney and soothing the liver as well as removing blood stasis and eliminating stagnation".

Keywords: Ovarian endometrial cyst; Collective visualization system; Wang Xiuxia; Medication experience; Traditional Chinese medicine; Tonifying the kidney and soothing the liver; Removing blood stasis; Eliminating stagnation.

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Clinical Observation of Lumbar Disc Herniation Treated by Floating Needle Combined with Dong's Acupoint

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Abstract

To observe the clinical effect of floating needle therapy combined with Dong's acupoint in the treatment of lumbar disc herniation. 40 patients were randomly divided into two groups, 20 patients in the treatment group were treated with floating needle combined with Dong's acupoint, and 20 patients in the control group were treated with conventional acupuncture. Visual analogue scale (VAS) and serum inflammatory factor levels were compared between the two groups, and the efficacy was statistically analyzed. To evaluate the effectiveness of floating acupuncture combined with Dong's odd points in the treatment of lumbar disc herniation, in order to provide reference for clinical practice.

Key words: Clinical Observation; Lumbar Disc Herniation; Floating Needle; Dong's Acupoint

Lumbar disc herniation is the degenerative change of the lumbar intervertebral disc, the annulus fibrosus ruptures and protrudes under the action of external force, and it can also together with the nucleus pulposus and cartilage endplates protrude out, causing the sinus vertebral nerve and (or) the cauda equina nerve root to be compressed. A lesion that causes pain in the lower back and legs^[1-2]. The author adopts floating needle combined with Dong's odd acupoints to treat lumbar disc herniation and conduct clinical observation. The observed cases in this study were all from outpatients and inpatients at the Epilepsy Treatment Center of the First Affiliated Hospital of Heilongjiang University of Traditional Chinese Medicine from March 2021 to March 2022.

Objective

To evaluate the effectiveness of floating acupuncture combined with Dong's odd points in the treatment of lumbar disc herniation, in order to provide reference for clinical practice.

Materials and methods

Floating needle device: one-time use floating needle (Nanjing Paifu Medical Technology Co., Ltd., Specification: Medium, Medical Device Registration Certificate No.: Su Machinery Note 20152270832, Production Batch No.: 20210212)

Acupuncture device: 0.30 mm×40 mm stainless steel needle (Guizhou Andi Medical Instrument Co., Ltd., batch number: 20210118)

Floating Needle Combined with Dong's Extraordinary Point Group

Float operation: The patient takes a comfortable position and exposes the painful area. The doctor looks for the lumbar trigger point (MTrP)^[3]. If there is pain in the lower extremity, the doctor places the right thumb on the skin surface of the lower extremity to look for the pain point or cord-like protrusion, and walks against the meridian at a distance of 5-8 cm from the pain point or protrusion. Acupuncture. After the patient feels less or less pain, the needle core is removed and the needle is retained for 24 hours. If pain also occurs in the lower extremities, the same operation method can be

applied to the lower extremities for treatment, until the pain is relieved or disappeared, then stop and keep the needle for 24 hours, and fix it with a special tape for floating needles.

Dong's special point acupuncture: Acupuncture was performed at Linggu and Dabai points on the healthy side of the patient^[4]. Linggu point was located at the junction of the first and second metacarpal bones on the back of the hand, and Dabai point was located 1 cun away from Linggu point on the radial side of the second metacarpal bone on the back of the hand. Acupuncture deeply to the bone surface. While performing the lifting, inserting and twisting manipulation, the patient was instructed to move the muscles of the lower back on the affected side, and to walk. After the symptoms were relieved, the needle was retained for 40 min.

The above treatment was given once every other day, with 5 times as a course of treatment, a total of 4 courses of treatment.

conventional acupuncture group

Acupoint selection: Jiaji acupoints and Yaoyangguan on both sides corresponding to the prominent parts, ring jumping on the affected side, if there is lower extremity pain, match with Yanglingquan, Weizhong, Kunlun, Chengshan, Juegu, Yinmen and other acupoints on the affected side .

Operation: When acupuncture at Jiaji point, the needle tip should be slightly in the direction of the midline, and the other points should be punctured straight. , the needle was retained for 40 min.

The above treatment was performed once every other day, with 5 times as a course of treatment, a total of 4 courses of treatment.

Results and discussion

The treatment results showed that the total effective rate was 90% in the treatment group and 65% in the control group. There was a statistically significant difference between the two groups ($P < 0.05$), and the treatment group was significantly better than the control group. The VAS score after one course of treatment showed that the treatment group improved from (7.61 ± 2.16) to (1.25 ± 2.07) , and the control group improved from (7.43 ± 2.05) to (3.67 ± 1.59) . Acupuncture is effective in improving the pain symptoms of patients with lumbar disc herniation, which is better than acupuncture alone. Comparison of serum inflammatory factor levels between the two groups after 4 courses of treatment showed that the treatment group improved from IL-6 (139.02 ± 25.48) $\mu\text{g/L}$, TNF- α (2.05 ± 0.45) ng /L to IL-6 (103.25 ± 0.45) 14.37 $\mu\text{g/L}$, TNF- α (1.09 ± 0.18) ng /L, the control group was improved from IL-6 (138.27 ± 25.43) $\mu\text{g/L}$, TNF- α (2.04 ± 0.42) ng /L to IL-6 (116.78 ± 21.04) $\mu\text{g/L}$, TNF- α (1.75 ± 0.27) ng /L, indicating that the combination of floating acupuncture and acupuncture at Dong's extraordinary points is also beneficial in reducing inflammation and analgesia, and is superior to acupuncture alone.

To sum up, floating acupuncture combined with Dong's extraordinary points in the treatment of lumbar disc herniation has definite curative effect, high safety, and convenient operation.

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Isolation and Identification of Phenylpropanoids from *Taraxacum ohwianum* Kitam leaves

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Abstract

These compounds were identified by physicochemical properties and spectral data as sinapyl alcohol(1), dihydromustard alcohol(2), lawsorosemarinol(3), caffeic acid(4), caffeic acid methyl ester(5), caffeic acid butyl ester(6), chlorogenic acid(7), 3, 5-di-*O*-caffeoylquinic acid(8), 3, 4-*O*-dicaffeoylquinic acid n-butyl ester(9), isorinic acid(10), butyl p-coumarate(11). Compounds 1~3, 10 and 11 were isolated from the *Taraxacum* for the first time.

Key words: *Taraxacum ohwianum* Kitam.; leaves; Chemical compositions; Phenylpropanoids; Structure identification

Dandelion for composite dandelion perennial herb, also known as milk grass, mother-in-law ding. It has antibacterial, diuretic, antiviral, antioxidant and other pharmacological effects. Different species of dandelion have certain health care functions, and its flowers, roots and other parts also have edible value. Ancient books record that it is "essential medicine for antipyretic and cooling blood" and "extremely cheap and effective". As traditional Chinese medicinal materials, it contains phenylpropanoid, phenolic acids, flavonoids, triterpenoids and other chemical components, among which phenylpropanoid compounds such as chlorogenic acid have antioxidant activities. In order to further develop and utilize the pharmacodynamic substances of Dandelion, 11 phenylpropanoid compounds were isolated and identified by multiple chromatographic methods. The compounds were erucinol (1), dihydroerucinol (2), Lawsorosemarinol (3), caffeic acid (4), caffeic acid methyl ester (5), caffeic acid butyl ester (6), chlorogenic acid (7), 3, 5-*O*-discaffeic acid quinic acid (8), 3, caffeic acid methyl ester (5), caffeic acid methyl ester (6), chlorogenic acid (7), 5, 5-*O*-discaffeic acid quinic acid (8), Compounds 1~3, 10 and 11 were isolated from the genus Dandelion for the first time.

Objective

To study the phenylpropanoid constituents in the leaves of *Taraxacum ohwianum* Kitam. Eleven compounds were isolated and purified by silica gel, ODS column chromatography and preparative HPLC.

Materials and methods

Waters E2695 High Performance Liquid Chromatography; Lc-20ar preparation liquid chromatography (Shimadzu Instrument Co., LTD., Japan); Bruker-500 Superconducting NMR (Bruker, Switzerland); Chromatographic grade reagents for liquid phase and analytical grade reagents for the rest.

The acidic fractions of n-butanol (97 g) were separated by silica gel column chromatography with gradient elution of methylene chloride and methanol (20:1-1:1). Eight fractions were obtained by HPLC and THIN layer chromatography combined. Fr.3, Fr.7 and FR.8 were separated by reverse silica gel column chromatography to obtain Fr.3.1-Fr.3.2, Fr.7.2-Fr.7.4 and Fr.8.1-Fr.8.5. Compound 6(13.0 mg) and compound 7(11.0 mg) were obtained by preparative HPLC, respectively.

Compound 8(19.0 mg) was isolated from Fr.7.2 and 5(14.5 mg) was isolated from Fr.1 by preparative HPLC. Compounds 9(21.9 mg), 11(7.8 mg), 10(26.4 mg) and 4(14.5 mg) were isolated from Fr.8.1, Fr.8.3 and Fr.8.4 by preparative HPLC.

The basic fractions of n-butanol (64 g) were separated by silica gel column chromatography and eluted by gradient elution of methylene chloride and methanol (50:1-1:1). Six fractions were obtained by HPLC and THIN layer chromatography. Fr.11 was separated by reverse silica gel column chromatography to obtain Fr.11.1-Fr.11.5, and Fr.11.1 were separated by preparative HPLC to obtain compounds 1(15.4 mg), 2(13.7 mg) and 3(5.6 mg).

Results and discussion

Dandelion, as a traditional herbal medicine with a long history, has the functions of clearing heat and detoxifying, reducing swelling and dispersing knot, etc. Traditional Chinese medicine believes that dandelion can nourish and dispel evil by playing the functions of clearing heat and detoxifying. At the same time, it has edible value and is widely used in clinical, food, cosmetics and other aspects. At present, studies on dandelion mainly focus on flavonoids, polysaccharides and other active substances, while less attention is paid to other types of components.

In this paper, the chemical constituents of phenylpropanoids from dandelion were studied. Eleven phenylpropanoids were isolated, among which compounds 1-3, 10 and 11 were isolated from Dandelion for the first time. Studies have found that organic acids such as caffeic acid in dandelion can reduce lipopolysaccharide (LPS) induced respiratory tract inflammation and other inflammation by affecting the TLR4/IKK/NF- κ B signaling pathway in human bronchial epithelial cells. In addition, chlorogenic acid in dandelion also has broad spectrum antibacterial and other pharmacological effects. This study enriched the chemical constituents of dandelion, and provided a certain material basis for its clinical application and pharmacology research.

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Chemical constituents from the root of *Taraxacum ohwianum*

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Abstract:

To study the chemical composition of the root of *Taraxacum ohwianum*. Using methanol ultrasonic extraction Thirteen compounds were separated by forward silica gel column chromatography, ODS column chromatography and preparative HPLC. Three compounds were isolated and identified as maricaffeolyide A (1), 3,4-*O*-dicaffeoylquinic acid n-butyl ester (2), 4-allyl-2,6-dimethoxyphenyl glucoside (3), All the compounds are isolated from *Taraxacum* genus for the first time.

Key words: *Taraxacum ohwianum* Kitam; chemical constituents; structural identification

Dandelion is compositae dandelion plant, a perennial herb, first recorded in the Tang Herb, folk also known as Mother-in-law ding, Pu Pu ding, Huang Hua Di Ding, Huang Hua Lang, etc. Dandelion resources are widely distributed, varieties are diverse, and functional components are rich. Currently, more and more studies have been conducted on the chemical components of taraxacum. Phenolic acids, terpenoids, flavonoids and other components are the main components of dandelion, which can protect liver and promote gallbladder, regulate immunity, and fight fatigue^[1,2].

Dandelion plants also profoundly embody the characteristics of food and medicine homology, because of its medicinal and nutritional value has been processed into dandelion tea and other health food. In recent years, the application of dandelion as medicine and food homology is increasing day by day, and the research on its chemical composition and pharmacological action is increasing day by day. In the process of storage and transportation of medicinal materials, its stems and leaves are easy to be damaged, and its roots are easy to be preserved and transported. Its roots are rich in resources, high yield, cheap and easy to obtain. In this paper, a variety of modern separation methods were used to separate and identify the chemical components of dandelion roots, and three compounds were obtained.

Objective:

According to the study of its chemical components, the study of the activity of the medicinal materials of dandelion is carried out to provide a theoretical basis for the development of new medicines and health products of dandelion.

Materials and methods:

Dandelion root 10.0 kg, soaked in 7 times the amount of 80% methanol for 12 hours, ultrasonic extraction 3 times, 40 minutes each time. The extracts were filtered and combined, and the filtrate was recovered under reduced pressure with a rotary evaporator until there was no alcohol taste, resulting in 2.6 kg of methanol extract. After the methanol extract is diluted and suspended with water, petroleum ether is added for extraction for 3 times, and the petroleum ether extract is recovered under reduced pressure with a rotary evaporator to obtain petroleum ether extract. Adjust the PH value of the remaining water layer to 2.5 with HCl solution, saturate n-butanol with water in the ratio of 1:1 for three times, and recover the n-butanol extraction solution under reduced pressure to obtain the n-butanol acidic component.

Take the sample of n-butanol acid component, use 80-100 mesh silica gel to mix the sample at 1:1.5

after methanol suspension, and dry it to loose shape. Soak 200-300 mesh silica gel with dichloromethane, directly mount the column, and then load the dried sample. Using dichloromethane methanol (20:1~1:1) in different proportions as the mobile phase, gradient elution, HPLC and thin-layer chromatography were combined, and three compounds were separated by ODS column and semi preparative HPLC.

Compound **1** is a white amorphous powder. ESI-MS gave an $[M+H]^+$ ion peak at m/z 321, ^{13}C -NMR (150 MHz, CD_3OD) δ : 127.2 (C-1), 114.7 (C-2), 146.8 (C-3), 149.2 (C-4), 116.1 (C-5), 122.5 (C-6), 147.4 (C-7), 114.6 (C-8), 167.8 (C-9), 174.6 (C-1'), 37.6 (C-2'), 19.6 (C-3'), 31.3 (C-4'), 31.2 (C-5'), 71.7 (C-6'), 66.0 (C-7'), 13.6 (C-4'-Me). The above data is consistent with the literature data, so it is identified as maricaffeolylyde A^[3].

Compound **2** is a white amorphous powder. ESI-MS gave an $[M-H]^-$ ion peak at m/z 571, ^{13}C -NMR (150 MHz, CD_3OD) δ : 75.4 (C-1), 41.0 (C-2), 74.8 (C-3), 69.5 (C-4), 65.9 (C-5), 36.4 (C-6), 175.4 (C-7), 64.4 (C-8), 31.3 (C-9), 19.7 (C-10), 13.6 (C-11), 127.3 (C-1'), 114.8 (C-2'), 146.9 (C-3'), 149.2 (C-4'), 116.1 (C-5'), 122.8 (C-6'), 147.0 (C-7'), 114.6 (C-8'), 168.1 (C-9'), 127.3 (C-1''), 114.7 (C-2''), 146.3 (C-3''), 149.2 (C-4''), 116.1 (C-5''), 122.7 (C-6''), 147 (C-7''), 114.6 (C-8''), 168.0 (C-9''). The above data is consistent with the literature data, so it is identified as 3,4-*O*-dicaffeoylquinic acid n-butyl ester^[4].

Compound **3** is a white amorphous powder. ESI-MS gave an $[M-H]^-$ ion peak at m/z 379.1, ^{13}C -NMR (150 MHz, CD_3OD) δ : 138.4 (C-1), 154.2 (C-2), 107.5 (C-3), 134.7 (C-4), 107.5 (C-5), 154.2 (C-6), 41.3 (C-7), 138.7 (C-8), 116.2 (C-9), 102.9 (C-1'), 75.2 (C-2'), 78.3 (C-3'), 71.3 (C-4'), 77.8 (C-5'), 62.6 (C-6'), 55.5 (2-OMe). The above data is consistent with the literature data, so it is identified as 4-allyl-2,6-dimethoxyphenyl glucoside^[5].

Results and discussion:

Dandelion is a traditional Chinese medicine with a long history of food and medicine homology. At present, the clinical demand for dandelion is increasing. It has a wide variety, rich resources, complex chemical composition, and has a variety of activities. Phenolic acids and sesquiterpenoids have antioxidant, anti-tumor, hypoglycemic, anti-inflammatory, antibacterial and other pharmacological activities. In this study, three phenylpropanoid compounds were isolated and identified, which were all isolated from The genus Dandelion for the first time. The results of this study enriched the compound library of Dandelion, and provided theoretical basis for the development of new drugs and health care products of dandelion, so as to better develop and utilize this drug.

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Study on triterpenoid saponins in the tender leaves (shoots) of *Aralia elata*

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Abstract

The tender leaves (shoots) of *Aralia elata* (Miq.) Seem. They are common wild vegetables in northeast China. They have the effects of protecting liver, invigorating qi, strengthening kidney, appetizer, tranquilizing and lowering blood pressure. In this paper, the triterpenoid saponins contained in prickly buds were isolated and identified by NMR and MS spectra. Altogether 15 compounds were identified and 5 of them were isolated from *aralia elata* for the first time. Compounds 2, 4, 5, 6, 7, 9, 10 and 13 are oleanolic acid type triterpenoid saponins, compounds 1, 8, 11, 12 and 14 are Ivy type triterpenoid saponins, and compounds 3 and 15 are acantholic acid type triterpenoid saponins. It provides guidance for the further research, development and utilization of *Aralia elata* tender leaves (shoots).

Key words tender leaves (shoots) of *Aralia elata*, Triterpenoid saponins

Aralia elata is a *Aralia* plant of Acanthaceae. The root bark and stem bark of *Aralia elata* are often used as medicine in traditional Chinese medicine of the motherland, which is bitter, pungent and mild in nature. *Aralia elata* mostly have the functions of protecting the liver and invigorating qi, strengthening the kidney and appetisement, calming the nerves and lowering blood pressure, and have certain therapeutic effects on malignant tumors, cardiovascular and cerebrovascular diseases, diabetes and its complications and other chronic diseases. The chemical components of *Aralia continentalis* mainly include triterpenoid saponins, flavonoids and volatile oil, which have anti-tumor, anti-inflammatory, liver protection, anti-aging, anti-diabetes and other activities.

The tender leaves (shoots) of *Aralia elata* are common wild herbs in northeast China and are consumed in large quantities. In order to ensure safe consumption, the ethanol extract of the tender leaves (shoots) of *Aralia elata* was isolated and identified. It provides guidance for the further research, development and utilization of *Aralia elata* tender leaves (shoots).

Objective

In order to study the chemical constituents of triterpenoid saponins in the tender leaves (shoots) of *Aralia elata*, It provides guidance for the further research, development and utilization of *Aralia elata* tender leaves (shoots).

Materials and methods

The compounds were extracted by ethanol reflux, After the extract is dissolved in water, add sodium hydroxide solution to the water layer, adjust the pH to 10-12, saturate n-butanol with water for 3 times, and recover the n-butanol layer under reduced pressure to obtain the alkali extract of n-butanol layer; After the components of n-butanol alkali extract are completely adsorbed by AB-8 macroporous resin, they are successively eluted with water, 30% ethanol, 60% ethanol and 90% ethanol. Semi preparative HPLC (MeOH:H₂O=34:66) obtained compound 1 (10.1 mg), compound 2 (12.3 mg), compound 3 (12.7 mg); (MeOH:H₂O =36:64) to obtain compound 4 (10.8 mg), compound 5 (8.5 mg), compound 6 (10.1 mg); 8g of 60% ethanol was partially eluted by reversed-phase ODS column chromatography, gradient elution with methanol: water (30%~100%),

and compound 7 (12.3 mg) was obtained by semi preparative HPLC (MeOH:H₂O =42:58); (MeOH:H₂O =50:50) to obtain compound 8 (15.3 mg) and compound 9 (12.1 mg); (MeOH:H₂O =48:52) to obtain compound 10 (13.1 mg) and compound 11 (12.3 mg); (MeOH:H₂O =62:38) to obtain compound 12 (14.1 mg) and compound 13 (13.4 mg); (MeOH:H₂O = 81:19) to obtain compound 14 (14.6 mg) and compound 15 (12.5 mg). The structures of the compounds were identified by NMR and MS.

Results and discussion

15 triterpenoid saponins were isolated from the tender leaves(shoots) of *Aralia elata* as hederagenin-3-*O*- β -*D*-glucopyranosyl-(1 \rightarrow 3)- α -*L*- arabinopyranoside(1), araloside A(2), echinocystic acid-3-*O*- β -*D*-glucopyranosyl-(1 \rightarrow 3)-*O*- α -*L*-arabinopyranoside(3), oleanolic acid-3-*O*- α -*L*-arabinopyranosyl-(1 \rightarrow 2)- β -*D*-glucopyranoside(4), oleanolic acid-3-*O*- β -*D*-glucopyranoside(5), anchusosid 2(6), oleanolic acid-3-*O*- β -*D*-glucopyranosyl-(1 \rightarrow 2)- β -*D*-glucopyranosyl(7), hederagenin-3-*O*- β -*D*-glucopyranosyl-(1 \rightarrow 3)- β -*D*-glucopyranoside(8), chikusetsu saponin IVa(9), randianin(10), macranthoside A(11), hederagenin 3-*O*- β -*D*-glucopyranoside (12), oleanolic acid-3-*O*- β -*D*-glucopyranosyl-(1 \rightarrow 2)- β -*D*-galactopyranosyl(13), hederagenin-3-*O*- α -*L*-arabinofuranosyl-(1 \rightarrow 4)- β -*D*-glucuronopyranosyl-28-*O*- β -*D*-glucopyranosyl ester(14), echinocystic acid-3-*O*- α -*L*-arabinopyranoside(15). Compounds 4, 8, 11, 13and14 were isolated from this genus for the first time. Compounds 2, 4, 5, 6, 7, 9, 10 and 13 are oleanolic acid type triterpenoid saponins, compounds 1, 8, 11, 12 and 14 are Ivy type triterpenoid saponins, and compounds 3 and 15 are acantholic acid type triterpenoid saponins.

Most of the saponins isolated from the tender leaves (shoots) of *Aralia elata* are triterpenoid saponins, and the main ones are oleanolic acid type, Ivy saponin yuan and thorn bursa acid type triterpenoid saponins. Most of the triterpenoid saponins isolated have anti-inflammatory, anti-tumor and liver protective effects, low toxicity, and high medicinal value.

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Study on Chemical Constituents in Leaves of *Astragalus membranaceus*

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Abstract

To study triterpenoid saponins in the leaves of *Astragalus membranaceus*. The chemical constituents of *Astragalus membranaceus* leaves were isolated by silica gel and ODS chromatography, The compounds were identified by 1D-NMR and 2D-NMR. Three compounds were isolated and identified from the extract of *Astragalus membranaceus* leaves. Cyclounifolioside D(**1**) , Astraverrucin I(**2**) , Cycloaraloside A(**3**). Compounds **1**, **2**, **3** were isolated from *Astragalus membranaceus* leaves for the first time.

Key words: *Astragalus* leaves; Triterpenoids; Chemical composition

Astragalus membranaceus (fish.) Bge. is a perennial herb of *A. membranaceus* Linn belonging to Leguminosae, which was published in Shennong Materia Medica. It has the effects of invigorating qi and consolidating exterior, detoxicating and expelling pus, promoting urination and promoting granulation [1]. With the increase of clinical application of *A. membranaceus*, the number of wild *A. membranaceus* decreased sharply. In order to protect natural resources and promote the sustainable development of wild *A. membranaceus* medicinal resources, the chemical constituents of *A. membranaceus* leaves were isolated and identified, and three triterpenoid saponins were obtained.

Objective

In order to study the chemical constituents in the leaves of *A. membranaceus* and provide the basis for further research.

Material and methods

SHIMADZU LC-6AD Preparative High Performance Liquid Chromatography (SHIMADZU), AB Sciex Q-TOF™5600+ESI Mass Spectrometer (AB Sciex), Bruker DMX-600 superconducting NMR spectrometer (Bruker, Switzerland), Bruker DMX-400 Superconducting NMR spectrometer (Bruker, Switzerland); The semi-preparative column was Sunfire Prep™ C18(10×250mm, 10μm). The preparative chromatographic column was Sunfire Prep™ C18(19×250mm, 10μm).

The dried leaves of *A. membranaceus* (10.0 kg) were heated and extracted 3 times with 15 times volume of 75% ethanol for 2 h each time. The extracted solution was filtered and combined, and the extracted solution was decompressed to recover the solvent. The extract was 1395.0 g. Petroleum ether (3 times ×6 L), ethyl acetate (3 times ×6 L) and water-saturated n-butanol (3 times ×6 L) were successively extracted, and 50.0 g of petroleum ether, 190.0 g of ethyl acetate and 195.0 g of n-butanol were obtained by decompression recovery of solvent, respectively. Fr.1-Fr.11. Fr.4(9.0g) was separated by reversed-phase ODS column chromatography and eluted by methanol-water mixture system (60%~90%), followed by semi-preparative HPLC eluting with methanol-water (80%), to obtain 3(12.7 mg), Fr.7 (12.4 g) was separated by reversed-phase ODS column and eluted by gradient elution of methanol and water mixture system (40%~85%). Preparative HPLC eluted by methanol-water (64%) and MeOH: H₂O (80:20), respectively. Compound 2(187.3 mg) and 3(16.2 mg) were obtained.

Results and discussion

Compound 1: White amorphous powder; ESI-MS m/z 741 $[M+HCOO]^-$; 1H -NMR (C_5D_5N , 600 MHz) δ : 3.95(1H, m, H-3), 1.74(1H, m, H-5), 3.96(1H, m, H-6), 1.26(1H, m, H-11a), 1.81(1H, m, H-11b), 5.51(1H, m, H-16), 1.90(1H, m, H-17), 1.25(3H, s, H-18), 0.30 (1H, d, $J=4.6$ Hz, H-19a), 0.56 (1H, d, $J=4.6$ Hz, H-19b), 1.03(3H, d, $J=7.0$ Hz, H-21), 2.01(3H, s, H-26), 1.39(3H, s, H-27), 0.98(3H, s, H-28), 1.31(3H, s, H-29), 1.25(3H, s, H-30), 2.07(3H, s, 16- CH_3CO), 4.99(1H, d, $J=7.5$ Hz, H-1'); ^{13}C -NMR (C_5D_5N , 150 MHz) δ : 88.4(C-3), 42.4(C-4), 70.4(C-6), 34.0(C-7), 46.1(C-8), 20.4(C-9), 29.5(C-10), 75.6(C-16), 18.8(C-18), 27.8(C-19), 31.5(C-20), 19.1(C-21), 32.7(C-22), 27.8(C-23), 79.0(C-24), 26.4(C-27), 19.2(C-28), 29.6(C-29), 16.4(C-30), 104.0(C-1'). The data of this compound were basically consistent with those reported in the literature^[2], so the compound was identified as Cyclounifolioside D.

Compound 2: White amorphous powder; ESI-MS m/z 653 $[M+H]^+$; 1H -NMR (C_5D_5N , 600 MHz) δ : 3.64(1H, dd, $J=15.8, 4.1$ Hz, H-3), 5.00(1H, m, H-16), 1.40(3H, s, H-18), 0.21(1H, d, $J=3.5$ Hz, H-19a), 0.54(1H, d, $J=3.5$ Hz, H-19b), 1.28(3H, s, H-21), 1.57(3H, s, H-26), 1.30(3H, s, H-27), 2.01(3H, s, H-28), 1.33(3H, s, H-29), 0.99(3H, s, H-30), 5.00(1H, d, $J=7.5$ Hz, H-1'); ^{13}C -NMR (C_5D_5N , 150 MHz) δ : 88.9(C-3), 42.5(C-4), 67.9(C-6), 38.5(C-7), 46.9(C-8), 20.8(C-9), 29.4(C-11), 33.3(C-12), 46.5(C-15), 73.3(C-16), 21.4(C-18), 30.4(C-19), 87.1(C-20), 27.0(C-21), 34.8(C-22), 26.3(C-23), 81.6(C-24), 71.2(C-25), 28.(C-26), 28.5(C-27), 28.9(C-28), 16.6(C-29), 20.1(C-30), 106.9(C-1'). The data of this compound were basically consistent with those reported in the literature^[3], so the compound was identified as Astraverrucin I.

Compound 3: White amorphous powder; ESI-MS m/z 651 $[M-H]^-$; 1H -NMR (C_5D_5N , 600 MHz) δ : 3.65(1H, m, H-3), 3.74(1H, m, H-6), 3.59(1H, m, H-8), 5.01(1H, m, H-16), 1.41(3H, s, H-18), 1.28(3H, s, H-21), 3.87(1H, d, $J=5.9$ Hz, H-24), 1.57(3H, s, H-26), 2.01(3H, s, H-28), 1.33(3H, s, H-29), 0.99(3H, s, H-30), 5.01(1H, d, $J=7.5$ Hz, H-1'); ^{13}C -NMR (C_5D_5N , 150 MHz) δ : 87.6(C-3), 42.5(C-4), 67.9(C-6), 46.9(C-8), 20.9(C-9), 29.4(C-10), 44.9(C-13), 45.9(C-14), 73.4(C-16), 58.3(C-17), 21.4(C-18), 30.4(C-19), 87.1(C-20), 27.0(C-21), 34.8(C-22), 26.3(C-23), 81.6(C-24), 71.2(C-25), 28.1(C-26), 28.5(C-27), 28.9(C-28), 16.6(C-29), 20.1(C-30), 106.9(C-1'). The data of this compound were basically consistent with those reported in the literature^[4-5], so the compound was identified as Cycloaraloside A.

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A meta-analysis on the efficacy and safety of promoting blood circulation and removing stasis in the treatment of endometriosis

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Abstract

Objective: To evaluate the efficacy and safety of activating blood circulation and removing blood stasis in treating endometriosis (EMS). **Methods:** Randomized controlled trials (RCT) of promoting blood circulation and removing blood stasis for EMS in PubMed, CNKI, Wan Fang Data and CBM databases were retrieved by computer. Two researchers independently screened and extracted literature according to inclusion and exclusion criteria, and evaluated the risk of bias and quality of included literature, and used RevMan 5.3 software to analyze the outcome indicators. **Result:** Finally, 15 RCTs were included, including 1528 patients, 772 in the experimental group and 756 in the control group. Meta-analysis showed that in clinical efficacy, serum CA125, recurrence rate, ectopic cyst size, enhanced erythrocyte immune function, increased RC3bR, and decreased RIcR. The efficacy of the treatment group was better than that of the control group. **Conclusion:** The method of activating blood circulation and removing blood stasis can effectively improve the clinical symptoms of EMS and improve the effective rate. However, due to the low quality of the included literatures, more high-quality RCT are needed to verify the conclusion.

Key words: promoting blood circulation and removing blood-stasis; endometriosis; Meta-analysis

Objective

Endometriosis (EMS) refers to the appearance, growth, and infiltration of endometrial tissue in the lining of the uterus and outside the uterus, resulting in repeated vaginal bleeding accompanied by pain, infertility, nodules, or masses ^[1]. Although EMS is a benign disease of gynecology, it is characterized by malignant growth ^[2]. The incidence of EMS in women of childbearing age is as high as 10%-15%, showing a significant upward trend in recent years ^[3]. The disease falls into the categories of "symptom" and "dysmenorrhea" in TCM. In TCM, EMS could be classified as qi stagnation and blood stasis, coagulative blood stasis, deficiency of kidney blood stasis, qi deficiency and blood stasis, mutual formation of phlegm and blood stasis, heat stasis and damp-heat stasis ^[4], suggesting that the main pathogenesis of EMS is stasis blocking uterine and blood veins ^[5]. At present, many RCTs have reported the efficacy of Huoxue huayu TCM in the treatment of endometriosis, but no researchers have systematically evaluated the treatment of EMS by huoxue Huayu TCM. In order to further clarify its efficacy, systematic evaluation method is used to evaluate the effectiveness and safety of promoting blood circulation and removing stasis in the treatment of EMS.

Materials and methods

RCT of promoting blood circulation and removing blood stasis for EMS in PubMed, CNKI, Wan Fang Data and CBM databases were retrieved by computer. Two researchers independently screened and extracted literature according to inclusion and exclusion criteria, and evaluated the risk of bias and quality of included literature, and used RevMan 5.3 software to analyze the outcome

indicators. When the outcome index was a continuous variable, the mean difference (MD) was used to analyze the same units of measurement, while the standard mean difference (SMD) was used to analyze the different units of measurement. When the outcome index was a dichotomous variable, the relative risk (RR) was used as the effect size. 95% confidence interval (CI) was given for each effect size. Heterogeneity analysis was carried out for the RCTS used. If $P \geq 0.1$ and $I^2 \leq 50\%$, it indicated that there was homogeneity between studies. Fixed-effect model was used for meta-analysis. If $P < 0.1$ and $I^2 > 50\%$, it indicates heterogeneity between studies, and random effect model is used for analysis.

Results and conclusion

Meta-analysis showed that in clinical efficacy (RR=1.16, 95% CI [1.07, 1.25], $P=0.0001$), serum CA125 (MD=-4.5, 95% CI [-7.39, -0.92], $P=0.01$), recurrence rate (RR=0.36, 95% CI [0.23, 0.57], $P < 0.00001$), ectopic cyst size (MD=-0.57, 95% CI [-0.79, -0.34], $P < 0.00001$), enhanced erythrocyte immune function, increased RC3bR (MD=1.76, 95% CI [0.27, 3.25], $P=0.02$), and decreased RIcR (MD=-1.58, 95% CI [-2.63, -0.53], $P=0.003$). The efficacy of the treatment group was better than that of the control group. The treatment of promoting blood circulation and removing stasis has the effect of "thinning qi and blood and regulating it". By improving abnormal hemodynamics and hemorheology and inhibiting abnormal tissue hyperplasia, human microcirculation disorders are improved and qi and blood flow is smooth^[6], preventing the formation of lesions. Under the combined influence of hormones and their receptors, inflammatory immunity, invasion adhesion, angiogenesis and other related factors, EMS patients develop abnormal microenvironment in the pelvic cavity^[7]. Studies have shown that Huoxue huayu TCM can inhibit the growth of endometrium and ectopic endometrium tissue blood vessels, improve local blood circulation, and also regulate the immune function of patients for anti-inflammatory treatment^[8]. The treatment of activating blood circulation and removing stasis can improve the curative effect of EMS patients, shorten the course of disease, reduce the use of drugs, reduce side effects and so on. This study showed that the therapeutic effect of the treatment group was better than that of the control group in improving the clinical effective rate, reducing the serum CA125 and recurrence rate, reducing the size of ectopic cyst and enhancing the RBC immune function. It is suggested that the method of activating blood circulation and removing blood stasis can effectively improve the clinical efficacy and reduce the recurrence rate as a supplement to western medicine and surgical treatment. In the future, a large number of high-quality and large-sample RCTS are still needed to verify the efficacy of promoting blood circulation and removing stasis in EMS treatment.

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Analysis of traditional Chinese medicine on obesity-related hypertension

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Abstract: The prevalence of obesity-related hypertension is increasing year by year, which seriously affects human health. The treatment of obesity-related hypertension by TCM has good clinical effect. From the etiology of obesity-related hypertension, the treatment of single Chinese medicine and the treatment of TCM compound syndrome differentiation, the studies of obesity-related hypertension are briefly reviewed.

Key words: obesity; hypertension; traditional Chinese medicine;

In recent decades, the prevalence of obesity and hypertension around the world has been increasing year by year. A summary analysis of a cross-sectional survey of 240,000 adults in China showed that the risk of hypertension in overweight people was three to 4 times higher than that of normal weight people, and more than 90% of obese patients (BMI 28 kg / m²) had hypertension and glycemic and lipid metabolism disorders or clusters of risk factors^[1]. An important feature of obesity-related hypertension is that the occurrence of hypertension is closely related to obesity, and weight control can effectively reduce blood pressure^[2]. Studies have shown that hypertensive patients combined with obesity are more likely to develop resistant hypertension. Obesity not only increases the difficulty of blood pressure control in hypertensive patients, but also promotes the aggregation of multiple cardiovascular and metabolic risk factors. Therefore, while controlling body weight and metabolic disorders, we should pay attention to and reduce blood pressure. The main interventions include medical nutrition therapy, exercise therapy, cognitive and behavioral intervention, drug therapy and surgical treatment^[3]. In recent years, TCM has the advantages of prevention first, significant curative effect and small toxic and side effects in the treatment of this disease. TCM therapy for the prevention and treatment of obesity-related hypertension has become the focus of the research and attention of doctors. This paper will briefly review the research on TCM therapy in the treatment of obesity-related hypertension.

1. Knowledge of obesity-related hypertension in traditional Chinese medicine

Obesity-related hypertension can belong to the category of "vertigo" in traditional Chinese medicine. This disease is located in the brain body, and it is closely related to the liver, spleen, kidney and other viscera. "Re-order Yan's aid side" cloud: "the so-called vertigo, six sexual external feelings, seven feelings and internal injury, can lead to." Explain that its causes include emotion, diet, constitution, work and rest, age and other factors. Pathness is nothing more than both ends of the virtual reality, this deficiency refers to the viscera deficiency or fine blood deficiency to make the brain marrow loss, deficiency is Yin deficiency and Yang partial kang, resulting in the liver wind internal movement, "Lingshu wei qi" said: "on the deficiency is dizzy." Standard is actually caused by phlegm turbidity obstruction, anger and blood stasis stagnation.

2. TCM for the treatment of obesity-related hypertension

2.1 Single taste of traditional Chinese medicine and medicine pair

In recent years, a large number of studies have shown that a variety of single traditional Chinese medicine and medicine have the effect of reducing fat and lowering blood pressure, including astragalus, ghost herb, white peony root, Ze diarrhea, and Poria cocos, etc. Astragalus is a representative Chinese medicine to tonifying qi. Modern pharmacological studies show that the main ingredients of Astragalus include flavonoids, polysaccharides and saponins. Astragalus agalside is one of the most popular ingredients in recent years. Astragalus methyloside can play an anti-obesity effect by improving the hypothalamic leptin sensitivity in obese rats, and it also has the efficacy of improving the endothelial function in the arterial tissue and then antihypertension. Ghost needle grass into the liver meridian has the function of regulating qi and blood. Because it has a benign bidirectional regulation effect of blood pressure, it is applied in the treatment of blood pressure. Zhang Yuanyuan et al^[4]Total flavonoids were found to reduce TC, TG levels, and to increase HDL-C in hyperlipidemic rats. Paeoniflorin in white peony root lowers blood pressure and vasodilation, while reducing blood lipid and thus inhibiting inflammatory cytokine production. The compatibility of Ze diarrhea and poria cocos has the synergistic effect of lipid reduction and weight loss, while poria cocos has the potential aldosterone receptor antagonistic components, which can promote the body water and salt metabolism to achieve the diuretic effect.

2.2 Treatment based on syndrome differentiation

There is no unified standard for the treatment of obesity-related hypertension by TCM syndrome differentiation. At present, most doctors use the methods such as liver clearing, qi nourishing, kidney nourishing, spleen strengthening, phlegm removal and blood stasis in the treatment of obesity-related hypertension.

2.2.1 Clear liver and kidney nourishing method

Shu-jie zhang^[5]Experimental study in rat showed clear liver effect in obese hypertensive patients. Other studies have shown that this method has obvious hypoglycemic effects, lipid regulation, improved metabolic effects, and can also significantly improve the heart structure and function of obese rats^[6].

2.2.2 Strengthen the spleen and reduce the phlegm method

Liu Shibao^[7]Including 90 cases of phlegm and dampness congestion obesity related hypertension patients, divided into control group and TCM group, control group using conventional antihypertensive drug treatment, Chinese medicine group using pinellia white gastrodia elata soup flavor treatment, observed 28 days found TCM group headache, dizziness, chest tightness, vomiting sputum saliva of Chinese medicine symptoms integral significantly lower than the control group.

2.2.3 Yi Qi and Tongluo method

Ye Rong et al^[8]It is found that the method of invigorating qi and promoting blood circulation can effectively reduce blood pressure, improve insulin sensitivity, reduce insulin resistance, reduce blood lipid and blood sugar, and relieve dizziness, headache, fatigue and other symptoms.

3. Conclusion

Nowadays, the prevalence of obesity-related hypertension is high and harmful. The occurrence of obesity-related hypertension can increase the risk and mortality of cardiovascular disease and kidney disease in obese people. Preventing and treating obesity-related hypertension can effectively prevent the occurrence of its complications. Based on the overall concept, traditional Chinese medicine attaches importance to the regulation of the whole viscera organs and meridians. TCM

plays an irreplaceable role in the clinical treatment of this disease.

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Observation on therapeutic effect of “Zhatiao” acupuncture technique combined with electroacupuncture on primary restless legs syndrome

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Abstract

Objective To observe and compare the clinical effects of the “Zhatiao” acupuncture technique on Xuehai and Zusanli combined with electroacupuncture as well as the ordinary acupuncture in the treatment of primary restless legs syndrome. **Methods** 60 outpatients diagnosed with primary restless legs syndrome were randomly divided into combination group (30 cases) and conventional acupuncture group (30 cases) according to a random number table. In the conventional acupuncture group, the scalp acupuncture selected the foot movement sense area and Baihui, the body acupuncture took Xuehai (double), the Diji (double), Zusanli (double), Sanyinjiao (double), Taichong (double). The needles were kept for 40 minutes, the frequency of acupuncture was once a day, 6 times a week, and the whole treatment cycle was 2 weeks. The point selection and operation of the combination group are basically the same as those of the conventional acupuncture group. The difference was that the “Zhatiao” technique was used, followed by the electric acupuncture on both sides of the Xuehai and Zusanli for 20 minutes, and the acupuncture needles are kept. The time, frequency of acupuncture and treatment cycle were the same as those of the acupuncture group. The restless legs severity scale (IRLS) and Pittsburgh Sleep Quality Index (PSQI) scores were compared between the two groups; the clinical effects of the two groups were counted and evaluated before treatment and 2 weeks after treatment. **Results** After 2 weeks of treatment, between the two groups of patients, the IRLS scores, individual scores and total scores of PSQI were significantly lower than before (all $P < 0.05$), and after comparison, the scores of the combination group improved significantly better than the conventional acupuncture group ($P < 0.05$). The total effective rate of the combination group was 90.0%, which was higher than the 73.3% of the conventional acupuncture group ($P < 0.05$). **Conclusion** “Zhatiao” acupuncture technique combined with electroacupuncture to treat primary restless legs syndrome can effectively alleviate the patient's lower limb discomfort and improve the patient's sleep status, and its curative effect is better than conventional acupuncture.

Key words: Xuehai; ZU Sanli; “Zhatiao” acupuncture technique; primary restless legs syndrome

As a kind of neurological sensorimotor disorder, restless legs syndrome (RLS) is mainly characterized by sleep disturbance as the first symptom, and then with the progression of the disease year by year, patients gradually develop indescribable deep paresthesias in both lower extremities, the symptoms are particularly aggravated when resting at night, and they often need to be forced to move both lower extremities to relieve their uncomfortable symptoms^[1]. RLS affects the sleep quality of patients, and even severe mental symptoms including anxiety and depression may occur in patients with severe symptoms. At present, western medicine mainly adopts symptomatic treatment of this disease, which generally lacks pertinence.

“Zhatiao” acupuncture technique refers to the phenomenon that the muscles at the acupuncture site can be observed from the outside in the process of acupuncture, resulting in local contraction. We chooses Xuehai, Zusanli "Zhatiao" combined with electroacupuncture to treat patients with primary RLS, and the curative effect is satisfactory.

Treatment and methods

Control group: given the conventional acupuncture treatment only, the scalp acupuncture selected the foot movement sense area and Baihui, the body acupuncture taked Xuehai (double), the Diji (double), Zusanli (double), Sanyinjiao (double), Taichong (double). The needles were kept for 40 minutes, the frequency of acupuncture was once a day, 6 times a week, and the whole treatment cycle was 2 weeks

Observation group: “Zhatiao” and electroacupuncture were used. When acupuncture at Xuehai and Zusanli, acupuncture needles with a size of 0.22×40mm should be used instead. With the cooperation of the pressing hand, the piercing hand should move the needle in a small, gentle and orderly fan shape until the muscle at the acupuncture site is inserted. When obvious beating occurs, the ipsilateral Xuehai acupoint and Zusanli are connected to Huatuo brand SDZ-II electroacupuncture, and the continuous wave band is selected. The selection and operation of the remaining points were the same as those of the control group. All acupuncture needles were kept for 40 minutes, the frequency of acupuncture was once a day, 6 times a week, and the whole treatment cycle was 2 weeks.

Results and discussion

The excellent rate of the observation group was 90.0%, which was higher than 73.3% of the conventional acupuncture group ($P < 0.05$). “Zhatiao” acupuncture technique combined with electroacupuncture to treat primary RLS can effectively alleviate the patient's lower limb discomfort and improve the patient's sleep status, and its curative effect is better than conventional acupuncture.

After long-term clinical practice, Professor Lu Biao summed up the “Zhatiao” method. It refers to the beating of the muscle after puncturing. After the needle is placed, the doctor can press the hand or the patient can clearly perceive the muscle where the acupuncture point is located. Sudden, short, transient contractions and beatings are a state of acquired qi visible to the naked eye, and this judgment of acquired qi is more objective and accurate. Relevant studies have shown that the mechanism of “Zhatiao” is quite similar to the stimulation of trigger points, that is, through a certain stimulation, a local twitching response is induced, and the muscle fibers are stretched, thereby relieving the compressed state of the capillaries, increasing the oxygen content of the local muscles, and then it promotes the restoration of local microcirculation, ultimately relieves muscle tension and inhibits the sensitization of nociceptors^[2].

Xuehai acupoint is an important acupoint for the treatment of RLS lower limb discomfort, which has the effect of promoting blood circulation and relieving itching. Zusanli can unblock the meridians and activate collaterals as well as regulate the power of lower extremity qi. The two acupoints are matched to regulate the qi and blood of the zang-fu organs, the qi movement of the meridians and collaterals, and the stasis of ying and wei.

Combined with the operation of “Zhatiao”, whichever is the meaning of dredging meridians and connecting qi, it can enhance the effect of meridian qi sensing, and has a particularly strong effect

on dredging meridians and regulating qi and blood. In addition, after “Zhatiao”, following the principle of “the meridian qi has arrived, be careful not to lose it”, connect the electroacupuncture to give a slight and continuous stimulation to help guard the qi, which can gradually stimulate the meridian qi, so that the qi guards and does not disperse. And modern research shows that continuous wave can not only regulate the diastolic and systolic function of muscle tissue and blood vessels, improve local blood flow, and promote the repair of neuromuscular tissue; it can also inhibit the abnormal excitation of nerves, and then relieve muscles from spasticity. The combination of “Zhatiao” and electro-acupuncture can reconcile yin and yang, qi and blood, and the effect is outstanding.

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Effect of Qi Zhi Capsule on the Expression Levels of PI3K and Beclin-1 in Cerebral Ischemia Reperfusion Injury

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Abstract

Objective and significance

Stroke is the first leading cause of death in Chinese residents, with a predilection for the elderly over 60 years old. Today's people are mostly qi deficiency, blood stasis and exuberant phlegm-damp in the background of sedentary, lack of exercise, stay overnight, diet with more hypertrophy and high work stress. Thus, the prevention and treatment of stroke has great significance and application value.

The present study was undertaken to explore the mechanism of the Qi Zhi capsule's antagonism to cerebral ischemia reperfusion injury (CIRI) through the study on the related molecules of PI3K-Akt-mTOR signaling pathway.

Materials and Methods

Sixty SD rats were randomly divided into six groups, sham group, model group, 3-MA group, rapamycin group, LY294002 group and Traditional Chinese medicine (TCM) group with 10 rats in each group. Before MCAO model replication, the corresponding inhibitor and Chinese medicine intervention were respectively carried out. After that, the neurological function of animals in each group was analyzed using the Neurological Severity Score. The cerebral infarct size was detected by TTC staining. And the expression of PI3K, p-PI3K and Beclin-1 protein in brain tissue was tested by Western Blot.

Results

1. The results of the Neurological Severity Score showed that compared with the sham group, all the other groups showed symptoms of neurological impairment, with significantly higher scores ($P < 0.05$). Compared with the model group, the rapamycin, LY294002, and TCM groups showed reduced neurological impairment symptoms and significantly lower scores ($P < 0.05$). Compared with the TCM group, the neurological impairment was more severe in the LY294002 group ($P < 0.05$). Our analysis revealed that Qi Zhi capsule exerted therapeutic and protective effects on the neurological function of CIRI rats.

2. The results of TTC staining showed that compared with the sham group, significant infarcts were observed in the other groups ($P < 0.05$). Compared with the model group, the 3-MA group and LY294002 group had further enlarged infarct volumes ($P < 0.05$). And similarly compared with the model group, the cerebral infarction volume of the rapamycin group and the TCM group had significantly reduced ($P < 0.05$). Compared with the TCM group, the rapamycin group showed weaker brain protective effect in CIRI rats ($P < 0.05$). It is known that Qi Zhi capsule can

effectively alleviate the degree of cerebral infarction in CIRI rats.

2.The expression of PI3K, p-PI3K and Beclin-1 protein in Western Blot assay showed:

① PI3K: Compared with the sham group, the expression of PI3K was significantly decreased in the model or TCM groups ($P < 0.05$). Compared with the model group, PI3K expression was significantly increased in the 3-MA group ($P < 0.05$).

②p-PI3K: Compared with the sham group, p-PI3K expression was significantly decreased in the model, rapamycin, LY294002, and TCM groups ($P < 0.05$). Compared with the model group, p-PI3K expression was further decreased in the LY294002 group and the TCM group ($P < 0.05$).

③Beclin-1: Compared with the sham group, Beclin-1 expression in the other groups was significantly increased ($P < 0.05$). Compared with the model group, It's expression was significantly decreased ($P < 0.05$) in the 3-MA group and significantly increased ($P < 0.05$) in the rapamycin or TCM groups. It is known that Qi Zhi capsule further activates autophagy by reducing the expression of p-PI3K and increasing the expression of Beclin-1.

Conclusion

Qi Zhi capsule can reduce NSS score and brain tissue injury after CIRI, and further activate autophagy by inhibiting the activation of PI3K and upregulating the expression of Beclin-1 protein, thus greatly protecting brain tissue and playing an antagonistic role against CIRI.

Key words: Qi Zhi capsule; Cerebral ischemia reperfusion injury; Autophagy; PI3K; Beclin-1

Clinical Efficacy of Conventional Treatment Methods versus Kaiqiao Fucong Combined with Feijing Zouqi Acupuncture in the Treatment of Sensorineural Hearing Loss

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Abstract:

Objective To compare the clinical efficacy of conventional treatment methods versus Kaiqiao Fucong combined with Feijing *Zouqi* acupuncture in the treatment of sensorineural hearing loss (SNHL); **Methods** 60 patients meeting the diagnostic criteria were randomly divided into 2 groups, and the control group was promoted microcirculation and neurotrophic drug treatment; the treatment group used acupuncture, some of acupoints using Kaiqiao Fucong combined with Feijing *Zouqi* acupuncture methods. Every process of treatment should keeps the needles for 50 minutes; the treatment methods of the two groups were once a day for a total of 21 days. **Results** The total effective rate of the treatment group was 86.67%, and that of the control group was 76.67%, it indicated statistical significance ($P < 0.05$). **Conclusion** Compared with intravenous drugs, the application of Kaiqiao Fucong combined with Feijing *Zouqi* acupuncture methods can treat sensorineural hearing loss (SNHL) better .

Key words: Sensorineural hearing loss; Acupuncture; Kaiqiao Fucong; Feijing *Zouqi*

Sensorineural hearing loss (SNHL) is the most common type of deafness, with accounting for about 90% of people suffer from this type in this disease. The main clinical manifestations of the disease is hearing loss caused by lesions of the auditory receptor, auditory nerve or auditory center of the inner ear. At present, the specific cause of the disease is not clear, and the clinical understanding and treatment of the disease are mostly from the aspects of infection, immunity, inner ear microcirculation and so on ^{[1]-[2]}. There is no significant gender difference in the disease, and it can occur at all ages. With the continuous increase of age, the relationship between the disease and inner ear microcirculation is getting closer and closer. Doctors mainly use the combination of anti-infection, improving local blood circulation, nerve nutrition and other drugs to treat SNHL. This study mainly aims at treating hearing loss caused by microcirculatory disorders through acupuncture.

Treatment and methods

Control group: treatment with drugs that promote microcirculation and nutrient nerves: such as *Salviae Miltiorrhizae* And *Ligustrazine Hydrochloride Injection*, *Monosialotetrahexosylganglioside Sodium Injection* once a day, and continuous treatment for 21 days.

Treatment group: Acupuncture treatment was added on the basis of the control group. The doctor punctured Baihui(DU20) to the affected side and the acupuncture points around the ears such as Ermen(SJ27), Tinghui(GB2), Jiaosun(SJ20) and Yifeng(SJ17) were pricked towards the ear canal, and the direction of Fengchi(GB20) acupoint is toward the contralateral mouth angle with 8~10mm depth, and the method of twisting is applied after obtaining *qi*; the two points of Waiguan(SJ5) and Zhongzhu(SJ3) adopt the technique of Feijing *Zouqi*. That is, when pricking at Zhongzhu(SJ3) and Waiguan(SJ5) points, the doctor pierced the acupuncture into subcutaneous tissue about 3~5mm,

twisting the needle until obtained *qi*, pressed down the needle body, made the needle point toward the shoulder, pressed the distal end of the acupuncture point by the other hand. At this acupuncture depth, slowly shook the needle handle to the left and right. The above-mentioned acupoints were left with a single needle for 50 minutes, and the treatment course was the same as that of the control group.

Results and discussion

After treatment, the total effective rate of the treatment group was 86.67%, and that of the control group was 76.67%. It can be concluded that compared with intravenous drugs, the application of Kaiqiao Fucong combined with Feijing Zouqi acupuncture methods can achieve better curative effect in SNHL.

The causes of SNHL are diverse, and many researchers tend to identify with blood circulation disorders in the inner ear. Guo Hao et al. [3] summarized the predecessors' understanding of sensorineural deafness through multi-angle analysis, and concluded that inner ear microcirculation disorders is an important reason for the decline or even loss of auditory function. The labyrinth artery that supplies blood to the inner ear does not have collateral circulation. If the hair cells of the inner ear release a large amount of free radicals due to the metabolic disorder caused by ischemia and hypoxia, the neuronal cells and hair cells of the inner ear will undergo a large number of apoptosis and cause hearing function decline [4]. Experiments^{[5]-[6]} have shown that if there are small emboli in the cochlear blood vessels, the cochlear microphone potential and action potential can drop rapidly within 1 min. Ear microcirculation disorders caused by arterial spasm or sclerosis, basilar artery stenosis or slow blood flow, hyperlipidemia, and abnormal blood coagulation are all important factors to SNHL.

This disease belongs to the category of "deafness" in Traditional Chinese Medicine, and the application of acupuncture has its own characteristics and advantages. Based on many years of clinical experience, professor Zou Wei has used the acupuncture technique of Kaiqiao Fucong combined with Feijing Zouqi to treat SNHL, which is clinically effective. The technique of applying Baihui(DU20) stab toward Qubin(GB7) can change the expression of P-selectin(CD62p) and factors such as PI3K and p-AKT in the serum. It can reduce damage to nerve cells and increase excitability. It can also improve the excitability of nerve cells to a certain extent. Improve the vasomotor function. In the meridian circulation, the meridians distributed around the ear and passing through the ear mainly include the SanJiao Meridian and the GallBladder Meridian. The auricular acupoints of these two meridians are used for resuscitating the hearing. Ermen(SJ27), Tinghui(GB2), Jiaosun(SJ20) and Yifeng(SJ17) as well as the Fengchi(GB20), the twirling method is applied to open the ear orifice and restore the hearing. There are vertebral arteries and veins in the deep anatomy of Fengchi (GB20) acupoint, so acupuncture at it can alleviate vasospasm, thus increasing the blood supply of vertebral-basal artery, increasing the oxygen content in the blood, and helping to restore the function of damaged nerve cells^[7]. Waiguan(SJ5) and Zhongzhu(SJ3) points, using the technique of Feijing Zouqi to make the *qi* under the acupuncture rapidly spread to the path of the disease and to the ear orifices. *Acupuncture and Moxibustion Questions* stated that this technique has the effect of "prosperity". Therefore, the combination of the Feijing Zouqi techniques at the two points of the meridian not only strengthens the sense of acupuncture *qi*, but also promotes the movement of blood during the *qi* movement, and promotes the curative effect of

the disease. The two points of Waiguan(SJ5) and Zhongzhu(SJ3) points belong to the SanJiao Meridian while Ermen(SJ27) and Jiaosun(SJ20) share the same meridian with them. The relational acupoints have the same effect, dredges the Shaoyang Meridian, and have the effect of combining acupuncture for near or far cure effect.

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Observation on the therapeutic effect of scalp acupuncture combined with "transcranial repeated acupuncture" in the treatment of chronic fatigue syndrome

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Abstract

Objective To observe the comparison of clinical efficacy between scalp acupuncture and western medicine in the treatment of patients with chronic fatigue syndrome. **Methods** A total of 66 patients who met the CFS diagnosis and inclusion criteria were collected, 3 patients dropped out in each group, a total of 6 patients, and the patients were divided into a treatment group (scalp acupuncture group) of 30 cases and a control group (western medicine therapy group) of 30 cases by random number table method. example. There was no significant difference between the two groups in terms of gender, age and course of disease, and they were comparable ($P > 0.05$). The treatment group was treated with scalp acupuncture and repeated transcranial stimulation, while the control group was treated with western medicine oryzanol and vitamin B1 orally. The efficacy of the two treatments was evaluated by four scale scores. **Results** After the treatment, the FS-14 score of the two groups were significantly improved compared with those before treatment, and the difference was statistically significant ($P < 0.01$); After treatment and before treatment, the PSQI, SAS and SDS scores were compared within groups, and the difference was statistically significant ($P < 0.05$); after treatment, the difference was statistically significant ($P < 0.05$); **Conclusion** Scalp acupuncture has obvious effects on improving fatigue symptoms, sleep quality, anxiety and depression symptoms in CFS patients, and the curative effect is better than that of the western medicine group, which is worthy of further clinical research.

Key words

Chronic fatigue syndrome, Scalp acupuncture, Transcranial repeated acupuncture, Western medicine, Clinical efficacy

This study used Sun's scalp acupuncture, which was first proposed by Professor Sun Shentian of Heilongjiang University of Traditional Chinese Medicine, to improve and innovate traditional scalp acupuncture. He emphasized meridian syndrome differentiation, and on this basis inherited and innovated traditional acupuncture and acupoint selection methods^[1]. In the application of scalp acupuncture, practice and theoretical research confirmed the correctness of acupoint selection for the relationship between brain function positioning and scalp, and emphasized the correctness of acupoint selection^[2,3,4]. The importance of manipulation and curative effect expands the scope of treatment of scalp acupuncture, and it is proposed that scalp acupuncture is a new therapy of integrated traditional Chinese and western medicine independently innovated in my country.

In this study, scalp acupuncture combined with transcranial repeated acupuncture was used to treat 60 patients with CFS, and it was compared with oral administration of western medicine oryzanol and vitamin B1.

Objective

To compare the clinical efficacy of scalp acupuncture combined with "transcranial repeated acupuncture" and oral oryzanol and vitamin B1 in the treatment of chronic fatigue syndrome.

Methods

A total of 66 patients who met the CFS diagnosis and inclusion criteria were collected, 3 patients dropped out in each group, a total of 6 patients, and the patients were divided into a treatment group (scalp acupuncture group) of 30 cases and a control group (western medicine therapy group) of 30 cases by random number table method. example. There was no significant difference in gender and age between the two groups of cases after statistical analysis, and they were comparable ($P > 0.05$). The treatment group was treated with scalp acupuncture and repeated transcranial stimulation, while the control group was treated with western medicine oryzanol and vitamin B1 orally. All patients were required to sign an informed consent form before enrolling in the group, and each scale was filled out before and after treatment. The curative effect was evaluated by observing the FS-14 scale, SAS, SDS scores and the overall curative effect of the two groups of patients before and after treatment.

Results

The scores of sleep scale, anxiety scale, and depression scale were compared between the two groups before and after treatment. The scores of the two groups were compared before treatment. The t test showed that the difference was not statistically significant ($P > 0.05$), which was comparable. After the treatment, the intra-group comparison of the two groups of patients showed that the scores in the treatment group were significantly improved compared with those before treatment, and the difference was statistically significant ($P < 0.01$);

Conclusion

Scalp acupuncture combined with "repeated transcranial acupuncture" can significantly improve the symptoms of fatigue, anxiety and depression in patients with CFS, and the effect is better than that of the western medicine group. Scalp acupuncture is an effective method for the treatment of CFS, and it is worthy of clinical application.

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Innovative advances in the TCM big health industry

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Abstract

The Traditional Chinese Medicine (TCM) big health industry is an important foundation for the innovative development of Chinese medicine in China. By giving full play to various advantageous innovative resources, the TCM health industry can achieve the overall goal of going international and meeting the needs of human health services. This paper reviews the methods and paths of development and innovation in the TCM health industry.

Keywords: Big Health Industry, TCM

Health is the basis and necessary condition for all-around human development. The health industry is linked to people's well-being and economic development. With the development of society and the economy, people's health demand is becoming increasingly urgent. In particular, the change in the spectrum of diseases, the arrival of an aging society, the change in lifestyle, and the constant pursuit of health have brought huge market demand and development opportunities to the health service industry. The health service industry is an important part of the modern service industry. At present, the output value of China's health service industry only accounts for about 5% of the gross domestic product (GDP), while the output value of the health service industry in developed countries accounts for more than 10% of the GDP, so the development potential of China's health service industry is huge[1][2].

Objective

By discussing the definition of the TCM health industry and the cooperation between China and Russia in recent years, we will clarify the direction of innovation and future development of the TCM health industry.

Materials and methods

Relevant literature was sorted out using a literature review.

Results and discussion

In the context of the development of the times, and based on the development of health and related industries to a new stage, Big Health is a holistic concept of health based on social needs[3]. As an outstanding representative of Chinese civilization, TCM is a medical science that has been gradually formed and continuously enriched and developed by Chinese people of all ethnic groups during thousands of years of practice in production and life and struggles against diseases and has not only made remarkable contributions to the prosperity of the Chinese nation but also had a positive impact on the progress of world civilization.

The dissemination of Chinese medicine culture is the first and foremost driver for China's Chinese medicine to go global and can provide a constant impetus for the development of Chinese medicine culture and the modernization of Chinese medicine in China during the 13th Five-Year Plan period. We believe that by making full use of existing science and technology, the Internet, and the media, combining the broad coverage and long industrial chain of big health, and with the concerted efforts

of all relevant departments to effectively promote and popularise Chinese medicine knowledge, the modernization and internationalization of Chinese medicine will certainly be realized shortly. Therefore, in addition to inheritance, we must also insist on keeping up with the times and introducing new ideas. We should not only inherit the unique advantages of Chinese medicine but also dare to innovate and make full use of modern science and technology to develop a set of Chinese medicine standards with Chinese characteristics, to promote the development of Chinese medicine theory and practice in the world and thus modernize Chinese medicine in China.[4]

The efficiency of the health systems of Russia and China has been good in recent years[5] and 2020-2021 is the Year of Science, Technology, and Innovation between Russia and China. Cooperation in science, technology, and innovation between Russia and China has grown by leaps and bounds in recent years, especially during the 2020-2021 Year of Science, Technology, and Innovation between Russia and China, which has seen changes in the development of cooperation in the medical field.

The health industry is market-oriented, providing health products and services through optimal resource allocation. In the TCM industry, cross-regional cooperation in TCM trading is an important way to optimize TCM resources, and TCM has the advantage of cross-regional trading, especially in the development of the TCM industry chain and the development of TCM health tourism. In the development of the TCM industry chain, as the climate, temperature, and humidity vary from region to region, the authentic herbs grown in each region are also different, so it is possible to negotiate between regions to establish a targeted cooperation system for TCM and promote cross-regional cooperation and trade. On the one hand, it will promote the development of Chinese medicine cultivation, processing and preparation, manufacturing and storage, and distribution of Chinese medicine in both regions, thus realizing the economic value of Chinese medicine in both regions, thereby raising the income level of the people in both regions and improving the ecological environment. On the other hand, the cultivation of Chinese herbal medicine can also promote the development of Chinese medicine health tourism and realize cross-regional trade. The TCM health tourism industry, as a new form of TCM industry, is an extension of the TCM health service industry and an expansion of the traditional tourism industry[6][7].

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Clinical study of acupuncture combined with ear acupuncture on sleep disorder patients with Alzheimer's disease based on “Du channel”

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Abstract

Objective Acupuncture combined with auricular acupuncture and needle acupuncture treatment based on the theory of governing veins is used to treat patients with Alzheimer's disease and sleep disorders, and a comparison is made to provide more effective clinical treatment for patients with Alzheimer's disease and sleep disorders. **Methods** 72 clinical patients met the criteria for inclusion and diagnosis of dementia with sleep disorders. According to the random number table method, they were randomly divided into a treatment group of 36 cases and a control group of 36 cases. In the treatment group, acupuncture combined with auricular acupuncture was used to acupuncture the needle based on the theory of Du channel, and the main points were selected: Baihui, Fengfu, Dazhui, Mingmen, Yaoyangguan; Acupoints: Anmian(bilateral), Sanyinjiao(bilateral), Taixi (bilateral), Zusanli(bilateral), ear points select bilateral Shenmen, subcortical, sleep, heart, kidney. the control group is based on supervising were selected: Baihui, Fengfu, Dazhui, Mingmen, Yaoyangguan; Acupoints: Anmian(bilateral), Sanyinjiao(bilateral), Taixi(bilateral), Zusanli(bilateral). Pulse theory acupuncture method. The selected patients were treated once a day, 6 times a week, 6 times as a course of treatment, a rest day after each course of treatment, a total of 4 courses of treatment. Both groups of patients used the Pittsburgh Sleep Quality Index Scale(PSQI), before and after treatment to evaluate the treatment effect. **Results** After 4 weeks of treatment, between the two groups of patients, total scores of PSQI were significantly lower than before (all $P < 0.05$), and after comparison, the scores of the combination group improved significantly better than the conventional acupuncture group ($P < 0.05$). The total effective rate of the combination group was 87.5%, which was higher than the 76.47% of the conventional acupuncture group ($P < 0.05$). **Conclusion** Acupuncture based on Du channel combined with acupuncture at ear points and acupuncture based solely on Du channel can significantly improve the sleep status, daytime sleepiness and cognitive function of patients with dementia and sleep disorders.

Key words: Du channel; acupuncture at ear points; dementia; sleep disturbance

Alzheimer's disease(AD) is one of the primary and degenerative diseases of the central nervous system and has three characteristics: insidious onset, slow progression, and progressive development. For a long time, non-cognitive psycho-behavioral symptoms such as sleep disturbance, depression, and apathy accompanying Alzheimer's disease have been neglected, but the incidence of psycho-behavioral symptoms in Alzheimer's patients is as high as 70%~100%.

“Du channel” is closely related to the physiology and pathology of the brain. And when a disease occurs in the human body, certain reaction points can appear in the corresponding area on the ear shell. Thus, we choose auricular combined with governor vessel acupuncture to treat patients with

AD, and the curative effect is satisfactory.

Treatment and methods

Control group: Acupuncture based on the theory of Governor Vessel: Select the main points: Baihui, Fengfu, Dazhui, Mingmen, Yaoyangguan. Matching points: Anmian (bilateral), Sanyinjiao (bilateral), Taixi (bilateral), Zusanli (bilateral). The needles were kept for 30 minutes, the frequency of acupuncture was once a day, 6 times a week, and the whole treatment cycle was 4 weeks.

Observation group: Acupoint selection: Auricular acupuncture treatment was performed on the basis of the control group. Select bilateral Shenmen, subcortical, sleeping, heart, and kidney. The needles were kept for 30 minutes, the frequency of acupuncture was once a day, 6 times a week, and the whole treatment cycle was 4 weeks.

Results and discussion

The total effective rate of the combination group was 87.5%, which was higher than the 76.47% of the conventional acupuncture group ($P<0.05$). Acupuncture based on Du channel combined with acupuncture at ear points and acupuncture based solely on Du channel can significantly improve the sleep status, daytime sleepiness and cognitive function of patients with dementia and sleep disorders.

The auricle is the place where all the meridians pass, terminate and meet. When the human body suffers from disease, certain reaction points can appear in the corresponding area on the ear shell. When there is a disease in the internal organs or a certain part of the body, a pathological connection occurs between these pathological impulses and the neurons corresponding to the auricular points, thereby greatly increasing the excitability of these neurons, and this excitability can generate electrical energy.

The nerve axis, one of the three specific axes in the ear area, starts from the tip of the ear and ends in the dreamy area, which can adjust the function of the human nervous system and reflect the state of the nervous system. This nerve axis runs through four of the six main acupoints of insomnia from top to bottom, Shenmen, kidney, subcortical, and pillow, which is enough to show that the principle of acupoint selection is to regulate the nervous system as the main purpose.

Based on acupuncture on the Du channel, combined with auricular acupuncture treatment, it can strengthen the effect of treating insomnia, increase sleep time, and improve sleep depth. At the same time, it can slow down the progress of dementia development in elderly patients, enhance memory, and improve the quality of life of patients.

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Application of mountain-burning fire acupuncture method in the treatment of allergic rhinitis in cold regions based on regional characteristics

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Abstract Cold regions have cold climate, the residents in these regions are prone to consume milk, meat and wine, leading to the constitution of phlegm-dampness and yang deficiency, and therefore, allergic rhinitis occurs frequently. Based on the regional characteristics, guided by the unique mountain-burning fire acupuncture method, and following the idea of “guiding defense yang into interior through needling the 3 layers: the layer of skin, the layer of flesh and the layer between muscle and bone”, we aim to provide in this paper with more effective thought and method for the prevention and treatment of allergic rhinitis in cold regions.

Keywords Allergic rhinitis, cold regions, mountain-burning fire acupuncture; guiding defense yang into interior through needling the 3 layers

Allergic rhinitis (AR) is an allergic disease which is paroxysmal, refractory, relapsable, and with high incidence, particularly in cold regions. The clinical manifestations of AR are nasal congestion and itching, sneezing, runny nose, etc.

1. The concept of cold regions

The cold regions in China mainly include Heilongjiang, Jilin, and Liaoning in the northeast, and other places. These areas have a mainland monsoon type climate, with significant temperature difference between day and night, four distinct seasons, and windy and cold weather. Under the influence of the Siberian cold current which frequently goes south, the winter is very cold, and the freezing period is as long as half a year, forming a unique cold area.

2. The etiology and pathogenesis of AR in cold regions

2.1 Cold is prone to invade lung collaterals leading to failure of lung yin to be nourished

In cold regions, residents' rooms are warm and dry, and the exuberant heat damages body yin, resulting in failure of lung yin to be nourished, giving rise to the impossibility of lung yin to moisten the nose. Meanwhile, due to the long-term influence of wind and cold weather, lung qi in this regions is usually deficient, giving the opportunity for cold to invade lung exterior and for dryness to damage lung yin. Deficiency of lung yin may fail to enrich nose and lose its function of regulating the waterways, then, water, fluid and dampness will aggregate, and nasal orifices will be blocked, resulting in this disease.

2.2 Fatty food produces dampness, resulting in deficient spleen which fails in transportation

The spleen is the source of phlegm, and the lung is the container of phlegm; weak spleen and stomach are unable to transport and transform dampness, giving rise to phlegm and dampness production and aggregation in the body; disorder of the mother-organ may affect the child-organ, which means “earth does not generate gold” in this case, and as a result, the lung cannot get nourished from spleen essence and therefore cannot work well, leading to this disease.

2.3 Cold qi damages yang, giving rise to failure of kidney yang in its warming functions

Residents who grow up in cold regions are affected by the wind and cold, and therefore, most of them have yang deficiency constitutions. Because the kidney governs yang qi of the whole body, if kidney yang is deficient, the lung and the nose of the same body cannot get warmth from the kidney, water and dampness cannot be dissolved, and hence, cold and rheum will attack the nose orifices, leading to this disease.

3. AR treatment in cold regions using mountain-burning fire acupuncture method

3.1 Guiding defense yang into interior through needling 3 layers

Mountain-burning fire acupuncture is a representative of complex method of supplementation and drainage. In this method, the depth of the needling is divided into three layers, the first layer is intradermal layer of the needling, called the layer of sky, the deepest layer is the layer between muscle and bone, called the layer of earth, and the middle layer is within muscle, called the layer of people. Supplementation needling for this method is used 9 times (number 9 is regarded as yang by ancient people) in each layer from shallow to deep until the patient has “hot” feeling in the needling area.

Guiding defense yang into interior through needling 3 layers is the key manipulation for obtaining qi, maintaining needling sensation and conducting heat in the method of mountain-burning fire acupuncture. It was stated in the book *Jinzheng Fu* that supplementation is achieved by inserting the needle when the patient is exhaling; the needle is inserted first into intradermal layer, the layer of sky, then into the flesh layer, the layer of people, followed by the layer between muscle and bone, the layer of earth, which is the extreme depth.

It is said in the book *Nan Jing* that when you want to perform supplementation, you should obtain qi from defense area. The layer of people is the pivot of qi movement, which can guide the defensive yang qi into the interior, induce qi downward, and warm the layer of earth, “making yang qi arrive profusely”. The doctor, therefore, at this time, feels heat coming from the needle. Meridian qi includes nutrient qi, defense qi, ancestral qi and genuine qi, and functioning normally of these qi are the keys for the effectiveness of the method of mountain-burning fire acupuncture.

Guiding defense yang into interior through needling 3 layers makes yang qi exuberant for the spleen and kidney. Thereby, the lung qi will be exuberant, yin and yang will be harmonious, resulting in warming up and barrier free of the nose orifice. Thus all symptoms will disappear.

3.2 Regulating governor vessel and other meridians together

3.2.1 Regulating governor vessel to control the development of existing disease

Governor vessel, the meeting area of all yang meridians, descends along the forehead to the nose, and governs the yang qi and replenishes source qi of the whole body. The yang qi in governor vessel is the foundation of defense yang qi and the source of lung ancestral qi, and the acupoints on this vessel has miraculous effect of opening and moistening the nasal orifice. GB20, GV20 and EX-HN3 points are often selected in clinical practice. GB20 connects GV and governs yang qi of the whole body, where GB and yang link vessels intersect. Needling GB20 through the method of mountain-burning fire has the effects of warming yang, resolving phlegm and opening the orifices. In clinical practice, the mountain-burning fire is usually applied to GB20 points on both sides of the body to treat AR, for 3 courses. After this treatment, the symptoms of nasal congestion and runny nose usually disappear with no recurrence. GV20, located at the top of the head, is the key point of the governor vessel and is the place where great many meridians and vessels converge. EX-HN3 is

connected to GV above it and to the nose orifice below it, and is the hub where the meridians converge. Electro-acupuncture is often employed on the points such as GV20 and EX-HN3, which can regulate and harmonize yin and yang. When nasal orifice is unobstructed, and yin and yang are balanced, AR will disappear.

3.2.2 Regulating other meridians to prevent disease before it occurs

BL meridian can inspire yang qi of the whole body, support healthy qi, and drive pathogenic qi out of the body. Back transport points are the places where qi and blood of the viscera and bowels are infused and converged. Clinically, mountain-burning fire acupuncture method is often used on ST36, BL13, BL20 and BL23 to inspire the meridian qi, diffuse lung qi and fortify spleen qi, and warm and supplement spleen and kidney. Studies have found that needling back transport points in rats can regulate its gastrin and motilin well, and promote the growth of epidermal factors and protect gastric mucosa. The ability of the human body to resist external pathogenic qi lies in the abundance of yang qi in the spleen and stomach. ST36 is the sea point of the stomach meridian, and needling this point has the effect of regulating spleen and stomach, strengthening the healthy qi and eliminating pathogenic qi. When mountain-burning fire acupuncture method is used on ST36, the needling can strengthen the function of the spleen and stomach, cultivate earth and generate metal, supplement lung and fortify spleen, improve autoimmune function, reduce the rate of AR, and achieve the purpose of preventing diseases before it occurs.

4. Summary

Based on the regional characteristics of cold regions and the distinctive living habits of the residents, this paper first analyzed the unique etiology and pathogenesis of allergic rhinitis, then explored the theoretical basis and manipulation method of mountain-burning fire for the treatment of this disease in these regions, and hence, provided new ideas for clinical treatment of allergic rhinitis.

Exploring the prevention and treatment of ischemic heart disease with traditional Chinese medicine based on intestinal flora-from “Disease prevention and treatment” to “Big health industry”

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Abstract

The development of "big health industry" based on the theory of traditional Chinese medicine is of great significance to the prevention and treatment of ischemic heart disease. In this paper, the correlation between intestinal flora and the etiology and pathogenesis of ischemic heart disease was analyzed, and the metabolism of intestinal flora caused by traditional Chinese medicine treatment was analyzed from the perspective of "reconciliation of qi, blood and water - normal spleen and stomach function - intestinal flora". The impact mechanism of changes in products, nutritional status, etc. By exploring and analyzing the mechanism of Chinese medicine to improve intestinal flora to prevent and treat ischemic heart disease, the theoretical support for the prevention and treatment of ischemic heart disease can be provided for the "big health industry" guided by the theory of "preventive disease" of traditional Chinese medicine.

Key words: Big health industry, cure disease, intestinal flora, ischemic heart disease

Ischemic heart disease (IHD) refers to a state of insufficient blood supply and oxygen supply to part of the myocardium. Studies have shown that the mortality, disability, and morbidity rates of IHD are increasing year by year, and there are problems such as high treatment costs, poor efficacy of existing treatment plans, and increasing readmission rates year by year.

Chinese medicine believes that "the heart controls the small intestine", "the heart is the context of the small intestine, and the heart and the small intestine are related to the outside and inside", so the "intestine" and "heart" are closely related. "It is closely related to the heart, and can regulate the transportation and transformation of the spleen and stomach and intestinal flora, so it suggests that there may be a potential relationship between "gut flora - acquired spleen and stomach function - qi, blood and water - heart" with "Qi, blood and water" as the hub . Modern medical clinical studies have confirmed that the healthy intestinal flora is a key factor for the normal functioning of digestion. A large number of studies have found that the activation of pro-inflammatory mechanisms and metabolic toxicity of intestinal flora are related to the pathogenesis of IHD.

The big health industry is an emerging industry with huge market potential, including medical products, health products, nutritional foods, medical equipment, health appliances, leisure fitness, health management, health consulting and many other production and service fields closely related to human health^[1]. It is based on the prevention idea of "preventing disease" in traditional Chinese medicine culture, the self-cultivation concept of "harmony between man and nature", and the treatment principle of "diagnosis and treatment". The ecosystem and innovation chain of the health industry. In recent years, traditional Chinese medicine has gradually become a potential research hotspot for the prevention and treatment of IHD based on the theory of "Qi, blood and water" to improve the intestinal microbial environment and regulate the metabolites of intestinal flora^[2]. This

article will discuss the correlation between intestinal flora and IHD from the perspective of "Qi, blood and water", aiming to provide some theoretical support for the prevention and treatment of ischemic heart disease in the "big health industry" guided by the theory of "preventive disease" in TCM.

Objective

To understand the theory of "Qi, blood and water", "intestinal flora - acquired spleen and stomach function - reconciliation of qi, blood and water" and other theories, analyze the correlation between intestinal flora and ischemic heart disease, and discuss the traditional Chinese medicine to "prevent disease" as the The guiding significance of the theoretical basis for the "big health industry", and the guiding significance of regulating the intestinal microecology to the progress of the prevention and treatment of ischemic heart disease in the "big health industry".

Materials and methods

Combined with ancient and modern literature to analyze the pathogenesis of IHD, based on the theory of "Qi, blood and water" in traditional Chinese medicine to explore the correlation between intestinal flora and IHD, combined with the concept and function of "gut" in modern medicine and traditional Chinese medicine, an in-depth analysis of "intestinal flora- The relationship between acquired spleen and stomach function - qi, blood and water harmony - heart", discusses the therapeutic significance of regulating intestinal microecology based on the theoretical basis of "preventive disease", and summarizes theoretical basis and progress of the "big health industry" combined with traditional Chinese medicine theory to prevent and treat ischemic heart disease.

Results and discussion

IHD is a state of insufficient myocardial blood supply and oxygen supply or imbalance of supply and demand. Initially, it often manifests as shortness of breath, fatigue, or chest tightness. As the disease progresses, it can manifest as chest tightness, colic, or even severe pain that is not relieved. sense of death. Chinese medicine believes that the pathogenesis of IHD is closely related to "qi, blood and water". Modern medicine believes that the intestinal flora is the largest and most complex microbial community in the human body, and is called "the virtual endocrine organ of the human body".

As a result, the abnormal composition, function and metabolites of intestinal flora can affect the metabolism, immune defense and nervous system regulation of various organs of the human body^[3], which is of great significance to the occurrence and development of IHD^[4]. TCM regulates the acquired spleen and stomach function, which can improve the function of intestinal flora, thereby preventing and treating IHD.

Thus,the theory of "preventive disease treatment" in TCM has important guiding significance for the prevention and treatment of IHD in the "big health industry". The industrial chain of "big health industry" aiming at regulating intestinal flora to prevent IHD is embodied in lifestyle changes, dietary structure adjustment, reduction of risk factors, treatment of high-risk metabolic diseases, etc., including: prevention and treatment of diabetes, regulation of blood lipid metabolism, etc. , control high blood pressure, guide diet, quit smoking and limit alcohol, psychotherapy, exercise therapy, etc.

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Wnt signaling pathway in liver cirrhosis

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Abstract: Objective To assess the significance of Wnt signaling pathway in liver cirrhosis which will allow to judge indirectly the treatment effectiveness of Wnt signaling pathway in liver cirrhosis. **Methods** We reviewed the research progress of Wnt signaling pathway and liver cirrhosis pathogenesis and related molecular expression. **Results and discussion** We described the relationship of Wnt signaling pathway and liver cirrhosis in regulating hepatic stellate cells, hepatic Kupffer cells and hepatic progenitor cells, and its application in the treatment of cirrhosis. Wnt signaling pathway is one of the most important signaling pathways to the progress of cirrhosis, which plays an important role in cell fate determination, proliferation and cell polarity establishment, and these changes have key effects on maintaining tissue homeostasis.

Key words: Wnt signaling pathway, liver cirrhosis, review

Background

Cirrhosis is a disease with characteristics that liver parenchyma is replaced by fibrotic tissue and regenerative nodules, with excessive deposition of collagen and other extracellular matrix(ECM).It have been confirmed that it can restore normal liver structure by removing the causes of liver injury, activating myofibrocells and fiber scar, or promoting extracellular matrix degradation.Wnt signaling pathway plays an important role in the formation and development of liver fibrosis, which is a research hotspot of anti-liver fibrosis therapy in recent years.

Wnt signaling pathway

The Wnt signaling pathway is a very complex and intracellular signaling pathway controlling various physiological functions. In humans, there are 19 WNT encoding genes, 2 co-receptors, 10 coiled (Fzd) receptors, and various non-Fzd receptors to control functional kinases. They connect to various receptors and stimulate different intracellular signal transduction pathways^[1]. The pathway affects cell cycle, induces cell proliferation, simultaneously affects the cytoskeleton and mitotic spindle, mediates cell tissue morphology growth, which has an important role in tissue remodeling, hepatocyte renewal and regeneration proliferation^[2]. When liver injures, it drives bile duct proliferation mitosis, and induces bile duct epithelial cells to differentiate into hepatocytes^[3]. It have shown that we can limit hepatic stellate cells (HSCs) contraction, reduce portal hypertension, and alleviate liver inflammation to enhance anti-fibrotic therapy by blocking the pathway^[4].

Wnt signaling pathway in hepatic stellate cells

HSCs play important role in the liver cirrhosis, which is closely related to the Wnt signaling pathway. On the one hand, the pathway determinates cell fate and morphogenesis. The peroxisome proliferator activation receptor γ (PPAR γ) is required for the differentiation of adipocytes and HSC, and promotes fat storage in HSC. Wnt/ β -catenin interacts with PPAR γ , and is activated in the process of HSC transdifferentiation into myofibroblast^[5]. On the other hand, the expression of Polo-like kinase 1 (PLK1) is elevated in both primary HSC and LX-2 cells stimulated by TGF β 1 of CCl₄-induced liver fibrosis mice, while, the HSC activation can be reduced via knockdown of

PLK1 which inhibites intracellular α -SMA and Coll1 α 1 expression. Wnt/ β -catenin signaling may be required for PLK1-mediated HSC activation^[6]. Besides, small ribose Nucleic acid 708(miR-708) can directly target the transmembrane protein TMEM88 through the Wnt/ β -catenin signaling pathway, which promotes the activation of HSC and the accumulation of the extracellular matrix by regulating the expression of Wnt3a, Wnt2b, Wnt3 α and the PDZ domain of Dvl-1^[7].

Wnt signaling pathway in hepatic Kupffer cells

Akcora found that the Wnt ligands(Wnt1, Wnt3a, and Wnt10b) and receptors(Fzd1, Fzd2) and their co-receptors(LRP6) increase in liver fibrotic, and the chemokine CXCL12 could promote HSC activation through the classical Wnt/ β -catenin pathway, and stimulate Kupffer recruitment to the liver, which enhances intrahepatic inflammation, angiogenesis, and fibrosis, whereas Wnt/ β -catenin/TCF-mediated transcriptional inhibitors ICG-001 can mitigate these responses^[8].

Wnt signaling pathway in hepatic progenitor cells

Hepatic progenitor cells(HPCs) are undifferentiated cells in the liver with the function of stem cell. Study showed that expression reduction of the Atg5 gene can inhibit autophagy which could hinder HPC differentiation and inhibit the activation of Wnt/ β -catenin signaling, and autophagy can regulate the hepatocyte differentiation of HPC by regulating the signaling^[9].

Wnt signaling pathway in liver cirrhosis treatment

Inhibitors of Wnt signaling have be divided into two categories: Wnt-receptor inhibitors and β -catenin destruction complex inhibitors. Several therapeutic molecules, such as anti-Frizzled antibodies, mimetics of Wnt molecules, disheveled inhibitors, tankyrase inhibitors, axin stabilizers, and inhibitors of TCF/CBP interactions are being evaluated in different phases of clinical studies.

Challenges and opportunities

The safety and effectiveness of Wnt signaling-targeted drugs is the most concerning issue that we have to face. The majority of available Wnt inhibitors are broad spectrum, and it is challenging to achieve balance by controlling the dosage or appropriate time of drug administration. In addition, the effectiveness of Wnt signaling-targeted drugs needs to be further confirmed in clinical trials.

Conclusions

Wnt signaling plays a major role in hepatocyte and cell fate determination, proliferation, and cell fate determination as a bridge between hepatocytes and the liver cell microenvironment for cell polarity establishment. There is still room for further investigation to investigate and combat the side effects of utilizing the pathway, as it is important for cellular homeostasis.

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Effects and predictive value of serum uric acid level and insulin resistance index on new-onset atrial fibrillation in metabolic syndrome

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Abstract

Atrial fibrillation (AF) is a supraventricular tachyarrhythmia characterized by disturbed atrial electrical activity and ineffective mechanical atrial contractions. It is an important cause of stroke, heart failure, and sudden cardiac death. Patients with MS are susceptible to AF. Insulin resistance (IR) is the core mechanism of MS. Hyperuricemia is also an important component of MS. Both of them are associated with AF. Also, they both have good predictive value for new-onset AF.

Key word: metabolic syndrome; atrial fibrillation; serum uric acid; insulin resistance index; nested case-control study

Atrial fibrillation (AF) is the most common sustained cardiac arrhythmia and it is associated with an increased risk of stroke, thromboembolic events, heart failure and other comorbidities^[1]. Due to its high rate of disability and mortality, AF has become a worldwide health problem^[2]. Epidemiological surveys show that the lifetime risk of AF in European and American populations ranges from 21.6% to 23.8%. Metabolic syndrome (MS) is a group of clinical syndromes with abdominal obesity, glucose and lipid metabolism disorders, and hypertension as the main manifestations, and cardiovascular disease as the main clinical outcome^[3]. MS and its components may increase susceptibility to AF by inducing electrical and structural remodeling of the atrium^[4].

Objective

To investigate the effect and predictive value of serum uric acid (SUA) level and insulin resistance index on new-onset AF in a population with metabolic syndrome (MS).

Materials and methods

This study was a nested case-control study based on a retrospective MS cohort. The study cases were collected from MS patients who visited the First Affiliated Hospital of Heilongjiang University of Traditional Chinese Medicine between January 2015 and December 2016. Selected cases whose diagnosis were not AF and the data were complete at the baseline survey, excluding rheumatic heart disease, dilated cardiomyopathy, hypertrophic cardiomyopathy, myocardial infarction, hyperthyroidism, and cognitive dysfunction, a retrospective cohort was established and followed up. Screening 285 cases of new-onset AF within 5 years from the baseline survey were selected as the AF group. Moreover, based on the same gender and age (± 2 years) as the matching principle, 570 cases without AF were matched as the control group. Baseline data were collected, and the differences between groups were analyzed. Then, the effects of SUA level and Homeostatic Model Insulin Resistance Index (HOMA-IR) on new-onset AF were analyzed by constructing a logistic regression model and adjusting for confounding factors. Predictive value analysis was performed by receiver operating characteristic curve (ROC).

Results and discussion

The levels of SUA and HOMA-IR in the AF group were higher than those in the control group, and

the differences were statistically significant ($P<0.05$). SUA and HOMA-IR were independent factors for new-onset AF. Without adjusting for any confounding factors, the risk of new-onset AF in the Q2, Q3, and Q4 stratification of SUA was 2.087, 3.773, and 5.153 times of the Q1 stratification, respectively. Meanwhile, the risk in the Q2, Q3, and Q4 stratification of HOMA-IR was 1.632, 2.662, and 2.899 times of the Q1 stratification, respectively. After adjusting for some confounding factors, the risk of new-onset AF in the Q2, Q3, and Q4 stratification of SUA was 1.883, 3.052, and 4.791 times of the Q1 stratification, respectively. Meanwhile, the risk in the Q2, Q3, and Q4 stratification of HOMA-IR was 1.622, 1.989, and 2.350 times of the Q1 stratification, respectively. After adjusting for all confounding factors, the risk of new-onset AF in the Q2, Q3, and Q4 stratification of SUA was 1.752, 3.040, and 4.281 times of the Q1 stratification, respectively. Meanwhile, the risk in the Q3, and Q4 stratification of HOMA-IR was 1.922 and 2.403 times of the Q1 stratification, respectively. The area under the ROC curve (AUC) of SUA for predicting new-onset AF was 0.757. The AUC of HOMA-IR was 0.714. The AUC of the combined prediction of the two indicators was 0.828, which was higher than that of any single indicator, and the difference was statistically significant ($P<0.05$).

In MS population, SUA level and HOMA-IR are independent influencing factors of new-onset AF, and the risk of new-onset AF is positively correlated with SUA level and HOMA-IR. Both indicators have good predictive value, and the combination of the two has a higher predictive value.

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Study on processing mechanism of *Amomi Fructus* based on GC-MS and multivariate statistical analysis

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Abstract

The medicinal materials of *Amomi fructus* with four different processing method were analyzed by gas chromatography-mass spectrometry (GC-MS) metabolomics technique and hierarchical clustering analysis (HCA) chemometrics method. This study was to analyze differential volatile components of *A. fructus* from different processing method. The results showed that there had a large metabolic difference of volatile components between unprocessing and three processing *A. fructus*, and VIP and P of PLS-DA screened 15 different components from each processing method. Bornyl acetate is one of the main effective components of *A. fructus* to exert its pharmacological effects. The content of bornyl acetate in salt roasted and ginger roasted *A. fructus* increased, and the content of bornyl acetate in fried *A. fructus* decreased slightly, but the difference was not significant.. This shows that the three processing methods of salt roasting, ginger roasting and frying are scientific.

Key words: *Amomi fructus*; Gas chromatography-mass spectrometry (GC-MS); Metabonomics; Processing mechanism

A. fructus is pungent and warm in nature, and it can guide the spleen and stomach meridian. Clinically, it has the effects of eliminating dampness and appetizing the stomach, warming the spleen and stopping diarrhea, regulating qi and calming the fetus^[1]. It has been used as a traditional Chinese medicine for both medicine and food for more than 1300 years in China. The processing of *A. fructus* was firstly recorded in the *Yi Xue Qi Yuan* (Jin Dynasty), in which there is a record of "smashing and using". With the development of the times, there have been methods such as frying and processing with auxiliary materials.

The correct processing method makes the drug give better play to its curative effect. Although there are many records about the processing methods of *A. fructus* in medical books, they lack scientific basis. Therefore, this paper explores the differences of volatile components of *A. fructus* after ginger roasting, salt roasting and frying by means of metabonomics, and its impact on the traditional efficacy of *A. fructus*. The purpose is to provide a scientific basis for processing *A. fructus* into medicine and developing new medicinal activities of *A. fructus*.

Objective

To explore the processing mechanism of *A. fructus* , the method of GC-MS and multivariate statistical analysis was adopted to study the component differences of *A. fructus* after four different processing methods, to provide scientific basis for processing method of *A. fructus*.

Materials and methods

A. fructus produced in Yunnan.

GC-MS and multivariate statistical analysis

Results and discussion

Some volatile components of *A. fructus* were changed after different processing methods. For example, the content of D-limonene in ginger roasted and salt roasted *A. fructus* has decreased significantly. Although this substance is widely used in cosmetics and other fields, it will cause skin irritation to humans and experimental animals, eye irritation to rabbits, and induce contact dermatitis in guinea pigs. Extremely high doses of D-limonene will cause reproductive toxicity. Although D-limonene no obvious adverse effects in other aspects, there are still risks^[2]. The content of camphor (+)-2-Bornanone in water fried, ginger roasted and salt roasted *A. fructus* decreased. It is reported that accidental intake of camphor can cause serious liver and central nervous system damage, and routine use often leads to mild hepatic neurotoxicity. The symptoms may not be obvious, but there is still a certain risk^[3]. In water fried and salt roasted *A. fructus* γ -Terpinene content has decreased. Although γ -Terpinene no perfect study on the toxicity at present, it may cause respiratory tract, skin and eye irritation. Therefore, the decline of these components makes *A. fructus* have less side effects when playing its pharmacological role.

Bornyl acetate is the main effective component of *A. fructus*, which has pharmacological effects such as fetal protection, insecticidal, anti-inflammatory, anti-tumor, cardiovascular activity, relieve pain and diarrhea, memory improvement and so on. In the Ben Cao Yan Yi Bu Yi (Yuan Dynasty) said: 'it can calm the fetus, relieve pain, and promote qi, so it is also true'. Those who have bad resistance to pregnancy and are cold should be matched with ginger, After being roasted with salt, *A. fructus* mainly returns to the kidney. They can induce medicine downward, enhance the effect of regulating qi, calming the fetus, warming the kidney and shrinking urine, and can be used for bad resistance to pregnancy and restless fetal movement. Therefore, the increase of bornyl acetate content in salt roasted and ginger roasted *A. fructus* can enhance the traditional efficacy of *A. fructus*, while the slight decrease of bornyl acetate content in fried *A. fructus* may be related to processing temperature and other factors, but it has little difference with salt roasted and ginger roasted *A. fructus*.

According to the analysis of differential metabolic components, the three processing methods of salt roasting, ginger roasting and frying have certain scientificity, which provide a scientific basis for the study of the processing mechanism of traditional Chinese medicine.

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Based on network pharmacology and molecular docking to explore the mechanism of *Scutellaria baicalensis*-*Coptis chinensis* in the treatment of *H. pylori* infection

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Abstract: Objective: To explore *Scutellaria baicalensis*-*Coptis chinensis* in the treatment of *Helicobacter pylori* infection through network pharmacology. Methods: The drug components and targets were screened through the TCMSP database, and disease targets were screened by GeneCards, OMIM, TTD, Drugbank, and Pharmgkb platforms. GO and KEGG analysis were performed on the drug-disease intersection targets through the DAVID, and the "component-target-signaling pathway" network was made with Cytoscape 3.8.0. Results: GO functional involves apoptosis, transcription and other processes; KEGG enrichment results show that the drug mainly acts on cancer, TNF and other signaling pathways. Conclusion: *Scutellaria baicalensis*-*Coptis chinensis* drug pair may exert its anti-*Helicobacter pylori* effect through changing the process of apoptosis, transcription, inflammatory response and so on.

Key words: *Scutellariae Radix*; *Coptidis Rhizoma*; *helicobacter pylori*; network pharmacology

As a common clinical disease, the global infection rate of *Helicobacter pylori* (Hp) is about 50%^[1]. At present, western medicine mainly uses triple or quadruple therapy for antibacterial. Traditional Chinese medicine (TCM) think Hp is a dampness and heat pathogenic, causing spleen-stomach dampness heat when deficiency of healthy qi, lack of spleen and stomach and neglecting of life nurturing. *Scutellaria baicalensis* can "treat heat diseases, boils and purulent disease", *Coptis chinensis* can clear heart, stomach, intestines and liver and gallbladder heat. Herbs can improve the eradication rate, alleviate adverse reactions and reduce the amount of antibiotics, which is one of the new methods to eradicate Hp^[2]. The key to the infection of Hp lies in the spleen-stomach dampness heat and the deficiency healthy qi, as recorded in the *Huangdi Neijing: Diseases caused by damp pathogens such as edema belong to the abnormal function of the spleen*.

TCM prescriptions have the characteristics of complex components and acting on multiple targets. Network pharmacology integrates a large number of published biological information to construct a component-target-pathway, which is a powerful tool to explore the principle of herbs efficacy and screen herbs components and provides a reliable basis for confirming the mechanism of TCM efficacy. Therefore, this study conducted a network pharmacology study on the mechanism of *Scutellariae Radix*-*Coptis chinensis* in the treatment of Hp infection in order to provide some ideas for subsequent research.

1 Methods

The TCMSP platform was used to retrieve the components of *Scutellaria baicalensis* and *Coptis chinensis*. The ADME affect whether they can work in the body therefore, when screening active ingredients, $OB \geq 30\%$ and $DL \geq 0.18$ were used as criteria and supplemented by literature. Using "helicobacter pylori" and "helicobacter infection" as keywords, disease targets were searched in Genecards, OMIM, TTD, Drugbank and Pharmgkb platforms. Uniprot was used to correct the target

name and organize the data to obtain the target.

The targets of drugs and diseases were imported into the venny 2.1.0 website to get intersection targets, using the STRING 11.5 platform to get tsv file, set the species to Homo sapiens (Homo sapiens). Import the obtained tsv file into Cytoscape 3.8.0, perform topology analysis through Analyze Network, and use the MCC and Degree algorithms to obtain their respective Top10 targets and Top4 components. The DAVID platform was used to analyze intersection targets, and the GO and KEGG analysis results were obtained, with the data with $P \leq 0.01$ was screened. According to the corrected P value (FDR/qvalue) from small to large, the top 10 KEGG and GO items were selected. The "component-target-pathway" network diagram was drawn by Cytoscape 3.8.0 software.

2 Results

A total of 48 components and 221 potential targets in *Scutellaria baicalensis*-*Coptis chinensis* and 2051 disease targets obtained from each platform. 126 intersection targets of effective components and diseases were obtained by venny mapping. 11 key targets including AKT1, TP53, IL6, JUN, TNF, IL1B, CASP3, MYC, HIF1A, PTGS2, MMP9 and 4 main active components including quercetin, wogonin, acacetin and baicalein were obtained by Cytoscape 3.8.0. GO analysis showed that therapeutic targets were mainly enriched in 850 biological processes including enzyme binding, protein binding and initiation of RNA transcription. KEGG analysis showed that therapeutic targets were mainly enriched in 151 pathways involved in cancer, lipid and atherosclerosis, and IL-17, p53, TNF and other signaling pathways.

The "component-target-pathway" network diagram drawn by Cytoscape (Fig.1) contains 172 nodes and 722 edges. The larger the nodes in the network, the larger the Degree value, and the thicker the edge line, the closer the connection relationship. The green arrow represents the first 10 pathways enriched by KEGG, the yellow circle represents the component used for the pathway, and the purple box represents the target used for the pathway. The relationship between the components-targets-pathways shown in the network diagram indicates that a variety of components and multiple targets act synergistically in different pathways of disease.

3 Discussion

Hp is a common, persistent infection-causing bacterium, according to the symptoms of patients, TCM classifies them into "stomach pain" and "fullness". In terms of treatment, the method of drying dampness and strengthening the spleen combined with promoting qi is often used clinically to achieve the purpose of restoring the body's health qi, removing pathogenic factors and regulating the internal environment. This study proves that four compounds such as quercetin are the main

compounds in the drug pair. A number of studies have shown that wogonin has the effect of inhibiting *Hp*^[3], while quercetin can down-regulate the increase of p38 MAPK and BAX caused by *Hp* infection and increase the level of BCL-2^[4]. Acacetin can prevent cancer cells over-expression of RAR γ activation of AKT to restore normal p53 signal transduction^[5] and baicalein inhibits the *Hp* virulence factor VacA, reduces the adhesion and invasion of *Hp* to host cells^[6]. *Hp* is a clear carcinogen, and there is substantial experimental and investigative evidence to support eradication therapy for all *Hp*-infected, KEGG

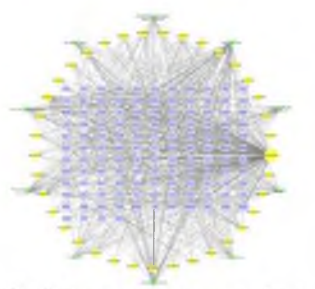


Fig.1 Component-target-pathway network

enrichment results suggest target genes are concentrated in the cancer pathway.

Previous studies have focused on the therapeutic effect of compounds containing *Scutellaria baicalensis*-*Coptis chinensis* drug pairs on Hp infection, this time we focused on drug pairs to explore the main components and possible targets of Hp infection treatment, revealing the main components of drug pair have inhibition of inflammation, tumor, and apoptosis. We hope our study can provide the basis for the mechanism of drug pair in the treatment of Hp and theoretical support for subsequent studies and clinical research.

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Ancient and modern literature research and application development direction of deer antler in heilongjiang Nine Herbs

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Abstract

Objective: Velvet antler is one of the homologous Chinese medicinal materials published by ministry of Health and one of the key brands recommended by Heilongjiang Traditional Chinese Medicine Administration .This study was conducted to summarize the concoction method, efficacy, active ingredients and pharmacological effects of antler based on ancient and modern literature, in order to provide a certain literature base and development direction for basic research and product development of antler in Longjiang region.

Methods: A search of ancient medical texts such as Materia Medica and Fang Shu, and journal databases such as China Knowledge Network and web of science was conducted to crawl through the contents of deer antler.

Results: Deer antler concoction is mainly divided into two types of concoction methods: with and without ingredients. The ancient potency of deer antler was mainly continued from Shennong Ben Cao Jing before Song Dynasty, aand later expanded the efficacy of velvet antler in the treatment of asthenia.. The main active ingredients and pharmacological effects of deer antler are: antler polypeptide has the effects of anti-inflammation, protecting nerve cells, improving liver fibrosis, accelerating cell proliferation and differentiation; deer antler protein has the effects of kidney protection and improving myocardial ischemia; deer antler polysaccharide has the effects of anti-aging, anti-oxidation, improving bone density and preventing osteoporosis. The clinical applications of deer antler in cardiac system diseases, bone and joint diseases, neurological diseases, and skin diseases are summarized from them. Based on the ancient potency and active ingredients it is proposed that deer antler can be used to develop weight loss meal replacement powder, nutritional oral solution, etc.

Conclusion: Deer antler as a natural as a kind of dual-use medicine with antioxidant, anti-inflammatory, anti-aging and other pharmacological effects, has significant advantages in the direction of health food and health care drugs, and has considerable market potential, traditional theory and modern technology should be combined to accelerate the research and development of deer antler food and drugs, and improve the social and economic benefits of deer antler.

Keywords: deer antler; pharmacological effects; literature research; development direction

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Association between polymorphisms of miR-146a and miR-149 and ischemic stroke: a meta-analysis

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Abstract

Objective: Polymorphisms of miR-146a C>G (rs2910164) and miR-149 T>C (rs2292832) have been confirmed to be associated with atherosclerotic mechanisms. We conducted a meta-analysis to investigate whether the polymorphisms of miR-146a and miR-149 are associated with IS. **Methods:** Six databases were searched for relevant studies published before April 2022. Meta-analysis, sensitivity analysis, and publication bias analysis were performed using Stata software 16.0. **Result:** The results of meta-analysis indicated that there were no significant associations between miR-146a and IS risk. MiR-149 was associated with an increased IS risk under the allelic model (C vs. T, OR = 1.16, 95% CI = 1.04–1.29), homozygote model (CC vs. TT, OR = 1.40, 95% CI = 1.13–1.74) and recessive model (CC vs. TC+TT, OR = 1.33, 95% CI = 1.15–1.53). **Conclusion:** The polymorphism of miR-146 was not associated with ischemic stroke; miR-149 T>C (rs2292832) C alleles increase the risk of IS under the allelic model (1.16-fold), homozygote model (1.40-fold) and recessive model (1.33-fold).

Key words: ischemic stroke, polymorphism, meta-analysis, miR-146a, miR-149.

Introduction

Stroke is the second-leading cause of death and a major contributor to disability worldwide, which affects roughly 13.7 million people and kills around 5.5 million annually and approximately 87% of strokes are ischemic infarctions [1-3]. Previous evidence shows that the miR-146a and miR-149 contribute to vascular damage responses and inflammation-related atherosclerosis, may increase susceptibility to ischemic stroke and serve as potential predictors of ischemic stroke.

Materials and methods

We conducted a comprehensive search across PubMed, Embase, Web of Science, the Cochrane Library, China National Knowledge Infrastructure, and China Wanfang Database for studies published up to March 2022. Keywords: [“ischemic stroke” AND (((“microRNA” OR “miRNA” OR “miR”) AND (“polymorphism” OR “SNP” OR “mutation” OR “variant”)) OR (“rs2910164” OR “rs2292832”))]. Two researchers independently screened the literature according to the selection criteria, extracted essential data from the included studies, and then cross-checked to reach a consensus. All statistical analyses were completed by Stata software 16.0 (StataCorp, College Station, TX, USA).

Results

No significant association was observed between miR-146a C>G (rs2910164) polymorphism and risk of IS under all models (allelic model: G vs. C, OR = 1.06, 95% CI = 0.96–1.17; homozygote model: GG vs. CC, OR = 1.19, 95% CI = 1.00–1.43; heterozygote model: CG vs. CC, OR = 1.05, 95% CI = 0.96–1.14; recessive model: GG vs. CG+CC, OR = 1.15, 95% CI = 1.00–1.33 and dominant model: CG+GG vs. CC, OR = 1.09, 95% CI = 0.98–1.21). The overall analysis showed

that the miR-149 T>C (rs2292832) polymorphism increased the risk of IS under the allelic model (C vs. T, OR = 1.16, 95% CI = 1.04–1.29), homozygote model (CC vs. TT, OR = 1.40, 95% CI = 1.13–1.74) and recessive model (CC vs. TC+TT, OR = 1.33, 95% CI = 1.15–1.53) but no significant association was observed for the heterozygote model (TC vs. TT, OR = 1.07, 95% CI = 0.97–1.19) and dominant model (TC+CC vs. TT, OR = 1.14, 95% CI = 1.00–1.30).

Conclusion and Discussion

MiR-146a polymorphism has been found to regulate inflammation and atherosclerosis by targeting inflammatory mediators such as TNF- α , IRAK1, TRAF6, CRP and NF- κ B [4-6]. In addition to mediating inflammation, TNF- α was found to be involved in atherosclerosis by inducing CD47 expression and rendering vascular cells resistant to phagocytic clearance [7]. However, we did not find a significant association between miR-146a and IS.

Our overall analysis found that the C alleles of miR-149 rs2292832 increase the risk of IS under the allelic model (1.16-fold), homozygote model (1.40-fold) and recessive model (1.33-fold). MiR-149 polymorphism influence the function and level of mature miR-149, and further changes the level of MTHFR, increasing susceptibility to coronary heart disease [8]. Therefore, this polymorphism is also considered to be potentially associated with IS.

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“Tongdu Tiaoshen” Acupuncture Combined with Moxibustion for the Treatment of Subthreshold Depression (Liver Stagnation and Spleen Deficiency Type): A Randomized Clinical Trial

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Abstract

Objective: To observe the efficacy and safety of “Tongdu Tiaoshen” acupuncture combined with moxibustion in the treatment of subthreshold depression and the improvement of life treatment. **Methods:** 90 patients were randomly divided into acupuncture group (n=45) and moxibustion group (n=45). The acupuncture group was intervened mainly by “Tongdu Tiaoshen” acupuncture combined with moxibustion. Acupuncture selected Baihui (GV20), Shenting (GV24), Hegu (LI4), Taichong (LR3), Ganshu (BL18) and Pishu (BL20), the needle was retained in acupoint place for 20 minutes with Deqi. After acupuncture treatment, moxibustion was used. Acupoints Baihui (GV20), Zusanli (ST36), Ganshu (BL18) and Pishu (BL20) were used for moxibustion every time 20min. The acupoints in the moxibustion group were the same as those in the acupuncture group, each time 20min. Both groups were treated 3 times a week. HAMD-24 and SF- 36 scale were evaluated before and after treatment, and SPSS25.0 statistical software was used to analyze the collected data. **Results:** After 4 weeks of treatment, the total effective rate was 93.61% in the acupuncture group and 81.63% in the moxibustion group, which was better than that in the moxibustion group ($P<0.05$). The score of SF- 36 scale in acupuncture group was higher than that in moxibustion group ($P<0.05$). **Conclusion:** “Tongdu Tiaoshen” acupuncture combined with moxibustion can effectively improve the depressive symptoms and quality of life of patients with subthreshold depression (liver depression and spleen deficiency).

Key words: “Tongdu Tiaoshen” acupuncture, moxibustion, subthreshold depression, RCT

Introduction

Subthreshold depression is characterized by depression, decreased interest, mental exhaustion and slow thinking and action. People with subthreshold depression have a relatively higher risk of depression [1]. A study calculated the treatment and health costs of 36 low-and high-income people. The results show that the cost of counseling and antidepressants is estimated at \$147 [2]. Therefore, effectively controlling the transition from subthreshold depression to depression can effectively alleviate and reduce the pressure and burden of national medical care. At present, the efficacy of antidepressants in the treatment of subthreshold depression has not been determined, and the adverse reactions caused by antidepressants may do more harm than good. Therefore, it is imperative to find a safe, effective, less side effect and low-cost treatment.

Acupuncture, as a kind of complementary replacement therapy, is an important part of traditional Chinese medicine. It has been developed for more than 2500 years and has been widely used in clinical practice in China. In recent decades, with the increasing attention of the international community to acupuncture, it is becoming popular in western countries. Acupuncture has become a promising and effective alternative therapy for depression. This study takes patients with

subthreshold depression as the research object to explore the clinical effect of acupuncture in the treatment of subthreshold depression.

Objective

This trial aims to (1) evaluate the efficacy and safety of the treatment of subthreshold depression by "Tongdu Tiaoshen" acupuncture combined with moxibustion; (2) observe the improvement of life treatment of patients with subthreshold depression by "Tongdu Tiaoshen" acupuncture combined with moxibustion

Materials and methods

90 participants were randomly assigned to acupuncture group or moxibustion group. During the 4-week treatment, the patient received 12 acupuncture treatments. The acupuncture group was intervened mainly by acupuncture method of "Tongdu Tiaoshen" combined with moxibustion. Baihui (GV20) and Shenting (GV24) were selected as the main acupoints, and Hegu (LI4), Taichong (LR3), Ganshu (BL18) and Pishu (BL20) were matched according to the characteristics of liver depression and spleen deficiency. 20min was obtained by acupuncture 3 times a week. After acupuncture treatment, moxibustion was used. Acupoints Baihui (GV20), Zusanli (ST36), Ganshu (BL18) and Pishu (BL20) were used for moxibustion every time 20min. The acupoints in the moxibustion group were the same as those in the acupuncture group. Intervention used Hwato disposable sterile needle (0.35× 40mm, Suzhou Medical device Factory), moxibustion material selected warm moxibustion column (18mm×27mm branch, Nanyang Shennong Biological Products Co., Ltd.). The location of acupoints refers to the "Nomenclature and location of meridian points" (GB/T12346-2021) implemented by the people's Republic of China. The scores of Hamilton Depression scale (HAMD-24) and the MOS items short from health survey (SF-36) were evaluated before and after treatment, and the adverse reactions were recorded at the same time. SPSS25.0 statistical software was used to analyze the collected data.

Results and Discussion

After 4 weeks of treatment, a total of 4 patients in the two groups dropped out, including 3 patients in the acupuncture group, 1 patient was unable to continue the treatment as required due to work change, 2 patients dropped out due to loss of follow-up, and 1 patient in the moxibustion group dropped out due to loss of follow-up. There were 47 patients in the acupuncture group and 49 patients in the moxibustion group who finally completed the treatment. The two groups were comparable in gender, age and baseline data of pre-treatment scale scores ($P>0.05$). After 4 weeks of treatment, the effective rate was evaluated by calculating the reduction rate of HAMD-24 total score. The total effective rate of the acupuncture group was 93.61%, and that of the moxibustion group was 81.63%. The acupuncture group was better than the moxibustion group ($P<0.05$). The scores of HAMD-24 scale decreased in both groups, and the scores of the acupuncture group were lower than those of the moxibustion group after treatment ($P<0.05$). The scores of SF-36 scale in the acupuncture group were increased higher than those in the moxibustion group ($P<0.05$). The improvement of moxibustion group was not obvious in terms of physiological functions and health changes. There were no adverse events in the two groups during the treatment.

Clinical studies have shown that "Tongdu Tiaoshen" acupuncture combined with moxibustion can effectively improve the depressive symptoms and quality of life in patients with subthreshold depression, and the method is safe.

Because subthreshold depression is easy to develop into depression, which seriously affects patients' health, social function and daily life, there is a high burden of disease^[3]. Clinicians and researchers must find treatments to improve subliminal depression to avoid the development of the disease. In the previous study of our research group, it was found that “Tongdu Tiaoshen” acupuncture could significantly improve the macroscopic behavior and microcosmic molecular biological indexes of depression model rats^[4]. Through the method of randomized controlled trial, we selected the type of subthreshold depression, observed the efficacy and safety of “Tongdu Tiaoshen” acupuncture combined with moxibustion and simple moxibustion on patients with subthreshold depression. It further confirms the efficacy and safety of acupuncture and moxibustion in the treatment of subthreshold depression, which is helpful to improve the depressive symptoms of patients with subthreshold depression, and reduce the negative effects of subthreshold depression on overall health.

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Rehabilitation application progress of CAM therapy based on virtual reality technology in patients with cognitive impairment

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Abstract

Objective

Based on the cutting-edge research in this field, this paper provides ideas for the follow-up exploration of virtual reality technology as a common complementary and alternative therapy to patients with cognitive impairment.

methods

Seven databases, including China Journal full-text Database (CNKI), Wanfang academic Journal full-text Database (Wanfang), VIP Chinese Sci-tech Journals Database (VIP), China Biomedical Literature Database (Sino Med), PubMed, Cochrane Library and Embase database, were searched with the keywords of "virtual reality", "AND", "cognitive impairment", "OR", "cognitive dysfunction" and corresponding Chinese. The search time limit was before July 2022. Included articles were summarized and analyzed.

Results

Cognitive impairment has a significant impact on the sufferers' ability to live a quality life, and puts a heavy burden on his/her families and community. However, conventional cognitive rehabilitation training usually requires input of a large amount of human resources, and the process is monotonous and tedious, and the patient's compliance is poor. Many studies have demonstrated that virtual reality, as one of the most innovative and cutting-edge intelligence complementary and alternative therapy technology, can not only ecologically and efficiently improve the condition, but also enhance compliance through its interesting and diverse characteristics, which has been a hot spot for research and application in the field of the rehabilitation of cognitive impairment.

The feasibility and effectiveness of virtual reality technology application in cognitive impairment rehabilitation has been confirmed, but the related research is still in its infancy and there remain some problems. For example, there is a lack of comparative study on how to select a more appropriate virtual reality system for different types of cognitive impairment caused by different diseases and the effectiveness of the same virtual reality system for the rehabilitation of different types of cognitive impairment caused by different diseases; how to develop virtual reality devices and systems that can be applied to the rehabilitation of patients with cognitive impairment accompanied by motor dysfunction.

Discussion

It is expected that with the continued growth of virtual reality technology and the advent of other high and emerging technologies in the future, virtual reality technology will be promoted to playing

a more significant advantageous role in the field of cognitive impairment rehabilitation. In the era of artificial intelligence, the development of intelligent virtual reality devices and systems that integrate cognitive impairment rehabilitation assessment and rehabilitation treatment without relying on rehabilitation practitioners is just around the corner.

Key words: virtual reality, Rehabilitation of Cognitive Impairment, Complementary and Alternative Therapy

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Data mining to explore the dominant diseases of "transcranial repeated acupuncture"

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Abstract

Objective: To explore the dominant diseases of "transcranial repeated acupuncture" by data mining. **Methods:** Taking "transcranial repeated acupuncture" or "transcranial acupuncture stimulation" as the theme word, CNKI, VIP and Wanfang Data databases were retrieved by computer, and the clinical randomized controlled trials related to "transcranial repeated acupuncture" collected from the establishment of the database to November 2021 were collected. **Results:** a total of 24 literatures were included, involving 10 diseases, of which the articles related to stroke sequelae were the most. **Conclusion:** the dominant diseases of "transcranial repeated acupuncture" are stroke sequelae, insomnia and peripheral facial paralysis.

Key words: acupuncture and moxibustion; Sun Shentian; transcranial repeated acupuncture; dominant disease

Professor Sun Shentian is one of the founders of acupuncture and moxibustion in Heilongjiang Province. His "transcranial repeated acupuncture" has been widely used in clinic ^[1]. In this method, the function of cerebral cortex is located in the corresponding area on the scalp surface as the acupuncture part, and the repeated twisting manipulation is applied to twist continuously for 3 ~ 5 minutes, with a frequency of about 200 times /min, with remarkable results. This paper explores the dominant diseases of "transcranial repeated acupuncture" through data mining, hoping to comprehensively present the application scope of this method from the perspective of data mining.

Objective

This paper explores the dominant diseases of "transcranial repeated acupuncture" through data mining, hoping to comprehensively present the application scope of this method from the perspective of data mining.

Materials and methods

With "transcranial repeated acupuncture" or "transcranial acupuncture stimulation" as the theme word, CNKI, VIP and Wanfang Data databases were retrieved by computer, and the clinical randomized controlled trials related to "transcranial repeated acupuncture" collected from the establishment of the database to November 2021 were collected.

Results and discussion

A total of 24 literatures were included, including 7 sequelae of stroke, 4 insomnia, 3 pain, 2 peripheral facial paralysis, 2 tremor paralysis, 2 facial spasm, 1 depression, 1 restless legs syndrome, 1 urinary retention after spinal cord injury, and 1 functional dyspepsia. The article systematically presents the dominant disease of "Sun Shentian transcranial repeated acupuncture". Mr. Sun Shentian's academic thought is the treasure of the academic session of acupuncture and moxibustion in Heilongjiang Province. It is our duty to promote its application, development and dissemination.

I hope this article will play a certain role in promoting the study, promotion and even development of "transcranial repeated acupuncture"!

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A brief discussion on the prospect of joint development of TCM between China and Russia in B&R from the "14th Five-Year Plan"

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Abstract

The joint construction of B&R is a national cooperation initiative proposed by General Secretary Xi in 2013. It includes many aspects such as politics, economy and culture. In 2017, China and Russia formally proposed to jointly build the "Ice Silk Road". The "14th Five-Year Plan for the Development of TCM" proposes 10 key tasks in various aspects, including accelerating the open development of TCM. This paper summarizes the past and current situation, and discusses the prospect and direction of Sino-Russian joint development of TCM in the future from four aspects: strengthening Sino-Russian cooperation, establishing TCM standards, cultivating TCM talents, and accelerating the development of TCM trade.

Key words: The Belt and Road(B&R), Sino-Russian, traditional Chinese medicine (TCM)

"The Belt and Road" (B&R) is the abbreviation of "Silk Road Economic Belt" and "21st Century Maritime Silk Road". It was proposed by Chinese President Xi Jinping in September and October 2013 respectively. The purpose of B&R is to jointly build a community of interests, a community of destiny and a community of responsibilities featuring political mutual trust, economic integration, and cultural inclusiveness. On March 28, 2015, "Vision and Actions to Promote the Joint Construction of B&R" was released. Among it, the position of Inner Mongolia, Heilongjiang, Jilin, Liaoning and Beijing is to build an important window opening to Northeast Asia. On July 4, 2017, when President Xi met Medvedev in Moscow, he proposed: "We should carry out cooperation on Arctic waterways and jointly build the 'Ice Silk Road'."

In the "14th Five-Year Plan for the Development of Traditional Chinese Medicine(TCM)" issued by the State Council in March 2022^[1], it is proposed to speed up the opening and development of TCM, promote the participation of TCM in international cooperation in the prevention and control of major infectious diseases such as Covid-19, and promote the high-quality integration of TCM into B&R Construction, implement the special project of international cooperation in TCM, help build a community of human health, deepen exchanges and cooperation in TCM, expand international trade in TCM, and build a high-quality national export base of TCM services. In view of the joint development prospects of TCM between China and Russia, the following points are summarized.

1. Strengthen Sino-Russian cooperation in TCM

In April 2015, a seminar on the implementation plan of B&R Sino-Russian TCM Cooperation Demonstration Project organized by World Federation of Chinese Medicine Societies (WFCMS) was held in Beijing^[2]. The project gives full play to the resource advantages of WFCMS in the field of TCM to establish a model medical institution of TCM in Russia. It regulates the medical practice of TCM in Russia with the standards of WFCMS international organizations, and takes the lead in

forming an example of management based on the standards of the international organization of TCM in the world. On June 16, 2016, the Sino-Russian Chinese Medicine Innovation and Development Alliance initiated by Heilongjiang University of Chinese Medicine and Amur State Medical College of Russia was officially announced^[3]. A total of 70 units from China and Russia, as the first members of the alliance, jointly issued the "Common Declaration", expressing the desire to "jointly promote the healthy, orderly and mature dissemination and development of TCM in Russia and the world". In the future, relying on B&R, under the current international environment, to strengthen cooperation in Northeast Asia, we will strengthen cooperation with Russia, increase the influence of TCM in Russia, and organize relevant universities and research institutes in China and Russia, strengthen research and promotion in the field of innovation and development of TCM-related botanicals and traditional medicine, realize resource sharing and cross-border cooperation, and make positive contributions to the health of the people of China and Russia and the development of human health.

2. Establish international standards of TCM and promote the "legalization" of Russian TCM

In March 2022, on the official website of the World Health Organization (WHO), the "WHO International Standards for Chinese Medicine Terminology" was officially released. The standardization and internationalization of medicine provides a unified Chinese-English blueprint, which plays an important role in promoting the international exchange and informatization construction of TCM. However, there is currently a lack of normative provisions for TCM in the Russian legislative system, which makes the level of TCM in Russia uneven. In the future, the legal status of TCM in Russia should be established from the 3 levels of government dialogue - think tank media/enterprises and universities - the public. In the context of the development of B&R and the current situation that covid-19 is still raging around the world, the Chinese government can strive for more legalization opportunities for TCM in Russia through political, economic, legal and other means. In the future, the Chinese and Russian governments can increase the attention of Russian think tanks and media to TCM through the exchange of think tanks between the two countries, emphasizing that TCM is effective in preventing and treating common diseases, frequently-occurring diseases, chronic diseases and certain major diseases. TCM attaches great importance to the concepts of health preservation, fitness, and dietary supplements, which are conducive to improving human immunity, and thus can be widely recognized by Russian society.

3. Cultivate local practitioners and let TCM benefit a wider range of people

High-quality TCM services depend on the cultivation of high-quality TCM talents. In 2016, the St. Petersburg TCM Center of Beijing University of TCM was established, becoming the first Chinese medicine hospital in Russia to be legally recognized. Colleges and universities should make use of abundant educational resources to cultivate international-oriented TCM professionals. If TCM wants to develop in Russia for a long time, doctors should have the basic ability to communicate with the Russian people during diagnosis and treatment. If TCM physicians in Russia can communicate with patients in Russian, "observation, auscultation and olfaction, inquiry, and pulse feeling and palpation" can avoid obstacles caused by language barriers. The cultivation of compound TCM talents is inseparable from the joint efforts of the two countries. There can be academic exchanges between Chinese and Russian medical universities, joint training of talents and collaborative research in scientific research.

4. Accelerate the process of internationalization of TCM and empower the development of international trade of TCM

The internationalization of TCM is an indispensable link for TCM to move towards B&R. In 2021, the Sino-Russian pharmaceutical export trade volume was US\$2.83 billion, of which the export of TCM was US\$38.568 million, a year-on-year increase of 68.5% of 2020, and there was a steady increase in 2022. In the first quarter of 2022, the export of proprietary Chinese medicines increased by 274.39%. On July 7, 2022, the BRICS Traditional Medicine Standardization Seminar was held in Hangzhou. The TCM Technical Committee, promoted by China and established in the International Organization for Standardization, has issued 86 international standards for TCM. International exchange is not only one-way output, but also two-way communication. Since 2020, Heilongjiang Province has innovatively implemented the "Russian low-risk plant-derived Chinese medicinal materials trial import" free trade pilot zone. As of March this year, 1,629 tons of low-risk plant-derived Chinese medicinal materials have been imported from Russia in the two years. To this end, the construction of the evaluation mechanism of foreign TCM should be stepped up, which will surely provide a scientific guarantee for the effectiveness and safety of foreign medicinal materials. At the same time, it will revitalize the international TCM market and empower the development of international trade in TCM.

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THE CLINICAL STUDY ON TREATMENT OF CONGNITIVE FENCTION OF SUBCORTICAL ARTERIOSCLEROYIC ENCEPHALOPATHY BY SCALP ELECTROACUPUNCTURE

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Abstract: Acupuncture has been widely used in the treatment of subcortical arteriosclerotic encephalopathy (SAE). In this study, scalp electroacupuncture was used to treat subcortical arteriosclerotic encephalopathy, and the efficacy was compared with conventional acupuncture methods commonly used in clinical practice. Both groups were treated with the Mini-mental state examination (MMSE), the Montreal Cognitive Assessment (MoCA) and Event-related potentials (ERP) before and after treatment. According to the analysis, scalp electro-acupuncture is superior to conventional acupuncture in the treatment of SAE.

Keywords: Subcortical arteriosclerotic encephalopathy, Cognitive imparment, Scalp electroacupuncture, Conventional acupuncture

The clinical incidence of subcortical arteriosclerotic encephalopathy is also increasing. Studies have shown that in the elderly, the incidence of this disease is about 1% to 5%. The progression of the disease is gradual, and the main symptoms are progressive intellectual decline and cognitive dysfunction. In the current clinical treatment of this disease, methods to reduce vascular risk factors and improve cerebral blood perfusion are mainly used (such as drugs to lower blood pressure, blood lipids, blood sugar, vasodilators), physical therapy methods (such as acupuncture, transcranial electrical stimulation) therapy), etc. Although there are various treatment methods, and some therapies have achieved certain clinical therapeutic effects, the clinical needs have not yet been met. Therefore, there is a clinical need for new and less side effects of treatment.

Objective: This clinical observation uses scientific research and statistical methods to observe the effect of scalp electroacupuncture on cognitive function impairment of subcortical arteriosclerotic encephalopathy and to perform statistical analysis. program approach.

Materials and methods

1. Sixty patients with cognitive impairment of subcortical arteriosclerotic encephalopathy were selected and divided into a treatment group (scalp electroacupuncture group) and a control group (conventional acupuncture) according to the randomized control method.

2. In treatment group Baihui, Sishencong, Shenting, Fengchi, Benshen, Zusanli, Taixi, Xuanzhong were selected. Among them, Baihui, Sishencong, Shenting and Benshen was connected with the G6850 electroacupuncture apparatus to diffuse the density wave and lasted for 30min. After the electroacupuncture, pull out the body needle and the acupuncture needle of Fengchi, Baihui, Sishencong, Shenting and Benshen retained the needle for 6h. In the control group, Baihui, Sishencong, Shenting, Fengchi, Benshen, Zusanli, Taixi and Xuanzhong were selected and treated with conventional acupuncture. After acupuncture for 30min, the body needle and the acupuncture needle at fengchi point were removed, and the acupuncture needle of Fengchi, Baihui, Sishencong, Shenting and Benshen retained the needle for 6h. Both groups were treated 6 days a week for 5 weeks.

3. Both groups were treated with the Mini-mental state examination (MMSE), the Montreal Cognitive Assessment (MoCA) and Event-related potentials (ERP) before and after treatment.

Results and discussion

In this clinical study, 60 patients with subcortical arteriosclerotic encephalopathy and cognitive impairment were randomly divided into a scalp electro-acupuncture group and a conventional acupuncture group. Before treatment, 60 patients who were divided into two groups were statistically compared with the basic information of age, gender and education time, $P>0.05$, indicating that there was no significant difference in the basic conditions of the two groups before treatment. Before and after treatment in the two groups, the Simple Mental State Scale, Montreal Cognitive Assessment Scale, and Event-related Potential P300 were used to evaluate the effect before and after treatment, and the results were compared and statistically analyzed. After treatment, the total score of MMSE in the treatment group and the control group was significantly improved compared with that before treatment ($P<0.01$), and the total score of MoCA was improved ($P<0.05$). SAE cognitive impairment was improved. After treatment, the MMSE and MoCA scores of the treatment group and the control group were compared, and the treatment group was higher than the control group ($P<0.05$). <0.05). It shows that scalp electro-acupuncture is superior to conventional acupuncture in treating SAE cognitive impairment. Comparing the scores of MoCA in the treatment group before and after treatment, the scores of visuospatial/executive power, naming, attention, computing power and recall ability were improved after treatment, which was statistically significant compared with that before treatment ($P<0.05$). Compared with before treatment, the language and abstraction ability of the treatment group did not have statistical significance after treatment ($P>0.05$). The P300 latency and amplitude of event-related potential before and after treatment in the treatment group and the control group were significantly shortened ($P<0.01$), while the amplitude was significantly increased ($P<0.01$). Compared with the P300 latency and amplitude after treatment in the treatment group and the control group, the incubation period in the treatment group was shorter than that in the control group ($P<0.01$), and the amplitude in the treatment group was higher than that in the control group ($P<0.01$).

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Observation on the effect of improving the quality of life of patients with heart failure from "liver raising and lung lowering"

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Objective: Based on the theory of "liver raising and lung lowering", to study the clinical efficacy of the treatment of heart failure patients with the method of soothing the liver and regulating qi, clearing the internal organs and saving the lungs, and to explore its mechanism of action. **Methods:** A total of 64 elderly patients with heart failure admitted to the Department of Cardiology of the First Affiliated Hospital of Heilongjiang University of Traditional Chinese Medicine from January 1, 2021 to July 1, 2022 were randomly divided into a treatment group and a control group with 32 cases in each. The control group was given conventional anti-heart failure treatment, and the treatment group was given self-prepared formula on the basis of the control group. The clinical efficacy of TCM syndromes, plasma N-terminal precursor B-type natriuretic peptide (NT-proBNP), left ventricular ejection fraction (LVEF), cardiac function classification and quality of life (MLHFQ score) of the two groups were observed. **Results:** After treatment, the total effective rate of TCM syndromes in the control group was 93.8% higher than that in the control group (69.8%); the cardiac function classification in the treatment group was significantly higher than that in the control group ($P < 0.05$). There was no significant difference in NT-pro BNP and LVEF between the two groups before treatment (all $P > 0.05$). After treatment, NTproBNP and LVEF in the two groups were improved compared with those before treatment, and the treatment group was more significant than the combination group (all $P < 0.05$). There was no significant difference in the MLHFQ scores between the groups before treatment ($P > 0.05$). After treatment, the MLHFQ scores of the two groups were decreased compared with those before treatment, and the quality of life score of the treatment group was lower than that of the control group ($P < 0.05$). **Conclusion:** Based on the theory of "liver raising and lung lowering", the combined treatment of heart failure patients with the method of soothing the liver and regulating qi and unblocking the internal organs and saving the lungs can effectively reduce serum BNP, improve cardiac function, improve pulmonary infection, relieve inflammatory response, and improve quality of life. , can improve the clinical symptoms of patients with chronic heart failure and blood stasis syndrome, prevent disease reversal, and has high safety.

Key Words: Liver raising and lung lowering, Heart failure, Quality of Life

Clinical observation of Mediterranean diet combined with acupoint catgut embedding therapy in the treatment of simple obesity

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Summary

This paper introduces a new treatment of simple obesity - Mediterranean diet combined with acupoint catgut embedding therapy. In this study, 60 patients with simple obesity were randomly divided into two groups, with 30 cases in each group. The control group was given Mediterranean diet therapy, and the treatment group was given acupoint catgut embedding therapy on the basis of the control group. It was observed that Mediterranean diet combined with acupoint catgut embedding therapy could significantly reduce the body weight (BW), waist circumference (WC), body mass index (BMI), and blood lipid (TG,TC,LDL-C) levels of patients.

Keywords : Simple obesity, acupoint catgut embedding, Mediterranean diet, clinical study.

Traditional Chinese medicine believes that obesity is due to a variety of reasons leading to excessive accumulation of ointment in the body, abnormal weight gain, and accompanied by dizziness, fatigue, laziness, shortness of breath and other symptoms of a class of syndromes. If there is no obvious etiology of endocrine metabolism, it can be called simple obesity. At present, simple obesity has become a public health problem that has attracted much attention in the scientific community. The side effects of drug weight loss and surgical weight loss are large and easy to rebound. Mediterranean diet combined with acupoint catgut embedding therapy achieves therapeutic effect through the comprehensive adjustment of nervous system, endocrine system, digestive system and energy metabolism, which is not easy to rebound, has long-term curative effect and no side effect.

Objective

This study aims to explore the clinical efficacy of Mediterranean diet combined with acupoint catgut embedding therapy in the treatment of simple obesity.

Materials and methods

Sixty patients who met the requirements of this study were collected and randomly divided into treatment group and control group, with 30 cases in each group. There were 5 males and 25 females in the treatment group, aged from 20 to 38 (28.8 ± 5.0) years, 50% of them were overweight, 44.6% were grade I obesity and 5.4% were grade II obesity. In the control group, there were 3 males and 27 females, aged 18–45 (29.5 ± 6.3) years old. Overweight accounted for 46.6%, I degree obesity accounted for 45.3%, and II degree obesity accounted for 8.1%.

Inclusion criteria : (1) in line with simple obesity diagnostic criteria, and no history of alcohol, animal protein allergy ; (2) Willing to accept the treatment of this study, and signed informed consent.

Exclusion criteria : (1) pregnancy or lactation women ; (2) secondary obesity patients with severe heart, brain, liver, kidney, endocrine diseases ; (3) Patients who cannot adhere to the course of treatment ; (4) Patients who participated in other ways of weight loss during treatment.

The Mediterranean diet was used in the control group: the diet history, dietary habits and hobbies were asked, and the diet was formulated according to the overweight and physical labor of the patients. Vegetables, fruits, fish, beans and nuts were the main foods, followed by cereals. Vegetable oil was used to replace animal oil in cooking, especially olive oil, drinking more water, and adhering to the principle of eating less and eating more. At the same time told patients not to eat beverages, sweets, fried food during treatment. Doctors were given a nutritional intervention for 2 weeks, and provided a diet for the next 2 weeks for 4 weeks.

The treatment group was treated with acupoint catgut embedding therapy on the basis of the control group : the main acupoints were selected as abdominal eight needles, including water point, Guanyuan point, Daheng point, Daimai point, Zhongwan point, Qihai point, Tianshu point, Huaroumen point, spleen deficiency and dampness stagnation plus Pishu, Yinlingquan ; patients with excessive stomach fire were added Liangqiu and Quchi ; liver qi stagnation plus Taichong, Ganshu ; spleen and kidney deficiency to close the gate, life. Will the patient lying, routine disinfection, with sterile tweezers put the line into the buried needle, with the left hand to tighten the skin around the acupoint, right hand quickly into the needle, when the needle feel twist flat out the needle. Two weeks of treatment once, twice for a course of treatment, a course of treatment after the efficacy of observation.

Results and discussion

Before treatment, the baseline data of all patients were statistically analyzed, and the difference between the two groups was not statistically significant ($P>0.05$).

BW, WC and BMI of the two groups after treatment were significantly lower than those before treatment, and the differences were statistically significant ($P<0.05$). After treatment, BW, WC and BMI in the treatment group were lower than those in the control group, and the differences were statistically significant ($P<0.05$). See Table 1.

Table 1 Comparison of BW, WC and BMI between the two groups before and after treatment

Group	time	cases	BW(kg)	WC(cm)	BMI
Treatment group	before treatment	30	79.53±5.05	98.73±2.52	28.62±2.93
	after treatment	30	66.40±3.68	74.13±3.79	23.91±2.54
Control group	before treatment	30	79.21±7.21	99.00±2.90	29.24±2.80
	after treatment	30	72.06±6.87	82.33±2.69	26.59±2.60

TG, TC and LDL-C of the two groups were significantly decreased after treatment, and the differences were statistically significant ($P<0.05$). After treatment, TG, TC and LDL-C in the treatment group were lower than those in the control group, and the differences were statistically significant ($P<0.05$). See Table 2.

Table 2 Comparison of blood lipids between the two groups before and after treatment (mmol/L)

Group	time	cases	TG	TC	LDL-C
Treatment group	before treatment	30	1.74±0.17	5.29±0.46	3.66±0.39
	After treatment	30	1.11±0.04	4.29±0.52	1.91±0.39
Control group	before treatment	30	1.75±0.17	5.27±0.47	3.65±0.47
	After treatment	30	1.40±0.12	4.53±0.56	2.64±0.40

After treatment, the total effective rate of the treatment group (93.3%) was higher than that of the

control group (73.3%) ($P < 0.05$), indicating that the Mediterranean diet combined with acupoint catgut embedding therapy was superior to the control group in the treatment of simple obesity.

Acupoint catgut embedding therapy, as a new treatment method extending the acupuncture therapy, has the effect of long needle retention. After the line body is implanted into the human body, through this continuous stimulation to adjust the body's viscera and meridians, yin and yang balance. Therefore, it has the characteristics of long-term stimulation and no side effect. The Mediterranean diet is more comprehensive than the general diet, and the intake of more vitamins can improve the sub-health state while treating obesity. It is nutritionally healthy and does not rebound. The combination of Mediterranean diet and acupoint catgut embedding therapy forms a cyclic induction process, which produces mutual excitation and mutual synergy, thus inducing physiological amplification effect and achieving the purpose of treating simple obesity.

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Advances in the study of signaling pathways associated with ulcerative colitis

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[Abstract]Ulcerative colitis(UC)is a chronic non-specific inflammatory bowel disease of unknown etiology, with clinical manifestations of abdominal pain, mucopurulent stools and urgency, and lesions mainly in the mucosa and submucosa of the rectum and colon.Studies have shown that the pathogenesis of UC may be related to the transduction of signaling pathways. combined with domestic and international related literature,we found that Chinese herbal medicine has significant effect on the treatment of UC. This article provides a review on the role of UC-related signaling pathways in pathogenesis. In order to provide some scientific basis for the treatment of UC in Chinese medicine and the development of new anti-UC drugs.

[Key words]ulcerative colitis;signaling pathways;chinese medicine;research advances

UC is characterised by recurring episodes of inflammation limited to the mucosal layer of the colon. Inflammatory episodes give rise to rectal bleeding, diarrhoea, and abdominal pain^[1].In recent years,through the in-depth study of cellular signaling pathways, more and more pathogenic mechanisms of UC have been discovered. The main signaling pathways affecting UC are NRF2/HO-1, JAK/STAT, PI3K/Akt, MAPKs, NF-κB, hippo and so on.Therefore, this paper presents a review of UC-related signaling pathways with reference to domestic and international literature, in order to improve the understanding of UC pathogenesis and provide ideas for UC therapy and the development of new anti-UC drugs.

1 Nrf2/HO-1 signal pathway

Nrf2/HO-1 signal pathway is the most classical effect pathway of Nrf2.Nrf2 is involved in many oxidative stress-related diseases. HO-1 is a member of the heme oxygenase family and plays an important role in anti-inflammation and antioxidation. Nrf2 contains seven conserved domains. Under physiological conditions, Nrf2 binds to Kelch epichlorohydrin-related protein 1 (Kelch-like ECH-associated protein 1,Keap1) to form a complex in the Neh2 region,and the 40th amino acid is the phosphorylation site.Keap1 is a negative regulator of Nrf2,which can mediate proteasome degradation of ubiquitinated Nrf2, thus maintaining the inhibitory state of low Nrf2 activity. When under oxidative stress or other chemical stimulation, Nrf2 dissociates from Keap1 by phosphorylation, transfers to the nucleus, binds to the related gene promoter antioxidant response element (ARE) sequence, and then regulates the expression of downstream genes, such as HO-1, NADPH:quinone oxidoreductase 1, glutathione peroxidase, etc, which play the role of antioxidant stress, anti-inflammation and additional cytoprotection^[2]. Zhang Xuexiaet al. found that the levels of IL-6, TNF-α, MDA and ROS in the serum of mice treated with Sishen Pills decreased, while improving the histopathological damage of the colon. Sishen Pills intervention significantly increased the expression of UC Nrf2 and was able to significantly enhance the expression of Nrf2-induced phase II coenzymes NQO-1 and HO-1, suggesting that Sishen Pills may play a protective role against oxidative stress by activating the Nrf2/HO-1 signaling pathway^[3].

2 JAK/STAT signaling pathway

JAK is a kind of important tyrosine protein kinase. STAT3 is an important member of the signal transduction pathway family, which is closely related to cell proliferation, differentiation and apoptosis. The abnormal expression and activation of STAT3 participate in the development of many diseases. IL-6 binds to its corresponding receptors to form a complex IL-6/IL-6R/gp130. The complex molecules are dimerized to activate the coupled JAK kinase, and the activated JAK phosphorylates STAT3 to form a STAT3 protein dimer, which is transferred to the nucleus, induces the transcription and synthesis of corresponding regulatory target genes, and activates the expression of related inflammatory factors. Mediate and regulate inflammatory response^[4]. An Mingwei et al. found that the expression of IL-6, JAK2 and STAT3 genes and proteins were reduced in UC rats after treatment with gegenqinlian decoction, suggesting that the decoction can inhibit JAK2/STAT3 gene transcription^[5].

3 PI3K/Akt signaling pathway

PI3K family is a kind of protein kinases. Their activation is secondary to the activation of Ras molecules induced by growth factors and cytokines or tyrosine phosphorylation of some signal molecules to produce corresponding inositol lipid substances, which is a new intracellular second messenger. After binding to the signal molecules containing the homologous domain of platelet-leukocyte kinase C substrate in the cytoplasm, it can regulate the activity of the corresponding molecules. AKT is a direct target protein downstream of PI3K, which is mainly responsible for the biological information transduction initiated by PI3K. After the site is phosphorylated, the AKT binding to the cell membrane is completely activated. Activated AKT is released from the cell membrane to the cytoplasm to phosphorylate its downstream FOXO (forked transcription factor). After phosphorylation, FOXO goes out of the nucleus and initiates the downstream signal pathway. After AKT activation, NF- κ B activates the retrograde nucleus, which acts as a transcription factor to initiate the downstream inflammatory response^[6]. Yang Xianjuan et al found that the single use and combination of *Coptis chinensis* and *Magnolia officinalis* could inhibit the positive expression of PI3K and Akt and the expression level of p-Akt protein in rat colon^[7].

In addition to the pathways listed above, there are multiple pathways related to UC. MAPK and NF- κ B pathways are more common in UC, they are common downstream pathways that regulate the expression of inflammatory factors. With the deepening of research on Hippo signaling pathway, it has been found in recent years that Hippo signaling pathway is also involved in regulating the occurrence and development of inflammation in the body^[8].

Summary

UC is characterized by refractoriness, recurrence, continuity, high recurrence rate, and difficulty of cure. The drugs currently used to treat UC are not effective for all patients and have significant side effects when taken for long periods of time. In-depth study on the mechanism of action of traditional Chinese medicine in the treatment of UC from the signaling pathway, to identify the key links in the signaling pathway, eliminate the adverse effects and utilize the beneficial effects, can provide new ideas for the development of new anti-UC drugs.

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Advances in acupuncture treatment of Parkinson's disease

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Abstract

Parkinson's disease (PD) is most common in middle-aged and elderly people. It is characterized by abnormal symptoms such as tremor, myotonia, bradykinesia and dyskinesia caused by dysfunction of extracone system. Clinically, body acupuncture, electroacupuncture,scalp acupuncture, Eye of acupuncture are commonly used to improve the motor symptoms and non-motor symptoms of Parkinson's disease.

Key words: Parkinson's disease; Acupuncture; treatment

Parkinson'sdisease (PD) is a chronic progressive disease caused by the disturbance of the substantia nigra striatum pathway, which is mostly seen in middle-aged and elderly people. The main symptoms of PD are muscle tremor and rigidity, dyskinesia and dyskinesia caused by dysfunction of the extracone system. In severe cases, it may be accompanied by complications such as constipation, depression and sleep disorders.The main pathological features are the decrease of dopamine transmitters in the striatum due to the loss of dopaminergic neurons in the substantia nigra dense region and other factors.At present, the best results of PD treatment are :(1) controlling symptoms and reducing complications;(2) Prolong disease progression and improve quality of life;(3) Prolong the service life of drugs;(4) Reduce the adverse reactions of drugs ^[1].As a common treatment, levodopa has obvious therapeutic effect in the early stage, but the therapeutic effect gradually decreases with the decrease of the regulating ability of dopamine in the body after long-term use, and has obvious side effects.After taking PD, patients may develop gastrointestinal symptoms, "on/off" phenomenon and dyskinesia ^[2].

Objective

Clinical studies have found that acupuncture is effective in improving Parkinson's symptoms, and there are no side effects.

Materials and methods

This article summarized the acupuncture treatment of Parkinson's disease in recent years.

Result and discussion

1. Body of acupuncture

Studies have found that increased glucocorticoid secretion is caused by hyperactivity of hypothalamic pituitary-adrenal axis, and a large amount of glucocorticoid acting as brain can cause cognitive dysfunction in PD patients ^[3].Yu Huan ^[4] used Kidney-tonifying Shenshen acupuncture to treat Parkinson's disease patients. Baihui, Fengfu, Ganshu, Shenshu, Taixi and Yongquan were selected as the main points, and daily activity ability score and motor function score were used to evaluate the therapeutic effect. It was found that kidney-tonifying Shenshu acupuncture could effectively improve the activity ability and quality of life of Parkinson's disease patients.

2.Electric acupuncture

Electroacupuncture can improve cerebral blood flow and promote PD clinical rehabilitation. Electroacupuncture can increase the trend of dopamine content in PD striatum and enhance the ability to resist oxidative stress in human body, so as to improve PD symptoms [5-8]. Studies have shown that electroacupuncture stimulation with a certain frequency can promote the release of strong peptides in vivo and inhibit the excitability of spinal cord anterior horn cells, proving that electroacupuncture can relieve muscle spasm [9-11]. Li Jing [12] found that electroacupuncture of Baihui, Taichong and Sanyinjiao could inhibit neuronal apoptosis in PD rats and increase the number of Th-positive neurons in the brain and the content of DA in the striatum.

3. scalp acupuncture

Parkinson's disease is located in the brain, and the head acupoint area is an important acupuncture site. Clinically, tremor area, motor area, sensory area, skull base acupoint and Du Meridian point of the head are mostly selected for treatment. Its mechanism of action is that acupuncture stimulates corresponding acupoints of the head and acts on the corresponding parts of the cerebral cortex to stimulate the release of neurotransmitters in the brain [13]. Huang Yong et al. [14] found in their study that acupuncture combined with mdopa treatment could improve blood flow in basal ganglia, cerebellum and occipital lobe of PD patients, and significantly improve motor function and cognitive level of patients.

4. Eye of acupuncture

Eye acupuncture therapy is characterized by small needles, less acupoint selection, shallow acupuncture depth, simple operation, quick effect and two-way adjustment. Dong Liyu [16] used eye acupuncture combined with cephalic acupuncture combined with madopa to treat PD. The results showed that the clinical efficacy of eye acupuncture combined with head acupuncture combined with western medicine in the treatment of PD was significantly better than that of head acupuncture combined with western medicine.

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Effect of Bining decotion on gouty neph¹ropathy based on network pharmacology

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Abstract

Bining decotion (BN) is a new traditional Chinese medicine formulation.BN has been designed to treat gouty nephropathy. Despite the therapeutic benefits of BN, its underlying mechanism of action is not known. We explored the efficacy of BN against gouty nephropathy by network pharmacology and experimental verification to elucidated its mechanism of action. The Pathways in cancer has the most significant node, and it has the strongest correlation with Mandenol and MAPK8.These results represent how BN works against gouty nephropathy and provide a reference for further studies.

Keywords: network pharmacology, gouty nephropathy, Bining decotion

Gouty nephropathy (GN) is mainly caused by the deposition of uric acid(UA), usually in the form of monosodium urate (MSU) crystals, precipitates in synovial cavities and other anatomic location to induce severe inflammation and debilitating pain ^[1]. In particular, deposits of uric acid in the kidney causes gouty nephropathy.Disease progression may even cause renal failure.

GN has undergone a revolutionary development since the introduction of corticosteroids and nonsteroidal anti-inflammatory drugs(NSAIDs) . However, presently therapies often have severe side effects have hindered further clinical application^[2].Therefore, more attention has been paid to the research and development of drugs with greater efficacy and lower toxicity, especially those derived from natural products.

Bining decotion(BN) is a traditional Chinese herbal decotion , include Dioscoreae Hypoglaucae Rhizoma, Plantaginis Semen, Atractylodes Lancea (Thunb.)Dc. , Coicis Semen, Pseudobulbus Cremastrae Seu Pleiones, Phellodendri Chinrnsis Cortex, Chuanxiong Rhizoma, Cyathulae Radix and Lonicerae Japonicae Caulisand .Under the guidance of traditional Chinese medicine theory and clinical practice, BN is a diuretic decotion, and it has the characteristics of mild drug and little side effects.

Objective

To explored the mechanisms of Bining decotion for treating gouty nephropathy by applying network pharmacology to provide credible evidence for the mechanism of Bining decotion treating gouty nephropathy .

Materials and Methods

Traditional Chinese Medicine Systems Pharmacology Database and Analysis Platform (TCMSP) (<https://old.tcm-sp-e.com>) is used to search for the useful active components of GN .The human genes associated with GN were screened from GeneCards(www.genecards.org/),Genbank (<http://www.ncbi.nlm.nih.gov>) ,Online Mendelian Inheritance in Man(www.omim.org/),and Disgenet (<https://www.disgenet.org/home/>) databases to search for disease targets. Then, all the target proteins obtained above were converted into standardized gene names through the UniProt

database (www.uniprot.org/). Construction of a Protein–Protein Interaction (PPI) Network. The therapeutic targets of BN against GN were determined by mapping the targets of active compounds to GN-related targets. The therapeutic targets of BN were entered into the Search Tool for the Retrieval of Interacting Genes/Proteins (STRING) database (<https://string-db.org>) and analyzed with organism species limited to Homo sapiens and a high confidence score (>0.9). The obtained PPI data were entered into Cytoscape 3.7.2 (<https://cytoscape.org/>),^[3] then we selected top-ranked 10 cDEGs as a set of key genes (KGs) by cytoHubba plugin in Cytoscape. We used the Metascape database (<https://metascape.org/gp/index.html#/main/step1>) to conduct analyses of signaling pathway enrichment via the KEGG database. The diagram for signaling pathway enrichment was obtained using R 3.5.2. Then drawing network diagram of Bining decoction in the treatment of GN.

Results and discussion

After removing duplicate targets, the databases yielded 413 pharmacological targets related to BN. A total of 1085 GN-related targets were obtained from the databases, and GN-related targets were mapped to 118 active ingredient targets. We used Venny 2.1 (<https://bioinfo.gp.cnb.csic.es/tools/venny/>) to obtain the therapeutic targets of BN against GN (Figure 1A). Visualization of the PPI networks of BN was achieved using the STRING database. Significantly more interactions were seen in the PPI network with 90 nodes and 416 edges (Figure 1B). At the same time, the cytohubba plug-in Cytoscape was used to screen out the core targets. Combined with the score of the calculation method, the top 10 genes were considered as core genes. Those for Proto-oncogene tyrosine-protein kinase Src (SRC), Mitogen-activated protein kinase (MAPK)1, Heat shock protein HSP 90-alpha (HSP90AA1), Tyrosine-protein phosphatase non-receptor type (PTPN)11, Transforming protein RhoA (RHOA), Mitogen-activated protein kinase (MAPK)14, Estrogen receptor (ESR)1, Tyrosine-protein kinase JAK (JAK)2, Signal transducer and activator of transcription 1-alpha/beta (STAT)1, Mitogen-activated protein kinase (MAPK)8 (Figure 1C). These genes may be key targets for BN to have a role in lowering of uric acid concentrations^[4]. To further elucidate the molecular mechanism of action of BN on GN, analyses of pathway enrichment were undertaken on the 10 core genes mentioned above using the KEGG database 157 metabolic pathways were identified, Based on the core genes obtained from these twenty signaling pathways and network pharmacology, an integrated network map of Bening decoction for the treatment of GN was drawn (Figure 1D).

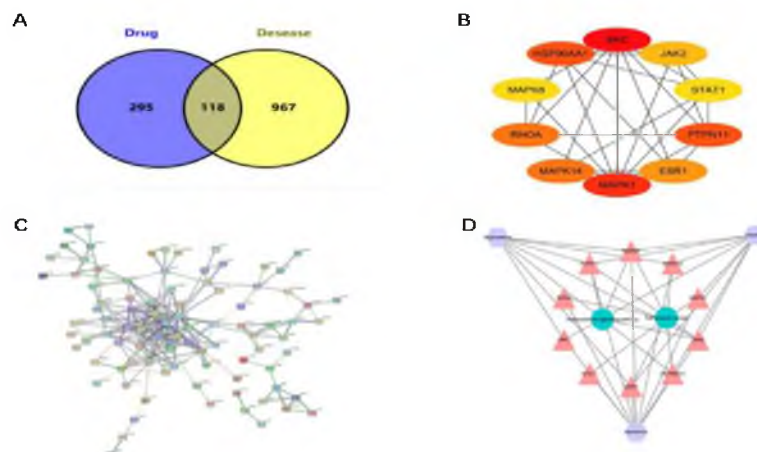


FIGURE1 (A) Venn diagram of the common targets of BN in GN treatment. (B) The protein–protein interaction (PPI) network is based on the targets of BN. (C)The top 10 core genes.(D)Comprehensive network diagram of Bining decoction in the treatment of GN.

The network pharmacology revealed that ten major targets, including SRC,MAPK1,HSP90AA1,PTPN11,RHOA,MAPK14,ESR1,JAK2,STAT1,MAPK8and their essential metabolites (sitosterol, Stigmasterol, Mandenol) and pathway (Pathways in cancer and Adipocytokine signaling pathway).The Pathways in cancer has the most significant node, and it has the strongest correlation with Mandenol and MAPK8.These results demonstrate that the network pharmacology could be used to reflect the effects of BN works against gouty nephropathy.

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Investigation on molecular mechanism involved in anti-knee osteoarthritis effect of active components contained in lycopodium clavatum based on network pharmacology

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Abstract

It's to study the target and molecular mechanism of lycopodium clavatum extensiae in the treatment of KOA based on network pharmacology. The active compounds were screened in TCMSP database, PubChem and SwissTargetPrediction targets were obtained. Disease targets were searched from GENECRADS and OMIM databases. Establish drug-disease cross-targets Venny diagram, screen out the specific targets of lycopodium clavatum Hyacinth for the treatment of KOA, and analyze them by Cytoscape. The drug-disease intersection targets were uploaded to the STRING website, and a protein-protein interaction (PPI) network model was constructed with enrichment analysis of their signaling pathways by Cytoscape software. On the basis of the analysis it was noted that *esculenta tenuifolia* has the potential to treat KOA, which is mainly regulated by multi-target and multi-pathway.

Key words: *tenuifolia*; network pharmacology; KOA; target prediction; molecular mechanism
KOA, a degenerative and inflammatory disease of the knee, has a high prevalence in our country as high as 5.4% to 30.5% [1], traditional Chinese medicine has been proved to be effective in the treatment of KOA with low cost. The herb has the effects of anti-inflammation, analgesia, anti-oxidation and anti-platelet aggregation in the treatment of orthopaedic diseases. The network pharmacological method was used to explore the mechanism of the treatment of KOA and provide theoretical support for clinical treatment.

1. Objective

It's to study the target and molecular mechanism of lycopodium clavatum extensiae in the treatment of KOA based on network pharmacology

2. Materials and methods

2.1 To screen predictive targets and disease targets and to obtain drug-disease intersection genes
Active compound components with oral bioavailability $OB \geq 30\%$ and drug-like $DL \geq 0.18$ were searched in the TCMSP database with the keyword "*Tenuifolia*". The chemical structure was obtained by PubChem, and the drug action prediction targets were obtained by SwissTargetPrediction, and the targets with a score greater than 0 were selected as the predicted drug targets. Search the GENECRADS and OMIM databases with "Kneeosteoarthritis" as the key words, and then merge them to get the disease targets. Mapping Venny diagram via the online Wayne map site and obtaining the intersection genes.

2.2 Construct component-target network and perform PPI, GO and KEGG enrichment analysis
Drug-disease intersection genes were imported into Cytoscape for component-target network analysis and uploaded to STRING website for PPI analysis, and analyzed using

Cytoscape3.8.0.Potential acting targets were uploaded to METASACPE construct biology,and GO enrichment analysis and KEGG metabolic pathway enrichment analysis were performed according to p-value as well as count-value screening.

3.Results

3.1 Genes intersect with geniculate KOA

Seventy-four compounds were retrieved from the TCMSP database,and five compounds were screened for subsequent studies.109 drug action prediction targets were obtained,of which Mol005419 was 0,to be eliminated.2110 disease-related targets were obtained by integrating and de-weighting GeneCrads and OMIM databases.The disease genes and drug genes were transferred to an online Venn diagram website to obtain 43 overlapping genes.

3.2 Enrichment analysis of PPI, GO and Kegg was performed according to component-target network

The drug-disease intersection genes were uploaded to the STRING website for PPI analysis with a confidence of greater than 0.4 and a total of 43 nodes,98 edges,and an average nodal degree value of 4.56 were obtained after hiding the isolated protein.There were 18 targets with degree values greater than average,among which the degree values of EGFR,PPARA, ESR1 were greater than 8,indicating that these targets play a key role in PPI.The drug-disease overlapping genes were analyzed by GO and KEGG enrichment analysis,the functions of target-associated molecules include nuclear receptor activity,ligand-activated transcription factor activity,steroid binding,dna-binding transcriptional activator activity,RNA polymerase II specificity,adenosine triphosphatase binding and so on.The biological pathways shown include cancer pathway,Th17 cell differentiation,insulin resistance and arachidonic acid metabolism.

4.Discussion

KOA belongs to the category of "Bone arthralgia" in traditional Chinese medicine.In this study, four compounds with oral bioavailability $\geq 30\%$ and drug-like activity ≥ 0.18 were obtained by network pharmacological method,the molecular mechanism and pathway of the treatment of KOA were predicted based on the results of the analysis.The results showed that lycopodium clavatum plays a role,and has the potential to treat KOA.Four active components,including sitosterol,formononetin,stigmasterenol and α -ornoserin,were scree-ened from the composition-target network^[2,3].PPI network analysis showed that EGFR,PPARA,ESR1,CYP19A1,IL2 had higher target degrees,which indicated that these genes were closely related to each other.These findings reveal the genes and pathways that may play a role in the treatment of KOA^[4].They are consistent with modern research and show that the research is credible^[5].KEGG analysis shows that Shenjincao can be used as an antagonistic molecular drug to treat KOA^[6-10].However, since this research is based on various data platforms,there are still some limitations.The results of this study can provide a basis for the further study of the mechanism of the treatment of KOA and a certain theoretical basis for the clinical formulation.

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Clinical observation of ultrasound-guided acupotomy combined with ozone in the treatment of suprascapular nerve entrapment syndrome

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Abstract:

From September 2020 to September 2021, the clinical data of 60 patients with suprascapular nerve entrapment syndrome treated by ultrasound-guided acupotomy combined with ozone in the Third Department of Bone Injury, the First Affiliated Hospital of Heilongjiang University of Traditional Chinese Medicine were collected. The Constant-Murley shoulder score (CMS), pain analog visual scale (VAS) score and clinical effective rate were recorded and analyzed before and after treatment, so as to evaluate the clinical efficacy of this treatment. On the basis of the analysis it was noted that the ultrasound-guided acupotomy combined with ozone in the treatment of suprascapular nerve compression syndrome has the advantages of visualization and targeted treatment, quick and good effect, and is worthy of clinical application.

Key words: acupotomy visualization; Suprascapular nerve compression; Medical ozone

Shoulder on neural viega profi-press syndrome refers to caused by trauma, strain and surrounding tissues variation on the shoulder nerve conformity, with one side shoulder pain caused discomfort, shoulder joint activity limitations, lift on outreach extorsion weakness, difficulty, passive activity is not affected as the main symptoms of the disease, is one of the most common disease of the shoulder pain caused by [1]. With the popularization of ultrasound technology in recent years, ultrasound-guided suprascapular nerve release has been gradually applied in clinical practice with many advantages such as precision, simplicity, less trauma and fewer complications [2]. In this study, ultrasound-guided acupotomy and ultrasound-guided acupotomy combined with medical ozone were used to treat this disease, and the clinical efficacy was observed by VAS score and Constant-Murley shoulder joint function score, in order to provide a more effective reference for the clinical treatment of suprascapular nerve compression syndrome.

Objective

To analyze the clinical efficacy before and after ultrasound-guided acupotomy combined with ozone treatment in patients with suprascapular nerve entrapment syndrome, and to obtain the effectiveness and advantages of ultrasound-guided acupotomy combined with ozone treatment.

Materials and Methods

From September 2020 to September 2021, 60 patients with suprascapular nerve compression syndrome were selected to be treated by ultrasound-guided acupotomy combined with ozone in our hospital. Patients were divided into experimental group and control group by random number table method, with 30 patients in each group. The control group was given ultrasound-guided acupotomy treatment, and the experimental group was given ozone injection on the basis of ultrasound-guided acupotomy treatment. Constant-murley shoulder score (CMS), pain analog visual scale (VAS) score before and after treatment were recorded. The clinical efficacy was evaluated by statistical analysis.

The control group was treated with ultrasound-guided acupotomy. The patient took the prone position, pillow under the chest, arms naturally droop; The above equipment was used to conduct ultrasonic exploration around the scapulae of the patient, and the anatomical morphology of the patient was clear. The echo disorder of the diseased tendon was found, and the calcified transverse shoulder ligament, lesions and surrounding tissues presented high echo area or light spot or spot. There were traces, edema and increased blood flow signals at nerve entrapment^[3]. Operation method: Determine the needle entry route on the skin with a marker pen, disinfect the skin and probe surface with iodophor for 3 times, inject 5mL of 2% lidocaine mixed with 5mL of sterilized water for local infiltration and anesthesia. After applying coupling agent on the shoulder, the doctor wears a disposable mask and sterile gloves, holding the probe in one hand. A handheld old cases of medical card Φ 0.8 mm x 50 mm disposable needle knife, the needle body alignment nest on the bone surface Pierce, under the ultrasonic probe real-time dynamic observation, according to the operation method of the needle knife basic and clinical medicine for loose on scapula ligament and the adhesion around organization solutions for stripping, stay under the ultrasonic echo area high dispersion or disappear after take out the needle knife and local press after hemostasis, The eye of the needle was covered with plaster, and the eye of the needle was prohibited from water for 2 days. Follow-up was conducted 1 month later.

The experimental group was given ultrasound-guided acupotomy combined with ozone therapy. The patient took the prone position, pillow under the chest, arms naturally droop; Operation methods: ultrasound guided needle knife therapy in control group operation, on the basis of the original needle points under ultrasound guided needle knife parts precision injection of medical ozone 3 ml (such as effusion, first drew effusion), observe the ultrasound real-time dynamic visible liquid dark area gradually expanded, with sterile dressing after compression bandage, needle ban water for two days. Follow-up was conducted 1 month later.

Results and discussion

The effective rate of experimental group was 96.7% and control group 93.3%, the experimental group was higher than control group, the difference was statistically significant . After 1 week of treatment and 1 month of follow-up, VAS scores of the two groups were lower than before, and the experimental group was lower than the control group, the difference was statistically significant . The Constant-Murley shoulder score of the two groups was higher than before treatment, and the experimental group was higher than the control group, the difference was statistically significant . Scapular nerve contorts the parts on the anatomical location, a pain in the broad, compared with the traditional needle knife blind operation, ozone combined with ultrasound guided needle knife can hit the bull 's-eye, accurate to nerve conformity of parts, without injury and peripheral vascular nerve to cut, cause conformity of soft tissue release, dredge stripping method to release, to lift its state of nerve compression, Restore local blood circulation, promote inflammatory cells dissipation absorption, relieve the purpose of pain symptoms. Ultrasound-guided acupotomy combined with ozone can not only relieve pain, but also make up for the disease development caused by suprascapular nerve compression due to inadequate treatment.

Thus,the Ultrasound-guided acupotomy combined with ozone in the treatment of suprascapular nerve entrapment syndrome is prospective and advanced. Real-time ultrasound can make acupotomy and ozone direct to the lesion for treatment. Compared with traditional acupotomy and

local sealing, ultrasound guidance has the advantages of visualization and targeted therapy, and can make acupotomy and local injection more standardized, which is worthy of clinical application.

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20 cases of cubital tunnel syndrome treated by acupotomy

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[Abstract] Cubital tunnel syndrome is also called traumatic ulnar neuritis, late-onset ulnar neuritis, etc., is the ulnar nerve in the elbow away by the surrounding structures in the line in the ulnar nerve groove press-fitting, which in turn leads to the neuropathy, and a feeling of ulnar nerve dominate regional barriers, between thumb adductor muscle and bone atrophy, little finger flexion and abduction dysfunction as the main performance of clinical syndrom, see more at manual workers, More men than women. It is common clinically and has various treatment methods. The author used acupotomy to treat 20 patients with mild to moderate cubital tunnel syndrome, with good results.

[Key words]: cubital tunnel syndrome; acupotomy

1. Materials and methods

1.1 Subjects In this group, there were 20 patients with mild to moderate cubital tunnel syndrome, including 15 males and 5 females, aged 30-60 years, with an average age of 45 years. The course of the disease is as short as 2 months and as long as 5 years, with a history of chronic strain.

1.2 Diagnostic criteria^[1] Diagnosis was made based on patient history, clinical manifestations and neuroelectrophysiological data.

(1) It conforms to the diagnostic criteria of cubital tunnel syndrome in the third edition of Hand Surgery: ① In the early stage, people often feel semi-numbness and discomfort in the ulnar side of little finger and ring finger. Sometimes writing and chopsticks are not flexible. ② When the symptoms are aggravated, the strength of flexor carpi ulnar and flexor digitorum profundus is weakened, and the internal muscles of the hand atrophy, resulting in mild clawed hand deformity of the ring little finger. Froment sign is positive.

(2) It meets the diagnostic criteria of nerve electrophysiology: ① MCV of cubital ulnar nerve < 50m/s. ② the MCV of the ulnar nerve of the elbow was slower than that of the ulnar nerve of the lower elbow by more than 10m/s. A diagnosis can be made if either meets the criteria.

2. Treatment Position: client is prone with the affected elbow bent at 90° on the edge of bed. Body surface positioning: arcuate ligament, fixed point in the medial edge of the medial humerus epicondyle and olecranon, the medial edge of the medial humerus epicondyle and olecranon line, the selected point marked with marker, iodophor disinfection 3 times, spread sterile tissue. Anesthesia: local infiltration anesthesia was performed with 2% lidocaine. 2mL drugs were injected at each of the two treatment sites of the medial epicondyle of the humerus and the medial edge of the olecranon, but the midpoints of the connection between the medial edge of the olecranon and the medial edge of the medial humerus were not injected. Tool: I type 4 straight needle knife. Acupotomy operation: the first acupotomy was used to release the epicondyle point of the humerus, the cutting line was consistent with the shape direction of the ulnar nerve, and the acupotomy body was vertical to the skin. The acupotomy was carried out in strict accordance with

the four-step acupotomy procedure, and the acupotomy went through the skin, subcutaneous tissue and arcuate ligament to the bone surface, and then the acupotomy was carried out 3 times along the bone surface with a range of 4cm. The second acupotomy was used to release the medial edge of the olecranon of the ulna. The operation was the same as the first acupotomy to release the adhesion, scar and contracture of the starting and ending points of the arcuate ligament. The third acupotomy was inserted between the epicondyle of the humerus and the olecranon of the ulna. The knife edge line was parallel to the ulnar nerve, and the acupotomy body was perpendicular to the skin. The acupotomy was carried out in strict accordance with the 4-step needle procedure. The acupotomy passed through the skin, subcutaneous and arcuate ligament, and reached the elbow canal. Then, lay down the needle body and point the knife toward the arcuate ligament, dredge the knife 2-3 times along the direction of the nerve, and pay attention to avoid the nerve. After the operation, the acupotomy was pulled out, local fingerpress hemostasis was performed for 3min, and the acupotomy was disinfected and covered with infusion patch. Course of treatment: once a week, three times as a course.

Precautions: (1) Master the body surface positioning of the operation site, accurately identify the two points of the medial epicondyle of the humerus and the medial edge of the olecranon; (2) Keep the direction of incision line consistent with the direction of ulnar nerve; (3) The acupotomy operation should be carried out slowly. The acupotomy operation should be carried out on the bone surface, and the acupotomy operation should not be carried out away from the bone surface. Strictly in accordance with the above 3 points of attention, needle knife, it is difficult to encounter ulnar nerve, even touching the ulnar nerve, the patient will soon have a sense of hemp, the operator can adjust the direction of the edge line, avoid the ulnar nerve, which can be effectively release the arcuate ligament while avoiding injury ulnar nerve, to ensure the safety and effectiveness of needle knife surgery.

3. Observation of therapeutic effect

3.1 Efficacy evaluation criteria^[2] Cured: the symptoms and signs disappeared, and there was no recurrence after six months of follow-up. Significant effect: the symptoms and signs were significantly improved and alleviated, and the general life was not affected. Invalid: the symptoms and signs are not relieved, and the daily life is obviously affected.

3.2 Treatment Results In this group, 12 cases (60%) were cured. 7 cases (35%) had obvious effect. One case was invalid, accounting for 5%, the total effective rate was 95 %.

4. Discussion Cubital tunnel syndrome (CUBital tunnel syndrome) is a clinical syndrome of progressive damage to the ulnar nerve caused by compression at the elbow, second only to carpal tunnel syndrome. Common clinical manifestations are hypoesthesia in the distribution of ulnar nerve, atrophy and weakness of internal hand muscles, and "claw hand" deformity may occur in severe patients, resulting in severe hand dysfunction^[3]. According to clinical observation and statistics, the common compression points of the ulnar nerve at the elbow include Struthers ligament, Osborne's fascia, medial septum, flexor carpi ulnar and fascia, medial epcondyle of the humerus, etc. The causes of local nerve compression due to ectopic ossification, elbow synovitis and rheumatic diseases have also been found^[4]. Cubital tunnel syndrome is western medicine traditional surgical methods ulnar nerve front, mainly including subcutaneous front, muscle under the preconditions, resection of the condyle inside humerus, obvious effects of the operation, suitable for medium and

severe cubital tunnel syndrome, but large trauma, ulnar nerve is completely free of its local branch nerve damage probability is bigger, the late local feel numbness and discomfort symptoms, After anterior ulnar nerve, it is more likely to suffer discomfort caused by external stimulation and more surgical complications. At present, in-situ ulnar nerve release is widely used in the clinical treatment of cubital tunnel syndrome [5].

Compared with traditional surgical treatment, acupotomy treatment has smaller wounds and less trauma to the soft tissues around the elbow joint. Therefore, postoperative fixation of the elbow joint is unnecessary, which will not affect the normal life of patients, let alone cause elbow joint mobility disorders caused by long-term fixation of the elbow joint.

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Needknife with shock wave for gluteus medius myofasciitis

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Objective: To observe the clinical efficacy of needle knife combined with shock wave in the treatment of hip myofasciitis. **Methods:** The VAS score and JOA hip function score of 35 patients with middle hip myofasciitis treated with needle knife combined with shock wave before and after treatment were analyzed. **Results:** The clinical symptoms of the patients were significantly improved, the VAS score after treatment was lower than that before treatment, the JOA hip function score was significantly higher than that before treatment, and the differences had statistical significance ($P < 0.05$). **Conclusion:** Needle knife combined with shock wave in the treatment of hip myofasciitis has quick effect and good effect, which is worthy of clinical application.

Key words: hip myofasciitis; needle knife therapy; shock wave therapy;

Gluteus medius myofasciitis is a common chronic pain disease of the waist and hip in the clinic, to strain or feel the wind, cold and wet is more common. The clinical manifestations are mainly obvious hip pain, acid distension, low back pain and limited movement, aggravation after fatigue or radiation pain in the lower limbs of the affected side. Due to the lack of specific clinical signs, it is more similar to the symptoms of lumbar disc herniation, piriformis injury, sciatica and so on, and so the diagnosis is also easy to be confused. Clinically, drug treatment, massage therapy, acupuncture therapy, acupuncture and knife therapy, medium frequency pulse treatment instrument, TDP treatment instrument are mainly used to treat gluteus medius myofasciitis, but the curative effect is not ideal.

Objective

This study is mainly to explore the effect of needle knife with shock wave in the treatment of gluteus medius myofasciitis.

Materials and methods

All 35 patients with gluteus medius myofasciitis were outpatients from September 2020 and orthopedics Department of the First Affiliated Hospital of Heilongjiang University of Chinese Medicine in July 2021, 19 females and 16 males; oldest was 64 years old, youngest was 35 years old, average of 48.74 years old. The disease course ranged from 6 days to 109 months. All were unilateral gluteus mediomofasciitis, including 14 patients on the left side and 21 patients on the right side.

The treatment group was treated with a needle knife and a shock wave treatment. In the prone position, the femoral greater trochanter is point A, the posterior superior iliac spine is point B, the inferior iliac crest is point C, and the three-point line of ABC is the projection of the gluteal medius body surface. Select 2~3 shock pain points, apply the hip coupling agent, and focus the shock wave on the shock pain points, the speed is medium speed, the frequency is 10~15HZ, and the number of shocks is 2500~3000 times. Treatment was treated once in 1 week for three times. Needknife treatment can be performed after shock wave treatment. The patient took the healthy limb in the lower side decubitus position, flexion of the healthy lower limb, adductor in the affected thigh and

slightly flexion the hip 30. The surgeon looked for 2 to 3 pain points and marked them. In the surgical area, iodine disinfection, sterile napkins, marking points for local infiltration anesthesia, vertical injection, needle blade direction should be parallel to the muscle fiber direction as far as possible. Four-step needle injection to reach the bone surface after the needle, with vertical cutting, pendulum, push the needle. Compress the needle eye for 3~5min, and the band-aid covers the needle eye to prevent infection. Treatment was treated once in 1 week for three times.

Results and discussion

In 35 patients, the VAS score was decreased compared with before treatment, and the JOA hip function score was significantly higher compared with before treatment, comparative differences were statistically significant($P < 0.05$). See Table 1.

The anatomical upper upper gluteus medius is subcutaneous, the outer lower part is below the gluteus, the lateral fascia, the medial gluteus and piriformis, and the lower gluteus, ending at the greater trochanter of the femur. The gluteus medius is the hip abductor and also an important stable muscle, involved in hip rotation and posterior extension. The gluteus medius plays an important role in stabilizing the pelvis while standing, walking, or running, as well as in daily bending, stretching, squatting, and sitting and waiting. Therefore, for a long time by traction stimulation and repeated friction, resulting in increased muscle tissue tension, contracture and adhesion. Along with the continuous daily exercise, frequent stimulation of the injury site, make the local tissue congestion and swelling, and eventually cause the disease.

According to the patient's body size, the depth and location of the shock pain point, the appropriate needle knife type is selected to direct the treatment of the shock pain point. According to the clinical experience of the operator: during the needle knife treatment, if the patient's strong sense of acid distension and the pain inducing mode of the induced shock pain point, the treatment target of the needle knife is accurate. The mechanism of acupuncture knife treatment of gluteus medius myofasciitis is to cut off the closed loop formation of pain points and reinduce muscle tissue regeneration. In addition, acupuncture knife also has the effect of "needle", which has the effect of "analgesia and anti-inflammatory".

This paper through 35 cases of needle knife with shock wave treatment of gluteus medius myofasciitis, treatment points in the gluteus medius muscle fascial shock pain points, some patients 2 treatment points, some patients 3 treatment points, after treatment, VAS score and JOA hip function score showed that all patients have significantly improved clinical symptoms.

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Accupotomology buttock epithelial nerve viega profi-press syndrome

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Abstract:

Superior gluteal nerve entrapment syndrome is caused by lumbar and hip pain caused by compression and traction of the gluteal epithelium, which can radiate to the posterolateral thigh, but not beyond the plane of the knee joint, mainly manual labourers. It is more common in middle-aged and elderly obese women. Its treatment with needle knife, acupuncture, massage manipulation, closure and other methods of single or combined use of conservative treatment, can improve the symptoms of waist and leg pain. Among them, needle knife has the advantages of remarkable curative effect, short course of treatment, simple operation, less trauma and so on.

Key words: superior gluteal nerve entrapment syndrome needle knife

Superior gluteal nerve entrapment syndrome, is a disease damaged by compression and traction of the gluteal epithelium, which is mainly characterized by diffuse persistent tingling pain in the waist and buttocks, especially in the buttocks. Can radiate to the posterolateral thigh, most of which do not exceed the plane of the knee joint. Feng Tianyou^[1] research believes that the incidence of superior gluteal nerve entrapment syndrome is mainly manual workers, the incidence rate is about 1.98%, more common in middle-aged and elderly obese women. At present, the main clinical treatment is conservative treatment, including needle knife, acupuncture, massage manipulation and blocking treatment.

1. Objective

At present, there are many treatment methods for this disease, but they all have different limitations. Therefore, the search for a treatment with good curative effect, simple operation, less trauma and low cost has become the key direction of clinical treatment of this disease. With a view to clinical promotion, for more patients with superior gluteal nerve entrapment syndrome to provide the best treatment.

2. Materials and methods

Randomly collected several clinical observation literatures about the common treatment methods of superior gluteal nerve entrapment syndrome in Chinese and western medicine, including needle knife, acupuncture, massage and blocking. Comprehensively compared the curative effect, the simplicity of operation, the size and cost of trauma to patients, and selected a relatively better treatment plan.

3. Results

Liu Haiyong^[2] treated superior gluteal nerve entrapment syndrome by acupuncture at Ashi acupoint. Among the 102 patients observed, the total effective rate is 99.0%. Ma Zhiming^[3] used sitting muscle relaxing manipulation to treat superior gluteal nerve entrapment syndrome. 54 patients were observed, with a total effective rate of 96%. Liu Xinming et al^[4] used blocking injection therapy to treat superior gluteal nerve entrapment syndrome. 53 patients were treated with 2% lidocaine 5ml, 0.9% normal saline 10ml, triamcinolone acetonide 40mg/ml, B122mg/4ml, lysine aspirin 0.58/2ml

mixture for pain point nerve block, once every 5-7 days, 3 times a course of treatment. Among them, the total effective rate was 99%. Song Min^[5] used closure and manipulation to treat superior gluteal nerve entrapment syndrome. Among the 42 patients, the total cure rate is 100%. Chen Xinli^[6] used needle knife to treat superior gluteal nerve entrapment syndrome, focusing on releasing the pain point cord. Among the 79 patients, the total effective rate was 95.9%. Zhong Kanghua et al.^[7] 82 cases of superior gluteal nerve entrapment syndrome were treated with pain point small needle knife release and massage with a total effective rate of 100%. The treatments of this disease can improve the symptoms of waist and leg pain. On the whole, the combined treatment is better than the single treatment. Due to the closure treatment, the short-term effect is obvious, the long-term is not good, therefore, the small needle knife treatment has an advantage.

4. Discussion

The superior gluteal nerve belongs to the sensory nerve, which is composed of the cutaneous branch of the posterolateral branch of the spinal nerve between the T12-L3 segments, mainly walking in the soft tissue. After the nerve sends out from the intervertebral foramen, it passes through the back of the transverse process of the vertebral body, walks from the sacral spine muscle into the deep fascia, from the deep fascia out of the superficial subcutaneous fascia, and finally from the bony fibrous tube of the lumbar dorsal fascia into the buttocks, which is called the "gluteal point"^[8]. When fatigue, trauma and feeling cold cause long-term muscle tension or spasm, some nerves or fiber bundles above the iliac crest are injured by relative displacement between the fascia and fascia, or due to fat incarceration and oppression. it can lead to congestion and edema of the nerve and its surrounding soft tissue, and degenerative reactions can occur in the axons and myelin sheath of the nerve for a long time, resulting in waist and hip pain^[9]. Superior gluteal nerve entrapment syndrome belongs to the category of "muscle injury" and "arthralgia syndrome" in traditional Chinese medicine. Most of the patients feel cold and dampness, injury, loss of work and rest, incorrect posture or kidney deficiency for a long time, resulting in poor meridians or loss of nourishment in the waist and buttocks, resulting in pain. That is, "if there is no communication, there is pain" and "if there is no tolerance, there is communication"^[10]. Among them, the mechanism of needle knife in the treatment of superior gluteal nerve entrapment syndrome is to release muscles, peel off adhesions, dredge meridians and collaterals, and reconcile qi and blood. Through the local stimulation of needle knife, promote blood circulation, can accelerate metabolism, but also let the lesion site quickly get the blood supply, so that the symptoms are relieved.

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Clinical study of needle knife and tuina on the treatment of radiculopathy cervical spondylosis

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Abstract

Cervical spondylosis is a degenerative lesion of the cervical spine, of which radiculopathy is the most common, which can be accompanied by typical nerve root symptoms such as cervical pain, neck and back stiffness, and different degrees of arm numbness, which seriously affect the daily work and life of patients [1-2]. At present, the clinical treatment of the disease is mainly conservative treatment, and nonsteroidal anti-inflammatory drugs are commonly used treatment drugs, which can reduce the inflammatory response around the lesion and reduce the production of analgesic substances to alleviate clinical symptoms. However, conventional pharmacotherapy is limited, and cervical spine function is poorly restored in some patients [3-4]. Chinese medicine classifies cervical radicular spondylosis into the category of "paralysis", believing that its onset is closely related to the lack of meridians and stagnation of qi and blood, and clinical treatment needs to pay attention to activating blood to reduce stasis and dredge meridians. Small needle knives and techniques are traditional external treatment methods of Traditional Chinese Medicine, both of which are of great significance in activating blood and reducing stasis, which can improve local blood circulation, enhance cervical spine function, reduce pain in the cervical spine, promote disease recovery, and improve quality of life.

Key words: Cervical radiculopathy; Small needle knives; technique

Cervical radiculopathy can cause neck and shoulder pain and upper extremity radiation pain, numbness, fatigue and other symptoms, adversely affecting the daily life and work of patients. In recent years, small needle knife therapy has been widely used in the treatment of cervical spondylosis and has achieved good results. During treatment, the needle is selected from the obvious pain points of the neck, which can effectively release the adhesion of the lesion tissue, reduce the mechanical compression of the nerve roots, relieve the spasm of the surrounding muscles and ligaments, thereby improving the surrounding microcirculation, correcting the ischemia and hypoxia of the cervical spine, promoting the absorption of inflammatory substances, and accelerating the repair of damaged tissues. After the small needle knife relieves the pain point, it can also block the vicious circle between muscle tension and pain, and play a good analgesic effect. The technique is a traditional external treatment method of traditional Chinese medicine, which has a variety of effects such as dredging meridians, activating blood and dissolving stasis, and the first two points and one side reduction can restore the original structure of the cervical spine, correct the partial spinous process, maintain the balance between the joints of the cervical spine, thereby relieving nerve root compression and accelerating the biomechanical recovery of the cervical spine. At the same time, cervical traction can improve cervical curvature, restore cervical spine sequence, and relieve spasm of surrounding muscles, helping to reset the nucleus pulposus and fibrous rings of the extrusion to alleviate the pain in the neck. Then massage shoulder points, water gutter points,

wind pool points, etc., with the effect of relieving muscles and vitality, aphrodisiacs, clearing heat and opening the trick, helping to improve neck stiffness and eliminate shoulder soreness. In addition, manual pressing on the neck and affected limbs can relax the surrounding muscle tissue, loosen soft tissue adhesions, and improve local blood flow, accelerate the absorption of pain-causing substances, alleviate clinical symptoms, and promote the recovery of cervical spine activity.

1.Objective

Currently, there are many treatments for this disease, but they all have different limitations. Therefore, finding a treatment method with good efficacy, simple operation, less trauma and low cost has become the key direction of clinical treatment of this disease. Focus on clinical promotion, to provide the best treatment plan for more patients with radiculopathy cervical spondylosis.

2.Materials and methods

2.1100 cases of CSR patients admitted to our hospital were randomly selected.

2.2The number table method is divided into two groups of 50 examples each.

There were 28 males and 22 females in the control group Example; Age 29 to 58 years old, average (41.56±4.69) years old; Physical index (BMI) : 19~27 kg/m², the average (24.18±1.23) kg/m²;Course 1 to12 months, average (6.58±1.13) months. Observation group 27 males and females23 cases; Age 28 to 57 years, average (41.53±4.65)years; BMI: 19~27kg/m², the average (24.16±1.21) kg/m²;Duration of illness 1 to 12 months, average(6.62±1.15) months; The two sets of general data were compared, and the difference was not statisticalMeaning (P>0.05). Comparable.

3.Results and discussion

Through clinical trials,it shows that the effect of small needle knife combined with manual manipulation in the treatment of radiculocaria cervical spondylosis is remarkable, which can improve the clinical efficacy of patients, reduce VAS score, reduce pain in the body, promote the recovery of cervical spine function, and improve the quality of life. Huang Yongqiang^[5] the use of small needle knife combined with "Wang's" chiropractic hand to treat radiculopathy cervical spondylosis, the observation group of the clinical bed efficacy rate of 95.45%, higher than the control group of 77.27%, after treatment VAS score of (2.27±0.53), lower than the (3.16±0.68) score of the contrast group, suggesting that the small needle knife combination can enhance the treatment effect of radiculomotorhea cervical spondylosis, reduce neck pain, and the results of this study are basically consistent with the results of this study.

In summary, small needle knife with manual treatment can improve the clinical efficacy of patients with radiculopathy cervical spondylosis, enhance cervical spine function, reduce pain in cervical spine, promote disease recovery, and improve quality of life, which is worth further promotion.

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Treatment of Cervical Spondylotic Radiculopathy with Acupotomy and Put Technique Combining Rotating Combination

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Abstract:

Objective: By observing the clinic effect of the small needle knife combined with lifting, traction, and rotating bone setting manipulation in the treatment of cervical spondylotic radiculopathy, we evaluate the improvement of various clinical symptoms and signs before and after treatment. Then this paper evaluates the safety and effectiveness of this comprehensive therapy in clinical application and provides a scientific basis for the clinical application of the small needle knife technique in the treatment of cervical spondylotic radiculopathy. **Methods:** A total of 30 outpatients with cervical spondylotic radiculopathy were collected from August 2020 to August 2021. They were treated with acupotomy combined with lifting and pulling rotation bone-setting, and their pain and function improvement was observed before and after treatment. **Result:** The effective rate is 87%. **Conclusion:** The minimally invasive needle-scalpel therapy is effective in the treatment of cervical spondylotic radiculopathy, which is worthy of clinical application.

Keywords: acupotomy; cervical spondylosis; the combination of traditional Chinese medicine and western medicine

Cervical spondylosis is a chronic cervical spine disease that often occurs in people who work at desks for a long time, also known as a cervical syndrome or cervical shoulder syndrome^[1]. Its pathological changes are caused by degenerative diseases of the human body or neck. This disease is closely related to age, and often occurs among middle-aged people aged 40 to 60^[2-3]. The prevalence rate of males is higher than that of females. Cervical spondylotic radiculopathy is one of the main manifestations of cervical spondylosis in the clinic, mainly due to degeneration and hyperosteo-geny of the cervical intervertebral disc in cervical lesions, with sensory, motor, and reflex disorders in the lesion segments as the main manifestations. Clinically, there are many treatments for cervical spondylotic radiculopathy, including acupuncture, massage, medication, minimally invasive treatment, and surgical treatment^[4].

Materials and methods

(1) Needle knife operation Position: The patient takes the prone position, and a soft pillow is placed in front of the neck to make the soft tissue behind the neck tense and easy to operate. Fixed point: ① The spinous process is 1.5 — 2cm apart, and the cervical tenderness point behind the articular process joint or the induration and cord; ② The upper angle of the scapula, at the levator scapulae point; ③ The inner edge of the scapula, at the insertion point of rhomboid muscle; ④ There is tenderness or induration at the posterior midline nuchal ligament of the neck or the apex of a cervical spinous process.

Disinfection: Routine preoperative disinfection preparation, disinfection with freshly prepared iodophor cotton balls for 3 times. The performer wears a mask and surgical gloves, spreads a sterile hole towel and prepares sterile gauze to stop bleeding.

Anesthesia: In principle, neck anesthesia is not advocated, but according to the patient's tolerance, for patients with sensitive pain, 0.25% lidocaine is used for local anesthesia, and the dosage is about 0.3 ml each time.

Needle knife operation^[5]: Select a medical marker to mark the positioning point, sterilize it with iodophor for 3 times, spread the hole towel and make the operation site in the center of the hole towel, with the point of the needle perpendicular to the skin, the line of the knife edge parallel to the long axis of the posterior midline of the neck, and enter the needle at an angle of about 70 with the posterior coronal plane, then stab it downward at the midline ligament of the posterior neck, and enter the needle at an angle of about 45 with the horizontal plane of the neck, according to the four-step operation rules of the needle knife. After the needle reaches the bone surface of the focus point, dredge and peel it vertically layer by layer, and swing the needle handle transversely. If there is induration or cord, cut the needle for 3-5 times according to the size of the focus, and then take out the needle. Press the needle eye until there is no bleeding. After acupuncture, compress sterile gauze for 24 hours, and do not touch water within 3 days to prevent infection.

(2) Manipulation therapy: the patient is in the supine position, the operator puts his hands behind his neck, and rubs with 2~5 fingers on the tense part of his neck for several minutes. After the soft tissue is completely relaxed, the technique of supine lifting, pulling and rotating bone setting is performed: the operator holds the head with one hand behind the pillow, pinches the mastoids on both sides of the temporal bone with his thumb and forefinger respectively, so that the patient's neck bends forward by about 25, and the other palm presses on the patient's cheek and mandibular angle, so that the cervical vertebra rotates to one side to the maximum extent under traction, and the cervical vertebra suddenly rotates again by about 10-15 along the sagittal column of the spine with both hands. At this time, several loud and crisp sounds can often be heard. Then, rotate it once more^[6].

Results and discussion

Cervical spondylosis is a group of syndromes caused by an imbalance of the internal and external spinal column, stimulation/compression of the cervical nerve root, vertebral artery, spinal cord, and sympathetic nerve^[7].

Knife medicine believes that the most fundamental pathological mechanism of tissue injury is dynamic imbalance^[8]. Knife-acupuncture is used to treat cervical spondylosis by loosening the starting and stopping points of cervical soft tissue lesions, the ligaments of the articular process of cervical spondylosis and the soft tissue of tubercle behind the transverse process, peeling off adhesion, cutting scar, correcting contracture, dredging blockage, improving local microenvironment, improving blood circulation state of injured parts, correcting ischemia and hypoxia of cervical tissues, improving local long-term spasm state, and restoring cervical soft tissues. Using acupotome to release the adhesion, paralysis marks and contracture of high-stress points of soft tissues can eliminate the stress imbalance, cooperate with a manipulative reduction to correct the misplaced neck joints and adjust the mechanical balance of cervical vertebrae, which can effectively eliminate symptoms and restore the soft tissue function of the neck^[9].

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Clinical observation on 89 cases of third lumbar transverse process syndrome treated with needle knife combined with ozone

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Abstract

Objective: To observe the clinical efficacy of needle knife combined with ozone in the treatment of the third lumbar transverse process syndrome. **Methods:** Patients with the third lumbar transverse process syndrome were diagnosed and treated in the outpatient department of orthopedics and traumatology of the First Affiliated Hospital of Heilongjiang University of traditional Chinese medicine from early September 2020 to March 2021. There were 89 patients, including 48 males and 41 females; The average age was (41.26 ± 11.89) years old; The average course of disease was (2.11 ± 1.17) months. After screening according to the inclusion criteria, observe the changes of clinical symptoms and signs before and after treatment, observe the curative effect, and use VAS score and JOA to evaluate lumbar symptoms to compare the scores before and after treatment. **Results:** all 89 patients were followed up after 6 months. 73 cases were cured, 14 cases were significantly effective, 1 case was effective and 1 case was ineffective. **Conclusion:** needle knife combined with ozone in the treatment of lumbar three transverse process syndrome can overcome the shortcomings of long treatment period of external use of drugs, and can also avoid the recurrence of local closure. It has the advantages of small trauma, stable and reliable curative effect, simple and safe operation, and is worthy of clinical promotion.

Key words: Third lumbar transverse process syndrome Needle knife Ozone

At present, the third lumbar transverse process syndrome is a relatively common disease in clinic. Its causes are mostly chronic strain, such as long-term bending work and labor, acute lumbar sprain has not been effectively treated, chronic and intermittent acid swelling, pain and fatigue in the waist, rigidity in the waist, and inability to sit and stand for a long time^[1].

Data and Method

Patients with the third lumbar transverse process syndrome were selected from the outpatient department of orthopedics and traumatology of the First Affiliated Hospital of Heilongjiang University of traditional Chinese medicine from early September 2020 to March 2021. There were 89 patients with lumbar three transverse process syndrome treated in outpatient department, including 48 males and 41 females; The average age was (41.26 ± 11.89) years old; The average course of disease was (2.11 ± 1.17) months.

Give needle knife combined with ozone (O₃) injection treatment, and ozone treatment after 10 minutes of needle knife operation.

Results and discussion

The transverse process of the third lumbar vertebra is longer than that of other lumbar vertebrae, and its end bears relatively large tensile stress of muscle fascia^[2]. Therefore, when performing flexion and extension activities at the waist here, it is easy to cause friction, extrusion, and traction damage between the tip of the three transverse processes of the waist and the surrounding soft tissue,

resulting in capillary hemorrhage, muscle fiber breakage, and adhesion due to mechanization, thus causing the dynamic balance imbalance of the functional activities of the lumbar back, resulting in the protective spasmodic pain of the fascia of the lumbar back and spinal muscles^[3]. Modern medicine believes that the third lumbar spine is the center of the lumbar spine, which is the most prominent place of lumbar physiological lordosis, and also the hub of lumbar flexion, extension, left and right lateral bending and left and right rotation activities; The transverse process on both sides is the longest and bears the greatest force. There are lumbar muscles, ligaments and other tissues attached to the top. The movement anywhere in the waist can make the top of the transverse process of the third lumbar vertebra bear repeated traction and grinding, so the probability of injury is large, and clinical cases are common^[4].

This disease is mostly caused by kidney qi deficiency, qi stagnation and blood stasis, cold and dampness invasion and other causes . Needle knife therapy can take effective relaxation according to the causes of the disease. At the same time, it has the mechanism of traditional medical needle acupuncture therapy, so as to achieve the therapeutic purpose of dredging the meridians, so as to "relieve pain" and "relieve pain contracture". Before needle knife treatment, we must take X-rays of the lumbar spine in the anterior and lateral positions to understand the specific location of the L3 transverse process, whether there is abnormal development, and exclude other diseases. When entering the needle knife, press your finger on the outer end of L3 transverse process to assist in positioning. The knife tip moves up and down slowly to explore the needle entry, so as to avoid unnecessary damage. Needle knife treatment does not cut the skin and tissue, and the closed minimally invasive surgery is performed to loosen it.

Needle knife surgery is to directly stab the lesion of the body through fixed point, positioning, orientation and a certain approach under non direct vision, and to loosen the adhesion, restore the mechanical balance and eliminate the symptoms by cutting, stripping and shoveling the lesion. In a word, needle knife combined with ozone in the treatment of lumbar three transverse process syndrome can overcome the shortcomings of long treatment period of external use of drugs, and can also avoid the recurrence of local closure. It has the advantages of small trauma, stable and reliable curative effect, simple and safe operation, and is worthy of clinical promotion.

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Needle-knife+block therapy for acute gouty arthritis

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Abstract:

Objective To explore the clinical application value of needle-knife plus block in the treatment of acute gouty arthritis. **Methods** 30 cases of acute gouty arthritis were retrospectively summarized. **Results** Twenty-eight cases were cured at one time, local swelling disappeared, and joint function was normal. The joint functions of two patients recovered to normal after two times of treatment. The total effective rate reaches 100%. **Conclusion** Acupuncture-knife+block therapy for acute gouty arthritis is safe and effective, with high patient satisfaction, and worthy of clinical promotion.

Key words: needle-knife therapy; Block therapy; Acute; gouty arthritis

In recent years, the incidence of gout increases year by year, which is related to the metabolic disorder of uric acid. Typical acute gouty arthritis is mostly monoarthritis, and the invasion of the first toe joint is the most common(95%), followed by the ankle, knee, elbow, wrist, hand and other joints of the foot .

Materials and methods

1.1 diagnostic criteria

① Acute arthritis occurs more than once, and the peak of attack is reached within 1 d. ② Acute arthritis is limited to individual joints, and the diseased joints are dark red^[1]. ③ Hyperuricemia. ④ Asymmetric joint swelling and pain. (5) attack can stop on its own. Having more than three of the above conditions can confirm the diagnosis.

1.2 General information

There were 29 males and 1 female in this group, and they were aged from 45 to 63 years old, with an average of 55 years old. All the 30 patients presented with swelling, burning sensation and refusal to press at the first metatarsophalangeal joint. The above diagnostic criteria were met.

1.3 therapeutic method

In the supine position, the patient sought the fixed point where the fluctuation was most obvious at the inflamed part of the affected joint. The mark was made with a marker pen, and the skin was routinely sterilized^[2]. Two to three mL of blocking solution (1% lidocaine 5 mL and dexamethasone 5 mg) was injected from the mark. The needle-knife was inserted at the mark, and it reached to the bone surface. The joint capsule was broken through to the joint space. The joint capsule was cut and peeled open. The results showed that the yellow effusion with white urate crystal secretion flowed out from the eye of the needle through the needle-knife. The active joint expels fluid more quickly^[3]. When no effusion flows out, the small-diameter vacuum negative pressure suction device is used for suction, and about 5–10 mL of mixed liquid such as blood, tissue fluid and effusion can be sucked out. If it was not cured, it was done once after 5 d.

Results

Among the 28 cases cured at one time, the local swelling disappeared and the joint function was normal. The joint functions of two patients recovered to normal after two times of treatment. The total effective rate reaches 100%.

Discussion

Gout is a disease in which urate is deposited in articular capsule, bursa, cartilage, bone, kidney, subcutaneous and other tissues to cause corresponding lesion and inflammatory reaction^[4]. It is a hereditary disease of purine metabolism disorder, characterized by the increase of urate in blood. Alcohol consumption, drugs and trauma were the inducing factors. It is mainly distributed in men aged 30–50 years old. The onset of typical gouty arthritis is sudden, sometimes even explosive, and it usually occurs at night. Suddenly, joint swelling and severe pain occur. The affected joints and the surrounding soft tissues are obviously red, hot and swollen. The severe pain is unbearable, and the joint motion is limited. Gouty arthritis is characterized by hyperuricemia and sodium urate crystalloidy of connective tissue structures, particularly cartilage synovial membrane. The oxidative decomposition of nucleic acids (DNA and RNA) produces purines, which are oxidized in the liver to (2,6,8-trioxopurine) called uric acid. Accounting for about 80% of the total uric acid in the body, it is called endogenous uric acid^[5]. The other part is broken down from nucleotides in food. It accounts for 20% of the total uric acid in the body and is called exogenous uric acid. Therefore, endogenous metabolic disorder of COVID-19 is more important than exogenous factors, and it has familial tendency. The genetic model is still unclear. In gout, the sodium urate crystals released by the synovial tissues and articular cartilage are swallowed by the white blood cells in the joint fluid, and the white blood cells are destroyed to release protease and inflammatory factors into the synovial fluid. The enzyme inflammatory factors increase the white blood cells in the joint fluid, so that more white blood cells that devour urate crystals burst in succession to release enzyme and inflammatory components, forming a vicious circle, further leading to acute synovitis and articular cartilage destruction. Different-sized granulomas of crystals formed around urate crystals. Needle-knife penetrating stripping synovial bursa^[6]. It causes the synovial fluid to overflow, promotes the removal of urate crystals precipitated in the bursa, lowers the pressure in the bursa, relieves the pressure on nerve endings, recovers the microcirculation, and causes the spasmodic and ischemic pain to disappear.

Needle knife treatment of acute gouty arthritis is a new method, not only can quickly control the pain, eliminate swelling, restore joint function, reduce blood uric acid, avoid drug-induced gastrointestinal reactions, and is effective for the prevention of the formation of advanced osteoarthritis, worthy of promotion.

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Clinical observation on treatment of neck shoulder syndrome with Zhengji Tiao Qu combined with needle knife

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Abstract:

To observe the clinical efficacy of Zhengji tiaoku combined with small needle knife in the treatment of neck shoulder syndrome. 90 patients with neck shoulder syndrome were randomly divided into small needle knife group, Zhengqu group and observation group, 30 cases in each group. The Needle knife group was treated with small needle knife, the Zhengqu group was treated with Zhengji tiaoku, and the observation group was treated with small needle knife combined with Zhengji tiaoku; One week is a course of treatment, a total of three courses of treatment. The changes of VAS and NDI scores before and after treatment were observed, and the clinical efficacy and safety were evaluated. after 3 weeks of treatment, the VAS score of the observation group was (1.58±0.86), NDI index score (5.93±3.62) and the total effective rate (93.33%) was better than that of the needle knife group (2.43±1.11), (9.48±5.87), (86.67%) and Zhengqu group (3.05±1.07), (9.04±5.81), (83.33%), the difference was statistically significant (P < 0.05). Zheng Ji Tiao Qu method combined with small needle knife has good clinical efficacy in the treatment of NSS with low price, simple operation and safety, which is worthy of clinical promotion.

Key words: acupotomy, Zhengji tiaoku, clinical, neck shoulder syndrome.

Neck shoulder syndrome (NSS) is caused by degenerative diseases such as passive change of cervical physiological curvature, hyperosteogeny, intervertebral disc herniation, vertebral facet joint disorder and so on; Thus, the nerve is compressed, resulting in congestion and edema of soft tissue, causing aseptic inflammation, secondary neck and shoulder local pain, numbness, and clinical syndrome with limited activity^[1]. With the change of current life and work style, the disease is getting younger, which seriously affects the quality of life and work of patients^[2]. The clinical treatment of the disease includes acupuncture, massage, oral medicine, external medicine, physiotherapy, closed therapy and other methods. The above treatment methods are conservative, and the short-term and long-term effects cannot be achieved at the same time^[3]. The purpose of this article is to explore the clinical efficacy of Zhengji Tiaojiao therapy combined with needle knife in the treatment of NSS, in order to obtain a better clinical treatment plan.

1.Objective

It's to observe the clinical efficacy of Zhengji tiaoku combined with small needle knife in the treatment of neck shoulder syndrome.

2.Materials and methods

90 patients with neck shoulder syndrome were randomly divided into small needle knife group, Zhengqu group and observation group, 30 cases in each group. The Needle knife group was treated with small needle knife, the Zhengqu group was treated with Zhengji tiaoku, and the observation

group was treated with small needle knife combined with Zhengji tiaoqu; One week is a course of treatment, a total of three courses of treatment. The changes of VAS and NDI scores before and after treatment were observed, and the clinical efficacy and safety were evaluated.

3.Results and Discussion

after 3 weeks of treatment, the VAS^[4]score of the observation group was (1.58±0.86), NDI^[5]index score (5.93±3.62) and the total effective rate (93.33%) was better than that of the needle knife group (2.43±1.11)、(9.48±5.87)、(86.67%) and Zhengqu group (3.05±1.07)、(9.04±5.81)、(83.33%), the difference was statistically significant (P < 0.05).

In this study, spine flexion combined with needle knife was used to treat neck shoulder syndrome. The VAS score and NDI index score of patients in the observation group after 3 courses of treatment were significantly lower than those before treatment, and the effective rate was 93.33%, which was better than that of the control group (p<0.01), and there was no obvious recurrence or adverse reactions in patients, indicating that spine flexion combined with needle knife in the treatment of neck shoulder syndrome can significantly alleviate symptoms^[6], combine bow and string adjustment, and give consideration to dynamic balance and static balance, Not only the initial effect is remarkable, but also the long-term effect is very ideal.

However, there are still some deficiencies in this study, such as small sample size, lack of more direct and objective observation indicators, and under the guidance of the overall concept of the spine^[7], the mechanical relationship between neck and shoulder diseases and chest, lumbar, sacral and pelvis is worthy of further study

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Clinical review of acupuncture-knife release combined with chiropractic fine-tuning manipulation in the treatment of neck and shoulder syndrome

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[Abstract] Objective: To retrospectively analyze the clinical effect of acupotomy release combined with chiropractic fine-tuning manipulation in the treatment of neck and shoulder syndrome. Methods: 64 cases of patients with neck and shoulder syndrome treated with acupuncture-knife release combined with chiropractic fine-tuning manipulation were followed up and analyzed, and the numerical rating score (NRS) was used as the observation index. Results: Comparison of NRS scores before and after treatment: the pain was significantly reduced, and the difference was statistically significant ($p < 0.05$). Conclusion: Acupuncture-knife release combined with chiropractic fine-tuning manipulation can effectively improve blood circulation, accelerate the absorption of inflammatory factors, relieve neck pain and promote the recovery of neck function, so as to achieve the purpose of treatment.

[Key words] acupotomy; chiropractic fine-tuning; neck and shoulder syndrome

Neck and shoulder syndrome refers to a series of clinical manifestations such as soreness, weakness, pain in the neck, shoulders or to the elbows, as well as corresponding joint dysfunction, soft tissue damage, etc. The lesions of the soft tissue in the upper part of the body can compress the cervical spinal nerve, which leads to the spasm and contracture of the shoulder-related muscles it innervates, and the shoulder joint syndrome is caused [1]. The disease is more common in middle-aged and elderly people, and the incidence rate is higher in women. Because there is no effective treatment, it is one of the common clinically refractory diseases [2]. Traditional Chinese medicine treatment of neck and shoulder syndrome mostly adopts traditional Chinese medicine oral administration, acupuncture, massage, thread embedding, and prickling. Modern medicine mainly focuses on symptomatic treatment in the treatment of neck and shoulder syndrome, including drug therapy, traction, physiotherapy, and sealing [3]. From July 2020 to July 2021, 64 patients with cervical radiculopathy treated with acupotomy release combined with chiropractic reduction manipulation were retrospectively analyzed. The reports are as follows:

1 Clinical data

1.1 General information

Among the research subjects, there were 30 males and 22 females: the youngest was 18 years old, the oldest was 50 years old, the average age was 34.8 years old, and the course of disease was 5.1 months. Its main clinical manifestations include pain, soreness, fatigue, and dysfunction in the muscles and tendons of the neck, shoulders, and elbows.

2 methods

2.1 Treatment methods

Chiropractic fine-tuning method: Mainly based on the general routine of the head and neck, first use the rolling method to relax the muscles of the neck, shoulders and back, and then use the pushing

method, kneading method, and pinching method to alternately treat the neck, shoulders, and back, and repeat each method. 3-5 times, and then use the neck lift method, the patient is in an upright sitting position, the surgeon stands on the healthy side, the thumb of one hand presses the pain point of the lesion, the tiger's mouth and four fingers are placed on the opposite side of the neck, hold the operation neck, and use the other hand. Hold the patient's head with one upper limb and ask the patient to hold the chest on the pillow, tilt the head slightly forward, and suddenly lift it upwards with force. The patient immediately felt clear head and eyesight, and then performed pillow-relief manipulation and neck-shaking manipulation, placing one hand on the patient's headrest, the other hand supporting the mandible, and pressing both hands upward, followed by stretching back the neck, and then using After 3-5 times of head wrapping activities, do double upper limb massage with push, hold, kneading, pinching, shaking points, etc., and then put the pillow. Fu, Dazhui, Jianjing, Tianzong, Quchi, Waiguan, Hegu, Neiguan, Shenmen, etc., and finally relax the upper limbs by kneading and shaking.

Needle-knife release: "Take pain as the sting" in needle-knife release, select the point where the tenderness is obvious or touch the cord as the operation point, mark it with gentian violet, and apply 2% towel after routine skin disinfection. Lidocaine-enhanced Songlong local anesthesia, 1ml per acupoint, the operator wears sterile gloves, selects a small needle knife of size 3, and quickly penetrates the subcutaneous to reach the application anatomical position, and searches for sensitive painful nodules at the corresponding pain points. Horizontal stripping method, incision stripping method and vertical stripping, dredging stripping three separation techniques^[4], the operation is completed. Sterilize the incision of the needle, seal it with a Bondi Band-Aid and pressurize it for 5 minutes to prevent tissue oozing. The doctor instructed the patient to keep the wound from water for 2 days, and perform the operation once a week, and 3 times as a course of treatment.

3 Efficacy and results

There were 64 patients in total, of which 34 were cured, 30 were improved, and 0 were ineffective

4 Discussion

In addition, the following points should be paid attention to in the treatment of neck and shoulder syndrome with acupotomy release combined with chiropractic fine-tuning manipulation: 1. Clear diagnosis and strict screening of indications; 2. Strict aseptic operation is required; 3. Strict physical examination combined with careful film reading, accurate positioning, and clear release levels and locations; 4. It is necessary to cooperate with chiropractic fine-tuning techniques to consolidate the curative effect; 5. Guide patients to perform functional exercises.

To sum up, the use of needle knife release combined with chiropractic fine-tuning manipulation in the treatment of patients with neck and shoulder syndrome is effective and can effectively relieve the clinical symptoms of patients. It has the advantages of simple operation, quick effect and good effect, and it is worthy of clinical promotion. application.

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Traditional Sports and health care of ethnic Minorities living in Heilongjiang Province

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Abstract: With the advent of the era of great health, physical and mental health and emotional cultivation have become more and more important directions of people's attention. In the long life of production and struggle, the minorities in Heilongjiang province have gradually formed rich and colorful traditional national sports. Ethnic minority sports are suitable for the broad masses of the people and easy to operate. This paper analyzes the health care function of all nationalities in Heilongjiang province by means of literature and logical analysis, and expounds the great significance of its development, so as to promote the strategy of "healthy China", promote the fitness of the whole people, improve the fitness level of the whole people, and strengthen the constitution of the whole people.

Keywords: Heilongjiang Province; Indigenous minorities; Traditional sports; Health care;

Objective : This paper analyzes the health care value of physical activities of ethnic minorities living in Heilongjiang province, expounds the great significance of its development, so as to promote the strategy of "healthy China", promote the fitness of the whole people, improve the fitness level of the whole people, and strengthen the constitution of the whole people.

Research Methods: This paper adopts the method of literature and logical analysis.

Results and discussion:

1. Classification and health care of traditional ethnic Sports in Heilongjiang Province

Heilongjiang province is located in the northeast of China, far from the Central Plains and inaccessible. In daily life and production, various ethnic minorities have formed colorful traditional national sports. Due to the wide distribution of ethnic minorities, great differences in natural conditions in various regions, a wide variety of sports activities and a few traditional sports events, it cannot be carried out according to the classification standards of modern sports events. In view of the above situation, we will classify sports into performance category, competitive category and entertainment category.

1.1 Performance category

Performance sports activities are a combination of entertainment, performance and art, mainly produced in ethnic festivals of ethnic minorities. Through the combination of unique forms, music and dance, they can not only give people physical and mental health, but also show a strong ethnic customs. For example, in order to celebrate the harvest, Mongolian people hold the Nadam Fair in June and July every year. There are thrilling horse racing, wrestling, archery, chess, and charming singing and dancing performances on the "Nadam" fair. Appropriate sports activities can directly promote people's physical and mental health. When people participate in sports activities, their attention is diverted, the pressure in life and work is relieved, and the nervous emotions are adjusted. Some scholars have pointed out that sports activities have a direct effect on psychological stress [1]. National festivals tend to deepen the communication between people, the festival atmosphere is strong, promote the harmonious relationship between people, but also more conducive to relieve

physical and mental pressure, improve the ability to adapt to the society.

1.2 Competitive category

Competitive sports come from the people and are closely connected with the way of production and life. Such as archery, pearl ball, cuju, horse racing, skiing and so on. Oroqen people living in the forest have been engaged in hunting and production for generations. When hunting, the hunters need good insight, vision and hearing to accurately determine the location of the animals, and take decisive shoot, traditional archery motion coordinator can not only balance ability, can also enhance the cardiopulmonary function, relieve eye fatigue and strengthen the back muscles, enhance people's physical quality [2].

1.3 Entertainment category

Recreational sports activities are sports activities that people carry out in order to enrich their cultural life and adjust their spirits. The role of recreational sports lies in relaxation, recreation and rest. Such as deer chess, tug-of-war, skating, hide-and-seek and so on. Games are children's nature. There are running, jumping and throwing in all kinds of entertainment items, which have an important impact on children's balance, coordination, intelligence and physical quality. Studies show that sports games are irreplaceable in improving preschool children's cognitive ability, enriching their emotions and forming good will quality [3].

2. The significance of developing traditional ethnic sports activities

Fitness is a normal state that should be contained in life, and everyone should actively enjoy the physical exercise fully. It is of great significance to excavate and protect the sports activities of minority nationalities. First, with the increase of life pressure, many people do not have more time to do physical exercise, so the incidence of "occupational disease" and "chronic disease" is on the rise. In recent years, countries pay more and more attention to the importance of health, the State Council for approval, since 2009, the annual "on August 8," set to "health day", the national physical quality of the depth value in our country, modern national fitness advocate recreational sex, entertaining, not only limited to focus on people's body health, pay more attention to people's mental health, mental health, etc., The active ethnic minority sports are suitable for the broad masses of the people, with the advantages of being suitable for all ages, in time and place, simple and easy to learn, and more easily accepted by the people, so as to achieve the effect of physical exercise; Second, in recent years, the heilongjiang province actively respond to a nation, the minority games, ethnic minority sports can not only promote the heritage and development of minority national sports, more can promote the national fusion and harmonious ethnic relations, rich people's competitive spirit and the spirit of entertainment, promote health of body and mind's attention; Third, the state advocates and promotes the protection of ethnic minority cultural resources, and traditional ethnic sports are an indispensable part of national culture. Inheriting the active and progressive spirit of the Chinese nation, traditional ethnic sports are indispensable means for developing a strong country in sports, which complement and promote each other to build up confidence in Chinese culture . Therefore, excavating, sorting out, protecting and inheriting ethnic minority sports activities not only enrich the cultural connotation of ethnic minorities, but also give full play to their own value, better serve to improve people's health and make them become the wealth of all mankind.

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Application of Medicinal Diet in Regulating Chest Obstruction Based on TCM Syndrome Differentiation

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Abstract

Chest pain is one of the common heart diseases, which seriously threatens the life and health of the elderly. In this paper, chest pain is taken as the research object, conditioning from different syndrome type, using edicinal diettherapy on the basis of focusing on the whole, dialectical diet for different syndromes, qi and blood yin and yang deficiency tonic yin and yang, cold coagulation heart yang scattered cold, Phlegm obstruction should be dispelled, qi stagnation and blood stasis to promote blood circulation to relieve pain. It can enhance the pertinence of treatment and maintenance and maximize the efficacy of medicinal diet.

Key words : chest pain ; medication diet ; chinese medicine ; syndrome differentiation ; dialectical diet

Chest pain^[1] refers to chest pain, even chest pain through the back, shortness of breath, wheezing can not lie in the main disease, a serious threat to life and health of the elderly. Due to the change of modern social life style, the incidence trend is gradually increasing, the disease is more and more attention. Chinese medicine has a very early understanding of this disease, and some studies^[2] have shown that Chinese medicine has the advantages of low drug dependence, small toxic and side effects, and obvious effects in the treatment of chest pain. Medicinal diet is the combination of Chinese medical classics and cooking experience, and the compatibility of medicinal materials and food materials. Since ancient times, there has been a theory of ' medicine and food homology '. It ' s ' medicine in food ', and the two complement each other, and more easily accepted by patients.

Objective

The TCM idea of dialectical diet of TCM diet is applied to the prevention and treatment of chest pain, which provides ideas for promoting the research and development of TCM diet and provides theoretical reference for exploring effective treatment methods of chest pain.

Materials and methods

Through the analysis of the correlation between TCM syndrome differentiation and etiology and pathogenesis of chest pain, the principle of diet treatment applied to patients with chest pain is discussed based on different syndrome types of patients. At the same time, the diet prescriptions suitable for patients with chest pain of different syndrome types are listed.

Based on the different syndrome differentiation of patients with chest pain and heartache, we should apply different medicinal diet prescriptions, dialectical diet, pay attention to the whole, add and subtract drugs according to their pathogenesis characteristics, so that it is more targeted.^[3-7]

Cold coagulation heart type

This type is mostly manifested as sudden heartache, suffocation in the chest, accompanied by cold sweat, heartache thorough back, and pale face. This disease is mainly due to deficiency of body yang, deficiency of chest yang, stagnation of cold coagulation and obstruction of chest yang. The

principle of food treatment should be warming yang to dissipate cold. Diet should choose tonic yang warm powder food, avoid cold food. Can give Xiebai porridge, ginger porridge for daily diet.

Qi stagnation chest type

This type of clinical manifestation is often chest tightness, bloating pain or pricking pain, and sometimes occurs and stops; or accompanied by two hypochondriac bloating pain, irritability, mood can easily induce or aggravate. Apply the method of promoting qi and activating blood to remove blood stasis and relieve pain. Should eat light and easy to digest, low salt, low fat nutritious food, eat fruits and vegetables. Patients with liver qi stagnation and chest obstruction can eat such as bergamot porridge, regulate qi stagnation and promote blood circulation.

Phlegm Obstruction Type

This type is common chest tightness and heartache, shortness of breath and phlegm, obesity, heavy limbs, anorexia, loose stools. This disease is mainly caused by improper diet of patients, accumulation of dampness and phlegm, and obstruction of chest yang. It should be based on the principle of eliminating phlegm and removing blood stasis, and eat more food for tonifying qi and invigorating spleen. Plain edible medicinal meals such as yam porridge and coix seed porridge.

Results and discussion

The etiology and pathogenesis of patients with chest obstruction and heart pain with different syndrome types are not only related, but also show different characteristics. Conditioning from different syndrome types and applying the TCM thinking of “ dialectical diet ” of traditional Chinese medicine diet therapy to the prevention and treatment of chest obstruction and heart pain can enhance the pertinence of treatment and maintenance and maximize the efficacy of medicinal diet, which is of great significance to reduce the occurrence of chest obstruction and heart pain and slow down the development of chest obstruction and heart pain.

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Meta-analysis of progressive relaxation training on sleep quality in hemodialysis patients

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Abstract

Objective To evaluate the effect of progressive relaxation training on sleep quality in hemodialysis patients. **Methods** The CNKI, Wanfang, VIP, PubMed, Embase, Web of Science and the Cochrane Library were searched from the establishment of the database to January 3, 2021, to find the randomized controlled comparison of the effect of progressive relaxation training on the sleep quality of hemodialysis patients. **test.** Analysis was performed using RevMan5.3 software. **Results** A total of 8 articles were included. Meta-analysis shows that progressive relaxation training can improve overall sleep quality in patients with hemodialysis sleep disorder, and help to improve depression and fatigue. **Conclusion** Progressive relaxation training can improve the overall quality of sleep, relieve depression and improve fatigue in hemodialysis patients.

Key words: progressive relaxation training; hemodialysis patients; sleep quality; meta-analysis

End-stage renal disease (ESRD) refers to end-stage renal disease in which the basic structure of the kidney is damaged and the renal function is abnormal due to long-term chronic kidney disease [1]. As of 2016, related studies report that the number of patients with end-stage renal disease worldwide will reach 5.1 million, and the number of patients will continue to rise . Hemodialysis (HD) is one of the ways of renal replacement therapy for ESRD patients. According to relevant research reports at home and abroad, progressive relaxation training has obvious effects on improving sleep disorders, relieving fatigue and negative emotions in hemodialysis patients, but there is still a lack of systematic evaluation data. Meta-analysis was performed on studies related to sleep quality in dialysis patients, and the research evidence was systematically summarized to provide high-quality evidence for clinical practice.

Objective

To evaluate the effect of progressive relaxation training on sleep quality in hemodialysis patients.

Materials and Methods

By searching Chinese databases, including: China National Knowledge Infrastructure (CNKI), Wanfang Data Knowledge Service Platform (WANFANG DATA), and VIP Full-text Database (VIP). English databases include: PubMed, Embase, Web of Science, the Cochrane Library. The time limit is from the construction of the database to January 3, 2021. The retrieval method adopts a combination of subject words and free words, and the Chinese retrieval method is: (progressive relaxation training OR relaxation training OR relaxation therapy OR relaxation training) AND (maintenance hemodialysis OR hemodialysis OR hemodialysis) AND (sleep quality).

Results and Discussion

A total of 7 literatures [2-8] reported the total PSQI score. The lower the PSQI score, the better the sleep quality. In the 7 literatures, the total PSQI score of the intervention group was lower than that of the control group. The results of the study showed that there was a statistically significant difference in the total PSQI score between the two groups of patients after intervention, and

progressive relaxation training was beneficial to reduce the score. A total of 2 studies^[5-8] reported the effect of progressive relaxation training on depression, and Meta-analysis showed that there was a statistically significant difference in depression between the two groups. A total of 4 studies^[3-5] reported progressive relaxation. The effect of training on fatigue status, Meta-analysis showed that there was a statistically significant difference in fatigue status between the intervention group and the control group

The results of this study show that, as a practical training method, progressive relaxation training can significantly improve sleep quality, relieve depression, and relieve fatigue in hemodialysis patients. Because sleep quality is affected by a variety of factors, subjective and objective indicators can be used to comprehensively evaluate the effect of progressive relaxation training on patients with hemodialysis sleep disorders.

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Based on the type of TCM certificate, the research status of TCM diet on functional dyspepsia is discussed

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Abstract

Functional dyspepsia is not a serious life-threatening disease, but its symptoms can persist. Greatly reduces their quality of life. This paper takes functional dyspepsia as the research object, and provides a reference for the treatment of functional dyspepsia and the prevention and treatment of functional dyspepsia in traditional Chinese medicine dietary therapy.

Key words: Medicinal diet; Dietary therapy; Functional dyspepsia

Functional dyspepsia^[1] FD is one of the most common disorders of functional gastrointestinal disorders. D is not a serious life-threatening disease, but its symptoms may persist. It greatly restricts people's social life and reduces their quality of life.

Objective

It provides a reference for the treatment of functional dyspepsia and the prevention and treatment of functional dyspepsia in traditional Chinese medicine dietary therapy.

Materials and methods

Electronic databases were searched, including Pubmed, CNKI, Wanfang and Weipu, to find clinical articles related to functional dyspepsia and TCM diets by June 2022. Our search strategies are traditional medicine, dietary therapy and functional dyspepsia.

Results and discussion

China's medicinal diet has a history of thousands of years, and many ancient books have recorded the treatment of functional indigestion. Such as good spleen cake, eight treasure cake, baizhu pork belly porridge and so on. The most prominent feature of Chinese cuisine is the integration of Traditional Chinese medicine culture with dietary culture. At present, according to xiang ming research statistics^[2] the hot spot of medicinal diet research mainly lies in clinical application research, and it is currently in a period of accelerated research development. China's emphasis on Chinese dietary therapy has been increasing, and medicinal food is highly favored. Lei Chunli^[3], Shen Chaoqun^[4] and others selected Healthy spleen and qi porridge, and Healthy spleen japonica rice porridge with good clinical efficacy

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Research progress on the treatment of primary dysmenorrhea with Chinese dietary therapy and medicine

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Abstract

TCM therapeutic medicine diet is a special diet based on TCM theory, which combines medicine and food with unique cooking and processing techniques to prevent and cure diseases and to maintain health and wellness. In this paper, we review the current situation of primary dysmenorrhea in Chinese medicine by tracing the origin, etiology and pathogenesis of dysmenorrhea, identifying and classifying the symptoms, and the application of Chinese therapeutic diets.

Keywords: dietary therapy and medicinal food; traditional Chinese medicine; dysmenorrhea treatment

Dysmenorrhea is defined as abdominal pain or lumbar discomfort before or during menstruation, and in severe cases, nausea, vomiting or even fainting [1]. Primary dysmenorrhea refers to dysmenorrhea in which there is no organic damage to the female reproductive organs themselves [2]. In modern society, work and study pressures follow each other, and dysmenorrhea has seriously affected the quality of life of women. TCM therapeutic medicine is a special diet based on TCM theory, which is processed or cooked with food and medicine to achieve the purpose of disease prevention and health care [3], with the characteristics of green and safe, convenient and effective, and economical and practical.

Objective

To summarize the experience of medicinal dietary treatment for dysmenorrhea in recent years and to provide reference for the prevention and treatment of primary dysmenorrhea.

Materials and Methods

Electronic databases, including Pubmed, CNKI, Wanfang, and Wipu, were searched for clinical articles related to dysmenorrhea and TCM dietary therapy until June 2022. Our search strategy was traditional medicine, dietary therapy, and primary dysmenorrhea.

Results and Discussion

The culture of Chinese dietary therapy and medicine is profound and has great advantages in disease prevention and treatment as well as health care. Meng Xiangyun and Yuan Renzhi [4] treated dysmenorrhea through the aid of medicinal food, which was divided into two groups: conventional medication and consumption of medicinal food on the basis of medication, and the result was that the efficiency of the group adding medicinal food therapy reached 93%, with significant pain relief. Liu Qian et al. treated primary cold clotting and blood stasis type dysmenorrhea with angelica ginger and mutton soup, and randomly divided the dysmenorrhea patients into medicinal food group, moxibustion group, and western medicine group. The results showed that the treatment effect of the medicinal food group on primary dysmenorrhea with cold clotting and blood stasis was better than that of the Western medicine group alone, and the difference in treatment effect with the moxibustion group was not significant.

In the process of treatment, different prescriptions should be given to patients according to their individual conditions; the same applies to dietary supplementation, which should take into account the different trends of dysmenorrhea, the characteristics of the symptoms, the physical characteristics, and the presence of physical disorders.

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Innovation and Development of TCM Health

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Abstract:

With the development of the times, people are enjoying a happy life and pursuing a higher quality of life, so the health industry is gradually being emphasized, and Chinese medicine has a profound cultural heritage in disease prevention, treatment and body care, and it is gradually becoming one of the most popular aspects of the health industry, and it is constantly innovating and has a very good development trend. The development trend is very good.

Keywords: Chinese medicine; big health industry; innovation and development

Big health medical service is a new type of medical model, which contains the future direction of medical development. In essence, "big health" is not a simple idea, but the integration and fusion of multiple ideas. With the introduction of the "Health China Strategy" in the 19th National Congress, "people's health is an important symbol of national prosperity and national wealth and strength" has become the new orientation of the development of big health, and "providing people with all-round and comprehensive health services" has become the new goal of big health development. This has undoubtedly provided a fundamental guideline for promoting the innovative development of the TCM health industry. As an outstanding representative of Chinese civilization, TCM has not only made outstanding contributions to the reproduction and prosperity of the Chinese nation, but also has a positive impact on the progress of world civilization [1].

Objective

To summarize the innovative advantages of TCM in general health, in order to better understand the current research progress in TCM in general health industry in China, to provide some theoretical basis for future research, and to be able to understand the development trend and prospect of TCM in general health industry.

Materials and Methods

Electronic databases, including Pubmed, CNKI, Wanfang, and Wipu, were searched for relevant clinical articles. Our search strategy was Chinese medicine, big health industry, and innovation development.

Results and Discussion

With the increasing number of aging people in China and the intensification of social aging, the "gray hair wave" has become a hot spot of social concern for the elderly. Therefore, the combination of TCM advantages and elderly care model will become a new trend of elderly people's recuperation [2]. Chinese medicine has obvious advantages in treating chronic diseases of the elderly, such as hypertension and diabetes mellitus, which are highly prevalent in the elderly. Chronic diseases usually require lifelong medication, and the elderly often suffer from imbalance of qi, blood, yin and yang, organ function decline, and changeable diseases [3]. Compared with chemical drugs, Chinese medicine has less toxic side effects, fewer adverse reactions, and longer lasting effects [4]. Therefore, TCM is widely used in chronic diseases and has a higher acceptance and credibility especially in the perception of the elderly. The TCM health industry should not be

stagnant and should follow the opportunities of the new era to achieve innovative and standardized development. We should strengthen the integration with the Internet and national development strategies, education, etc., meet the technological needs of talents and product development, promote the transformation and upgrading of traditional medical services, and realize the multi-modal and international development of TCM health industry.

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Effect of ethyl acetate extract of hematoxylon on chronic rejection in rat heart allograft model

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Abstract

This study successfully established an animal model of chronic rejection of heterotopic heart transplantation in rats. After treatment with ethyl acetate extract of hematoxylon, the pathological model and related immune indexes of the model were observed, which confirmed that ethyl acetate extract of hematoxylon has anti-immune rejection effect.

Key words: hematoxylon ethyl acetate extract; heterotopic heart transplantation; chronic rejection; effectiveness;

Objective

To explore the curative effect and possible mechanism of ethyl acetate extract of hematoxylon on animal model of chronic rejection of heterotopic heart transplantation, and confirm that the effective part of ethyl acetate of hematoxylon has anti immune rejection effect.

Materials and methods

Using the improved Ono operation, the ascending aorta and pulmonary aorta of the donor heart were end-to-side anastomosed with the abdominal aorta and inferior vena cava of the recipient respectively, so as to provide blood circulation for the transplanted heart. An animal model of chronic rejection of heterotopic heart transplantation in rats was established. Those who can stand awake within 2h after transplantation, and whose fingers can touch the abdominal heart beating with a little force from the back of the spine, and who do not stop beating within 24h, were used as the experimental animal model. The rats with successful operation were randomly divided into 3 groups, 8 rats in each group, which were model group, hematoxylon group and cyclosporine a group respectively. Another control group was set. The levels of TGF- β 1, IL-4 and IL-10 in serum were detected by ELISA. The pathomorphological changes of the grafts were observed by HE staining.

Results and discussion

Both ethyl acetate extract of hematoxylon and cyclosporin A can significantly increase peripheral serum TGF in rats with chronic rejection of heterotopic heart transplantation- β 1. The levels of IL-4 and IL-10 can improve the pathological morphology of transplanted myocardium.

TGF- β 1 is a key fibrogenic cytokine secreted by renal tubular and glomerular epithelial cells, which is involved in the expansion of matrix in the process of chronic rejection. Several subsets of T lymphocytes, including Th1, Th2 and Treg (mainly CD4⁺ and CD25⁺ regulatory T cells), are closely related to transplantation rejection. The activation of Th2 cells is mainly related to the induction of immune tolerance. Promoting the transformation of Th1 subgroup to Th2 subgroup is considered to be an important factor to promote the tolerance of allograft organs. Th2 cytokines such as IL-4 and IL-10 can inhibit the proliferation of Th1 subsets and promote the differentiation of Th1 into Th2 subsets, which is negatively related to transplantation rejection. This study explored that ethyl acetate extract of hematoxylon has obvious anti immune rejection effect by increasing peripheral serum TGF in rats with chronic rejection of heterotopic heart transplantation- β 1. The secretion of

IL-4 and IL-10 plays an immunosuppressive role.

Scholars have begun to study hematoxylon and its active components, confirming that it has strong in vitro inhibition of tumor cells, inhibition of platelet aggregation and immunosuppression. Immunosuppressants play an important role in the treatment of organ transplantation rejection and autoimmune diseases. At present, transplantation has become the most important treatment for the end stage of tissue and organ failure. However, acute rejection after transplantation is still the main complication after transplantation, and it is also the most important risk factor leading to chronic rejection and graft failure. It is of great significance for the new medicinal value of hematoxylon and the development of immunosuppressants of traditional Chinese medicine to further study the immunosuppressive mechanism of hematoxylon and continue to separate its effective parts and groups of effective parts.

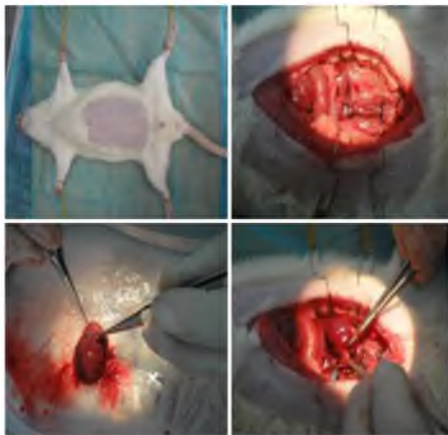


Fig.1 Model preparation process

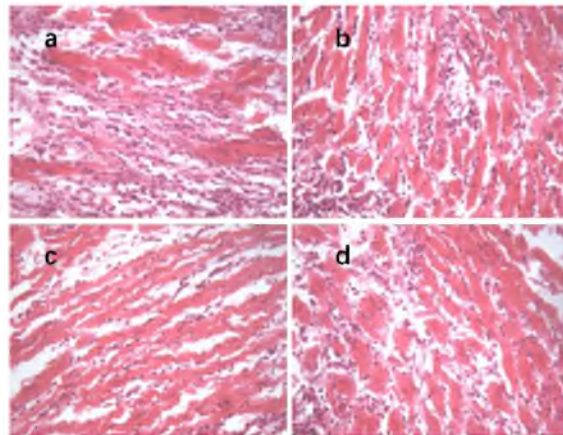


Fig.2 HE staining results

(a: model group, b: hematoxylon group, c: control group d: cyclosporine a group)

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Progress in TCM Research on Obesity

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Abstract

with the change of lifestyle and eating habits, obesity and overweight people showed a significant rising trend, obesity as one of the global common chronic metabolic diseases, often concurrent or combined with a variety of diseases, serious harm to human health, so the modern medical research on obesity is becoming more and more urgent, is the focus of scholars research and attention. Traditional Chinese medicine has long been studied on obesity, and traditional Chinese medicine has a remarkable effect in the treatment of obesity. This article makes a general description of the research progress of traditional Chinese medicine on obesity by consulting literature and reading ancient books.

Key words: obesity, etiology and pathogenesis, traditional Chinese medicine treatment

1. Purpose and significance

Obesity is to point to a variety of reasons such as food, lack of physical activity and excessive accumulation of fat in the body, weight over a certain range, or accompanied by dizziness, fatigue, less shortness of breath and other symptoms, is the basis of a variety of other diseases. Obesity is not only an independent disease, but also a risk factor for type 2 diabetes, cardiovascular disease and tumors, which the WHO lists as one of the top ten risk factors for disease burden ^[1]. According to the classification standard (Chinese standard) recommended by the Guidelines for the Prevention and Control of Overweight and Obesity published by the Department of Disease Control (WHO) of the Ministry of Health in 2003: Body mass index (BMI), BMI greater than 24 is overweight, and more than 28 is obesity ^[2]. Studies show that in China BMI > 28 men and women accounted for 17.10% and 13.37% of the statistical population ^[1], and showed an obvious upward trend, obesity and obesity caused by related diseases not only damage patients' physical health, but also caused serious harm to psychology, reduces the quality of life of patients, hit the self-confidence of patients, so it is of great significance to further research on obesity.

2. Traditional Chinese medicine understanding of the etiology of obesity

2.1 The understanding of the ancient doctors

Traditional Chinese medicine has a long history of understanding of obesity, the first recorded in the "Huangdi Neijing", such as the "Su Wen Tong Comment on the reality and the real" has a "fat noble people" description. "Su ask strange disease theory" mentioned: "sick mouth sweet..., its people must eat sweet and more fat also", "Su ask different method Yi Bo Zhong also pointed out:" the West, the domain of gold and jade... its people eat and fat fat ", pointed out that obesity and fat and eat sweet taste related. And lingshu. Wei qi disorder "according to the amount of human skin, meat, qi and blood, obesity is divided into" fat, paste, meat " three types. "Lingshu reverse fat shun thin" ^[3] cloud: "this fat people also, wide shoulder... its blood color black to turbidity, its gas astringent to late", weak kidney gas, gasification loss, the body wet turbidity difficult to discharge, accumulation in and induce obesity. Splen deficiency can not transport water to the stomach, long time and the stomach is dry, good hunger lead to obesity. It clearly discusses that the disease position closely

related to obesity lies in the liver, kidney and spleen. The Huangdi Neijing also believes that obesity is related to a variety of other diseases, which can be transformed into thirst elimination, but also with the attack, partial dry, impotence, full qi and other diseases.

3.Traditional Chinese medicine for the treatment of obesity

3.1Medicine and food treatment of traditional Chinese medicine for obesity treatment

The history of Chinese medicinal diet has a long history. As early as the Han Dynasty, the historical fact of the application of medicinal diet has been established. After successive research and improvement, it has developed into a nutrition discipline of traditional Chinese medicine, and is the health care basis of "medicine and food", and is of great significance for the prevention and clinical treatment of diseases. Medicinal diet for the treatment of obesity, such as chapter breeze ^[4] according to the theory of traditional Chinese medicine to the understanding and classification of obesity, syndrome differentiation, diet diet can be divided into five categories, for spleen deficiency damp resistance fat can choose soup, white poria porridge medicine dietary treatment, by astragalus, poria, poria, diarrhea, pinellia pinellia, rhubarb, lentils, broad beans, peas, etc.

3.2 Exercise therapy

Exercise is indispensable in the treatment of obesity. The traditional TCM health exercise "Wuqinxi", "six-character" formula ", " BadJin ", " Qigong "and" Tai Chi " have been highly praised by people. If obese patients can insist on exercise, the combination of static and static will make qi and blood smooth, and the disease will naturally heal ^[5].

3.3 Treatment with single-flavor traditional Chinese medicine

The research of Chinese herbal medicine has a long history and many effects. It is of great significance for many researchers to find effective weight loss drugs from modern Chinese medicine. Wang Yong through consulting the literature on the treatment of obesity by traditional Chinese medicine, established a database analysis of hawthorn, astragalus, white, angelica dahurica, lotus leaf, diarrhea, rhubarb, licorice, cassia, grey and other most frequently, indicating that these single taste drugs in the treatment of obesity is effective.

3.4 Chinese patent medicine treatment

With the continuous progress and development of traditional Chinese medicine, the treatment methods are also diversified. The application of proprietary Chinese patent medicine is born. Compared with the decoction, the proprietary Chinese patent medicine has less side effects and is easy to carry, and it is loved by the majority of patients. There are also plenty of proprietary Chinese patent medicines to treat obesity. Such as reducing weight soup, three flower tea, seaweed soup, light fat light body, body can be light, reducing weight loss, light body, light body number one, day goose tea, reduce weight, fat capsule, fat spirit, light drink, spleen weight loss, spleen kidney powder, supplement diet, clear drink, clear drink, fat reduce weight bodybuilding drink Chinese patent medicine has been proved to have significant curative effect.

3.5 Acupuncture and moxibustion treatment

Acupuncture and treatment of obesity is a characteristic of traditional Chinese medicine, and the treatment effect is obvious. Li Weiqin treated 60 patients with simple obesity with warm acupuncture, acupuncture middle pole, bilateral Fenglong, bilateral valley, bilateral Tianshu, Zhongwan, bilateral foot for 30 minutes, every other day for a total of 8 weeks, and the total effective rate was 90.0%, significantly effective.

3.6 Ear acupoint pressing treatment

Ear point sticking pressure is mainly by pressing the corresponding positive reaction point of the patient's ear, in order to dredge the meridians, and then adjust the viscera qi and blood function, so as to achieve the effect of nourishing qi and blood, reducing fat and reducing weight.

4.preliminary summary

With the development of society and the improvement of living standards, the incidence of obesity has also increased year by year, which has become an epidemic, which not only harms people's health, but also greatly affects self-confidence and affects the quality of life. In This paper, through the summary of the etiology and TCM treatment of obesity, a more systematic understanding of the disease, on the basis of previous research, we can summarize its experience and make more in-depth development, better for clinical services.

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The theoretical basis and application of dog-days paste for “summer treatment for winter diseases”

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Abstract

Dog-days Acupoint Application is a unique characteristic therapy of traditional Chinese medicine,it was founded according to the principle of "spring and summer nourish the yang" in *Huangdi Neijing*.It is also a typical application of the theory of "summer treatment for winter diseases" in traditional Chinese medicine.Traditional medicine selects time to treat,acupoint plasters are applied when the condition is relieved in summer, in order to restore the patient's yang, enhance disease resistance.This article summarizes and discusses the theoretical basis and application of "Summer Treatment for Winter Diseases" dog-days paste, and provides a reference for its clinical practice.

Key words:dog-days paste,summer treatment for winter diseases,treating predisease

1. Objective And Significance:

With the increasing living standards of human beings, the requirements for health are also constantly improving, and the needs of patients are showing a diversified trend.Sanfu paste is a popular treatment and rehabilitation project, and it has a tendency to extend in the direction of health care. It has considerable practical application value and operability, and is conducive to showing the characteristics and advantages of traditional Chinese medicine .

2. Theoretical basis and clinical application:

2.1 Theoretical basis of "summer treatment for winter diseases" dog-days paste

Huangdi Neijing contains the idea of “preventive treatment of disease” and the viewpoint of "combination of nature and human",which are the theoretical sources of “summer treatment for winter diseases”.Mutual rooting of yin and yang, nourishing Yang in spring and summer, laying the foundation for nourishing yin in autumn and winter. Yin and Yang restrict each other, in the dog days of summer, it is easiest to dissolve the cold and condensed qi in the body, supporting yang and overcome cold with yang, which can achieve the purpose of curing winter diseases in summer.According to the five-phase theory, later summer is attributed to the category of earth, winter is attributed to the category of water.The human body raises Yang in the later summer season to Consolidate earth to control water. Supplement the yang qi of the spleen to prevent cold-evil in winter.

In summer, the meridians are full of qi and blood, interstitial striae are opened, the drug penetrates the skin easily, at this time, for patients with yang deficiency, the traditional Chinese medicine with the properties of pungent-warm to dissipate cold and warm yang to dispel phlegm is applied to the acupuncture points.It penetrates along the acupoints, meridians and viscera, amplifies the effect of the medicine, to achieve the purpose of peaceful yin and concreting yang, and adjusting the immune function of the body.

Modern research has confirmed that "dog-days paste" is involved in the regulation of cellular immunity and humoral immunity, at the same time scavenging oxygen free radicals, inhibiting

inflammatory reactions^[1]. It can effectively remove the release of inflammatory mediators caused by free radicals, improve the state of low immune function, and improve the body's disease resistance.

2.2 Indications for dog-days paste

The prevention and treatment of dog sticky paste involves various diseases in internal medicine, surgery, gynecological and pediatric fields. The most widely used are mainly respiratory diseases, such as allergic rhinitis, asthma, chronic bronchitis, chronic or variant cough, etc. In addition, it has a good therapeutic effect on 31 diseases such as diarrhea, dysmenorrhea, abdominal pain in children, frozen shoulder, cervical spondylosis, etc.

The effect of dog-days paste in the treatment of lung diseases is the most ideal. Syndrome differentiation is dominated by yang deficiency, or cold-heat complex dominated by cold. Such patients are usually prone to colds, runny nose with clear snivel, panting and coughing, easy to aggravate when the weather is cold, pale red tongue, thin white coating, and string-like pulse. Chinese medicine believes that the occurrence and outcome of lung diseases are closely related to the lungs, spleen and kidneys, the basic pathogenesis is that interior cold or yang deficiency leads to endogenous cold. "Wind-cold-dampness" three evils are the important pathogenic factors of impediment pattern. Innate Yang deficiency, coupled with the affected of wind, cold and dampness, the muscles and sinew are lost in warmth, the blood flow is not smooth, and the pain is caused by obstruction, which is the cause of bone impediment. Using dog-days paste for external treatment can support healthy qi and invigorating yang, being recovered when eliminating evil, and effectively prevent the recurrence of bone impediment. Therefore, dog-days paste therapy can be applied to all kinds of impediment pattern of yang deficiency and cold exuberate.

2.3 Medication and acupoint selection of dog-days paste

Clinical acupoint selection and medication should be differentiated according to the syndrome. Summarize the selection of acupoints and the regularity of drug use in the related research literature of dog-days paste^[2], for respiratory diseases, choose Feishu, Tanzhong, Tiantu and Dingchuan; For motor system diseases and bone impediment due to wind-cold-damp, choose Dubi, Neixeyan, and Shenshu; For other systemic diseases, Shenshu, Guanyuan, and Zusanli are mostly selected. For medicines, choose pungent-warm products such as white mustard seeds, asarum, and corydalis, crushed into powder, then spread with ginger juice. White mustard seeds are pungent-warm into the lungs, regulates qi and resolves phlegm, warms the lungs and disperses cold; Asarum warming the lungs and transforming the drink, dispelling wind and relieving pain, both have the effect of warming and dispelling cold phlegm. Introducing ginger juice into the lung, spleen and stomach meridians has the effect of resolving phlegm, relieving vomiting, dispelling cold and warming.

2.4 Precautions for "summer treatment for winter diseases" dog-days paste

The local skin should be washed before application, and the wearing should be comfortable and loose. Secondly, pay attention to the time of acupoint application. Generally, acupoint plaster application is carried out at the first, middle and last days of the lunar calendar dog-days every year, it can also be applied during the sanfu period. The interval between each application is 7 to 10 days. For adults, the time for each application is 2 to 8 hours, and most of them are 4 hours, pediatric patients should be applied for 0.5 to 2 hours, the specific application time depends on the patient's skin reaction, and is generally as tolerated by the patient. Pay attention to the skin reaction

after application. In most patients, local skin flushing is accompanied by burning sensation, slight tingling, or small blisters, which subside spontaneously after a few days. If severe redness, ulcers or systemic skin allergies occur, the ointment should be removed immediately to reduce further irritation to the application site and seek medical treatment in time. After treatment, the diet should be bland, cold and spicy food should not be eaten.

3. Results and Conclusion

Treating winter diseases in summer with dog-days paste is a concentrated expression of the thought of "treatment of prediseases" in traditional Chinese medicine, fully demonstrating the traditional philosophical thinking of "correspondence between nature and human". Therefore, the popularization and promotion of the dog-days paste business is in line with the transition to the new medical model of "biological-psychological-social-environmental", and is a way of benefiting people with the characteristics of traditional Chinese medicine.

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Experience in treating obesity with traditional Chinese medicine and traditional Chinese medicine

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Abstract

Obesity is a chronic endocrine and metabolic disease caused by specific biochemical factors and overweight. It is a high-risk factor for chronic diseases such as type 2 diabetes, cancer and cardiovascular diseases, and its development and spread seriously threaten human health. Controlling obesity is of great significance for improving residents' health level and quality of life and relieving medical pressure. At present, the cause of obesity is not clear. Most studies think that the cause of obesity is closely related to improper diet, internal injuries in seven emotions, sedentary and long-term lying, etc. Traditional Chinese medicine believes that obesity is a kind of disease caused by many reasons, such as excessive accumulation of cream and fat in the body, abnormal weight gain, dizziness, fatigue, lazy speech, little movement and shortness of breath. Traditional Chinese medicine (TCM) has a long history of understanding obesity. It emphasizes that treatment must be based on the foundation, with various treatment methods, obvious effect and no obvious side effects. In recent years, it has played an increasingly important role in the treatment of obesity. The treatment methods include supplementing method, descending method, harmonizing method and eliminating method.

Key words:obesity, traditional Chinese medicine, treatment, traditional Chinese medicine

1. Objective And Significance:

Obesity is caused by specific biochemical factors, and its roots are eating regulation and energy metabolism disorder. A chronic endocrine and metabolic disease caused by excess energy consumption, excess energy stored in the body in the form of fat, and overweight is a high-risk factor for chronic diseases such as type 2 diabetes, cancer, cardiovascular diseases, etc. Its development and spread seriously threaten human health, and is listed as one of the top ten risk factors leading to diseases by the World Health Organization. In 2019, China's BMI obese population has reached 250 million, making it the country with the largest number of obese people in the world. Controlling obesity is of great significance for improving residents' health level and quality of life and relieving medical pressure.

2. Etiology, pathogenesis and treatment rules

2.1 etiology and pathogenesis At present

the cause of obesity is not very definite, and it is often influenced by biological factors, behavioral factors, psychology and other factors, which are closely related to genetic factors and unhealthy lifestyle. At present, the lifestyle intervention combining diet, behavior and exercise is the basic treatment scheme for obesity, and it can also be treated with various drugs and operations. However, there are many adverse reactions in the treatment of obesity by western medicine, and the surgical treatment cost is high and the damage to people is relatively large. The long-term efficacy of the two drugs is still controversial, and the clinical application and promotion still need further scientific verification. In addition, due to the lack of treatment plans for individual causes, it is

difficult for patients to persist in lifestyle changes under the influence of intervention measures for a long time, and the research and treatment of obesity still has a long way to go. Traditional Chinese medicine (TCM) has a long history of understanding obesity. It emphasizes that treatment must be based on the foundation, with various treatment methods, obvious effect and no obvious side effects. In recent years, it has played an increasingly important role in the treatment of obesity.

2.2 treatment rules

Treatment method	Masanori
<p>Tonifying method: invigorating spleen and qi, invigorating qi and tonifying kidney. Lower method: eliminating dampness, inducing diuresis, eliminating phlegm, dredging fu organs and promoting digestion.</p> <p>Harmony: harmonizing liver and spleen and stomach.</p> <p>Elimination of drugs: promoting blood circulation and removing blood stasis.</p>	<p>Holism: coordination and balance of the five internal organs.</p> <p>Seeking the root of treatment: identifying the root of the disease.</p> <p>Take care of both specimens: people-oriented, prioritize.</p> <p>Treating the same disease differently and treating different diseases at the same time: three causes should be treated appropriately, and the treatment should be established.</p>

3. Results and Conclusion (medication experience):

3.1 Traditional Chinese medicine for eliminating phlegm and turbidity, promoting diuresis and lowering blood fat: raw rhubarb, giant knotweed, Rhizoma Atractylodis, Alismatis Rhizoma, Herba Artemisiae Scopariae, etc.

3.2 Traditional Chinese medicine for promoting blood circulation, removing blood stasis, losing weight and removing lipid: Salvia miltiorrhiza, motherwort, raw hawthorn, Spatholobus stem, Ligusticum wallichii, etc. Nourishing yin, reducing weight and lipid: Eclipta prostrata, Radix Rehmanniae, Cornus officinalis, Fructus Lycii, Rhizoma Anemarrhenae, Ganoderma lucidum, etc.

3.3 Traditional Chinese medicine for nourishing yin, reducing weight and lipid: raw rhubarb, giant knotweed, Rhizoma Atractylodis, Alismatis Rhizoma, Herba Artemisiae Scopariae, etc.

3.4 Traditional Chinese medicines for eliminating phlegm and turbidity, promoting diuresis and lowering blood fat: raw rhubarb, giant knotweed, Rhizoma Atractylodis, Alismatis Rhizoma, Herba Artemisiae Scopariae, etc.

3.5 Traditional Chinese medicine for invigorating spleen, eliminating dampness, losing weight and removing lipid: hawthorn, yam, dogwood, tuckahoe, ginseng, jujube, etc.

3.6 Traditional Chinese medicine for tonifying kidney, promoting diuresis, reducing weight and lowering blood fat: Herba Epimedii, Fructus Psoraleae, Semen Cuscutae, Fructus Ligustri Lucidi, Polyporus umbellatus, Eucommia ulmoides Oliv, Semen Cuscutae, etc.

3.7 Others: lotus leaf, oolong tea, Gynostemma pentaphyllum, cassia seed, Siraitia grosvenorii, Cortex Moutan, Gardenia jasminoides Ellis, Bupleurum root, Radix Paeoniae alba, Angelica sinensis, Coptidis Rhizoma, and Mel, etc.

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Treatment for Insomnia through Traditional Chinese Medicine in Heilongjiang Province

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Abstract

Insomnia refers to the disorder of the beginning and maintenance of the sleeping state, which makes the sleep quality of people concerned unable to meet their physiological demand and significantly affects their activities of patients, bringing great pain to patients. Sleep disorder is an independent risk factor for many high-risk diseases in cold zone areas. Effectively improving sleep disorder has become an important measure to prevent some high-risk diseases in cold zone areas.

Key words: Heilongjiang Province, TCM treatment, insomnia

As an astronomical high latitude zone, the Frigid Zone is within the latitude circle of 66°34' in the North-South latitude, due to the oblique sunlight, the solar heat obtained is less than that in other zones, its climate is cold all year round, and it is called the Frigid Zone. According to the classification of Frigid Zone in China, Heilongjiang province belongs to this zone, and Russia is located in the north of Heilongjiang Province, the winter is long and cold, while its summer is short and warm. Similar to the climate of Heilongjiang Province, it also belongs to the Frigid Zone. According to a survey of the sleeping quality of 307 Russian community residents, 62% of people were diagnosed with insomnia^[1], significantly higher than other social groups, showing that the study of insomnia in Frigid Zone has become significantly important.

Objective

In this paper, the clinical efficacy of traditional Chinese medicine in treating insomnia in Heilongjiang Province will be explored, thus providing new ideas for the clinical diagnosis and treatment of insomnia in Russia and promoting the healthy development of traditional Chinese medicine in China and Russia.

Materials and methods

Acupuncture treatment: The Xinshu “Three Shen” are mainly adopted to treat insomnia patients with less good heart and spleen. The “Three spirit” refers to the Benshen, Sishencong, Shenting, Shenmen, Shendao, as well as Shentang. The routine acupoints are taken in the control group. The effective rate of the treatment group was as high as 90%, which was significantly better than 83.33% of the control group. Acupuncture of Xinyu “Three spirit” can promote the recovery of heart and brain functions and effectively alleviate insomnia symptoms^[2].

Treatment by chinese herbs: According to the method of nourishing the body and eliminating accumulation, Guben Jieyu Decoction is established and applied to insomnia of liver depression and spleen deficiency type, which can significantly improve insomnia symptoms and liver depression, as well as the spleen deficiency syndrome. The total effective rates reached 96% and 98%, respectively. Guben Jieyu Decoction can reduce or eliminate patients' symptoms including difficulties in falling asleep, being easy to wake up, dreaminess, etc^[3].

Massage: Massage on the Du meridian, Shenmen, Neiguan, Anmian points reflects the concept of

Tongdu Tiaoshen, with obvious effect after treatment. Tongdu Tiaoshen massage therapy can improve the blood supply of brain tissue and the sleep efficiency of patients, and alleviate the anxiety and depression of patients in a certain degree^[4].

Acupoint injection: On the basis of routine acupuncture treatment, point injection of Bozhi Tangfu injection is added to treat insomnia with heart kidney disharmony. In the point injection, bilateral Shenmen, Sanyinjiao and Taixi are chosen, which plays the role of coordinating the heart and kidney, calming heart and nerves, and can significantly improve the sleep quality of insomnia patients^[5].

Acupoint catgut embedding: Through the research on the curative effect of catgut embedding method on insomnia patients with liver depression and fire. On the basis of traditional acupuncture, catgut embedding treatment at Siguan point (Taichong, Hegu) was added. After the treatment, patients' sleep time was shortened and prolonged^[6].

Others: Patients with coronary heart disease and insomnia were treated with auricular acupoints pressing beans at Shenmen, Jiaogan, Subcortical, heart, spleen, as well as stomach. After the treatment, the sleep symptoms of patients were significantly improved^[7]. Ordinary acupuncture combining acupuncture and cupping has a significant effect on the treatment of primary insomnia, which can effectively shorten the patient's sleep time and prolong the actual sleep time at night^[8].

Results and discussion

In the Frigid Zone, there are characteristics of early sunset and late sunrise in winter and late sunset and early sunrise in summer, and the length of illumination time will have certain influence on people's sleep rhythm to a certain extent. Moreover, it is very cold outside in winter in the Frigid Zone. People tend to close doors and windows for energy conservation and thermal comfort. Indoor carbon dioxide concentration increases, and the polluted indoor air will have certain influence on the sleeping quality. According to relevant researches, low ventilation rate or high carbon dioxide concentration will have a negative impact on sleep. To resist the coldness, people in Frigid Zone have their own unique diet habits, with meat as the main food, in addition, they drink alcohol, intake too much salt, and eat spicy foods like pepper and garlic, which results in their high blood lipids. After the application of lipid-lowering drugs, most people will have symptoms of insomnia and nightmares.

Currently, there are many ways to treat insomnia in cold zone areas. Western medicine mostly uses sedative hypnosis and melatonin drugs, which have obvious curative effect, but adverse reactions such as drug resistance, dependence and withdrawal effect can occur easily. Under the theoretical framework of the overall concept, combining flexible treatment methods, traditional Chinese medicine can effectively treat insomnia by adjusting the blood, Yin and Yang, viscera and meridians of the human body. Compared with western medicine, traditional Chinese medicine can be more readily accepted, and the side effects of drugs can be minimized, presenting obvious clinical effects.

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Research Progress on the Influence of Different Dietary Patterns on Parkinson's Disease

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Abstract

Parkinson's disease (PD) is a motor disease, the second most common neurodegenerative disorder. PD affects approximately 1% of women and men worldwide, particularly older than 60 years. Both China and Russia are facing the problem of aging population, and there are more and more PD patients. PD has serious influence on the life quality of patients. Therefore, in this paper, the progress of different dietary patterns on Parkinson's disease is reviewed, which provides appropriate treatment strategies for PD patients, and greatly promotes the development of the China-Russia health industry.

Key words: Parkinson's disease, Health strategies, dietary patterns

Both China and Russia are facing the problem of aging population. The aging population accounts for the increasing prevalence of neurodegenerative diseases such as Parkinson's which carry a significant health and economic burden. According to relevant statistics, the average annual expenditure for treating PD has reached 22673 euros. At present, scholars at home and abroad have found that dietary intervention plays a certain role in treating PD. Therefore, this paper mainly discusses the research progress of the impact of different dietary patterns on PD, which is of reference significance for the dietary treatment of PD.

Objective

In this paper, the progress of different dietary patterns on Parkinson's disease is reviewed. In addition, the impact of different dietary patterns on PD has been pointed out, which provides appropriate treatment strategies for PD patients, and greatly promotes the development of China-Russia health industry.

Materials and methods

Referring to relevant literature of dietary treatment of PD in Pubmed and summarizing them, it is found that Mediterranean diet is rich in dietary fiber, which can regulate intestinal function, alleviate constipation symptoms, and reduce the occurrence and development of PD^[1]. In an experiment on ketogenic diet, the intervention group was provided with ketogenic diet and the control group was given western diet. According to the result, the cognitive ability of PD patients receiving ketogenic diet was improved^[2]. Thygesen et al. investigated the difference between vegetarian diet and ordinary diet in PD patients, and found that there was no significant difference in the standardized incidence rate of vegetarian diet PD compared with the general population^[3]. Zapał A, B, et al. explored the difference between the dietary preference of PD patients and the general diet, and concluded that PD patients mainly had Western diet, becoming one of key factors of increased PD risk^[4]. Metcalfe-Roach et al. food Frequency Questionnaires from 167 participants with PD and 119 controls were scored for MIND and 2 versions of Mediterranean diet adherence. Later age of onset correlated most strongly with MIND diet adherence in the female

subgroup^[5]. Conversely, milk and its accessory products can increase PD risk. Diet intervention is essential for neurologists to improve clinical outcomes and reduce the disease progression of PD.

Results and discussion

The global prevalence of Parkinson's disease is steadily increasing due to the aging population. Both China and Russia are facing the problem of aging population, and there are more and more PD patients. Medicine cures diseases, it also exerts the unexpected effect which is harmful to organism. Diet therapy is cheap, has no side effects, and is deeply loved by the public. At present, scholars at home and abroad have found that dietary intervention plays a certain role in treating PD. PD and dietary habits, suggesting that nutritional strategies may be an effective tool to delay PD onset. Therefore, in the future, we can explore the dietary patterns suitable for PD patients in China and Russia by combining the cultural and regional characteristics of China and Russia, thus promoting the development of China-Russia health industry.

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ACUPUNCTURE-REHABILITATION THERAPY IMPROVED INTESTINAL FLORA OF STROKE PATIENTS AND THEIR SYMPTOMS IN NORTHEAST ASIA

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Abstract

Cities in Northeast China and the Far East of Russia belong to the cold region of Northeast Asia, and the incidence of stroke is high. Such geographical characteristics undoubtedly bring more challenges to stroke rehabilitation. In order to improve the therapeutic effects of rehabilitation after stroke, we reviewed through China National Knowledge Infrastructure and Wanfang databases the acupuncture-rehabilitation therapy (ART) and its effects on stroke and intestinal flora of stroke patients in Northeast Asia and found that ART has a positive effect on stroke and intestinal flora of post-stroke patients.

Key words: acupuncture-rehabilitation therapy; Northeast Asia; stroke; intestinal flora

Objective

To explore the effects of ART on stroke, intestinal flora and inflammatory factors in stroke patients. In northeast part of China, the winter temperature is low, the temperature difference is large, there are many cold waves, and the wind speed is strong. The incidence and mortality of acute cerebrovascular diseases, such as stroke, are significantly higher than those in other areas. Rehabilitation therapy or acupuncture therapy alone has not produced satisfactory results. However, it was reported that ART can systematically improve various functional disorders such as motor, sensory, speech and swallowing after stroke, with a total effective rate of 94.67% [1]. In order to find the effects of ART on stroke and on intestinal flora of stroke patients in Northeast Asia, in this study, we searched two databases, China National Knowledge Infrastructure (CNKI) and Wanfang and analyzed the results.

Materials and methods

We searched the databases of CNKI and Wanfang in recent 10 years with "acupuncture-rehabilitation therapy", "stroke", "intestinal flora" and "Northeast Asia" as keywords to collect data of acupuncture-rehabilitation effects on stroke and the intestinal flora of stroke patients in Northeast Asia. Outcome measures include intestinal flora, inflammatory factors (including IL-23, IL-17, IL-6, and TNF- α), motor function, quality of life, and verbal function. SPSS26.0 software was used for this study.

Results and discussion

57 articles were collected, but 7 randomized controlled trial (RCT) articles^{[2]-[6][8][9]} met our inclusion criteria and included in our study. Their results show that ART groups are significantly superior to acupuncture alone and to rehabilitation alone groups ($P < 0.05$) in the improvement of intestinal flora, inflammatory factors, motor function, quality of life, and verbal function. As for acupuncture, it appears that cluster needling of scalp point with long needles initiated by Professor Tang qiang of our university produced best effects.

Traditional Chinese medicine (TCM) believes that stroke has a complex pathological process. Wind and fire pathogens, phlegm turbidity and blood stasis are the main pathological factors, which can ascend, harass and impair the brain. Acupuncture can expel these pathological factors and activate blood. Modern medicine has proved that acupuncture therapy has various mechanisms of action on cerebral ischemia [7]. Acupuncture can directly dilate blood vessels, promote oxygen metabolism and improve cerebral blood circulation, reducing secondary damage to brain cell morphology and function.

Acupuncture-rehabilitation therapy has become one of the important components in the treatment of stroke in TCM. Acupuncture therapy has exerted a profound influence on the northeast areas of China and other surrounding countries and regions, especially in the border cities of China and Russia.

There are not many studies related to the treatment of intestinal flora in stroke patients with ART, among which Zhao Yidian^[8] analyzed the effect of ART on intestinal flora and inflammatory factors. We found in our studies that ART can significantly restore motor function of stroke patients, increase the content of beneficial bacteria such as Lactobacillus and bifidobacterium, reduce the content of some opportunistic bacteria such as Clostridium, optimize the structure of intestinal flora, and down-regulate the level of proinflammatory factors in serum. The serum levels of IL-6 and IL-10 in rats after cerebral ischemia can be down-regulated by ART, and the mechanism may be related to the reduction of the expression level of inflammatory factors. The ART can antagonize the inflammatory factors after cerebral ischemia by inhibiting the expression of IL-23/IL17/IL-6/TNF- α protein in ischemic penumbra brain tissue and intestinal tissue. [9]

China's northeast and Russia's Far East cities are the cold northeast Asia regions. Chinese experts have studied the relationship between daytime temperature and stroke incidence in 16 cities in China from 2007 to 2013. The results show that low temperature climate is closely related to the occurrence and mortality of stroke, and mostly involves men and the elderly.

Conclusion

ART has a positive effect on stroke and intestinal flora of post-stroke patients. It can improve inflammatory factors, motor function, quality of life, and verbal function, helping improve the total effective rate of treatment and improve the prognosis of patients. Due to the similarities of geopolitical factors, ART can be promoted in Blagoveshchensk and other Russian regions.

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Analysis of the current situation of acupuncture treatment in Patients with Alzheimer's Disease

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Abstract

Objective: To analyze and summarize the current situation of acupuncture treatment for Alzheimer's disease (AD), in order to provide some data support and acupuncture treatment experience for the future clinical treatment of AD. **Methods:** The Wanfang database was searched, collected the literature related to AD acupuncture treatment, and conducted the summary analysis. **Results:** More than 30 relevant documents were retrieved, among which body needle, electroneedle, scalp needle or self-created regimen were used in clinical studies. The basic animal research was mainly to make animal models of AD and study the protein expression levels of related brain regions before and after acupuncture treatment. Most studies in the literature showed that the protein expression level of animal-related brain regions was significantly improved compared with that before treatment^[1-3]. Clinical studies mainly compared the improvement of cognitive and mental symptoms before and after acupuncture. The score of the simple mental state examination scale, the score of the dementia-related scale, and the cognitive-related scale were improved somewhat after acupuncture treatment.^[4-10] **Conclusion:** The pathogenesis of Alzheimer's disease is not clear, and there is no specific treatment drug. The current treatment is mainly for non-cognitive mental symptoms and cognitive decline. Traditional Chinese medicine has rich clinical experience in AD treatment, and acupuncture treatment is a relatively common treatment method. AD treatment can improve patients' cognition and memory, with high safety, small adverse reactions, simple operation, and can be popularized and applied in clinical practice.

Key words: AD; acupuncture; status quo

AD is a chronic degenerative neuropathy disease, with a relatively insidious onset, mainly with memory loss, personality change, cognitive dysfunction, physical dysfunction and other manifestations. In the later stage, psychotic symptoms such as hallucinations and delusions will appear in^[11]. AD patients have serious impaired brain function, reduced communication ability with the outside world, decreased self-care ability, and seriously impaired social function.^[12-13] brings different degrees of burden to their family and society. Because the cause of the disease is unknown, there is no specific treatment plan at present. In the treatment of western medicine, it mainly takes support treatment and psychological and physical treatment, giving some drugs to improve cognition, such as cholinesterase inhibitors, glutamate receptor antagonists, etc. When psychiatric symptoms occur, low doses of antipsychotic drugs are given to control psychiatric symptoms.

The pathogenesis of dementia in traditional Chinese medicine is believed to fall within "root vacuity and tip repletion", basically characterized by the deficiency of the spleen and kidney and blood stasis due to qi stagnation. The kidney being the congenital foundation, governs the bones and generates marrow. Therefore, sufficient kidney essence nourishes brain mar

row. Conversely, when the deficiency of kidney essence leads to the insufficiency of the sea of marrow, “then the brain revolves, and there are noises in the ears. The lower legs cramp, and vision is dimmed. The eyes see nothing. Patients are relaxed and sleep peacefully.”

The loss of nourishment of brain marrow and the dysfunction of vital activity result in the occurrence of dementia-associated symptoms. As the spleen being the postnatal foundation is the origin of producing qi and blood, and essence and blood mutually transform, spleen deficiency can also lead to the deficiency of essence and blood. Acupuncture therapy in traditional Chinese medicine is aimed at tonifying the kidney, strengthening the spleen, circulating blood, and regulating qi through pattern identification and the selection of formulas and acupoints. For example, ST 36 (Zusanli), BL 20 (Pishu), BL 23 (Shenshu), BL 17 (Geshu), and GB 39 (Xuanzhong) are selected to strengthen the spleen, tonify the kidney, supplement essence and marrow, and nourish blood and tonify deficiency; GV 20 (Baihui), EX-HN 1 (Sishencong), GB 20 (Fengchi), and GV 24 (Shenting) function to open the orifices and induce resuscitation, and calm the mind and promote the intelligence; and LR 3 (Taichong), PC 6 (Neiguan) and SP 10 (Xuehai) have an effect on regulating qi and resolving stasis. Some scholars have analyzed the advantages of acupuncture for AD from the perspective of modern medicine, which is mainly reflected as: promoting the brain to establish collateral circulation, strengthening the compensatory effect of brain function, promoting the synthesis of neurotransmitters, regulating the nerve function; promoting the brain tissue to increase blood flow and volume, and improving the excitability of brain nerve cells.^[14] In short, acupuncture treatment for AD can improve patients' cognition and memory, with high safety, small adverse reactions and easy operation, which can be applied in clinical practice.

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Clinical Observation of Electroacupuncture at Cervical Jiaji Points Combined with Xuebijing Injection in the Treatment of Stroke Associated Pneumonia

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Abstract:

Objective To observe the clinical efficacy of electroacupuncture at Jingjiaji point combined with Xuebijing injection in the treatment of SAP and its effect on lung function. **Methods** 64 patients with SAP were randomly divided into observation group and control group. The control group was treated with Xuebijing injection intravenously; The observation group was treated with Xuebijing injection intravenous drip combined with electroacupuncture at Cervical Jiaji points. The inflammatory indexes, CPIs and NIHSS scores of the two groups were observed before and after treatment, and the improvement of main symptoms and signs and clinical efficacy were compared. **Results** the total effective rate of the observation group was better than that of the control group. After treatment, the CPIs score and NIHSS score of the two groups decreased; The levels of serum WBC, neutrophils, CRP and PCT decreased in the two groups; The indexes of the observation group were significantly higher than those of the control group. After treatment, the recovery of body temperature, disappearance of cough and disappearance of pulmonary rales in the observation group were shorter than those in the control group. **Conclusion** electroacupuncture at Jingjiaji point combined with Xuebijing injection in the treatment of stroke associated pneumonia can effectively improve clinical symptoms and reduce inflammatory indicators, which is worthy of further promotion.

Key words: Stroke-associated pneumonia; Electroacupuncture; Cervical Jiaji Points; Xuebijing injection; Simultaneous intervention for lung and brain

Stroke associated pneumonia (SAP) is one of the common complications after stroke, with an incidence rate of 7% - 22%^[1]. The occurrence of SAP can prolong the hospital stay and is closely related to the prognosis of patients. The pathogenic bacteria of SAP are mainly gram-negative bacilli and anaerobes, and most of them are multiple mixed infections. After the occurrence, the condition is easy to be prolonged and repeated, and its prognosis is poor. It is one of the main causes of death in stroke patients^[2]. The main reasons for its occurrence include body dysfunction caused by aspiration, stroke and decreased immunity, which are also closely related to nutritional factors and treatment methods^[3].

Objective

To observe the clinical efficacy of electroacupuncture at cervical Jiaji points combined with Xuebijing injection in the treatment of stroke associated pneumonia and its effect on pulmonary function

Materials and methods

Sixty-four patients with SAP were randomly divided into observation group and control group, with 32 cases in each group. The control group was given Xuebijing injection intravenously; The observation group was treated with Xuebijing injection intravenous drip combined with electroacupuncture at cervical Jiaji points, twice a day, 7 times as a course of treatment. The curative effect was evaluated after the course of treatment. The inflammatory indexes, clinical pulmonary infection score and National Institutes of Health Stroke Scale were observed before and after treatment, and the impro

vement of main symptoms, signs and clinical efficacy were compared.

Results and discussion

The total effective rate of the observation group was 90.63% (29/32), which was better than 71.88% (23/32, $P < 0.05$). After treatment, the scores of CPIs and NIHSS decreased in the two groups ($P < 0.05$); After treatment, the levels of serum WBC, NE%, CRP and PCT decreased in the two groups ($P < 0.05$), see Table 1; The indexes of the observation group were significantly higher than those of the control group ($P < 0.05$). The recovery of body temperature, disappearance of cough and disappearance of pulmonary rales in the treatment group were significantly shorter than those in the control group ($P < 0.05$).

Table 1 Comparison of WBC, ne%, CRP and PCT levels between the two groups of SAP patients before and after treatment ($\bar{x} \pm s$)

Group	N	Time	WBC ($\times 10^9 \cdot L^{-1}$)	NE%	CRP ($mg \cdot L^{-1}$)	PCT ($\mu g \cdot L^{-1}$)
observation group	32	Before treatment	13.22 ± 1.38	85.39 ± 3.90	48.69 ± 12.04	1.85 ± 0.33
		After treatment	7.77 ± 1.46 ^{①②}	61.92 ± 6.42 ^{①②}	12.14 ± 3.55 ^{①②}	0.98 ± 0.20 ^{①②}
control group	32	Before treatment	13.01 ± 1.35	85.79 ± 3.88	49.41 ± 11.76	1.88 ± 0.37
		After treatment	8.42 ± 1.51 ^①	70.66 ± 5.39 ^①	18.59 ± 5.51 ^①	1.27 ± 0.35 ^①

Note: compared with the same group before treatment, ^① $P < 0.05$; Compared with the control group after treatment, ^② $P < 0.05$.

Electroacupuncture at cervical Jiaji points combined with Xuebijing injection in the treatment of stroke associated pneumonia can effectively improve clinical symptoms and reduce inflammatory indexes, which is worthy of further promotion. It can be seen that electroacupuncture at Jingjiaji point combined with Xuebijing injection in the treatment of SAP can significantly improve symptoms, shorten the course of disease, and the operation is simple without adverse reactions, which provides a new idea for further research on the treatment of SAP.

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Effectiveness of astragalus membranaceus in treating diabetic nephropathy: from multi targets to therapeutic potential

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Abstract

Diabetic nephropathy (DN), a common complication of diabetes, is one of the leading causes that eventually lead to end-stage renal disease (ESRD). At present, effective therapeutic measures are lacking because the pathogenesis of DN has not been clarified. Astragalus membranaceus, as a traditional Chinese medicinal herb in China, is commonly used in the treatment of DN. Astragalus contains two main active components, astragaloside IV (as - IV) and astragalus polysaccharide (APS), which can effectively alleviate proteinuria and protect kidney function. This review summarizes the mechanisms of as - IV and APS in the treatment of DN from the regulation of oxidative stress, endoplasmic reticulum stress (ERs), anti inflammation, and reduction of apoptosis through searching the literature with the gopubmed tool, which may provide a basis for their further application in the clinical treatment of DN.

Key words: Diabetic nephropathy; Astragalus; Astragaloside IV; Astragalus polysaccharide

DM is a metabolic disease characterized by hyperglycemia. Among many complications, diabetic nephropathy (DN) due to long-term chronic microangiopathy such as impaired glomerular vasculature and sclerosis is one of the most serious. The antidiabetic chemical components mainly contained by Astragalus membranaceus are polysaccharides, saponins, and flavonoids. APS are divided into glucans and heteropolysaccharides. A large number of experimental studies and professional analytical detection can go to illustrate that the triterpenoid saponins from Astragalus membranaceus have bioactive effects on human health. In particular, astragaloside IV (ags-iv), a 3-o-b-d xylopyranosyl-6-o-b-d-glucopyranosyl-cycloastragalone, belongs to the triterpenoid saponins class and has a wide range of pharmacological effects.

Objective

In recent years, studies on the prevention and treatment of diabetic nephropathy in traditional Chinese medicine (TCM) have also been in depth. In this review, we mainly summarize the mechanisms of as - IV and APS in the treatment of DN, aiming to provide a theoretical basis for their further pharmacological studies and clinical applications.

Materials and methods

A total of 20 high-frequency research keywords, core authors, top-level journals and regional distribution of studies on Astragalus treatment of diabetic nephropathy literature were collated by entering search terms (Astragalus and diabetic nephropathy) within gopubmed.

2 Results

2.1 Amelioration of oxidative stress

Increased oxidative stress is caused by a persistent hyperglycemic state that can cause oxidative damage to macromolecular substances such as carbohydrates, nucleic acids, proteins. Kidney during the course of DN, it can make more oxygen free radical production in the body for many reasons,

meanwhile, antioxidant enzymes such as SOD and GPX in the renal cortex may cause it to oxidize and glycosylate due to glucose metabolism disorder and oxidative stress, thus leading to renal tissue damage [1,2]. Studies have reported [3] that, in the cellular antioxidant response, the Nrf2 signaling pathway acts as a central regulator and plays a protective role in the process of inflammatory response, oxidative stress and cell apoptosis in the organism.

2.2 Regulation of endoplasmic reticulum stress

The endoplasmic reticulum is a key site for secretory and biological membrane proteins to be processed and transported to the Golgi apparatus and an important site for intracellular calcium ion storage. It has been found that APS can restore endoplasmic reticulum functional homeostasis by reducing the homologous protein levels of the ERS marker CCA at / enhancer binding protein by inhibiting perk phosphorylation [4]. Guo et al [5] used two animal models of diabetes, spontaneous and induced, that is, DB / db mice and streptozotocin-induced diabetic mice, and both found perk, ire-1 in mouse kidney tissue α 、 ATF6 and its downstream targets were activated, chop expression was significantly elevated, and the expression of factors involved in ers induced apoptosis, such as phosphorylated c-Jun amino terminal kinase and cleaved caspase-12, were increased, which were all reversed by as - IV.

2.3 Anti inflammation

During the development of DN pathology, different metabolic pathways and cytokines are activated, such as the Janus kinase / signal transducer and activator of transcription signaling pathway, nuclear transcription factor κ B (the nuclear transcription factor kappa B, NF- κ B), nuclear transcription factor E2 related factor 2, and others [6]. As - IV can alleviate inflammatory response and cell apoptosis by acting on the above pathways or cytokines [7]. Monocyte chemoattractant protein-1 is the key that influences the accumulation of macrophages in vivo in DN patients, and MCP-1 expression induced by certain inflammatory factors serves as a priming factor for the development of renal inflammation.

2.4 Reduce podocyte apoptosis

Currently, protecting podocyte has become one of the effective ways to treat glomerular injury [8]. It was found that as - IV could elevate mir-378 expression in high glucose induced mouse podocytes, and mir-378 could target to negatively regulate TRAF5, therefore, as - IV could inhibit podocyte apoptosis through the mir-378 / TRAF5 signaling pathway, and mir-378 and TRAF5 could be used as novel targets for the treatment of DN [9].

Discussion

The research on Astragalus treatment of diabetic nephropathy is in the rising stage, and the heat of this research at home and abroad is also increasing year by year. As far as the current research achievements are concerned, Radix Astragali has a certain relevance for the treatment of diabetic nephropathy, therefore, in the future, it is necessary to more deeply and comprehensively mine the pharmacological effects of the active components of Radix Astragali in order to provide a more reliable theoretical basis for the clinical treatment of DN.

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Research progress on *in vitro* synthesis technology of natural medicines

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Key words: Natural medicines; Biotransformation; Plant tissue culture; Microbial cell factories

Abstract:

With the deepening of pharmacological research, more and more natural medicines have been excavated and showed unique pharmacological effects, especially for diseases that are currently difficult to treat clinically. The ever-increasing demand for natural medicines has made it difficult to meet the current market demand solely from plants. Therefore, more and more *in vitro* synthesis techniques have been explored for the product of natural medicines, and great progress has been made. As a result, new challenges are constantly emerging.

The *in vitro* synthesis of natural medicines can rely on both chemical synthesis and biosynthesis. Due to the diverse structures, only a small number of natural medicines can be synthesized by chemical synthesis, but the catalytic reaction is complex and the synthesis cost is high. Therefore, the exploration of biosynthesis technology has become the main means of increasing production. Plant cell and tissue culture, root culture and somatic embryogenesis are traditional methods for *in vitro* culture of medicinal plants. Using bioreactor optimization, a large amount of extracted raw materials can be obtained regardless of the season, and it has the characteristics of high yield, stability and high efficiency. Through the manipulation of synthetic pathways by molecular biology techniques such as transgenic technology and genetic stability, the production efficiency of target natural medicines has been further improved^[1]. In recent years, the biosynthesis of natural products by constructing microbial cell factories has become a research hotspot. Through multi-module engineering, new metabolic pathways have been constructed, from artemisinin, taxadiene, tanshinone, resveratrol to more complex ginsenosides and diosgenin, all of which have realized the efficient production of microbial *in vitro* production platforms^[2]. In order to further improve the yield, an artificial multicellular system with high efficiency and stability was also constructed by utilizing the cooperative relationship between strains^[3]. Microorganisms such as *Aspergillus oryzae* and *Aspergillus terreus* are also being developed as chassis cells.

The construction of an *in vitro* synthesis platform for natural medicines is of great significance to alleviate the shortage of natural medicine resources and obtain rare natural medicines. With the development of molecular biology technology, rapid progress has been made in the targeted and massive biosynthesis of natural medicines. Using *in vitro* synthesis platforms, more and more natural medicines will be used for large-scale industrial production in the future.

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Fermentation of natural products by lactic acid bacteria, a new idea for regulating human immune function

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Key words: fermentation, natural products, lactic acid bacteria (LAB), immunomodulatory

Abstract

Natural products, such as polysaccharides, triterpenes, flavonoids, alkaloids, volatile oils and phenols, have been widely served as immune modulators with minimal side effects to regulate the immune function. Fermentation is a microorganism-driven process which yields high value product from raw or low-grade substrates^[1]. More specifically, fermentation can decompose or convert undesirable substrates into new active entities under the action of enzymes, thereby improving the bioactivity of natural medicine. It has been shown that fermentation improves the biological activities of natural products mainly through the modification of naturally occurring molecules such as polysaccharides^[2], saponins^[3-4], polyphenols^[5] and bioactive amino acids^[6] that exert immunoregulatory effects. Moreover, the fermentation-induced structural breakdown of the plant or fungi cell walls may liberate and/or induce the synthesis of various immunoreactive compounds. Furthermore, some natural compounds also affect the metabolic pathways of microorganisms and then produce more abundant active secondary metabolites. In recent years, considerable attention has been paid to the beneficial action of probiotic bacteria and their fermentation products on human health. Lactic acid bacteria (LAB) has been proved to interact with human immune cells and regulate specific pathways involved in innate and adaptive immune processes in various inflammatory diseases^[7]. Particularly, probiotics and prebiotics, including exopolysaccharides^[8], short-chain fatty acids^[9], bacteriocins^[10], etc. in the fermentation system may have positive impacts on the microorganisms and activity within the human gut, further affecting the immune system. For the reasons discussed above, the fermentation of natural products by LAB is an effective strategy to improve the immunomodulatory activity of herbal products. This study provides an overview of the effects of LAB fermentation on the immune active substances of natural products and the immunomodulation mechanisms of fermented products.

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Research Progress on main active constituents and pharmacological activities of *Trichosanthis Radix*

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Abstract

Trichosanthis Radix is a commonly used Chinese medicinal in clinic, and the study of its active components has attracted great attention from researchers both in China and abroad. In recent years, a large number of basic studies have been conducted on the active components of *Trichosanthis Radix*, and a variety of compounds and active components have been isolated from *Trichosanthis Radix*, possessing multiple pharmacological effects. The active components and pharmacological effects of trichosanthin were reviewed in order to provide reference for the further development of new drugs of trichosanthin.

Key words: *Trichosanthis Radix*; active constituents; pharmacological activities; trichosanthin; Trichosanthin polysaccharide

Trichosanthis Radix, also known as the root of *trichosantheskirilowii* maxim, is the dried root of *Trichosantheskirilowii* Maxim. or *Trichosanthesrosthornii* Harms. of cucurbitaceae^[1]. It has the effects of clearing heat, purging fire, promoting salivation, and quenching thirst. It is commonly used in the clinical treatment of pyretic polydipsia, cough due to lung heat dryness, and internal heat-wasting thirst^[2]. *Trichosanthis Radix* is a commonly used Chinese medicinal material in clinical practices, and its main components are protein, polysaccharide, lectin, and saponin. It has a variety of pharmacological activities, such as lowering blood glucose, termination of pregnancy, anti-tumor, anti-inflammatory, antiviral, antibacterial and coagulation^[3]. In order to make better use of the resources of *Trichosanthis Radix*, the active components and pharmacological activities of *Trichosanthis Radix* were reviewed in this paper.

1 Trichosanthin

Trichosanthin (TCS) is an essential protein extracted from *Trichosanthis Radix*. It is a type I ribosomal inactivating protein, belonging to one of the members of the ribosomal inactivating protein family. Trichosanthin mature skin consists of 247 amino acid residues, with a molecular weight of about 24000 and is composed of 15 amino acids^[4]. Nishant Bhatia et al.^[5] extracted type I ribosome-inactivating protein from the root tuber of *Trichosantheskirilowii* using cation exchange chromatography in a one-step rapid and simple purification procedure for trichosanthin, and protein has been identified. The pharmacological effects of trichosanthin include anti-tumor, termination of pregnancy, regulation of immunity and many other aspects. Zhou et al.^[6] found that trichosanthin could inhibit the proliferation and induce the apoptosis of colon cell line CMT-93 in vitro.

2 Polysaccharides of *Trichosanthis Radix*

Trichosanthis Radix polysaccharide is also one of the main components of *Trichosanthis Radix*, and its content accounts for the highest proportion among several components of *Trichosanthis Radix*. Huang Xiaolan et al.^[7] believed that polysaccharides of *Trichosanthis Radix* was a heteropolysaccharide composed of rhamnose, arabinose, fructose, mannose, glucose and

galactose. The polysaccharides of *Trichosanthis Radix* has that effect of regulating immunity and resis tumor. Jiang et al.^[8] injected trichosanthin polysaccharide into mice and found that compared with the control group, the injection of polysaccharides of *Trichosanthis Radix* significantly stimulated lymphocyte proliferation and thus improved the immune ability of the mice.

3 *Trichosanthes kirilowii* lection

Trichosanthes kirilowii lection (TKL) was a galactose-specific protein consisting of two peptide chains separated from *Trichosanthis Radix*. The lectin had a molecular weight of about 60kD, an isoelectric point of about 5.5^[9]. *Trichosanthes kirilowii* lection is considered to be the main active component of *trichosanthis Radix* in lowering blood glucose. Using metformin in hydrochloride as the positive control, TKL was divided into low, medium and high (0.3, 0.6, and 0.9 g/kg) doses for intragastric administration of streptozotocin-induced diabetic rats. Three weeks later, the results showed that TKL could significantly improve blood glucose abnormalities in diabetic rats and enhance their antioxidant capacity^[10-11].

4 Saponin of *Trichosanthis Radix*

Saponins are formed by the combination of sugars and non-sugars and widely exist in roots, stems, leaves and other parts of plants, with a variety of pharmacological effects^[12]. Chen Ying et al.^[13-14] used ursolic acid as reference substance and vanillin-glacial acetic acid as color developer to determine the content of total saponins in *Trichosanthis Radix* by ultraviolet spectrophotometry. The results showed that *Trichosanthis Radix* contained about 1.9%–2.4% of total saponins, and the saponins showed strong antioxidant activity in vitro.

5 Conclusion and prospect

In summary, the studies on the components of *Trichosanthis Radix* have mainly focused on their separation and purification, content determination, and pharmacological effects. Although *Trichosanthis Radix* contains a variety of active components, TCS, TKL and polysaccharides of *Trichosanthis Radix* have been studied most widely, and TCS is the current research focus. However, studies on saponins and flavonoids were relatively rare. It should be further studied and clarified in the future to lay a foundation for later development.

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Advances in chemical constituents, pharmacological effects and biotransformation of *isatis indigotica* Fort

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Key words:

Isatisindigotica Fort, chemical constituents, pharmacological action, biotransformation

Abstract

Isatis indigotica Fort is a cruciferous herbaceous plant. Its dry root is *Isatidis Radix*, and its dry leaf is *Isatidis Folium*^[1]. It has the effect of clearing heat and detoxifying, cooling blood and promoting pharynx, and eliminating plaque^[2]. Modern pharmacological studies have shown that *I. indigotica* has antibacterial^[3], antiviral^[4], antitumor^[5], anti-inflammatory^[6], and immune regulation^[7]. In addition, *Radix Isatidis* and *Folium Isatidis* are commonly used as heat-clearing and detoxicating drugs, which are commonly used for the prevention and treatment of influenza virus, and also play an active role in the prevention and treatment of SARS and new coronavirus, which is directly related to its rich chemical composition. The main chemical components can be roughly divided into alkaloids, organic acids, amino acids, nucleosides, phenylpropanoids, polysaccharides and trace elements, among which indigo, 4(3H)-quinazolone and epigoYichun are the main alkaloids, organic acids mainly include palmitic acid, syringic acid and salicylic acid, amino acid content of arginine is the highest, followed by proline^[8]. Biotransformation refers to the physiological and biochemical reactions that occur when exogenous substrates are modified or structurally modified by enzymes in biological systems or biological systems^[9]. With the deepening of research, researchers also tried to improve the content of active ingredients in *I. indigotica* by biotransformation, and then improve its efficacy, mainly involving the biotransformation of edible fungi, molds, bacteria, intestinal flora and even genetic engineering bacteria. The use of biotransformation technology to modify the chemical structure or active sites of active compounds traditional Chinese medicine to obtain new components or increase the content of original components, which is of great significance for exploring active substances of traditional Chinese medicine, expanding and protecting traditional Chinese medicine resources.

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Research progress of sports nutrition food and functional ingredients

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Abstract

In recent years, as we pay more and more attention to physical health, a lot of people choose to keep healthy by doing exercises, which greatly promotes the development of the sports food industry. Sports nutrition food can meet the metabolic and energy needs of sports crowd, reduce exercise-induced injury and quickly eliminate sports fatigue. This article provides an overview of sports nutrition foods and their functional ingredients, in order to provide theoretical guidance for current research and development to meet the needs of the growing sports population.

Key words: sports nutrition food, anti-fatigue effect, functional ingredients

Sports nutrition food is a kind of functional food based on biology, combined with sports and nutrition science, and developed by modern biotechnology methods. The nutritional components of sports nutrition food can be divided into basic nutrients and functional components. Basic nutrition refers to the nutrients that the human body needs to maintain normal life activities; functional components are bioactive factors that can improve human function, such as protecting ligaments and joints, improving muscle mass, and accelerating human metabolism. Compared with ordinary food, sports nutrition food has a certain health care effect and can effectively supplement the energy consumption of the body during exercise. Under specific and non-specific circumstances, according to the analysis of nutrient consumption in human exercise, nutrients can be reasonably matched to meet the body's needs during exercise^[1].

Research status of sports nutrition food

At present, a variety of sports nutrition foods have been developed at home and abroad, including beverages, tablets, energy bars, and capsules. Many of these products have been shown to prolong the swimming time of mice with weight, increase the glycogen reserve, reduce the serum urea nitrogen content and the blood lactate level, etc. so as to achieve the purpose of improving exercise endurance, physical function, increasing the glycogen reserve and anti-fatigue effect^[2-4].

Due to the late start of the sports nutrition food market in my China and the lack of product types, the market demands faced by enterprises specializing in the research, development and production of sports nutrition food are mainly concentrated in professional athletes and fitness clubs, which are far from meeting the needs of non-professional consumers.

Functional ingredients in sports nutrition foods

The current sports nutrition food mainly relies on the functional components contained or added in it to effectively relieve the mild injury and exercise fatigue of the body before, during and after exercise. These functional ingredients include food-derived bioactive peptides, traditional Chinese medicine ingredients and plant-based active substances^[5].

Modern nutrition research believes that protein is digested in the digestive tract after being ingested, and more is absorbed in the form of peptides, and a small amount is absorbed in the form of free amino acids, and peptides are easier to digest and absorb than free amino acids. Bioactive peptides also have a variety of physiological regulation effects, such as antioxidant, anti-fatigue, blood

pressure lowering, antibacterial and so on. The sources of bioactive peptides are very wide, which can be divided into two categories: plant sources and animal sources. The addition of bioactive peptides is of great significance to the improvement of the anti-fatigue effect of sports nutrition foods and the development of new sports nutrition foods.

The latest research confirms that some traditional Chinese medicine ingredients also have a positive effect on repairing and relieving exercise-induced fatigue^[6-7]. Nutritional supplements containing traditional Chinese medicine ingredients have few side effects, can adjust and improve the physical state of the body, and have anti-fatigue, anti-oxidation, immune-enhancing effects. Traditional Chinese medicine in China has a long and profound history, and has good market acceptance and development prospects.

Plant active substances such as polysaccharides, flavonoids, saponins, polyphenols and other substances have been proved to have the effect of anti-exercise fatigue and are widely used in sports food^[8]. Purslane polysaccharide can increase the content of muscle glycogen and liver glycogen in the body, accelerate lactic acid scavenging, increase glycogen reserve to enhance the body's anti-fatigue ability; plant polyphenols have good antioxidant ability and can scavenge oxygen free radicals. It has a positive effect on relieving exercise-induced fatigue, such as tea polyphenols, grape polyphenols, etc. Most flavonoids have the ability to improve the body's antioxidant and scavenging free radicals, such as quercetin, silymarin, etc.; saponins are bioactive substances mainly distributed in terrestrial higher plants, many studies have shown that saponins bioactive substances There are many ways to eliminate exercise fatigue and improve exercise endurance.

Conclusion and prospect

With the development of the economy and the continuous improvement of living standards, people pay more and more attention to health, and a series of sports injuries, sports recovery and other issues arising from exercise have attracted everyone's attention. In order to meet the needs of the sports crowd, domestic and foreign efforts are devoted to the research on the functional ingredients of sports nutrition food, especially the various sports drinks that have emerged in recent years, in which various nutrients have been added to relieve exercise fatigue and repair after exercise damaged muscle tissue.

At present, the development of sports nutrition food is not mature enough, and continuous innovation is needed. In the process of research and development, it is necessary to fully consider the differences and diversity of nutrients required by the human body in different periods, and to build a unified and standardized sports nutrition food industry standard.

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Research progress on properties and health care effects of probiotic fermentation in traditional Chinese medicine

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Abstract

Objective: To study the advantages and health care effects of probiotic fermented traditional Chinese medicine. **Methods:** The related literature on probiotics fermented in traditional Chinese medicine in recent years were consulted, and its advantages and characteristics and their application in health care were reviewed and analyzed. **Results:** Traditional Chinese medicine fermented by probiotics has the effects of increasing the content of effective components, enhancing the efficacy, producing new substances, and reducing the toxicity of traditional Chinese medicine. It has the effects of relieving fatigue, enhancing immunity and lowering blood lipids. **Conclusion:** the combination of probiotics and traditional Chinese medicine can biotransform the effective components of traditional Chinese medicine, and the curative effect is significantly enhanced. It brings new ideas to the research and development of functional food and traditional Chinese medicine and has great development prospects.

Key words: probiotic, traditional Chinese medicine, property, health care effect

Probiotics are active microorganisms beneficial to human health, which can regulate the function of the immune system and improve the balance of intestinal flora. Traditional Chinese medicine (TCM) contains a variety of natural compounds, which can decompose macromolecular substances, improve bioactive components, enhance pharmacological activity, and reduce the toxic and side effects of TCM after probiotic metabolism or biotransformation. Therefore, using probiotics to ferment TCM has become a current research hotspot. This paper analyzes and summarizes the characteristics and health care effects of probiotic fermentation in TCM, in order to provide a reference for the development of TCM and functional products.

1. Properties of probiotic fermentation of TCM

1.1 Increase bioactive ingredients and improve drug efficacy

The research on ginseng and curcuma showed that the contents of total saponins and curcumin increased by 25.87% and 9.76% respectively after fermentation with *Lactobacillus fermentum*, and the effects of fermented TCM on lipid-lowering, liver protection and anti-inflammatory were significantly enhanced^[1,2].

1.2 Produce new bioactive substances

Through analysis, it was found that when *Ganoderma lucidum* was fermented with *Lactobacillus acidophilus* and *Bifidobacterium breve*, component ganoderic acid A was biotransformed by probiotics to produce a new component ganoderic acid C2, which promotes the enhancement of immunostimulatory activity^[3].

1.3 Reduce the toxicity

The toxicity of TCM can be degraded and transformed by microorganisms. Chen et al. found that *Strychnos nux vomica* has analgesic and anti-inflammatory effects, and is highly toxic. Using probiotics to ferment it can not only maintain its original efficacy, but also reduce its toxicity^[4].

2. Functions of health care

2.1 Relieve fatigue

The study found that the contents of saponins, phenolic acids, flavonoids, and other active substances in *Panax Notoginseng* Leaves (PNL) were significantly increased and showed good antioxidant stability capacity after co-fermentation by *S. cerevisiae* and *B. subtilis*. In vitro and in vivo experiments showed that fermentation PNL could improve exercise-related energy storage and alleviate fatigue^[5].

2.2 Immune enhancement

Research demonstrated that *Ganoderma lucidum* fruiting body extracts of probiotic fermentation could significantly improve the immunity, intestinal integrity, and gut microbiota dysbiosis in dexamethasone-treated mice, which is closely related to its direct regulation on the expansion of CD4 T cells in Peyer's patches of mice^[3].

2.3 Hypolipidemic

Black tartary buckwheat fermented by *Bacillus* sp. DU-106 can significantly reduce the levels of serum total cholesterol, triglycerides, and low-density lipoprotein cholesterol in high-fat diet induced hyperlipidemic rats, play a role in lowering blood lipids and regulating gut microbiota^[6].

3. Conclusion and prospect

The use of probiotics to ferment TCM is the focus of current research. This fermentation method can obtain more effective target ingredients to improve the efficacy, produce secondary metabolites, improve the utilization rate of TCM, reduce the toxicity of TCM, increase the biological activity of TCM, and maximize the medicinal value of TCM. However, the TCM fermented by probiotics also faces some problems that need to be solved, such as the screening of excellent strains, the selection of fermentation methods, and the establishment of fermentation technology. The combination of probiotics and TCM has good prospects for sustainable development, which is a new idea for the modernization of TCM. Therefore, constantly expanding the development potential and application value of probiotics in the fermentation of TCM, and exploring the transformation mechanism and action mechanism of active ingredients of TCM have far-reaching significance for the research and development of functional foods and TCM.

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A review of microbial folic acid biosynthesis pathways

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Abstract

Folic acid is distributed in plants, animal tissues and microorganisms, which is poor in stability and easy to decompose, even only a few plants and microorganisms have the ability to synthesize folic acid. People's demand for folic acid is high, the human body lacks the gene that can synthesize folic acid and can only rely on external intake, and long-term excessive consumption of synthetic folic acid will lead to the occurrence of unmetabolized folic acid in plasma, so it is very important to improve the natural production of folic acid. In this paper, the biosynthetic pathway of microbial folic acid was reviewed to provide research ideas for fortification, development and utilization of folic acid.

Keywords: Microbial ,Folic acid, Biosynthesis

Folic acid is a water-soluble vitamin composed of purine, p-aminobenzoic acid and glutamic acid, which is widely distributed in plants, animal tissues, algae and microorganisms. Folic acid is unstably and easy to degrade in acidic environment and light conditions. Human beings and other higher animals lack the gene to synthesize folic acid and cannot synthesize their own folic acid. At present, microbial synthesis of folic acid is commonly used in food to meet people's daily needs. Strains of *Lactococcus*, *Bifidobacterium*, *Streptococcus* and some *Lactobacillus* have been found to synthesize folic acid. Most yeast cells can also produce folic acid, among which prion producing yeast has the highest yield, ester producing yeast is the next, beer yeast is low, wine yeast and candida do not produce folic acid.

1. Microbial folic acid synthesis pathway

1.1 Synthesis of butterfly ridine

GTP produces 7,8-dihydroneopterin-3'-triphosphate (DHNTP) under the action of GTP cyclohydrolase I (GCHI). GCHI is a key enzyme in the synthesis of folic acid, encoded by gene *folE*. In *Escherichia coli*, DHNTP was dephosphorized to form 7, 8-dihydropterin-3'-phosphoric acid by *nudB* protein, and continued dephosphorylation to form DHN. DHN in two new hydrogens with poison aldolase dihydroneopterin aldolase (DHNA) under the action of dehydroxylation acetaldehyde generated in 6-hydroxymethyl-7,8-dihydro with poison 6-hydroxymethyldihydropterin (HMDHP), DHNA is encoded by *folQ* gene in lactic acid bacteria, while it is found that this step is regulated by *folB* gene in *E. coli* [1-2]. HMDHP pyrophosphokinase (HPPK) is catalyzed by ATP to generate 6-HMDHP pyrophosphate (HMDHP-P₂), and HPPK is regulated by *folK* gene.

1.2 Biosynthesis of pABA

Aminodeoxychorismate (ADC) is generated by aminodeoxychorismate synthase (ADCS). In *E. coli*, ADC is generated by AMinodeoxychorismate SYNthase I and II. Encoded by *pabB* and *pabA*, respectively. The next step is to generate p-aminobenzoic acid (pABA) by the action of aminodeoxychorismate lyase (ADCL) encoded by *pabC*. In *Lactobacillus lactis* MG1363, pABA production requires pABA alone open reading frame and *pabBC* fusion open reading frame. The fused *pabBC* gene was found not only in *Lactobacillus* but also in other Gram-positive bacteria and

several gram-negative bacteria^[3]. In *Lactobacillus lactis*, pABA is a key step in folic acid synthesis, and deletion of the gene prevents it from making folic acid, resulting in an inability to make purine bases and hence growth.

1.3 Add glutamate tail

Dihydropterin analogue HMDHP was pyrophosphorylated and coupled with p-aminobenzoic acid to generate dihydropteroate (DHP) under the action of folP-guided synthesis of dihydropterate synthase (DHPS). Then dihydrofolate (DHF) was synthesized by Dihydrofolate synthase (DHFS) under the guidance of folC and glutamic acid was added to produce DHF, which was reduced to THF by Dihydrofolate reductase (DHFR). In *E. coli*, folM and folA encode DHFR is synthesized, followed by glutamate tail addition under the action of Folylpolyglutamate synthetase (FPGS), and polyglutamate tetrahydrofolate is finally synthesized^[4].

2.Folic acid and human health

Folic acid can only be supplied through diet or through absorption of folic acid produced by the catabolism of the gut flora. Folic acid is involved in vital metabolic reactions, including nucleotide synthesis, DNA methylation, and plasma homocysteine levels. Folic acid is also involved in indispensable biochemical reactions in the body, such as the synthesis of purines and pyrimidines, and the formation of hemosiderin, etc. Folic acid also provides free carbon ions, which can be involved in the formation of nerve endings and precursors of nerve impulses, enabling the normal development of the human nervous system. So folic acid is of vital importance for the body. However, dietary folic acid cannot longer meet some specific groups of people, and synthetic folic acid emerged. An increasing number of studies have found that taking a large amount of synthetic folic acid will lead to an increase in unmetabolized folic acid in the blood, and a higher plasma folic acid concentration will also increase the risk of colorectal cancer^[5], which cover up VB₁₂ deficiency and change liver dihydrofolic acid reductase activity. Long-term high folic acid intake may increase the incidence of breast cancer in postmenopausal women. Natural folate can be metabolized directly in the body into 5-methyltetrahydrofolic acid which can be used by the body, though synthetic folic acid tends to accumulate in the body due to lacking of the enzymes to break down it, which can lead to disease. Therefore, natural folate can reduce this risk, growing number of microorganisms are reported to be able to synthesize folic acid.

3.Discusion

Above all, the amount of folic acid produced by microorganisms is relatively high, which is still not enough for daily needs. People can control the amount of folic acid produced by microorganisms according to the key nodes of folic acid synthesis. It is reported that folE, folP, folQ, folM, folA, are the key genes controlling folic acid synthesis. Overexpressing one of these genes or a combination of two or more genes is able to achieve folic acid fortification. It can also improve the stability of folic acid in microorganism, make it degrade slowly, knock out the gene of folic acid catabolism, improve the content of folic acid in cells, and provide theoretical basis for the rational development and utilization of folic acid.

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Theories and Methods of Epidemic Prevention with Characteristics of Traditional Chinese Medicine

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Abstract

This article summarizes the epidemic prevention theories and methods of traditional Chinese medicine scientists in the past dynasties by consulting relevant documents and books, including protecting the righteousness and strengthening the physique; diagnosis, treatment and isolation, and control of transmission; Ten methods such as taking medicine, bathing, acupuncture and moxibustion.

Key words: Chinese medicine; Prevention; Epidemic prevention; Epidemic diseases; Infectious diseases

With the outbreak of the COVID-19 epidemic in 2019, the world is facing severe challenges. All countries are preventing the spread of the epidemic, while actively seeking effective responses to COVID-19. In the process of fighting the epidemic, the traditional Chinese medicine system shines brilliantly. A number of traditional Chinese medicine researchers have jointly created Qingfei Paidu decoction. After clinical application, the treatment effective rate has reached more than 90%. However, the traditional Chinese medicine culture that has been inherited for thousands of years is not only effective in the treatment of epidemic diseases, but also has its unique advantages in the prevention and control of epidemic diseases.

Objective

By searching the books written by traditional Chinese medicine scientists and related literature in modern times, this paper preliminarily summarizes and lists the epidemic prevention theories and methods with the characteristics of traditional Chinese medicine, hoping to play a reference role in resisting the epidemic situation.

Materials and methods

Through the library of Heilongjiang University of traditional Chinese Medicine, China knowledge Network, VIP, Wanfang and other platforms to collect and consult relevant books and documents, statistics and list the theories and methods of epidemic prevention with the characteristics of traditional Chinese medicine.

Results and discussion

By looking up the books and literatures written by traditional Chinese medicine scientists in previous dynasties, it is preliminarily summarized and listed as taking care of righteousness, strengthening physique, diagnosis and treatment, isolation and control of transmission. There are three parts: characteristic therapy and disease prevention, in which the content of characteristic therapy is the most important, including ten epidemic prevention methods with the characteristics of the theoretical system of traditional Chinese medicine, they are: prescription medicine epidemic prevention law, burning epidemic prevention method, immune epidemic prevention method, admiring epidemic prevention method, nasal medicine taking medicine method, acupuncture epidemic prevention method, powder body epidemic prevention method, bath epidemic prevention

method, drinking and drinking epidemic prevention method and eye-catching epidemic prevention method.

It is undeniable that when the theoretical system of traditional Chinese medicine is not perfect, limited by the lack of times and cognition, some doctors have put forward some methods of preventing and controlling epidemic diseases with feudal superstition and more inclined to witchcraft, such as mantra and peach charm, and so on, these methods need to be identified and abandoned by the successors of the theory of traditional Chinese medicine. However, traditional Chinese medicine has a long history of prevention and treatment of epidemic disease. in the historical circulation of thousands of years, countless doctors have inherited, summarized, extended and passed on, giving full play to the characteristics of syndrome differentiation and treatment of traditional Chinese medicine and their advantages in preventing and controlling epidemic diseases. for the prevention and treatment of epidemic diseases with the theory and methods of traditional Chinese medicine has accumulated a lot of experience, these experiences are the most valuable wealth handed down to future generations. At present, it only preliminarily collates and lists the epidemic prevention thoughts and methods of traditional Chinese medicine scientists of different academic schools in history, which are worthy of more in-depth exploration and verification. it has a certain reference value for the prevention, control and treatment of modern epidemic disease, especially COVID-19 epidemic situation.

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Effect of Intervention with Traditional Chinese Medicine Monomers on JAK/STAT Signal Pathway in Psoriasis : A Review

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Abstract

Psoriasis is a chronic and inflammatory disease characterized by erythema, papules, plaques and covered with multi-layer silver-white scales. At present, it is known that a variety of immune signaling pathways play an important role in the occurrence and development of psoriasis. JAK/STAT signal pathway plays an important role in the pathogenesis of psoriasis. Some cytokines, such as interleukin 17 (IL-17) and IL-23, regulate the transcriptional expression of target genes in the nucleus through JAK/STAT signaling pathway, leading to the occurrence and development of psoriasis. Over the years, traditional Chinese medicine has achieved good clinical efficacy in the prevention and treatment of psoriasis. Through further research, many doctors have found that some Chinese medicine monomers have obvious regulatory effects on psoriasis-related JAK/STAT signal pathway.

Key words: Chinese Medicine monomers; psoriasis; JAK/STAT signal pathway ; mechanism

Psoriasis as an autoimmune disease, the core mechanism of its pathogenesis is immune abnormality. By consulting the existing research results, the efficacy of JAK inhibitors in the treatment of psoriasis is excellent, but the effect of JAK inhibitors is not stable, Over the years, experts and scholars have also carried out a lot of research on traditional Chinese medicine monomers to provide a more reliable scientific basis and more treatment plans for the treatment of psoriasis.

JAK/STAT signal pathway

JAK (Janus kinase) / STAT (signal transducer and activator of transcription) signal pathway, which mainly mediates the response of cells to various cytokines and growth factors. JAK is a kind of cytoplasmic tyrosine kinase. JAK activates downstream pathways by binding to different receptors and assisting receptors without kinase activity in signal transduction. STAT is a downstream protein of JAK. JAK activates phosphorylated STAT and binds to related promoters to regulate the transcriptional expression of target genes.

JAK/STAT signaling pathway and psoriasis

The pathogenesis of psoriasis is not clear. It is generally believed that local abnormal activation of helper T cells (Th) play an important role in the pathogenesis of psoriasis^[1]. Cytokines secreted by T cells affect the occurrence and development of psoriasis by activating JAK/STAT signal pathway. The results showed that the mRNA expression level of STAT1 and STAT3 genes in keratinocytes in the lesion area was significantly higher than that in the non-lesion area. The possible mechanism was that abnormally activated Th1 cells secreted cytokines such as IFN- γ and IL-2, and misregulated the transcriptional expression of target genes through JAK/STAT signal transduction pathway^[2]. STAT3 has a significant effect on cell cycle, inhibition of STAT3 pathway can induce apoptosis^[3]. Activating STAT3 signal transduction pathway can delay the error of apoptosis^[4].

The above studies show that abnormally activated T cells in patients with psoriasis can secrete IFN- γ , IL-2 and other cytokines, regulate the expression of corresponding genes through JAK/STAT signaling pathway, and produce psoriasis-like lesions.

Intervention of traditional Chinese Medicine monomer on psoriatic JAK/STAT trunk signaling pathway

Tripterygium wilfordii polyglycosides, one of the effective components of Chinese herbal medicine Tripterygium wilfordii, have been found to have anti-inflammatory and immunomodulatory effects. Tripterygium wilfordii polyglycosides inhibit the expression of JAK1 and STAT3 protein in skin lesions and inhibit JAK/STAT signal pathway, thus improving the inflammation of skin lesions^[5].

Triptolide (TP), studies have shown that TP may inhibit the secretion of Th17 cells and the expression of IFN- γ cytokines through JAK/STAT signaling pathway, inhibit the overproliferation of epidermal cells, and improve the performance of skin lesions^{[6][7][8]}. Triptolide inhibits mRNA transcription of IL-17 and phosphorylation of STAT3 induced by IL-6, and STAT3 is a key signal molecule involved in the development of Th17 cells.

Indirubin (IR) is a diindole compound extracted from the leaves of indigo chinensis. The main mechanism is to reduce the inflammatory response mediated by γ δ T cells produced by IL-17A, inhibit the activation of JAK3/STAT3, and then reduce the psoriasis-like lesions induced by ImQ^[9].

Chrysin pretreatment can inhibit the phosphorylation of JAK/STAT pathway and inhibit the expression of cytokines such as TNF- α , IL-17A and IL-22. At the same time, it can also reduce the release of CCL20 and antimicrobial peptides from epidermal keratinocytes^[10].

Rosmarinic acid (RA) is a natural bioactive molecule known to have anti-inflammatory potential, which can be extracted from cumin. RA can resolve psoriasis-like inflammation in human keratinocytes by interfering the JAK2/STAT1 signaling pathway^[11].

Berberine (BBR). The expression of CDC6 is up-regulated in psoriatic epidermis. IL-22/STAT3 signal pathway in keratinocytes can mediate the expression of CDC6. By interfering with IL-22/STAT3 signal pathway, the loss of CDC6 will lead to the weakening of keratinocyte proliferation^[12].

Summary and prospect of the exhibition

Although a large number of clinical datas show that traditional Chinese medicine has achieved good results in the clinical treatment of psoriasis, the complexity of the effective components of traditional Chinese medicine leads to the difficulty of research. More researchers are needed to participate in a wider range of research results. And lack of a large number of sample data support, its clinical application needs to be further confirmed.

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Acanthopanax senticosus extract improves Parkinson's disease by modulating gut microbial structure and function

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Abstract:

Parkinson's disease is the second most common neurodegenerative disease with an increasing incidence, but the pathogenesis is still unclear. Traditional Chinese medicine has a clear therapeutic effect on Parkinson's disease. In order to further explore the mechanism of action of Acanthopanax senticosus extract in the treatment of PD, the structure and function of intestinal microbes were analyzed by integrating metagenomics before and after the intervention of Acanthopanax senticosus in PD mouse model. The experimental results show that at the phylum level, Acanthopanax senticosus can up-regulate Firmicutes and down-regulate Actinobacteria; at the genus level, it can up-regulate Clostridium and down-regulate Akkermansia; it can recall 49 species from the phyla Firmicutes, Actinobacteria and Tenericutes. The research results show that the extract of Acanthopanax senticosus can improve the structure and function of intestinal flora in PD models, providing new targets and new ideas for the treatment of PD with Acanthopanax senticosus..

Key words: Acanthopanax senticosus extract; Parkinson's disease; metagenomics; gut microbes

Parkinson's disease is a common neurodegenerative disease^[1]. Movement disorders such as resting tremor, muscle rigidity, and bradykinesia often occur clinically ^[2], which seriously affects the quality of life of patients. Studies have found that the imbalance of intestinal bacteria may also be an important cause of PD . Therefore, maintaining the gut microbiota is an important factor in safeguarding the health of the host, and targeting the gut microbiota may be a potential therapy for the treatment and prevention of PD.

Acanthopanax senticosus (Rupr.et Maxim.) Harms is the dried root and rhizome or stem of Acanthopanax senticosus (Rupr.et Maxim.) Harms, a traditional Chinese medicine. The research group explored the therapeutic effect of Acanthopanax senticosus on PD through animal and cell experiments in the early stage, and found that the extract of Acanthopanax senticosus could exert anti-Parkinson's disease effects by anti-inflammatory, anti-oxidative stress, and protecting the structure and function of mitochondria.

Objective

The research group used α -syn transgenic mice to construct a PD model, and used the Illumina platform to perform metagenomic sequencing of intestinal contents to explore the possible mechanism of Acanthopanax senticosus in treating PD, providing new ideas and methods for the prevention and treatment of PD.

Materials and methods

After 7 days of adaptive feeding, α -syn transgenic mice were randomly divided into model group (PD group), Acanthopanax senticosus group (ASH group), and male C57BL/6 mice were selected as control group (Con group). The AS group was given 45.5 mg/kg of Acanthopanax senticosus extract by gavage [6], while the Con and PD groups were given the same amount of 0.5% CMC-Na solution by gavage for 20 days. 24h after the last administration, the mice were anesthetized with

1% sodium pentobarbital injection, and then sacrificed..

Results and discussion

The simpson index of the α -syn transgenic mouse group increased ($P < 0.01$), and the simpson index decreased after administration of *Acanthopanax senticosus* ($P < 0.01$), indicating that the species diversity of the model group increased. Based on sequence data, microbial structural and compositional changes were further analyzed at the phylum and genus levels. The results showed that at the phylum level, Firmicutes, Bacteroidetes, Actinobacteria, Proteobacteria, and Verrucomicrobia were the dominant flora. Compared with the blank group, Firmicutes of α -syn transgenic mice were significantly reduced ($P < 0.01$), and Bacteroidetes, Verrucomicrobia and Actinobacteria were significantly increased ($P < 0.01$, < 0.05 , 0.05 , 0.01); Firmicutes increased significantly ($P < 0.05$), and Actinobacteria decreased significantly ($P < 0.01$) after the intervention of *Acanthopanax senticosus* extract. At the genus level, 9 dominant genera with abundance greater than 1% were identified. Among them, *Clostridium* and *Lachnoclostridium* were significantly reduced ($P < 0.01$, 0.05), and *Akkermansia* was significantly increased ($P < 0.05$) compared with the blank group. The species abundance of *Clostridium* and *Akkermansia* decreased after that. In order to search for specific microbial species that may mediate the treatment of PD with *Acanthopanax senticosus* extracts, we analyzed the metagenomic data at the species level. MetagenomeSeq was used to perform pairwise comparisons at the species level, and the differential species were screened for differences greater than 2-fold between groups ($(|\text{Log}_2(\text{Fold_change_value})| > 1)$) and adjusted $P < 0.05$ (adj.P < 0.05). The results found that 49 species underwent differential changes and callbacks after the intervention of *Acanthopanax senticosus* extracts, mainly from Firmicutes, Actinobacteria, and Bacteroidetes phyla .

In order to search for specific microbial species that may mediate the treatment of PD with *Acanthopanax senticosus* extracts, we analyzed the metagenomic data at the species level. MetagenomeSeq was used to perform pairwise comparisons at the species level, and the differences between groups were screened for differences greater than 2-fold ($(|\text{Log}_2(\text{Fold_change_value})| > 1)$) and adjusted $P < 0.05$ (adj.P < 0.05). The results found that 49 species underwent differential changes and callbacks after the intervention of *Acanthopanax senticosus* extracts, mainly from Firmicutes, Actinobacteria, and Bacteroidetes.

Changes in gut microbiota also caused potential functional changes in gut microbiota, therefore, we further investigated the effect of *Acanthopanax senticosus* extract on gut microbiota function. Plotting PCA based on the KO results from the Kyoto Encyclopedia of Genes and Genomes (KEGG) annotation, the model group and *Acanthopanax senticosus* group were clearly separated. Comparative analysis at the level of KEGG1 found that metabolism and gene information processing pathways were the most important pathways, and were also the main pathways of *Acanthopanax senticosus* extract intervention. LEfSE analysis was performed on KEGG under the condition of $\text{LDA} > 2$. In the KEGG3 level, a total of 52 metabolic and gene information processing items were screened out in the blank group and the model group, of which the model group had 30 up-regulated metabolic pathways and 14 down-regulated genes compared with the blank group. There are 6 information processing pathways, and 2 are down-regulated. After administration of *Acanthopanax senticosus*, 24 metabolic pathways and 4 gene information processing pathways were recalled.

In this study, in order to elucidate the connotation of *Acanthopanax senticosus* extract in the treatment of PD, we used metagenomics to study the possible mechanism of *Acanthopanax senticosus* in the treatment of PD, and found that *Acanthopanax senticosus* extract can regulate the intestinal bacteria of PD model mice. Cluster structure and function, these results may provide new insights for the treatment of PD with *Acanthopanax senticosus*, and targeting the gut microbiota may be a potential therapy for the treatment and prevention of PD.

Based on metagenomic sequencing, this experiment explored the effect and mechanism of *Acanthopanax senticosus* extract in the treatment of PD. The results showed that the structure and function of intestinal microbes in PD model mice were changed, and *Acanthopanax senticosus* extract could reverse this change. Forty-nine bacterial species under the phylum Firmicutes, Tenericutes, and Actinobacteria may be potential targets for PD therapy. In conclusion, this study explored the possible mechanism of *Acanthopanax senticosus* extract to improve the structure and function of intestinal bacteria in PD model, and provided new targets and new ideas for the treatment of PD with *Acanthopanax senticosus*.

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Preparation and evaluation of animal model with blood deficiency syndrome

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Abstract

Animal models can effectively understand the law of occurrence and development of diseases, and have now become an important part of scientific experimental research. Syndrome of blood deficiency in traditional Chinese medicine is a common clinical syndrome. This article summarizes and collates the methods and characteristics of commonly used animal models of blood deficiency syndrome, and provides information for the study of the pathogenesis of blood deficiency syndrome and the evaluation of the effect of drugs on blood deficiency.

Keywords: Syndrome of blood deficiency ; Animal model ; Modeling

Blood deficiency syndrome is a common clinical syndrome^[1]. When explaining the pathogenesis and pathological characteristics of blood deficiency syndrome, as well as the therapeutic effect and mechanism of traditional Chinese medicine blood-enriching drugs, animal experimental research is indispensable, so the establishment of reliable animal models is a necessary prerequisite. However, there is no unified standard model for animal models of blood deficiency syndrome. Therefore, this paper reviews the establishment methods of blood deficiency syndrome animal models to provide reference for related researches on blood deficiency syndrome.

1 blood loss method

The blood loss method is to reduce the number of blood cells in the peripheral blood of experimental animals by taking blood from the orbital venous plexus, bloodletting from the tail artery or drawing arterial and venous blood, thereby simulating the blood deficiency syndrome caused by traumatic bleeding in the human body.

1.1 Acute blood loss method

Acute blood loss method is a one-time large-scale bloodletting to create an animal model of blood deficiency. Yin Yuting made this model by taking 0.5ml of blood from the orbital venous plexus of mice, and found that the model group mice had red blood cells (RBC), hemoglobin (HGB), serum erythropoietin (EPO), The content of iron and testosterone in serum was significantly reduced, indicating that the blood deficiency model was successfully constructed.

1.2 Chronic blood loss

1.2.1 Simple bloodletting method

The simple blood loss method is to create an animal model of blood deficiency by continuous bloodletting on a daily or daily basis. Shi Xuqin Shi created 3 models of chronic blood loss and blood deficiency in rats. Blood was collected from the fundus venous plexus at 2.5 ml/kg, 5 ml/kg, and 7.5 ml/kg every day. At 12 and 15 days, the changes of peripheral blood were observed. At the same time, considering the comprehensive factors such as the degree of inflammatory reaction of the rats, the rats were selected to collect blood 5ml/kg every day for 12 days as a reliable model of chronic blood deficiency in rats.

1.2.2 Comprehensive bloodletting method

The comprehensive bloodletting method uses the combination of tail vein bloodletting, swimming or starvation to create an animal model of blood deficiency with blood loss. simulating blood deficiency caused by improper diet, work and rest injuries and traumatic blood loss. certificate. Hu Liu^[2] created 4 different comprehensive bloodletting models. By observing the appearance changes of mice after modeling and measuring body weight, immune organ index, mortality, blood routine and other indicators, the optimal modeling parameters were determined as follows: Bloodletting 0.3 ml every other day + swimming for 10 min every day.

2.1 Cyclophosphamide injury method

Cyclophosphamide (CTX) can kill lymphocytes in the body, and can also induce blood deficiency syndrome by reducing leukocytes and damaging immune organs. Liu Yingxin used the method of intraperitoneal injection of 40 mg/kg of CTX saline solution for three consecutive days to prepare the blood deficiency model in mice. The thymus and thymus index, HCT, RBC, HGB and PLT in the peripheral blood of mice in the model group were significantly decreased, indicating that the blood deficiency model was successfully replicated.

2.2 Acetylhydrazine hemolysis method

Acephenhydrazine (APH) is a strong oxidant that can affect a variety of enzymes in red blood cells in the body, resulting in oxidative damage to red blood cells. Qian Hongliang created a blood deficiency model by subcutaneously injecting APH at a dose of 170 mg/kg on the 1st and 4th days, and found that the weight of the mice in the model group decreased significantly, and the red blood cells of the mice were significantly destroyed, Symptoms or cell membrane rupture, decreased mature annular nuclear cells in the bone marrow, and abnormal expression of Epo gene, granulocyte and macrophage colony-stimulating factor in the kidneys, indicating that acetophenone hydrazine can create a mouse model of blood deficiency.

2.3 Composite modeling method

The blood deficiency model was established by the combined use of acetophenhydrazine and cyclophosphamide. This modeling method can destroy the hematopoietic microenvironment, resulting in a significant decrease in the content of red blood cells, white blood cells and hemoglobin in the peripheral blood of the body. Yang Manqin used a compound modeling method (combining APH and CTX) to create a mouse model of blood deficiency. Compared with the normal group, the content of WBC, RBC, and HGB in the peripheral blood of the mice in the model group was significantly reduced, pathological sections showed that bone marrow hyperplasia in the model group was severely inhibited, hematopoietic cells were significantly reduced, and there were obvious pathological characteristics of blood deficiency.

3. Radiation damage method

Gamma ray irradiation is also one of the commonly used methods for establishing animal models of blood deficiency syndrome. This method will reduce the number of blood cells, change the ultrastructure of the bone marrow, destroy the hematopoietic microenvironment, and inhibit the hematopoietic function of the bone marrow.

4. Immune-mediated method

The principle of the immune-mediated method is to first severely damage the immune function of the model animal, and then enter some specific immune active cells. These cells inhibit the host's hematopoiesis, resulting in a significant reduction in the number of hematopoietic stem cells and

defects.

5. Multi-factor modeling method

Use a combination of two or three of the above methods. For example, Zhang Jianmin used cyclophosphamide and $^{60}\text{Co-}\gamma$ rays to create a blood deficiency model.

6. Discussion

Experimental animal models should have the characteristics of similarity, reproducibility and reliability with human diseases. At present, the existing modeling methods for blood deficiency syndrome are based on their physical signs and objective indicators. However, blood deficiency in traditional Chinese medicine may be caused by a variety of causes (such as exogenous infection, internal injury, etc.), so it needs to be combined with the basic theory of traditional Chinese medicine. Improve and expand, and apply modern research technology to study blood deficiency syndrome at the individual, tissue, cellular and molecular levels, so as to establish an animal model that is more in line with TCM blood deficiency syndrome, in order to accurately explain the pathogenesis of blood deficiency syndrome, pathological characteristics, and the therapeutic effect and mechanism of traditional Chinese medicine blood-tonifying drugs.

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The Role of Exosomes in Neurodegenerative Diseases

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Abstract: Neurodegenerative diseases are a class of diseases in which neurons and/or their myelin sheaths progressively decrease and gradually become dysfunctional over time. Clinically common neurodegenerative diseases include Alzheimer's disease (AD), Parkinson's disease (PD), Huntington's disease (HD), and amyotrophic lateral sclerosis (ALS). In recent years, with the aging of the population, the incidence of neurodegenerative diseases has also increased year by year. However, there is a lack of a gold standard for clear diagnosis and effective treatment methods in clinical practice. With the further development of research, it is found that exosomes can participate in the communication between cells. Since exosomes carry various active substances and can be directly released outside the cells, they can participate in various types of nerve cells and various glial cells. The material exchange and information exchange between them play an important role in exerting the function of synaptic regulation, promoting the development of the nervous system and maintaining neuronal homeostasis.

Keywords : exosomes; neurodegenerative diseases; Alzheimer's disease; astrocytes

The main cause of neurodegenerative diseases is the death of nerve cells, which is also a hallmark of many diseases such as Parkinson's disease, Alzheimer's disease, Huntington's disease and other neurodegenerative diseases. Almost all cells in the body can produce exosomes, which are widely found in blood, urine, saliva, cerebrospinal fluid and other body fluids. Cells that make up the central nervous system, such as astrocytes, microglia, oligodendrocytes, and neurons, can also secrete exosomes under pathological and physiological stimuli. Exosomes widely exist in the central nervous system, carry important biologically active molecules, and play an important messenger function in the communication between nerve cells.

Objective: This article briefly reviewed the role of exosomes in the occurrence and development of degenerative diseases of the central nervous system.

1 Exosomes in degenerative diseases

1.1 Exosomes and Alzheimer's disease

The pathological hallmarks of Alzheimer's disease are the presence of senile plaques (SPs) and neurofibrillary tangles (NFTs). Senile plaques are mainly composed of extracellular insoluble deposits of amyloid beta protein (A β) polypeptides produced during the processing of amyloid precursor protein (APP). The two main pathways for processing APP are the non-amyloidogenic and amyloidogenic pathways. NFTs are intracellular inclusion bodies formed by hyperphosphorylated and misfolded tau proteins. Some studies have suggested that Tau-like proteins produced by microglia spread through exosomes, and preventing the synthesis of

exosomes or reducing microglia can significantly reduce the spread of pathogenic Tau-like proteins . Due to their RNA transport ability , stability in body fluids, and ability to cross the blood-brain barrier, exosomes can be used as carriers to transport nucleic acid fragments such as miRNA and siRNA across the blood-brain barrier for the treatment of AD . Furthermore, neuron-derived exosomes can induce conformational modification of extracellular A β , transforming it into non-toxic fibers and promoting microglia uptake.

1.2 Exosomes and Huntington 's disease

Huntington's disease (HD) is a rare inherited autosomal dominant neurodegenerative disorder caused by the expression of mutant huntingtin (mHTT) with abnormal number of N-terminal glutamine repeats , characterized by mHTT aggregates in the brain. Studies have shown that astrocyte-derived exosomes (Asc -Exo) carry heat shock proteins and other neuroprotective substances, which can reduce the cytotoxicity of misfolded proteins and prevent neurodegeneration. Dysfunction of astrocytes may contribute to neuronal fragility. Although mHTT is not present in Asc -Exo, it can reduce Asc-Exo secretion and increase cytotoxicity in HD mice . Injecting Asc -Exo into the striatum of HD mice can reduce the aggregation density of mHTT , and overexpression of α B-crystallin can alleviate exosome defects and neuropathological changes, providing ideas for the treatment of Huntington's disease. ^[1] As Li Meizhen et al. studied the xenobiotic treatment of HD, the transfer of serum exosomes from young mice into an in vitro model of HD can effectively improve mHTT mutation, slow down cell apoptosis, promote mitochondrial biogenesis, and achieve therapeutic Purpose. ^[2]

1.3 Exosomes and amyotrophic lateral sclerosis

Amyotrophic lateral sclerosis (ALS) is a fatal neurodegenerative disease characterized by motor neuron (MN) degeneration and progressive muscle weakness that, in most cases, leads to breathing within 3 to 5 years of onset exhaustion. At present, the pathogenesis of ALS is still unclear, and changes in various signaling pathways are involved in the pathogenesis of ALS. For example, mitochondrial dysfunction, glutamate excitotoxicity, oxidative stress, protein aggregates, neurofilament aggregation, and neuroinflammation. Riluzole and edaravone are often used in clinical treatment, but these drugs can only moderately improve the survival rate, and there is currently no specific drug for ALS . Studies have found that astrocyte-derived exosomes contain proteins that cause ALS, such as superoxide dismutase 1 (SOD1). It was also found that other ALS-related proteins including TDP43, FUS, neurofilament light chain (NFL) and INHAT inhibitor (NIR) were isolated from patient cerebrospinal fluid and plasma exosomes .

2 Discussion

Exosomes play many important roles in neurodegenerative diseases. They are not only transporters for intracellular metabolic waste to be excreted out of cells, but also participate in the intercellular transmission and dissemination of abnormal substances, thereby playing a role in neuronal protection, degeneration and death. a process. Neurodegenerative diseases are a large class of

diseases in the central nervous system. Due to the unclear pathogenesis of the disease, the disease is "late diagnosis and difficult to treat", which brings a heavy burden to society, families and individuals. A large number of studies have shown that exosomes play an important role in neurodegenerative diseases, and they are mainly involved in the dissemination of abnormal proteins, resulting in the gradual increase of damaged cells and the progressive deterioration of the disease. Therefore, in-depth study of the specific molecular mechanisms of exosome formation, sorting and packaging contents, transport and dissemination of abnormal proteins in neurodegenerative diseases, exploring potential high-specificity diagnostic and prognostic biomarkers, and finding new targets for drug action, It is extremely important to develop new avenues for treatment, which can bring hope for the realization of "early detection and precise treatment" of the disease.

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Feasibility analysis of electroacupuncture to improve depressive symptoms through targeted regulation of pyroptosis

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Abstract

Pyroptosis is a hot research direction. In recent years, many reports have proved that pyroptosis plays a very important role in a variety of inflammatory diseases, such as endometriosis, cervical cancer, and ovarian cancer in gynecological diseases. , endometrial cancer, breast cancer, and other types of tumor diseases are also reflected, such as liver cancer, lung cancer, esophageal cancer, gastric cancer, colorectal cancer, cervical cancer, skin cancer [1], etc. The role of apoptosis in the pathogenesis of depression has only been reported in a small amount, and most of them are concentrated in the apoptosis of astrocytes in the hippocampus, which has a relevant impact on the occurrence and development of depression. The effect and its mechanism are currently in the preliminary research stage, and a large amount of strong evidence is currently lacking. This article aims to briefly explore the research feasibility of the effect and mechanism of electroacupuncture on depression through the pyroptotic pathway.

Key words: pyroptosis; depression; electroacupuncture

1. Pyroptosis and depression

Pyroptosis is a newly discovered pro-inflammatory programmed cell death, mediated by gasdermin, characterized by the formation of holes in the cell membrane by GSDMD (Gasdermin D) protein molecules, resulting in cell lysis and death and the release of inflammatory factors. Depression is a common chronic serious mental illness, which is mainly characterized by persistent low mood, sleep disturbance, appetite disturbance, and social anxiety. The pathogenesis of depression is complex and not yet fully understood. The widely accepted pathogenesis hypotheses mainly include neurotrophic hypothesis, neuroplasticity hypothesis, monoamine hypothesis, neuroendocrine hypothesis and cytokine hypothesis. More and more studies have confirmed that neuroinflammation is an important mechanism in the pathogenesis of depression. A large number of studies have confirmed that the activation of the inflammasome will induce the occurrence of pyroptosis, and the neuroinflammation mediated by the excessive activation of microglia is an important pathogenesis of depression. Studies have shown that stress activates the NLRP3 inflammasome in microglia, activates the downstream Caspase-1, and then releases IL-1 β and IL-18, leading to the occurrence of pyroptosis, which in turn mediates related immunity. Inflammatory response, involved in the pathological process of depression [2].

2. Depression and electroacupuncture

More and more reports have confirmed the effectiveness of acupuncture, especially electroacupuncture, in the treatment of depression, indicating that acupuncture can significantly improve the symptoms of depressed patients, and this has been validated in the CUMS animal model. Among them, electroacupuncture can improve depression symptoms by increasing the expression level of BDNF, increasing monoamine neurotransmitters 5-HT, DA, GABA, etc., and inhibiting the levels of pro-inflammatory factors IL-1 β , IL-6, TNF- α , etc. However, the study of

electroacupuncture to improve depressive symptoms through targeted regulation of pyroptosis still needs to be in-depth, and there is a lack of a lot of valuable reports.

3.Pyroptosis and electroacupuncture

At present, there have been a few reports in China that electroacupuncture can improve disease symptoms through targeted regulation of cell pyroptosis, but most of them are limited to cerebral ischemia-reperfusion injury, acute cerebral infarction, acute spinal cord injury, acute kidney injury and other diseases. Current research results show that electroacupuncture plays an antidepressant effect, possibly by inhibiting the pyroptotic signaling pathway of CASP-1/GSDMD cells, reducing neuroinflammation and improving synaptic plasticity [3]. Therefore, it is of great value to carry out in-depth research on electroacupuncture to improve depression symptoms through targeted regulation of pyroptosis.

Conclusion

In conclusion, it is of great significance to carry out in-depth research on the improvement of depression symptoms by electroacupuncture through targeted regulation of pyroptosis. The molecular mechanism of antidepressant effect by inhibiting cell pyroptosis will further reveal the mechanism of action of electroacupuncture in the treatment of depression, and provide strong scientific evidence for the treatment of depression by electroacupuncture.

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Research progress on extraction and separation methods and pharmacological effects of cannabidiol

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Abstract: Cannabis has a long history of drug use, mainly containing cannabinoids, alkaloids, flavonoids, coumarins, terpenoids and other chemical components. Among them, cannabidiol, as the main active ingredient of cannabinoid, has a wide range of pharmacological effects, such as anti-cancer, anti-inflammatory, liver protection, etc., and has no hallucinogenic addiction and toxic side effects, so it has high research value. At present, the commonly used extraction and separation methods mainly include solvent impregnation, thermal reflux extraction and enzymatic extraction. In this paper, the extraction technology and pharmacological effects of cannabidiol were summarized by summarizing the related research contents and achievements at home and abroad, in order to provide reference for further research of cannabidiol in the future.

Keywords: pharmacological effects of cannabidiol extraction methods

Cannabidiol (CBD) is one of the main active components of annual cannabis plant in Moraceae, which belongs to high lipophilic cannabinoids with poor water solubility^[1]. Cannabis is widely cultivated in China and all over the world, especially industrial cannabis, which is an important cash crop. However, it is classified as a drug because of its hallucinogenic and addictive components, and it is forbidden to cultivate it privately in China. CBD has low affinity for cannabinoid receptor, so it is not hallucinogenic and addictive^[2]. Therefore, the application prospect of cannabidiol in pharmaceutical industry and the value of continuous development are favored by researchers. In this paper, the extraction methods and pharmacological effects of cannabidiol are reviewed, in order to bring more thoughts and possibilities for further development of cannabidiol.

1 extraction method of cannabidiol

1.1 solvent impregnation method

Serna-Loaiza et al. used ethanol as solvent to extract cannabidiol, and studied the effects of temperature, time and pressure on the extraction process. The experiment showed that the extraction concentration of cannabidiol was the highest, which was 19.8mg/g, under the conditions of low pressure of 0.5×10^4 k Pa, extraction time of 60min and temperature of 100°C.

1.2 hot reflux extraction

Gao Zhe et al. extracted cannabidiol from hemp leaves. Taking the extraction rate and content of cannabidiol as the index, the best technology of hot reflux method of cannabidiol was selected by orthogonal test. The extraction solvent was n-hexane, hemp leaf powder was screened through a 20-mesh sieve, extracted at 80°C for 3h, and the ratio of material to liquid was 1 : 15. Under these conditions, the extraction rate and content of cannabidiol were 5.24% and 43.16 mg g⁻¹, respectively.

1.3 enzymatic extraction

Wu Junfeng et al. studied the best technology of cannabidiol in hemp leaves by enzyme-assisted solvent extraction. Taking cannabidiol content and extract rate as observation indexes, the types of

enzymes, enzymolysis time, enzyme dosage, ratio of material to liquid, extraction time and heating pretreatment methods were investigated. The results showed that the optimum technological conditions were as follows: compound plant hydrolase (Viscozyme L) and acid protease were used for enzymolysis, enzymolysis time was 60min, enzyme dosage was 0.5%, the ratio of material to liquid was 1 : 20, and hemp leaves were heated in oven at 100°C for 2h.

1.4 supercritical extraction method

Rochfort et al. used hemp buds as experimental raw materials, and the extraction volume was 1kg/time, and supercritical CO₂ fluid extraction was carried out. Taking CO₂ flow rate, extraction pressure and extraction time as indexes, the effects of these factors on the best recovery rates of THC and CBD were observed. The research shows that the flow rate of CO₂ has the greatest influence on the total yield and recovery rate of CBD, indicating that the highest extraction quality is 71 g(7.1%) under the conditions of high flow rate (150 g/m L) and high pressure (3.2×10⁴k Pa) for 600 min.

2 Study on pharmacological action of cannabidiol

2.1 anti-tumor effect

Cancer, also known as malignant tumor, is one of the main causes of human death. The global morbidity and mortality are increasing year by year, which is an important factor hindering the extension of human life expectancy. At present, it is mainly treated by radiotherapy, chemotherapy, surgery, etc., but its recurrence rate is high, the cure rate is low and the treatment process is painful. Therefore, the research on new anticancer drugs is a key task to be solved urgently all over the world. Studies have proved that cannabidiol has anticancer active ingredients.

2.1.1 Endometrial cancer

Zhang Lihong et al. found that CBD can inhibit proliferation rate, cell cloning and migration rate of Ishikawa cells with endometrial cancer in a concentration-dependent manner, and its mechanism is to up-regulate the expression of Bax, Cyto C and cleaved caspase 3 and down-regulate the expression of Bcl-2 to induce the apoptosis of Ishikawa cells.

2.1.2 Breast cancer

Sultan et al. studied the effects of CBD on ER-positive and triple-negative breast cancer cells, and found that CBD could promote apoptosis by down-regulating mTOR, AKT, 4EBP1 and cyclin D1, while up-regulating the expression and nuclear localization of PPAR γ . It shows that CBD treatment induces the interaction between PPAR γ , mTOR and cyclin D1, which is beneficial to the apoptosis of ER-positive and triple-negative breast cancer cells. CBD can treat different breast cancer subtypes.

2.3 Liver protection

CBD has protective effect on alcoholic fatty liver and acute liver injury induced by CCL₄. Shu Yuanhui et al. established acute liver injury model induced by 20% carbon tetrachloride. The effects of cannabidiol on the expression of alanine aminotransferase (ALT), aspartate aminotransferase (AST), superoxide dismutase (SOD), malondialdehyde (MDA), glutathione (GSH), PPAR- γ and COX-2 proteins were studied by enzyme-linked immunosorbent assay (ELISA) and WB method. The results showed that the contents of ALT, AST and MDA in mice decreased, but the contents of SOD and GSH increased, while PPA increased.

3 conclusion

In recent years, great progress has been made in the research of cannabidiol at home and abroad. Cannabidiol has attracted much attention because of its diverse pharmacological activities, no hallucinogenic addiction and extensive sources. The research on the extraction and separation technology and pharmacological action of cannabidiol has been deepened day by day, and the current research mainly focuses on pharmacological activity and signal pathway. As one of the non-psychoactive cannabinoids, cannabidiol has been proved to be effective and safe, and its pharmacological effects have not only been verified in animal experiments, but also widely used in clinic. For this kind of drug resource with great potential, it is expected that more scholars will conduct in-depth research and discussion on it in the future, so that it can be better developed and utilized, and bring into play remarkable economic benefits and extensive social benefits.

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Research progress of chuanxiong in the treatment of myocardial ischemia

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Abstract

In recent years, Chuanxiong and its preparations are often used clinically to treat cardiovascular and cerebrovascular diseases such as myocardial ischemia, coronary heart disease, heart failure and stroke. This article mainly summarizes and analyzes the use of chuanxiong and its preparations in the treatment of myocardial ischemia from the aspects of chemical constituents and extracts of chuanxiong, hoping to provide reference for the citation of chuanxiong in the treatment of myocardial ischemia.

Key words: Chuanxiong, myocardial ischemia, compatibility

Chuanxiong is the dry rhizome of *Ligusticum chuanxiong hort.* It has the effect of promoting blood circulation, dispelling wind and relieving pain. It is a traditional Chinese medicinal material commonly used in clinical treatment of myocardial ischemia. *Ligusticum chuanxiong* contains a variety of active ingredients, mainly including ligustrazine, ferulic acid, ligustilide, etc., which have the functions of protecting myocardial ischemia injury, anti-platelet aggregation, anti-atherosclerosis, protecting ischemia-reperfusion myocardium, and protecting vascular endothelium. the efficacy of cells. In recent years, Chuanxiong and its preparations have been commonly used in clinical treatment of myocardial ischemia, coronary heart disease, angina pectoris, and other cardiovascular and cerebrovascular diseases. The use of the treatment of myocardial ischemia, in order to provide a more comprehensive data basis for the application of traditional Chinese medicine in the treatment of myocardial ischemia.

1. Single herb – Chuanxiong

At present, the chemical constituents of Chuanxiong are mainly alkaloids and volatile oils as research hotspots. The alkaloids mainly include ligustrazine, ligustine A, ligustine B, adenosine, etc., among which ligustrazine is considered as a representative alkaloid. The chemical components of volatile oils account for about 1% of the composition of Chuanxiong, and phthalide compounds are also the main chemical components of volatile oils. Mainly include Ligustolide A ~ N, Q, R, S, E-Lisuginolide, Z-Lisuginolide, Z-butenylphthalide, 3-butenyl-7-hydroxyphthalide, 4,7-dihydroxy-3-butylphthalide, new cnidolide, ligustilide A, B, ligustide A, B, etc., in addition to the above-mentioned main phthalide compounds also include ligustrium triterpenes, cypress terpenes such as terpenes, and a small amount of organic acids such as ferulic acid, caffeic acid, and sinapic acid. Among these components, ligustrazine, ferulic acid, ligustolide A, butylphthalide and ligustilide are widely used in the treatment of myocardial ischemia.

2. Ligustrazine

Ligustrazine is a traditional Chinese medicine monomer commonly used in the treatment of cardiovascular diseases. Li Ruifang et al. used ISO to induce acute myocardial ischemia in mice to explore the protective effect of ligustrazine on it. The levels of CK-MB, LDH, H₂O₂ increased in the T-AOC level to protect myocardial injury, and its protective effect was concentration-dependent. Lv Lei established a rat model of myocardial ischemia-reperfusion injury, and the results showed

that ligustrazine 10mg/kg could reduce the apoptosis index, and its mechanism may be related to reducing the content of caspase3 in myocardial tissue, down-regulating the relative expression level of Bax mRNA, and up-regulating Bcl. The relative expression level of -2 mRNA was related to the activation of PI3K/Akt signaling pathway. He Yanqing used heart rate (HR), myocardial contractility (IT), left ventricular ejection fraction (LVEF), left ventricular peak pressure (LVSP), and left ventricular maximum rise/fall rate (\pm LVdp/dtmax) as indicators, to study the effect of ligustrazine on the cardiac function of isolated hearts of rats with acute myocardial ischemia, and then concluded that ligustrazine can significantly increase the levels of IT, LVSP, LVEF, HR and \pm LVdp/dtmax in isolated hearts of myocardial ischemia. Ligustrazine can also protect the myocardium from acute myocardial ischemia-reperfusion injury by increasing coronary blood flow, enhancing myocardial contractility, and reducing the scope of myocardial ischemia. Chen Chengbo and others concluded through research that ligustrazine can promote the activation of JAK2/STAT3 signaling pathway and the expression of Bcl2, while inhibiting the expression of Bax, thereby inhibiting myocardial cell apoptosis and protecting damaged myocardium. Wang^[1] studied the energy metabolism of ligustrazine on myocardial cells during myocardial ischemia-reperfusion injury in rabbits and found that ligustrazine could improve ischemia perfusion injury by increasing the energy production of myocardial cells, and its mechanism may be related to the reduction of ligustrazine's ability to reduce myocardial ischemia-reperfusion injury. The degradation of myocardial ATP is related to the increase of ATP production. In this way, the energy storage of myocardial cells can be increased, and the high-energy phosphate compounds in the myocardium can be protected, so as to achieve the effect of protecting the myocardium. Yang^[2] found that ligustrazine could improve the expressions of Cu, SOD1, MDA5, Bax-2, Bcl-2, p-PI3K, p-Akt and p-GSK-3 β in ISO-induced rats, and reduce the levels of MDA and p-GSK-3 β in serum. The levels of CK as well as the activities of SOD and LDH, while reducing the levels of pro-inflammatory cytokines, including IL-1 β , IL-6 and TNF- α , confirmed that ligustrazine can not only alleviate the ISO-induced inflammatory conditions and oxidative stress. AMI can also regulate the PI3K/Akt/GSK-3 β signaling pathway to protect the damaged myocardium.

3. Sodium ferulate

Sodium ferulate is the sodium salt of ferulic acid, the main active component of the traditional Chinese medicine Chuanxiong extract. Because of its rich source and various pharmacological activities, high safety and few adverse reactions, it is commonly used in clinical cardiovascular and cerebrovascular diseases. Zhang Bolun et al studied the protective effect and mechanism of sodium ferulate on myocardial ischemia-reperfusion injury (MIRI) in rats. Sodium ferulate had obvious protective effect on MIRI rats. Compared with the model group, the rats in each group had.

4. Ligustolide A

Ligusticum lactone A, as the main active component of lactones in Ligusticum chuanxiong, is widely used in the treatment of myocardial ischemia. Xiao Yongqing et al. concluded by observing the protective effect of ligustolide A pretreatment on reperfusion in isolated rat hearts, and concluded that ligustolide A pretreatment can significantly increase coronary flow and myocardial contractility during ischemia perfusion, and reduce ventricular fibrillation. (VF), the incidence of ventricular tachycardia (VT), increased myocardial homogenate SOD activity, decreased MDA and LDH content, so as to achieve the protection of ischemia-reperfusion injury.

5. Butylphthalide

Gu Jianguo established a myocardial injury model induced by ISO, studied the protective effect of butylphthalide (NBP) on the myocardium, and explored its possible mechanism. The results showed that compared with the ISO group, ISO+NBP group can significantly improve the degree of myocardial injury, reduce the left ventricular end-diastolic pressure, increase SOD activity ($P < 0.05$), and reduce MDA content ($P < 0.01$), thus indicating that NBP has the effect of protecting myocardium, and its mechanism may be related to anti-lipid quality peroxidation.

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Research status of intervention effect of Baduanjin on type 2 diabetes mellitus

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Abstract

This paper summarized and analyzed the research status of Baduanjin in the intervention of type 2 diabetes. The content of Baduanjin is rich and diverse. More and more modern studies show that Baduanjin can effectively improve the blood viscosity, blood glucose level, blood lipid level, psychological state and other aspects of type 2 diabetes. Therefore, the clinical application of Baduanjin should be increased and the mechanism of its intervention should be further studied.

Key words: Baduanjin; Kinesitherapy; Type 2 diabetes mellitus; Intervention effect

Diabetes is a chronic metabolic disease characterized by abnormal insulin secretion and insulin resistance. There are about 415 million adults with diabetes worldwide, and over 90% of them have type 2 diabetes^[1]. Type 2 diabetes mellitus (T2DM) is a disease with insulin resistance or insufficient insulin secretion leading to elevated blood glucose levels in which insulin resistance or a relative^[2]. Exercise therapy is the preferred intervention strategy for patients newly diagnosed with type 2 diabetes^[3]. Baduanjin is a traditional exercise therapy with the advantages of being easy to learn and effective^[4]. It can stimulate the curative effect by adjusting shape, breath and consciousness, and it's an effective method for the intervention of type 2 diabetes.

Objective

Baduanjin, as one of the traditional Chinese medicine sports therapies, first appeared in "Yi Jian Zhi". Developed from the Song Dynasty to today, its rich content and diverse forms can be roughly divided into two categories: standing and sitting^[5]. It is an aerobic exercise and exerts good health care effects mainly through mind control, breathing regulation and body movement. In this paper, the retrieval of Baduanjin in the intervention of type 2 diabetes related studies, to provide a reference for the clinical application of exercise therapy.

Materials and methods

The relevant researches on the intervention of Baduanjin in type 2 diabetes in CNKI and PubMed databases were searched by computer for the period from the self-built database to the present. Using the method of subject words combined with free words, according to the Inclusion and Exclusion Criteria, the 77 literatures that finally met the standard were summarized.

1. Intervention effect on blood viscosity

Studies have shown^[6] that Baduanjin exercise for 6 months can effectively reduce the levels of erythrocyte aggregation index, erythrocyte sedimentation rate, fibrinogen, sicAM-1 and Ps, reduce the whole blood high and low shear viscosity and plasma viscosity, and improve blood rheology.

2. Intervention effect on blood glucose level

Fasting plasma glucose (FPG) and glycosylated hemoglobin (HbA1c) are important indicators reflecting the changes of blood glucose in patients with type 2 diabetes. Exercise can promote the consumption of blood glucose by muscles and corresponding tissues, and reduce the blood glucose content, so as to achieve the purpose of controlling blood glucose and improving insulin sensitivity. Studies^[7] have shown that FPG and HbA1c in Baduanjin group decreased significantly after

treatment ($P<0.05$). After treatment, the SF-36 physical health score of Baduanjin group and walking group increased significantly, and the difference was significant compared with the control group ($P<0.05$). After treatment, sF-36 mental health score in Baduanjin group and walking group was significantly higher than that before treatment ($P<0.05$). Therefore, Baduanjin can more effectively reduce Fasting plasma glucose (FPG) and glycosylated hemoglobin (HbA1c) in patients with type 2 diabetes.

3. Intervention effect on blood lipid level

Studies have shown^[8] that Baduanjin can stably improve triglyceride, total cholesterol, low density lipoprotein cholesterol, high density lipoprotein cholesterol, body weight, BMI and other lipid levels.

4. Intervention effect on psychological state

Studies have shown^[9,10] that long-term regular practice of Baduanjin can effectively reduce the score of Self-rating Depression Scale (SDS), Self-rating Anxiety Scale (SAS) and improve the psychological state of type 2 diabetes patients.

Results and discussion

Diabetes belongs to the category of "consumptive thirst" in traditional Chinese medicine. The disease location is mainly in lung, stomach and kidney, and it is also related to spleen and liver. In the exercise therapy, every action of Baduanjin can be adjusted for the relevant viscera. This study shows that patients with type 2 diabetes can improve their blood viscosity, blood glucose level, blood lipid level and psychological state through systematic and long-term Baduanjin exercise. Therefore, this method can not only exercise health, enhance cultural identity, but also improve the quality of life of patients, reduce the medical economic burden of patients. It has a good promotion significance for kinesiotherapy in the treatment of type 2 diabetes. At present, most of the domestic clinical studies on the intervention effect of Baduanjin on type 2 diabetes are small sample and short-term trials. In the future, multi-center and large-sample randomized controlled trials should be conducted to increase the rigor of trial design, so as to provide new ideas and methods for the clinical prevention and treatment of type 2 diabetes.

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Longitudinal changes in the retinal and choroidal thickness in young children at low and high risk for myopia

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Key words: Myopia; Retinal thickness; Choroidal thickness; Young children with high or low risk of developing myopia.

Abstract

Objective

Breviscapine injection (BI) is made of the sterile aqueous of breviscapine which was extracted from *Erigeron breviscapus* whole plant. It is widely consumed concomitantly with conventional prescription drugs in clinics in China. Scutellarin is considered the primary active ingredient of breviscapine and used frequently in clinics to treat ischemic vascular diseases in China. However, the direct relationship between BI, scutellarin and CYP450 are unclear. The present study investigated the influence of BI and scutellarin on CYP450 2E1, 2C9 and 3A4, and compared these effects of scutellarin with its mixture, BI in rats.

Methods

Children (n=23, age=7.6±0.9 years) were categorized as low risk (LR) (n=12, age=7.9±0.8 years, axial length, AXL=22.8±0.3mm, RE=1.1±0.3D) and high risk (HR) (n=11, age=7.4±1.0 years, AXL=22.5±0.8mm, RE=0.8±0.5D) for myopia, based on parental history and cycloplegic autorefractometry at baseline. Wide-field SD-OCT (Spectralis, Heidelberg) radial scans centered on the fovea (55°, 12 lines) were collected at 3 points in time: baseline, 6 and 12 months. Images were processed in a custom Matlab program and corrected for lateral magnification using biometric data (Lenstar). RT and ChT were evaluated for retinal eccentricities of 1, 3, 5, 8 and 12 mm.

Results and discussion

At 12 months, AXL increased and RE decreased (less hyperopic) in the HR group (p<0.05 both) while only AXL increased in the LR group (p<0.05). At baseline, RT and ChT were not significantly different between the two groups at any eccentricity, although there was a trend for thicker choroid in the LR compared to the HR group at all eccentricities. There was also a significant increase in RT for the HR group at 1, 3 and 5 mm eccentricities, while RT increased at the central 1 mm only for the LR group (p<0.05 all). ChT increased significantly at all eccentricities for both groups, greatest superiorly (27.9±29.0 μm) and smallest nasally (19.9±20.7 μm) (p<0.05 both). Subfoveal ChT at 12 months increased significantly only in the LR group (26.2±27.8 μm, p<0.01).

Conclusion: At 12 months, there was greater ocular elongation and decreased hyperopia in children for HR of myopia, as predicted. Additionally, there were significant increase in RT and ChT, with different patterns of thickening for the HR and LR groups, which suggests differences in ocular growth patterns prior to myopia development. We will continue to follow up these children for 3 years, which will provide an understanding of changes associated with myopia development.

Study on the preparation of a drug for defecation and sleep improvement

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Abstract: In this study, dry Tremella fuciformis is used as the main raw material, together with Schisandra chinensis extract, peach gum extract, Sophora honey and Osmanthus fragrans dried products. It has the effects of Tonifying Qi and essence, nourishing yin and dryness, strengthening brain and intelligence, beauty and beauty. The best preparation technology of Tremella fuciformis, Schisandra chinensis and peach gum was determined by single factor experiment and sensory evaluation analysis. The proportioning process was optimized by orthogonal test, and the best proportioning of health drugs was determined with sensory evaluation as the evaluation index. Results: Tremella 1.5g, Schisandra chinensis 0.5g, peach gum 6g, Sophora japonica honey 7g, with a small amount of osmanthus, sealed in cans, boiled and sterilized for 3min. Under these conditions, the health care drugs produced are light reddish brown in color, soft in aroma, with Tremella flavor and honey sweetness, delicate in texture, sweet and sour and delicious, and have certain nutritional value.

Keywords: Tremella; Schisandra; Peach gum; Health care drugs; Processing technology

With the rapid development of social economy and the gradual improvement of material living standards, health issues have become the focus of social attention. People pay more and more attention to their physical quality and health status, and their health awareness is also increasing. The homology of medicine and food has become the mainstream of today's society, which reflects the functionality of food in physical health and health care. The dual use of medicine and food is mainly reflected in the two aspects of dietotherapy and feeding, especially in the aspect of feeding, which reflects the health care thought of today's society. In ancient herbal books, many Chinese medicinal materials that can be used for both medicine and food are recorded, and their medicinal effects are analyzed and explained to a certain extent. This has laid a solid foundation for the study of modern medicine and food homology theory and medicine and food dual supplies. Chinese traditional medicine nutrition believes that the application of medicinal diet can play a role in strengthening the body and treating diseases. Nowadays, as people pay more attention to health, health care drugs containing high nutritional components, natural organic, without additives, low sugar and low calorie, and with tonic and maintenance effects will be more popular. Therefore, the demand for health drugs will increase significantly and stimulate greater market space, thus promoting the development of the health drug industry.

Objective

To establish the preparation process of new health care drugs, and lay a certain foundation for the research and development of new health care drugs in the future.

Materials and Methods

Take a certain amount of Schisandra chinensis, remove impurities, wash and dry it, steam it in a steamer for 20 minutes, remove seeds while it is hot, and ensure that the distillate of Schisandra chinensis has no bitterness. Choose clean and impurity free peach glue and soak it in cold water above 40°C for 12 hours to completely soak it until there is no hard core. Choose fleshy tremella,

remove the yellow part, crush it into medium-sized fine particles, and set aside. Through single factor test and sensory evaluation analysis, the best preparation process of health drugs was determined. Then the mixing process was optimized by orthogonal test, and the best mixed health drink was determined by sensory evaluation. Finally, disinfect the cans. Before canning, disinfect the interior of empty glassware with boiling water, and let the water stand and dry for future use. After canning, ensure that the net weight of the drug is 40g, then put it into the tank, boil it for sterilization for 3min, take it out and cool it to room temperature.

Results and Discussion

Through single factor analysis, it was found that when the solid-liquid ratio was 1:50 and the cooking time was 50min, tremella had smooth taste, transparent color and unique fragrance. The best material to liquid ratio of peach glue is 1:6, and the best frying time is 40min. At this time, the peach glue solution has transparent color and delicate taste. The color, smell and taste of schisandra chinensis solution were better when the ratio of material to liquid was 1:40 and decocted for 35min. Through the above experiments, identified the best preparation technology of tremella, schisandra and peach gum in this health drink. In order to optimize the taste, color, smell and nutritional value of health drugs, orthogonal tests were carried out with tremella (A), schisandra fruit (B), peach gum (C) and sophora honey (D), shown in table 1. The results were shown , the order of influencing the sensory evaluation score of health drugs was C > D > A > B, that is, the amount of peach gum > sophora honey > Tremella > schisandra. The most influential factor is the amount of peach gum. Appropriate peach gum can enrich the taste of health drugs, make them smooth and easy to take. The optimal ratio combination is A₃B₁C₁D₃, that is, the dosage of flos fungus is 1.5g, schisandra chinensis is 0.5g, peach gum is 6g and sophora honey is 7g.

Through single factor experiment, orthogonal experiment and sensory evaluation analysis, the optimal ratio of health drugs was determined. With a small amount of osmanthus, sealed canned, boiled sterilization in the pot, the product color is even light brownish red, with a certain sense of permeability; Delicate taste, moderate sweet and sour, peach gum Q elastic smooth, tremella soft mouth melt; The fragrance of schisandra chinensis, Tremella chinensis and sophorae nectar is harmonious and soft. The structure is uniform, without precipitation and stratification. Collocation a few osmanthus ornament color, osmanthus fragrance is mixed with sophora honey sweet, make the person appetite soars. Peach gum enriches the drug taste, tremella and schisandra have high nutritional value, so this product has a great development prospect.

Table 1 Factors and levels of orthogonal experimental design

level	factors			
	tremella (A) /g	schisandra fruit (B) /g	peach gum (C) /g	sophora honey (D) /g
1	0.5	0.5	6	3
2	1	0.7	8	5
3	1.5	0.9	10	7

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Effects of Diazepam、 Buspirone、 Paroxetine and Jujube Seed on State Anxiety Rats

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Keywords: state anxiety; elevated plus maze; diazepam; buspirone; paroxetine; jujube seed

Abstract

Objective: To investigate the effects of diazepam、 buspirone、 paroxetine and jujube seed on state anxiety rats.

Methods: The experimental rats were randomly divided into 6 groups, namely blank group、 model group、 diazepam group (3.6 mg/kg)、 buspirone group (3.6 mg/kg)、 paroxetine group (4.5 mg/kg), and Suanzaoren group (5 g/kg), the 4-day state anxiety model was replicated by the conditioned fear method. On the next day after the model was replicated, each group was given gavage for 10 days, and the elevated plus maze test was performed on the 10th and 11th days. and recorded the percentage of animals entering the open arm (OE%) and the percentage of time entering the open arm (OT%).

Results: Compared with the model group, both Suanzaoren and diazepam could significantly increase OE% and OT% in state anxiety rats ($P < 0.01$); The effects of buspirone and paroxetine on OE% and OT% were not significantly different from the model group; the OE% and OT% of the diazepam group showed significant differences before and after drug withdrawal ($P < 0.01$).

Conclusion: Suanzaoren and diazepam have obvious anti-state anxiety effects, but diazepam has obvious rebound symptoms after drug withdrawal compared with Suanzaoren.

Effects of Suanzaoren decoction on synaptic plasticity in hippocampus of conditioned fear-induced anxiety rats

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Keywords: Suanzaoren decoction; anxiety disorder; glutamate; synaptic plasticity

Abstract

Objective: To investigate the effect of Suanzaoren decoction on hippocampal synaptic plasticity in conditioned fear-induced anxiety rats.

Methods: In experiment one, 36 male rats were randomly divided into blank group, model group, diazepam group and Suanzaoren decoction group. Except for the blank group, the conditioned fear model was replicated in each group. After 4 days of modeling, each administration group was administered with Suanzaoren Decoction (10 g/kg) and diazepam solution (3.6 mg/kg), respectively. The rats in the model group were given the same volume of double distilled water for 10 consecutive days. The effect of Suanzaoren decoction on anxiety-like behavior in rats was investigated by elevated plus maze; the contents of Glu and GABA neurotransmitters in serum of rats were detected by enzyme-linked immunoassay (ELISA); the hippocampus of rats in each group was observed by transmission electron microscopy. Ultrastructural changes in neural synapses. In experiment 2, 36 rats were randomly divided into groups. The modeling and administration methods were the same as above, and the change rate of PS amplitude in the vHPC area of the rats in each group was recorded by in vivo LTP detection technology.

Results: The results of the elevated plus maze test showed that the Suanzaoren decoction group could effectively increase the arm opening time, the percentage of arm opening in the total exercise time, the number of arm openings and the percentage of arm opening in the total arm entry times in anxious rats, showing a significant Anxiety effect; ELISA analysis results showed that compared with the model group, the content of Glu in the serum of anxious rats in Suanzaoren decoction group was significantly lower ($P<0.05$). Compared with the model group, the primary cells and organelles were improved, showing that the organelle structure was complete, the cell membrane and nuclear membrane were complete and clear, the chromatin was evenly distributed, the organelles were abundant, the synaptic vesicles were abundant and densely distributed, and the intrasynaptic microtubules and microfilaments were abundant. The LTP test results showed that compared with the model group, the change rate (%) of PS amplitude in the hippocampus of the rats in the Suanzaoren decoction group increased significantly from 5 min to 35 min ($P<0.05$, $P<0.01$).

Conclusion: Suanzaoren Decoction has significant anxiolytic effects, and its mechanism may be related to regulating the levels of Glu and GABA and improving the structural and functional plasticity of synapses.

Determination of effective parts of YERENHE and study on the mechanism of improving PCPA sleep deprivation in rats

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Key words YERENHE; Content determination; Sleep; PCPA; 5-HT; 5-HIAA

Abstract

Objective: Based on the determination of 8 active components in YERENHE active part by HPLC, the effects of YERENHE active part on sleep time and mechanism of P-chlorophenylalanine (PCPA) induced sleep deprivation rats were investigated.

Methods: Firstly, HPLC was used to determine the content of components in the effective parts of YERENHE. Secondly, 48 SD rats were divided into blank group, model group, positive group, low-dose, medium-dose and high-dose groups of the effective parts of YERENHE. Experimental animal monitoring system (CLAMS) and enzyme linked immunoassay (ELISA) were used to detect the sleep duration, frequency and duration of sleep and the content of 5-hydroxytryptamine (5-HT) and 5-hydroxyindoeacetic acid (5-HIAA) in hypothalamus and hippocampus of PCPA deprived rats.

Results: The linear relationship of active components of spinotin, ferulic acid, quercetin, schisandrae A, schisandrae A, schisandrae B was good ($R > 0.9993$). The average recoveries were 96.82%~100.49% with RSD values of 0.78%~1.38%. Compared to the control group, In model group, the sleep duration of all day, daytime and night decreased ($P < 0.05$ or $P < 0.01$), the sleep frequency of all day and daytime decreased ($P < 0.05$), the sleep duration of night decreased ($P < 0.01$), and the contents of 5-HT and 5-HIAA in hypothalamus and hippocampus decreased ($P < 0.05$ or $P < 0.01$). Compared with model group, all-day, daytime and night sleep time of rats in positive group, middle dose group and high dose group of YERENHE effective part were increased ($P < 0.05$ or $P < 0.01$); In positive group, low dose group, medium dose group and high dose group of YERENHE, the occurrence times of sleep all day and night were increased ($P < 0.05$ or $P < 0.01$); The contents of 5-HT and 5-HIAA in hypothalamus and hippocampus of rats in positive group, middle dose group and high dose group of YERENHE were increased ($P < 0.05$ or $P < 0.01$).

Conclusion: The method is simple, reproducible and stable, which can provide a basis for the quality standard of YERENHE. The effective components of YERENHE can improve sleep, and the mechanism may be related to the regulation of 5-HT and 5-HIAA content in hypothalamus and hippocampus.

Naphthoquinone and Quinonoid Xanthene from *Arnebia Euchroma*

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Abstract

Three new naphthoquinones named 2-hydroxyl-6-(11- β -dimethylacryl) isohexenylnaphthoquinone (**1**), 3-ethoxy-6-(11- β -acetyl)isohexenylnaphthoquinone (**2**), 3-ethoxy-6-(11- β -acetoxisovaleryl)isohexenylnaphthoquinone (**3**), and a new quinonoid xanthene named Onosmanones C (**4**), were isolated from the roots of *Arnebia euchroma*. The structures of these compounds were elucidated based on spectroscopic data and comparisons with previously reported data.

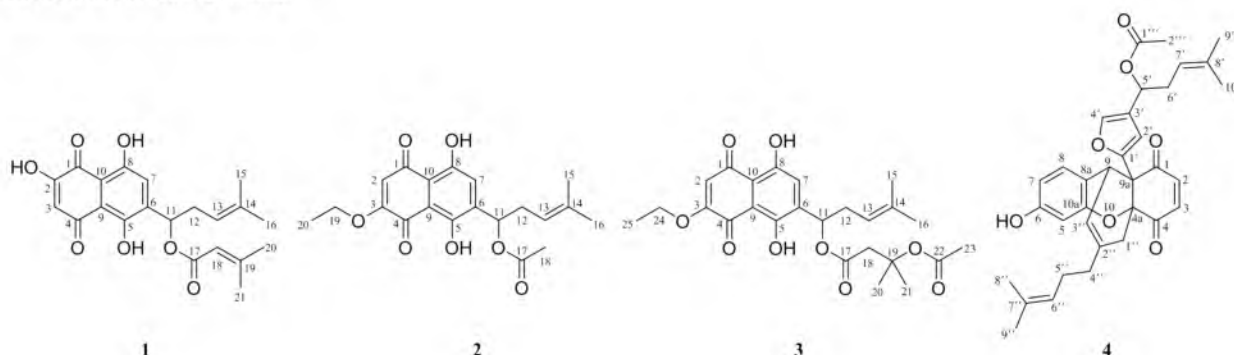
Key words: *Arnebia euchroma*, Boraginaceae, naphthoquinone, quinonoid xanthene

Zicao, the dried roots of *Arnebia euchroma* (Royle) Johnst., or *Arnebia guttata* Bunge.^[1] is an herbal medicine that has been used to treat many kinds of illnesses in China for centuries. Previous pharmacological studies have confirmed that *A. euchroma* has potential medicinal applications in the treatment and prevention of eczema, sores, measles impervious, water and fire scald^[2]. On the other research focus, the phytochemical investigation has revealed several types of secondary metabolites including naphthoquinones, dimeric naphthoquinones, monoterpene phenols, and phenolic acids from this plant^[3]. The most well-known second metabolites of *A. euchroma* are naphthoquinone compounds, such as shikonin, alkannin, and their ester derivatives. It has been shown that these compounds exhibit anti-inflammatory, antibacterial, and antiviral activities.

Objective

To isolate and identify the naphthoquinone constituents of dried roots of *Arnebia euchroma* (Royle) Johnst., and to provide a material basis for the subsequent research on its anti-eczema activity and mechanism.

Results and discussion



Compound **1** was obtained as a dark red powder. HR-ESI-MS analysis revealed the molecular formula to be C₂₁H₂₂O₇ based on the [M+H]⁺ signal at m/z 387.1444. The ¹H-NMR and ¹³C-NMR data of **1** were similar to those of 2-Phenylamino-6-(11- β , β -dimethylacryl) isohexenylnaphthazarin from artifacts^[4]. Because the chemical shift of C-2 moved to the lower field region, combined with HR-ESI-MS analysis, it was speculated that the phenylamino of C-2 was replaced by a hydroxyl group.

Compound **2** was obtained as a dark red powder. HR-ESI-MS analysis revealed the molecular formula to be C₂₀H₂₂O₇ based on the [M+H]⁺ signal at m/z 375.1444. The parent nucleus was identified as naphthoquinone by 1D-NMR data. In contrast to compound **1**, a hydroxyl linked at C-6 was lost, meanwhile, an ethoxy was attached at C-7, and dimethylacryl linked at C-11 was replaced by acetyl.

Compound **3** was obtained as a dark red powder. HR-ESI-MS analysis revealed the molecular formula to be C₂₅H₃₀O₉ based on the [M+H]⁺ signal at m/z 475.1968. Compared the ¹H and ¹³C NMR data of **3** with that of **2**, the two compounds were highly similar except the acetyl at C-11 was replaced by acetoxisovaleryl.

Compound **4** was obtained as a red-orange oil. HR-ESI-MS analysis revealed the molecular formula to be C₃₄H₃₆O₇ based on the [M+K]⁺ signal at m/z 595.2093. The ¹H and ¹³C NMR data of **4** were similar to those of Onosmanones A obtained previously from *Onosma paniculatum*^[5], and the only change was that the hydroxyl at C-6 was lost and it was attached at C-7.

Funding

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Clinical Research Progress of Acupuncture treatment of Post-stroke cognitive impairment

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[Abstract] Post-stroke cognitive impairment is a neuropsychological disorder with high morbidity and disability, which seriously affects the normal life of patients. This paper comprehensively analyzes the relevant data of acupuncture in the treatment of Post-stroke cognitive impairment from four aspects: scalp point acupuncture, Tongdu Xingshen acupuncture, eye acupuncture combined with transcranial direct current electric stimulation and wisdom three acupuncture combined with scalp acupuncture, in order to provide valuable reference for acupuncture treatment of Post-stroke cognitive impairment in the future.

[Keywords] Acupuncture; Stroke; Cognitive impairment; Research Progress

Post-stroke cognitive impairment (PSCI) is a clinical syndrome characterized by cognitive impairment that occurs after stroke and persists until 6 months after stroke. It is one of the most common sequelae of stroke, which is characterized by one or more impairment of memory, language, execution, calculation, comprehension and judgment^[1]. PSCI is an important subtype of vascular cognitive impairment with a high incidence^[2]. Some studies have also shown that the incidence of cognitive impairment in stroke patients is on the rise^[3]. At present, acupuncture treatment of PSCI has been widely recognized to some extent, which can effectively improve patients' memory, language, calculation and other functions. This article reviews the commonly used acupuncture therapy for the treatment of PSCI in order to provide new clinical treatment ideas.

1. Scalp acupuncture

Zhang Han et al.^[4] through the clinical study of 50 patients with mild cognitive impairment after stroke showed that the scores of Montreal Cognitive Assessment scale and Mini-Mental State examination scale were significantly improved in the scalp acupuncture group, and it was better than that in the control group of cognitive rehabilitation training. It can effectively improve the executive function and delayed recall function of patients.

2. Tongdu Xingshen acupuncture

Wang Yan et al.^[5] conducted a randomized controlled trial on 60 patients with mild cognitive impairment after stroke. Patients in both groups were given routine treatment and routine cognitive rehabilitation training. The study group was treated with Tongdu Xingshen acupuncture. The results showed that the scores of visual space and executive function, attention and calculation ability, delayed memory, language and abstract ability and orientation ability of the patients after treatment were higher than those of the control group. It shows that Tongdu Xingshen acupuncture is effective in the treatment of patients with mild cognitive impairment after stroke, and can effectively improve the cognitive function and mental and behavioral symptoms of the patients.

3. Eye acupuncture combined with transcranial direct current stimulation

Wang Heyi et al.^[6] divided 98 patients with PSCI into three groups according to different tr

treatment methods: trial group1(n=31),trial group2(n=33) and control group(n=34).The control group was given basic treatment,group 1 was treated with transcranial direct current stimulation,and group 2 was treated with eye acupuncture combined with transcranial direct current stimulation.The results show that group 2 can significantly improve the cognitive function and activities of daily living of patients with PSCI,and it is easy to operate, so it can be widely used in clinic.

4.Three-Needle of Wisdom Combined with Scalp Acupuncture

Wang Qiongfeng et al.^[7]randomly divided 100 patients with vascular cognitive impairment after stroke into treatment group (n=50) and control group (n=50).The control group was treated with scalp acupuncture,and the treatment group was treated with three-needle of wisdom on the basis of scalp acupuncture.The results showed that the total effective rate of the treatment group was 94.00%,which was significantly higher than that of the control group (84.00%).It can significantly improve the cognitive function of patients and help to quickly recover the damaged brain function of patients.

PSCI is a common symptom after stroke.At present,its pathogenesis is not completely clear. Studies have shown that it is mainly related to age,education,essential hypertension and so on.At the same time,it is related to cerebrovascular damage,cerebral neurodegenerative disease,molecular mechanism and other factors^[8].The prevalence rate ranges from 17% to 92%,so the active intervention of PSCI is very necessary.Acupuncture treatment of PSCI has a good clinical effect on improving the neurological function and cognitive function of patients.At the same time, acupuncture is a relatively simple,economical and safe treatment,and it is easy for patients to accept.Therefore,it is often used in the treatment of PSCI^{[9][10]}.However,there are still some shortcomings in the current research,such as small sample size and lack of multicenter,large-sample clinical randomized controlled trials.The duration of the study is short and there is a lack of long-term follow-up of treatment.Therefore,it is necessary to further improve the relevant clinical randomized controlled trials and prolong the follow-up time. At the same time,we should deeply study the mechanism of acupuncture in the treatment of PSCI,so as to provide a more reliable theoretical basis for acupuncture in the treatment of PSCI.

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Experience of treating labor pains after HyCoSy by using press needles of Baliao

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Abstract: Nowadays, the incidence of female infertility is increasing year by year, and tends to be younger, among which tubal infertility is the main factor of female infertility. HyCoSy as an important examination to evaluate the function of tubal passage, may cause patients panic because of the pain after the examination, and even affect the examination process and results. The second Department of Gynecology of Second Affiliated Hospital of Heilongjiang University Of Chinese Medicine carried out the treatment of HyCoSy labor pains by using press needles to stimulate the point, Baliao, which achieved a good curative effect and had embodied the unique advantages of traditional Chinese medicine, providing reference for clinical relief of HyCoSy labor pains.

Key words: press needles, Baliao, HyCoSy

Now the number of female infertility patients is increasing year by year. The etiology of female infertility is complex and involves many directions, among which tubal infertility is the main reason, accounting for about 20%-35% of female infertility patients. Therefore, accurate evaluation of fallopian tube function is very important for subsequent treatment options of female infertility patients. Hysterosalpingo-contrast sonography (HyCoSy) has gradually become the preferred method for evaluating the function of fallopian tubes due to its advantages of no radiation, little damage, high accuracy, repeatability and rapid examination, and has been widely used in clinical practice. In this study, traditional Chinese medicine press needles were applied in clinical practice as a non-drug analgesic method. Now, the Second Affiliated Hospital of Heilongjiang University of Chinese Medicine applied press needles of Baliao point to relieve labor pains during HyCoSy and achieved good clinical efficacy. The experience is introduced as follows.

1. The causes of pains during HyCoSy

With the deepening of clinical practice, the research on pain after HyCoSy is also deepening, and the related literature is gradually increasing. After comprehensive analysis, the main causes of pain are as follows: ① Tension during speculum placement causes pain; ② Uterine distension caused pain after contrast agent injection; ③ The contrast agent enters the abdominal cavity and causes pain[2]; ④ Pain caused by pulling the cervix when exiting the speculum; ⑤ Abnormal tubal patency causes pain; ⑥ Emotional stress and anxiety cause pain. Although the causes of labor pain during HyCoSy can be divided into several categories, in clinical practice, patients' pain is often a mixture of multiple pain, i.e., a combination of multiple factors. The most common one is to stimulate the vasovagal nerve, causing lower abdominal pain. Among the many causes of pain, the pain caused by the speculum placement and withdrawal is transient, and other reasons can produce persistent pain. However, our department has learned that there is a real fear of pain caused by HyCoSy examination and the need for pain relief after surgery. Therefore, the study of pain relief method, in order to low cost, easy to operate, safe and effective to meet the needs of patients.

2. Characteristics of Treatment

Baliao, located in the sacral region, is the neurovascular clustering place that controls the organs in the pelvic cavity. It is the main switch for regulating qi and blood of the whole body. Meanwhile, a large number of anatomical data showed that s1-S4 spinal nerve segments in the sacral region passed through the 1-4 posterior sacral foramina, forming the lumbosacral plexus. The parasympathetic nerves of the 2nd ~ 4th sacral nerves confluence into the pelvic plexus, which mainly distributes in the uterine body and cervix and innervates various sensations of the internal genitals, especially pain. Therefore, stimulating Ba Liao point can relieve postoperative pain caused by uterine dilation and contrast agent entering the abdominal cavity by regulating the sympathetic and parasympathetic nerve bundles in the sacral nerve cluster. There are a variety of rich clinical research and experience in applying Ba liao acupoint to gynecological pain relief. Compared with traditional acupuncture or electric acupuncture, acupuncture Ba Liao acupoint has obvious advantages. This therapy has the advantages of small trauma, long effect time, small side effects, high safety, simple and easy to be accepted by patients, and relatively low cost. It makes up for the disadvantages of traditional acupuncture therapy, such as many times, short lasting efficacy and poor patient compliance. The second Department of Gynecology, The Second Affiliated Hospital of Heilongjiang University of Traditional Chinese Medicine carried out the application of screw acupuncture Ba Liao point for the treatment of labor pains after hysterosalpingo-graphy. Specific operations: After the end of the contrast, the patient was instructed to lie prone, and the sacral skin was routinely disinfected with 75% alcohol. A single-use screw needle (specification: 0.25×1.3mm, Beijing Zhongyan Taihe Medical Instrument, 20172270935) was taken, and then the sterilized point was needled at Ba Liao point, and the adhesive tape was pressed to adhere and fixed. After the press, the operator warm both hands and gently and regularly press on the acupoints for 5 minutes until the patient feels acid, numbness, swelling, pain or local redness of the skin.

3 Discussion

Through clinical observation, it is found that many patients with pain after HyCoSy examination are mostly caused by "non-general pain", which is often empirical. This method is used to acupuncture Ba Liao point to clear collaterals and relieve pain, regulate qi and blood, assist massage to warm up the meridian, promote blood circulation and ease the mind, and jointly play the role of overall regulation. The selection of acupoints in this innovative method can relieve the pain after HyCoSy examination, and also produce auxiliary treatment for fallopian tube peristalsis and pelvic inflammatory disease to a certain extent[3]. In addition, a new technique combining acupuncture and massage is adopted. The selection of acupoints and treatment methods are in line with the needs of patients, and a good effect has been achieved. Acupoint massage is a traditional Chinese medicine treatment method, while acupuncture is a new form of improvement on the basis of traditional acupuncture and moxibustion, which is easy to operate and has no potential risks and side effects. In this study, we operated according to conventional norms, and no accident occurred in any patient. Therefore, it can be considered safe, feasible and innovative to relieve pain after HyCoSy examination by tapping Baliao point together with acupoint massage. At present, this method has a good effect in a small range of use in our department and is well received by patients. In the later period, on the basis of continuous application, patient data were collected and sorted out, and strict follow-up was conducted to comprehensively summarize the effective rate of patients. In addition, the theoretical basis of effectiveness was further explored to form a complete system, which was

further promoted to clinical application.

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Research progress of acupuncture in the treatment of spinal cord injury

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Abstract: This paper expounds the therapeutic effect of acupuncture and moxibustion on neurogenic bladder, neuropathic pain and deep venous thrombosis of lower limbs after spinal cord injury, and summarizes the deficiencies in the literature, in order to provide ideas and references for follow-up research.

Key words: Acupuncture; Spinal cord injury; The research progress

Spinal cord injury is a central nervous system injury caused by a variety of reasons, which can cause lifelong paralysis of patients. Due to the precise structure of the spinal cord, there is no radical cure so far, making the treatment of spinal cord injury become the focus of medical research and discussion. Acupuncture and moxibustion, as a safe and effective green therapy with little toxic and side effects, began to play its advantages. The author has read the relevant literature on acupuncture treatment of spinal cord injury, which is summarized as follows:

1、 Neurogenic bladder after spinal cord injury

1.1 acupuncture treatment

In traditional Chinese medicine, urinary system diseases are attributed to the bladder, and the Baliao points belong to the acupoints of the bladder meridian, and the anatomical position is close to the pelvic and other reproductive organs. It is not only the acupoint selection of this meridian, but also in line with the law of proximal acupoint selection, so clinically it is an important point for the treatment of urinary system diseases. Kuang Weichuan^[1] Selected points such as Shanglu, CILU, Zhonglu and Xialu for shallow and deep needling respectively. The results showed that both shallow and deep needling could improve bladder function and urinary retention symptoms after spinal cord injury.

1.2 Electroacupuncture

Ma Feixiang^[2] Treated 18 patients with neurogenic bladder after spinal cord injury with electric stimulation at point Ba Lu combined with the projection area on the surface of the bladder. Compared with the control group assisted with bladder training, the number of spontaneous micturition and maximum bladder capacity in the treatment group increased significantly. The mechanism may be that electric stimulation can strengthen the synergy between detrusor and sphincter and restore micturition reflex.

1.3 moxibustion treatment

Spinal cord injury makes the gasification function of the bladder lose its function, and the water channel cannot be adjusted, so urine retention in the body. Moxibustion has the function of warming and passing Qi. With the help of the heat of moxa fire, the efficacy can be transferred from the surface to the inside and reach the whole body. Wei Wei^[3] confirmed through experiments that moxibustion at Mingmen and Shenque points can reduce the expression of glucose regulatory protein 78, activating transcription factor 4 and cysteine aspartate specific protease 12 in rat bladder tissue, so as to reduce the apoptosis of bladder tissue cells and improve bladder function.

2. Neuropathic pain

2.1 acupuncture treatment

Zhang Jie^[4] treated 20 patients with neuralgia after spinal cord injury with acupuncture combined with respiratory training. The acupoints were Neiguan, Tongli, Houxi, Baihui, Yanglingquan and Ashi. The visual analog score (VAS) of the treatment group was significantly reduced and the analgesic effect was better.

2.2 electroacupuncture treatment

Zheng Qinghua^[5] compared the vas, neurological deficit score and tumor necrosis factor of the control group treated with oral pregabalin and the treatment group treated with scalp acupuncture combined with spinal electroacupuncture- α It was found that the treatment group could inhibit the transmission of pain information, inhibit central sensitization and improve pain threshold.

2.3 Puncture and cupping therapy

Patients with spinal cord injury are more likely to have blockage of Qi and blood stasis, and then there will be symptoms of blockage and blockage. Zhao Changying^[6] control group took western medicine orally, and the treatment group used three edged needle to prick and bleed the painful part, and then used flash fire cupping combined with acupuncture at Neiguan point. After the course of treatment, the total effective rate of the treatment group was higher than that of the control group. Puncture and cupping can relieve pain and improve sleep quality.

3. Formation of deep venous thrombosis of lower limbs after spinal cord injury

3.1 acupuncture treatment

Yu Jiansong^[7] observed the clinical efficacy of acupuncture combined with rehabilitation training on this disease, and found that there was no lower extremity venous thrombosis in the acupuncture combined group during the treatment period. The incidence of thrombosis in the simple rehabilitation training group is 32%. The combination of acupuncture and Kang can not only reduce the incidence of thrombosis in the lower limbs, but also restore the nerve function and independent living ability of patients, which is worthy of clinical application.

3.2 warm acupuncture treatment

Some studies believe that 11 venous stasis, blood hypercoagulation and vascular intimal injury are the three basic elements of thrombosis. Protein C system mainly plays the role of anticoagulation. After warm acupuncture treatment, it can improve the activity of protein C anticoagulation system, inactivate coagulation factors VA and VIIIa, and thus accelerate the speed of venous blood flow. Ge Xiaogang^[8] was treated with low molecular weight heparin and rivaroxaban, and the treatment group was combined with warm acupuncture. The results showed that the hemoglobin level, lower limb venous blood flow velocity and D-dimer in the treatment group were better than those in the control group, and the total effective rate was 93.33%.

4. Discussion

Our next step should focus on the study of the mechanism of acupuncture treatment of this disease, carry out animal experiments, expand basic research, apply academician Shi Xuemin's acupuncture manipulation metrology to clinical practice, in order to improve the reliability of the system in the trial.

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The application of traditional Chinese Medicine Constitution in treating diseases before treatment

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Abstract

With the development of economy and society, people pay more and more attention to health problems. TCM constitution is of great significance in the "prevention of disease". This paper comprehensively expounds the definition of "prevention of disease", focusing on the application of traditional Chinese Medicine Physique in "prevention of disease". According to the pathological constitution of patients, different treatment methods should be taken to prevent the occurrence of diseases; When the disease is in the critical state of onset, early detection, early diagnosis and early treatment should be done well; When the disease occurs, grasp the main factor of physique, treat the patients, and promote the disease to develop in a good direction. Based on the recent research and application status and future development trend of traditional Chinese Medicine Constitution and prevention of diseases, this paper discusses the application of traditional Chinese Medicine Constitution in "prevention of diseases", and provides ideas for further research on the development of traditional Chinese medicine.

Key words: TCM Constitution; Prevent disease; TCM Prevention

Objective

Prevention is to take certain measures to prevent the occurrence and development of diseases, which is traditionally called "prevention of diseases". Prevention, for healthy people, can enhance their physique and prevent the occurrence of diseases; For the sick, it can prevent the development and transmission of the disease.^[1] Traditional Chinese medicine academic qualifications to pay attention to prevention, as early as the "Neijing" put forward the prevention idea of "preventing disease before treatment". Sun Simiao put forward in his "Qianjin Yaofang · on diagnosis" that "the ancients were good at treating diseases that were not ill by medical treatment, diseases that were intended to be ill by traditional Chinese medicine, and diseases that were already ill by medical treatment". Diseases were divided into three categories: diseases that were not ill, diseases that were intended to be ill, and diseases that were already ill. This is the earliest concept of three-level prevention in traditional Chinese medicine, and it is also very consistent with the thought of three-level prevention in modern preventive medicine. The thought of "prevention of disease" is a characteristic academic thought of traditional Chinese medicine, which is of great strategic significance to the practice of healthy China. Physique refers to the relatively stable inherent characteristics formed by the joint influence of innate endowment and acquired in the process of human life in terms of morphological structure, physiological function and psychological state. In recent years, the research on TCM Constitution and prevention of diseases has gradually become a hot spot, providing reference for further research in the future.

Materials and methods

Physique refers to the relatively stable inherent characteristics formed by the joint influence of innate endowment and acquired in the process of human life in terms of morphological structure,

physiological function and psychological state. According to the cognitive method of "taking care of the outside and inferring the inside" in traditional Chinese medicine, there is an organic whole between the internal morphological structure and the external image, the external morphological structure is the external expression of physique, and the internal morphological structure is the internal basis of physique; The difference in physiological function is also a component of individual physical characteristics; Form and spirit are a unified whole. Constitution is a synthesis of specific morphological structure, physiological function and related psychological conditions. There is an internal correlation between morphological function and psychology. In addition, the characteristics of constitution include Congenital heredity, diversity, unity of form and spirit, group tendency, relative stability, dynamic variability, continuous measurability, and acquired adjustability.

"Prevention of disease" is guided by the theory of traditional Chinese medicine, through the adoption of preventive health preservation or early treatment, in order to achieve the purpose of preventing the occurrence and development of the disease.^[2] Traditional Chinese medicine emphasizes prevention over treatment. In the process of the development of traditional Chinese medicine prevention and health care, process and occupies an important position. According to the statements of doctors in various periods on "treating diseases before they occur", its connotation can be summarized into two aspects: first, prevent diseases before they occur, that is, pay attention to health care, maintain body and mind, and prevent the occurrence of diseases, including two points: health preservation to enhance healthy qi, and its measures mainly include: conforming to nature, nourishing nature and regulating spirit, protecting kidney and essence, physical exercise, regulating diet, acupuncture, massage, medicine and so on; The main measures to prevent the invasion of disease and evil are: avoiding its evil Qi, drug prevention to prevent the injury of disease and evil; Second, disease prevention refers to early diagnosis and treatment after the occurrence of the disease to prevent the transmission of the disease. It also includes two points: early diagnosis and treatment, "Su Wen · eight positive gods theory" said: "work to save its bud... Work to save it has become." To prevent the transmission of disease, the main measures are: ① block the way of disease transmission. ② Xian'an is a place free from evil.

Yu Bibo^[3] identified the constitution before pregnancy, guided and intervened in high-risk groups, and applied the thought of "prevention and treatment of diseases" in traditional Chinese medicine to the prevention and treatment of embryo suspension. Starting with the patient's constitution type, he used the advantage of "constitution adjustability" to guide and intervene in the susceptible constitution, so as to reduce the risk of recurrence of embryo suspension and provide a theoretical basis for the clinical treatment of embryo suspension, It also opens up a new foothold for traditional Chinese medicine to recognize and treat embryo suspension. When studying the relationship between various biochemical indexes of patients with polycystic ovary syndrome with blood stasis constitution and patients with polycystic ovary syndrome with non blood stasis constitution, Wang Jie^[4] pointed out that in clinical practice, the biased constitution can be adjusted through the method of body discrimination, so as to improve symptoms and prevent the occurrence of diseases, provide new ideas for the prevention of polycystic ovary syndrome, and also embody the idea of "prevention before disease" in traditional Chinese medicine.

Results and discussion

"Prevention of disease" is not only the prominent feature and advantage of traditional Chinese medicine, but also the core value of traditional Chinese medicine culture. To carry forward the excellent culture of traditional Chinese medicine, the fundamental point is to carry forward the fine tradition of "curing diseases before diseases" in traditional Chinese medicine. At the same time, with the continuous development of TCM constitution theory and the in-depth study of disease pathogenesis theory, it is more necessary to inherit and innovate the theory of "prevention and treatment of diseases", combine TCM Constitution with "prevention and treatment of diseases", and embody the treatment scheme with the characteristics of traditional Chinese medicine, which is of great strategic significance to solve the problems of disease prevention and control and health care, and promote the development of traditional Chinese medicine.

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Construction and prospect of Chinese medicine diagnosis and treatment system in Sino-Russian barrier-free intelligent holographic cloud platform

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Abstract

Objective

Based on the current development of science and technology as well as the establishment and use of different types of cloud platforms [1-7] at home and abroad, this paper introduces a new diagnosis and treatment system, aiming to overcome the obstacles such as distance language, develop and spread the cause of Chinese medicine, and further realize the exploration and application of the Sino-Russian great health field. Other endpoints included analysis of collaboration between participants, patient outcomes, and satisfaction.

Materials and methods

By professional engineers, artificial intelligence, the development and design of cloud platform software, holographic visualization technology and corresponding supporting services of TCM diagnosis and treatment are integrated and developed to ensure online communication between individuals, hospitals and departments and realize remote diagnosis and treatment services.

Results

The development of the software has certain feasibility, involving the communication and multidisciplinary cooperation of different disease entities and departments in China and Russia, to create the best TCM diagnosis and treatment path and the center radiation relationship for patients.

Conclusion

The diagnosis and treatment system provides a feasible opportunity for remote patient-centered optimization of TCM care management. High-quality visualization and smooth communication can save time and resources to a greater extent, complete the collection and exchange of clinical data across different borders, and is expected to continue to be promoted to enhance the multidisciplinary decision-making of TCM.

Key words: China and Russia, traditional Chinese medicine diagnosis and treatment, holography, cloud platform, barrier free, intellectual ability

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Research on the advantages of China-Russia TCM health industry under Belt and Road

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Abstract

Traditional Chinese medicine is the treasure of the Chinese nation. Taking thousands of years away from nature and giving back to the great health of human beings, it has accumulated rich experience in disease prevention and treatment. As global powers, China and Russia play a huge role in the face of public health emergencies. The strengthened cooperation between China and Russia against the background of Belt and Road will undoubtedly provide a guarantee for the innovative development of TCM in the field of big health. At present, people's health faces severe challenges: On the one hand, the epidemic situation of major infectious diseases is still severe, chronic non-communicable diseases and mental diseases pose increasing threats to people's health, and the potential threats of new infectious diseases and traditional severe infectious diseases cannot be ignored. On the other hand, changes in the ecological environment and production and life style, as well as food and drug safety, occupational injuries, drinking water safety and environmental problems, have had a more prominent impact on people's health. The contradiction between the supply and demand of medical and health services is becoming increasingly prominent, and the service concept and service mode urgently need to be adjusted accordingly. The big health industry has become the current sunrise industry. In this context, it is an important development opportunity to promote the traditional Chinese medicine industry, to apply it to the people in China and Russia and the world, and to promote the development of the big health field.

Key words: traditional Chinese medicine; China and Russia; innovation;

In 2013, Chinese President Xi Jinping proposed a cooperation initiative to build the "Belt and Road". By May 27, 2022, China had signed more than 200 Belt and Road " cooperation documents with 150 countries and 32 international organizations. As a major country, the mutual cooperation between China and Russia and the two countries plays a crucial role in the development of "Belt and Road". In the 14th Five-Year Plan for TCM Development released by the state in 2022^[1], it is clearly pointed out that we should vigorously develop the characteristic TCM health industry and actively promote the overseas cooperation and development of TCM by relying on the "Belt and Road" construction framework, and promote the construction of TCM academic exchanges, cultural communication, international education and other aspects. It has laid an important foundation for TCM to go global. With the change of human health concept and medical model, TCM has gradually been recognized and valued internationally.

Objective

China and Russia have a wide land area, rich traditional Chinese medicine resources and a long history. China and Russia are among the top three in the world. Rich in natural resources. The history of Traditional Chinese medicine in China has long been well known all over the world. As early as in "Shuo Wen Jie Zi", it was clearly pointed out that "medicine" is a cure, which has been continuously inherited and developed to this day. According to the results of the third national TCM

resources survey, there are 12,807 kinds of available medicinal resources in China, and there are very high-quality authentic medicinal materials producing area everywhere^[3,4]. The historical origin of Russian Traditional Chinese medicine is also relatively early. In the 10th century, copies of some Greek herbs were introduced to Russia and translated into Russian. In the 13th century, Russian medical scientists applied the herbs to their wounds for anti-inflammatory and analgesic effects. Currently, the Russian Federation follows the National Pharmacopoeia of the former Soviet Union (the 11th edition), which includes 83 individual plant monographs and is used in clinical practice^[5].

Materials and methods

The concept of TCM health management mainly comes from the traditional thought of "curing the disease". "Su ask four qi tune theory" pointed out: "eliminate the disease without omen" "because the sage did not cure the disease is not disease, do not cure the disorderly treatment is not chaos". It shows that the idea of treating no diseases and TCM health management has been contained in medical practice since ancient times. As early as two thousand years ago, traditional Chinese medicine has summarized the principles and methods of health care, such as adapting to nature, practicing Yin and Yang, avoiding evil outside, eating and drinking. These theories and methods, after thousands of years of verification, supplement, improvement and development, are enduring and still play an important role today. As General Secretary Xi Jinping has stressed that, Scientific and technological innovation Science popularization is the two wings of innovative development, To put the popularization of science is of equal importance to scientific and technological innovation, We must adhere to the ancient use for China, To deeply explore the connotation and value of traditional Chinese medicine health preservation culture, To realize its creative transformation and innovative development, To popularize the scientific knowledge of traditional Chinese medicine in a way that the people can understand, learn, and spread it widely, Scientific approach to maintaining health, Improve the scientific literacy of TCM, To advocate the idea that everyone is the first person responsible for their own health, Do my health, I decide, And I maintain my health, Be a gatekeeper of your own health, While enabling the people to fully enjoy the achievements of TCM innovation and development and improve their health literacy, Constantly improve their own ability to cure diseases, repair injuries and maintain health.

As China's new industrialization, informatization, urbanization, agricultural modernization further development, accelerating population aging process, health services booming, people's demand for Chinese medicine service more and more strong, urgent need to inherit, development, make good use of Chinese medicine, give full play to the role of Chinese medicine in deepening the reform of medical and health system, for the benefit of human health. In the process of deeply integrating the Internet and TCM and reconstructing the development model of the whole TCM industry chain, not only the game relationship between the traditional TCM business model and the stakeholders has been changed, but also the inheritance and communication model of TCM culture has also undergone profound changes.

Results and discussion

Response to national call, under the background of Belt and Road to promote the development of traditional Chinese medicine, with the development of the Internet, the new method of industry combining traditional Chinese medicine, heritage culture, promote the recognition of the world of traditional Chinese medicine, strengthen the close ties between the two countries, change the

traditional Chinese medicine business model and the game relationship between interests, strengthen the practice innovation of traditional Chinese medicine culture inheritance and development. It is of national strategic significance to make TCM gradually recognized and attach importance internationally, to promote the development of TCM "Belt and Road" strategy, and to deepen cooperation and exchanges with countries along the Belt and Road.

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Wake-sleep phase, energy expenditure, and activity frequency in VCD-induced menopausal transition mice

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Keywords: Menopausal transition; VCD; sleep; energy expenditure

Objective: In this study, VCD-induced menopausal transition mice were used as models. To explore the changes in the sleep-wake phase and energy expenditure in VCD mice, and provide experimental basis for the study of sleep disorders and metabolic diseases during menopausal transition.

Methods: 56-day-old female ICR mice were randomly divided into 6 groups (n=8), namely VCD 20 d, VCD 35 d, VCD 52 d, control 20 d, control 35 d, and control 52 d. The mice in the VCD group were intraperitoneally injected with VCD (160 mg/kg, 5 d/w, 20 d in total) to replicate the menopausal transition model. Mice in the control group were injected with an equal volume of sesame oil. On the 20th, 35th, and 52th days after the injection of VCD or sesame oil, the 24-hour EEG and EMG of the mice in each group were recorded. The mice in each group were put into the Comprehensive Laboratory Animal Monitoring System (CLAMS) on the next day, and their 24-hour Respiratory exchange ratio (RER), energy expenditure, and activity times were measured.

Results: At 20, 35, and 52 days after VCD treatment, Compared with the control group, awakening time at 24 h ($P<0.05$) and daytime ($P<0.05$) was prolonged, and duration of REM sleep was significantly shortened at 24 h ($P<0.01$), daytime ($P<0.05$), and nighttime ($P<0.05$) in the VCD group compared with that in the control group ($P<0.05$). Meanwhile, shortened duration of NREM sleep in the VCD group was recorded at a full cycle of 24 h either at 35 days ($P<0.01$) or 52 days ($P<0.05$) and at 12-h daytime and nighttime at 35 days ($P<0.01$). At 52 days of VCD treatment, the duration of awake episodes was reduced throughout all day ($P<0.05$) and daytime ($P<0.05$). The heat production values in the VCD group were lower than those in the control group throughout 24 h compared with those at at 20 and 52 days ($P<0.05$), and there was no significant difference at 35 days. During a 24-h day, compared with the control group, the RER of VCD mice was elevated at 35days ($P<0.01$) and 52d ($P<0.05$). VCD mice showed an increase in RER at 35 days compared with VCD mice at 20 ($P<0.05$) and 52 days. Moreover, all mice in the VCD group at different time points showed the increased locomotor activity in both dark and light cycles compared with those in the control group ($P<0.05$).

Conclusion: The decrease in sleep quality and the interconversion of fatty acid and carbohydrate oxidative metabolism would occur throughout the menopausal transition.

Effects of Schisandra Lignans on Learning and Memory function in Sleep-Deprived Rats

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Abstract

Keywords

Schisandra lignans, sleep deprivation, learning and memory, synaptic plasticity, hippocampus

Objective

Recently, there has been growing evidence that sleep deprivation not only contributes to cognitive impairment, but also increases the risk of dementia. Synaptic plasticity is generally considered to be the neurobiological basis for learning and memory processes, while sleep deprivation impairs the learning and memory function of experimental animals by affecting hippocampal synaptic plasticity. Our previous studies have shown that Schisandra lignans can antagonize the reduction of sleep duration in sleep-deprived rats, and can significantly improve the daytime function decline caused by sleep deprivation, such as anxiety, depression, as well as fatigue degree. However, its effect on the learning and memory of sleep-deprived rats remains unclear. In this study, the effect and mechanism of Schisandra lignans on learning and memory function in sleep-deprived rats are investigated.

Method

SD rats were randomly divided into four groups: control group, model group, melatonin group, and Schisandra lignans group. Rats were subjected to sleep deprivation by treadmill apparatus for consecutive three days. The rats in control and model groups were treated with the same volume of 1% sodium carboxymethyl cellulose suspension, and in Schisandra lignans group were treated with Schisandra lignan suspension (67.2 mg/kg) by oral gavage twice daily at 8:00 and 20:00, respectively. The rats in melatonin group was treated with melatonin suspension (10 mg/kg) at 8:00 in the morning, and 1% sodium carboxymethyl cellulose solution (50 mg/kg) at 20:00. The learning and memory abilities of rats were evaluated by hexagonal maze behavior method, and LTP changes in rat hippocampal CA1 region were detected by in vivo electrophysiological technology. The contents of Glu and Gln in the hippocampus were measured by ELISA technology and mRNA expression of Glu-related receptors and Glu transporters were tested by Q-PCR.

Results

As compared to the model group, melatonin and Schisandra lignans significantly shorten the searching time, increased search frequency and cognitive rate in the hexagonal maze test ($p < 0.05$). Additionally, melatonin and Schisandra lignans significantly increased the change rate of population spike amplitude in the hippocampal CA1 region, and enhanced the contents of Glu and Gln in the hippocampus ($p < 0.05$). Meanwhile, mRNA transcription levels of GluN1, GluN2A, GluN2B, AMPAR, CaMK II, GLAST, and GLT-1 were all elevated significantly in melatonin and Schisandra lignans group compared to model group ($p < 0.05$).

Conclusion

Schisandra lignans possess the potential to improve learning and memory function in treadmill sleep-deprived rats, which may be mediated by hippocampal synaptic plasticity.

Effect of freeze-dried powder of sour jujube on immune function and intestinal flora in mice with cyclophosphamide-induced immunosuppression

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Abstract

Keywords

Sour jujube, immune enhancement, cellular immunity, humoral immunity, cytokines, intestinal flora

Objective

To study the effect of sour jujube freeze-dried powder (including peel, pulp, date kernel, and seed kernel) on immune function and the regulation of intestinal flora in cyclophosphamide (CTX) mice.

Methods

BALB/c mice were randomly divided into four groups with 8 mice in each group: blank group, model group and sour jujube group. The mice in the blank group and model group were administrated with the same volume of saline water, and the mice in the sour jujube group were administrated with a freeze-dried aqueous solution of sour jujube water extract (20mL/kg/d) for 21 consecutive days. Mice in the model group and sour jujube group were intraperitoneally injected with CTX (8mL/kg/d) on the 16th and 17th day of intragastric administration, respectively. Organ index, ear swelling degree, half hemolysis value (HC₅₀), phagocytic index, small intestinal villus height and crypt depth, as well as serum cytokines IFN- γ and IL-4 levels were measured after 21 days of gavage. Meanwhile, fresh fecal samples from each mouse were collected, and the gut microbiota was analyzed using 16S rRNA sequencing data. **Results:** Compared with blank group, organ index ($P<0.01$), serum IFN- γ and IL-4 levels ($P<0.05$), ear swelling ($P<0.01$), HC₅₀ ($P<0.01$), phagocytic index ($P<0.01$), villus height ($P<0.01$), the ratio to crypt depth ($P<0.01$), richness and uniformity of intestinal flora ($P<0.05$) were significantly decreased in the model group. However, these changes in model group were all reversed by sour jujube. In terms of flora composition, the abundance of Rikenellaceae-RC9-gut-group and Prevotellaceae-UCG-001 was lower in the model group ($P<0.05$), while the abundance of Helicobacteraceae and Bacteroidaceae was higher ($P<0.05$). Compared with the model group, the abundance of Lactobacteriaceae and Bacteroidaceae in sour jujube group was down-regulated ($P<0.05$), and the abundance of Rikenellaceae-RC9-gut-group was up-regulated ($P<0.01$).

Conclusion

Sour jujube has immune-protective effects on CTX-treated mice, which may be regulated by gut microbiota.

Three new triterpenoid saponins from *Astragalus membranaceus* var. *mongholicus*

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Abstract

Phytochemical study of the ethanol extract of *Astragalus membranaceus* (Fisch) Bge. var. *mongholicus* (Bge) Hsiao resulted in the isolation of three new triterpenoid saponins (**1-3**), Astralanosaponins F-H. Structure analysis of these extracted compounds was performed by 1D-NMR and 2D-NMR spectroscopy, and their data were compared with similar compounds previously described in the document. The absolute configuration of sugar was determined by GC-MS.

Keywords

Astragalus membranaceus var. *mongholicus*; triterpenoid saponins

Objective

To rich chemical constituents of *Astragalus membranaceus* var. *mongholicus* and provide material basis for subsequent experiments.

Materials and methods

The chemical constituents of *Astragalus membranaceus* var. *mongholicus* were extracted by 70% ethanol reflux. Triterpenoid saponins were enriched by HP-20 macroporous adsorption resin, then separated and purified by silica gel, ODS, Sephadex LH-20, and preparative liquid chromatography. The structure of the compounds was identified by NMR, MS, and other modern spectroscopic techniques.

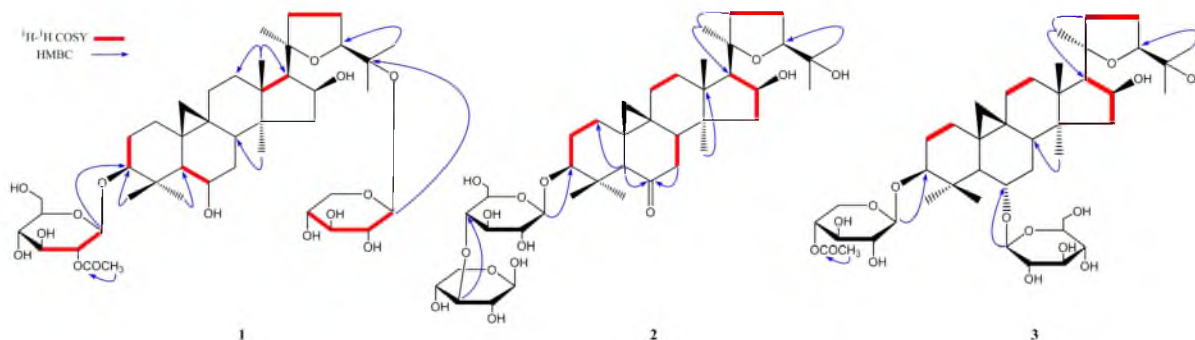
Results and discussion

Astralanosaponin F (**1**) was obtained as a white powder. In the $^1\text{H-NMR}$ spectrum of compound **1**, 7 methyl proton signals were observed, which are characteristic signals of triterpenoids. The signals of H-19a (δ_{H} 0.18) and H-19b (δ_{H} 0.55) were observed in the high field as the characteristic signals of cycloartane triterpenoids. The terminal proton signals of xylose and glucose were observed in the low field region. The 1D-NMR data of compound **1** were compared with that of the known compound Astralanosaponin A₂, and it was found that the chemical shifts of the two compounds were highly similar. The only difference was the glucose which was attached at position 27 converted into xylose. In addition, the long-range correlations of H_{1''} (δ_{H} 5.07)/C-27 (δ_{C} 78.3) in the HMBC spectrum could indicate the position of xylose.

The planar structure of astralanosaponin G (**2**) can be preliminarily predicted by $^1\text{H-NMR}$ and $^{13}\text{C-NMR}$. The $^1\text{H-NMR}$ spectra of compound **2** showed that the characteristic proton signals of cycloartane triterpenoids existed at H-19a (δ_{H} 0.26) and H-19b (δ_{H} 0.53). The terminal proton signals of xylose and glucose were observed in the low field region. In the $^{13}\text{C-NMR}$ spectrum of compound **2**, seven methyl carbon signals can be observed: C-18 (δ_{C} 21.7), C-21 (δ_{C} 27.1), C-26 (δ_{C} 28.1), C-27 (δ_{C} 28.5), C-28 (δ_{C} 25.6), C-29 (δ_{C} 15.3), C-30 (δ_{C} 20.1). Through data comparison, it can be seen that the structure was highly similar to the known compound astralanosaponin B. Meanwhile, the structure of the triterpenoid parent nucleus could be confirmed by $^1\text{H-}^1\text{H COSY}$. By

HMBC spectrum, the difference between **2** and known compounds was that glucose attached at position 27 changed into xylose linked at position 4'.

Figure1. Key HMBC and ^1H - ^1H COSY of compounds **1-3**.



Astralanosaponin H (**3**) showed as a white powder. In the ^1H -NMR spectrum of compound **3**, the signals of H-19a (δ_{H} 0.20) and H-19b (δ_{H} 0.58) were observed in the high field as the characteristic signals of cycloartane triterpenoids. In the low field region, the terminal proton signals of xylose H-1' (δ_{H} 4.90) and glucose H-1'' (δ_{H} 4.84) could be observed. Compared to the one-dimensional NMR data of the known compound astragaloside II, the xylose of compound **3** was acetylated at C-2 instead of C-2. In the HMBC spectrum, the correlations of H-4' (δ_{H} 5.38)/C-Ac (170.5) could be observed which confirmed that the position of the acetyl group changed.

Funding

Key Research and Development Projects of Heilongjiang Province (GA21D008) and Heilongjiang Touyan Innovation Team Program.

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A review of chemical constituents of the roots and rhizomes of *Dioscorea nipponica* Makino

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Abstract

Dioscorea nipponica Makino (*D. nipponica*) is one of the major medicinal plants of Northeast China, which is a species of the *Dioscorea* genus in the *Dioscoreaceae* family. The roots and rhizomes of *D. nipponica* were rich in steroidal saponins and used in traditional Chinese medicine to treat rheumatoid arthritis, chronic bronchitis, asthma, coronary heart disease, and so on. This review focuses on the progress of isolated compounds in the roots and rhizomes of *Dioscorea nipponica*.

Keywords

Dioscorea nipponica, Active ingredient, steroidal saponin

The roots and rhizomes of *D. nipponica* were rich in a variety of biologically active secondary metabolites, including steroid saponins, sterols, diarylheptanoids, coumarins, and phenanthrenes, modern pharmacological studies had proved that *D. nipponica* had anti-tumor, liver protection, immune regulation, hypoglycemic, anti-inflammatory, antiviral, and other pharmacological effects^[1-5].

Objective

This review focused on the phytochemistry of the roots and rhizomes of *D. nipponica*, which provided new insights into the study of the phytochemistry rational utilization of resources of *D. nipponica*.

Materials and methods

The information reported in this study was retrieved from the scientific database such as CNKI, ScienceDirect, PubMed, and Wiley, up until July 2022. The key search word was “*Dioscorea nipponica*”.

Results and discussion

1 steroidal saponins

In steroid saponins isolated from the roots and rhizomes of *D. nipponica* in recent years, the proportion of new compounds in steroidal saponins of the furosteroidal type was large. Liu^[1] isolated 23 furosteroidal saponins from the roots and rhizomes of *D. nipponica*, among which 15 were new compounds, were named diosnipponicosides A-O, their novelty was that the different types, numbers, and connection modes of sugars based on similar saponins. Liu^[1] also used UPLC-Q-TOF-MS to quickly identify total saponins and identified 38 other steroid saponins, 20 of which might be new compounds, indicating that there was a prospect for further research on the separation of compounds from the roots and rhizomes of *D. nipponica*. In contrast, the occurrence frequency of new compounds in isospiranol steroidal saponins was low, and only 3 new compounds were found in 20 compounds. By comparing the structure of the compounds, the number of sugars in the isospirosteranol steroid saponins was generally less than in the furosteranol type, so the

polarity was smaller. This has a guiding role in subsequent separation, if new compounds are to be obtained, the components with higher polarity should be selected for separation.

It was well known that the chemical structure of compounds is closely related to biological activity. The relationship between molecular biology research and the structure of steroidal saponins in *D. nipponica* was reviewed in the following. The content of isospirosteranol steroid saponins in the roots and rhizomes of *D. nipponica* was higher than that of furosteranol type, and its antitumor, antithrombotic and anti-inflammatory activities were also higher than those of furostanol^[2, 4]. Up to now, studies on anticancer activity of compounds isolated from the roots and rhizomes of *D. nipponica* are sufficient. Diosgenin was a precursor drug for the synthesis of steroid hormone drugs, but it had no anticancer and antithrombotic activity in itself^[2, 4]. The steroid saponins formed by the substitution of the 3-position hydroxyl by the sugar chain had strong biological activity, therefore, it was speculated that the 3-position sugar chain was a necessary condition for anti-cancer activity^[2]. Furostanol-type steroidal saponins were steroidal saponins of parent nucleosides with an F-ring cleavage ring. The anti-cancer biological activity of these steroidal saponins was generally weaker than that of isospiranol-type steroidal saponins, which might be due to the decrease in anti-cancer activity caused by the F-ring cleavage ring^[2]. Through literature comparison we could also draw the following conclusions: The formation of double bonded between 20 and 22 furostanol-type steroid saponins might weaken the anticancer activity, the 2 - position-linked rhamnose of glucose in the sugar chain had strong biological activity, the 6 - position esterification would weaken the biological activity, and the 14 - position-linked hydroxyl group in the aglycone would reduce the activity of the compounds^[2, 4].

2 Other compounds

In addition to steroid saponins, phenolic derivatives, sterols, coumarins, diphenyl heptanes, and flavonoids were found in the roots and rhizomes of *D. nipponica*^[3, 5]. Among these trace components, there were many new compounds in phenolic derivatives. Their novelty was in the different substituent groups and the introduction of sugar chains. Diphenylheptane compounds were not common in Dioscoreaceae plants but were the main active components in Zingiberaceae plants, which reflected the biological differences and relationships between Dioscoreaceae plants and Zingiberaceae plants.

These compounds had low content in the roots and rhizomes of *D. nipponica* and played an auxiliary role in the process of *D. nipponica*'s anti-inflammatory, anti-tumor, and other biological activities^[3, 5]. Some of these compounds showed good biological activity like 3,7-dihydroxy-2,4,6-trimethoxy-phenanthrene showed significant neuroprotective activity through the increase of NGF secretion in C6 glioma cells and inhibition of NO production in lipopolysaccharide-activated BV-2 cells, it showed an increase of neurite outgrowth in N2a cells^[3]. Therefore, *D. nipponica* and its active components might be used as a potential agent for the regulation of neurodegenerative diseases. In addition, the cytotoxic activity of the NCI-H460 lung cancer cell line was tested, and it was found that 2,2', 7,7'- tetramethoxy- [1,1'-biphenanthrene]- 4, 4', 6, 6'- tetrol had moderate cytotoxic activity^[5]. At present, the research on steroid compounds in the roots and rhizomes of *D. nipponica* was more in-depth, while the research on other compounds with biological activity was less. The main reason is that the content of such compounds was less, which makes it difficult to separate and enrich. By comparing the literature, it was found that these

compounds also had good biological activity, so the research on other compounds in the roots and rhizomes of *D. nipponica* also had a good prospect.

In this paper, the recent research progress of chemical constituents in the roots and rhizomes of *D. nipponica* was reviewed, and the relationship between the separation methods, structures, and biological activities of steroidal saponins was speculated and summarized, to guide the subsequent separation and molecular biology research of the roots and rhizomes of *D. nipponica*.

Funding

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Explore the ideas and methods of treatment of bronchial asthma (hot asthma) based on the theory of “rush, all belong to fire”

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Abstract

[Objective] To study the ideas and methods of treating bronchial asthma (hot asthma) from the theory of “rush, all belong to fire”. [Methods] Through long-term clinical experience, combined with the theory of “rush, all belong to fire”, the relationship between the three viscera of lung, stomach and intestine and hot asthma and its treatment were summarized, and the rational prescription of treating hot asthma from fire was perfected. [Results] In traditional Chinese medicine, bronchial asthma belongs to "asthma", and hot asthma is mostly caused by fire-heat pathogens, which has the characteristics of Qi upside down. In 19 articles, “rush, all belong to fire” points out that the disease mechanism of patients with rapid onset can be attributed to the evil of fire-heat, and in modern medical research, it is found that the disease of fire-heat in traditional Chinese medicine is closely related to western medicine inflammation. Through dialectical view of the relationship between lung, stomach, intestines and asthma based on the theory of “rush, all belong to fire”, the effect of modified Dingchuan Decoction in the treatment of patients with hot asthma is obvious. [Conclusion] The treatment of bronchial asthma (hot asthma) from the theory of “rush, all belong to fire” has a definite clinical effect and broadens the ideas for the treatment of bronchial asthma.

Keywords

Article 19 of pathogenesis;Bronchial asthma;Hot asthma;Theoretical discussion

Bronchial asthma is a heterogeneous disease characterized by the chronic inflammation of the airway involved by a variety of cells and cellular components. With the characteristics of recurrent attacks, the time stage of the attack or aggravation is often at night or in the early morning, and its symptoms can be relieved or relieved spontaneously after treatment. Asthma as one of the most common chronic diseases affecting human health in the world, due to the changes of people's lifestyle and environment today, the number of patients with asthma is increasing year by year, according to the global burden of disease research [Global Burden of Disease (GBD) Study] 2015 epidemiological survey on asthma prevalence increased by 12.6% compared with 1990, and Asian asthma prevalence rate is increasing year by year. Because of asthma cannot cure, long-term drug treatment brings patients the burden of life and body, so the author through the relevant literature learning and combined with years of clinical experience, to “rush, all belong to fire” based on the theory of the dialectical view of lung, stomach, intestinal viscera relationship with asthma, “self-proposed add flavor asthma-reliving decoction” treatment asthma patients, curative effect is obvious, specific as follows.

In the theory of traditional Chinese medicine, the treatment of wheezing should be done by clearing heat and reducing phlegm, reducing qi and relieving asthma. Therefore, the asthma soup in the “ Wonderful Square of Photography ” is selected to refine, and “self-proposed add flavor

asthma-relieving decoction” should be used to treat this syndrome. Modern pharmacological studies have found that the ingredients contained in ephedra have the effect of removing phlegm and relieving asthma, and relaxing the airway and smooth muscle, namely. Mulberry pisin component, has the effect of inhibiting asthma attack, its extract can dissolve phlegm and cough. Rhubarb has the anti-allergy, anti-inflammatory effect, but also can relax the airway smooth muscle, play the role of relieving asthma. Modern medical research believes that fixed asthma soup can significantly promote the excretion of allergic substances in the airway and reduce the local inflammatory reaction. Cui Ze Zhen, et al. found that fixed asthma soup can reduce the release of proinflammatory factors in bronchial asthma, and then reduce the airway inflammation.

The change process, diagnosis, treatment and prevention of diseases all need to master the pathogenesis. “Rush, all belong to fire” is not only the high summary of the disease pathogenesis, but also the embodiment of traditional Chinese medicine must seek the disease. In "rush, all belong to the fire" theory support, combined with bronchial asthma cannot be cured, lingering characteristics, seriously affect the quality of life and health, so the author will theory of the TCM literature as the basis, combined with pathology, modern medicine, physiology and other related knowledge practice and summary, Chinese medicine and western medicine inflammation, with dialectical thought dispel lung, stomach, bowel fire to treat heat, this method both follow the thought of traditional Chinese medicine asthma, and broaden the clinical thinking, hope you scholars continue to study, hand in hand to promote medical progress, try our best to reduce pain.

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Study on the critical quality chemical attributes of *Polygala tenuifolia*

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Abstract

Keywords

Polygala tenuifolia, Critical quality chemical attributes

Objective

Through the research, the critical quality chemical attributes of *Polygala tenuifolia* were determined, which laid a foundation for improving the quality control standard of *Polygala tenuifolia* by combining qualitative and quantitative methods.

Methods

① Establishment of fingerprint of *Polygala tenuifolia*: Based on the optimization of preparation methods, chromatographic conditions, and methodological investigation, 15 batches of *Polygala tenuifolia* samples from three producing areas were analyzed by the HPLC method. The similarity evaluation was carried out by using "Similarity evaluation system software of Chinese medicine chromatographic Fingerprint" to establish the HPLC fingerprint of *Polygala tenuifolia*. On this basis, the relevant components in 15 batches of *Polygala tenuifolia* were identified. ② Determination as chemical components in *Polygala tenuifolia*: The contents of sibiricose A5, sibiricose A6, polygalaxanthone III, 3, 6'-disinapoyl sucrose, tenuifoliside A, tenuifoliside C, and polygala tenuifolia saponin B in 15 batches of *Polygala tenuifolia* from three producing areas were determined by HPLC.

Results

① HPLC fingerprint of *Polygala tenuifolia*: The common pattern contains 28 common peaks. There were differences in non-common peaks between Xintai of Shandong province and Wenxi of Shanxi Province (4 more peaks appeared in Xintai of Shandong province than in Yulin of Shaanxi Province when the retention time is about 8min, 9min, 32min, and 46min, respectively). There are 3 more peaks in *Polygala* from Wenxi of Shanxi Province than from Yulin of Shaanxi Province, which appear when the retention time is about 8min, 9min, and 36min, respectively. ② After identification, in the HPLC fingerprint of *Polygala tenuifolia*, Peak 1 is Sibiricose A5, Peak 2 is Sibiricose A6, Peak 4 is Polygalaxanthone III, Peak 7 is 3',6'-Disinapoylsucrose, Peak 10 is Tenuifolin A, Peak 12 is Tenuifoliside C and Peak 27 is onjisaponin B. ③ There are differences among the seven identified components: the Sibiricose A6 content of *Polygala* in Yulin, Shaanxi is about twice that in Xintai, Shandong, and Wenxi, Shanxi; the content of *Polygala* Tenuifolin A in Yulin, Shaanxi is about 4 times that in Xintai, Shandong and about 2 times that in Wenxi, Shanxi. Determination of content limits of seven main chemical components in *Polygala tenuifolia*: the content limit of Sibiricose

A5 is $3.60 \pm 1.27 \text{ mg} \cdot \text{g}^{-1}$, the content limit of Sibiricose A6 is $2.15 \pm 0.95 \text{ mg} \cdot \text{g}^{-1}$, the content limit of Polygalaxanthone III is $3.05 \pm 0.91 \text{ mg} \cdot \text{g}^{-1}$, the content limit of 3',6-Disinapoylsucrose is $7.92 \pm 1.12 \text{ mg} \cdot \text{g}^{-1}$, the content limit of Tenuifolin A is $4.18 \pm 2.09 \text{ mg} \cdot \text{g}^{-1}$, the content limit of Tenuifoliside C is $1.44 \pm 0.19 \text{ mg} \cdot \text{g}^{-1}$, the content limit of onjisaponin B is $14.34 \pm 1.91 \text{ mg} \cdot \text{g}^{-1}$.

Conclusion

The critical quality chemical properties of *Polygala tenuifolia* could be characterized by HPLC fingerprint, 7 confirmed chemical components, and their content detection limits.

Behavioral impairments comparison of sleep-deprived rats by modified multiple platform, treadmill and para-chlorophenylalanine

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Keywords

Sleep deprivation, Anxiety, Depressed, Learning and memory

Background

Modified multiple platform, treadmill, and para-chlorophenylalanine (PCPA) are the most common method of sleep deprivation (SD), which are used widely to evaluate treatment effect of medicine for insomnia. Despite daytime functional deficits being the main symptoms of insomnia, these deficits are poorly characterized in SD animals. This study aimed to identify behavioral impairments associated with SD methods, and to investigate relationships between these impairments and the neuro-endocrine-immune system.

Methods

Sprague-Dawley rats were randomly divided into three groups: modified multiple platform (MMP), treadmill and PCPA, with model and control in the three groups. Model rats experienced SD for three consecutive days induced by MMP, treadmill and PCPA, respectively. The anxiety- and depression-like behaviors, fatigue, learning and memory, and heart rate variability were investigated. Furthermore, neuro-endocrine-immune-related indicators in the hypothalamus and serum were measured.

Results

Three SD Model rats exhibited all daytime function impairment, such as increased anxiety- and depression-like behaviors, decreased learning and memory function, increased fatigue behavior, elevated heart rate variability. Treadmill and PCPA displayed a similar overall degree of daytime impairment. However, Treadmill SD had correlations with more severe depression-related behaviors and learning and memory impairment, and PCPA SD was associated with higher anxiety-related behaviors and fatigue behaviors. In contrast, MMP led to less impairment but a relatively increased heart rate variability. In all three SD models, hypothalamic norepinephrine (NE) levels were elevated, and 5-HT, glutamate and γ -aminobutyric acid (GABA) contents were decreased. Serum levels of IL-1, IL-2 and melatonin were reduced, but TNF- α and corticosterone were increased. The ability involved in the homeostatic regulation of sleep was diminished and sleep-wake rhythms were disordered.

Conclusion

Increased depression-related behaviors and learning memory impairment induced by treadmill may be related to increased NE levels and decreased GABA levels. Higher anxiety-related behaviors and fatigue behaviors caused by PCPA may be related to immune stress.

A new sesquiterpene from the *Viscum coloratum* (Komar.) Nakai

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Abstract

A new sesquiterpene, named viscolterpene A (**1**), together with ten known compounds (**2-11**), were isolated from the root of *Viscum coloratum* (Komar.) Nakai. Their structures were elucidated by extensive analysis of 1 D and 2 D NMR spectra and from the HR-ESI-MS.

Keywords

Viscum coloratum (Komar.) Nakai, chemical composition, sesquiterpene

The dry leaves, stems, and branches of *Viscum coloratum* (Komar.) Nakai, which are called *V. coloratum* in Chinese, are widely used in traditional Chinese medicine for the treatment of rheumatism, neuralgia, hypertension, and hemorrhage^[1]. Phytochemical investigation of *V. coloratum* also showed the presence of many other types of compounds including flavonoids, triterpenoids, lignans, diarylheptanoids, and so on^[2]. Similarly, the whole-plant extract from *V. album* has been used in adjuvant cancer therapy in Europe. However, the current research on the pharmacological effects of the *V. coloratum* is still relatively simple, especially in chemical composition.

Objective

To screen for biologically-active natural products as well as make full use of the abundant medicinal plant resources in the *V. coloratum*, we investigated the chemical constituents of the *V. coloratum* to afford a new sesquiterpene.

Materials and methods

The dry leaves, stems, and branches of *V. coloratum* were extracted three times with 95% ethanol under reflux (3 h), and then the solvent was removed under reduced pressure to give a crude extract. The aqueous layer was chromatographed over a macroporous resin AB-8 column eluted with H₂O, 45% EtOH, and then 95% EtOH. The 95% EtOH fraction was used in silica gel, ODS, and preparation solution to separate compounds **1-11**.

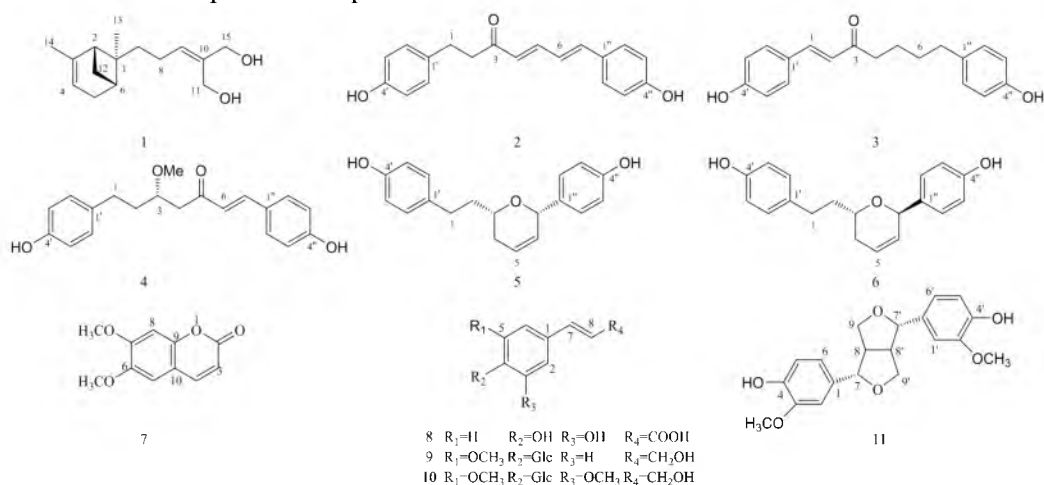


Fig.1 Chemical structures of compounds 1–11.

Results and discussion

Compound **1** was isolated as a light yellow oil. This compound's molecular formula was indicated to be C₁₅H₂₄O₂ by its positive HR-ESI-MS with m/z 237.1852 [M+H]⁺ (calculated to be 237.1854). ¹H-NMR (Table 1) of **1** shows two methyl groups [δ_{H} : 0.83 (3H, s, H-13) and 1.61 (3H, s, H-14)], two olefin protons [δ_{H} : 5.20 (1H, m, H-4) and 5.92 (1H, t, $J=7.3$, H-9)] and two methylene signals [δ_{H} : 4.73(2H, s, H-11) and 4.72(2H, s, H-15)]; In conjunction with the DEPT and HSQC spectrum, the ¹³C-NMR data of **1** indicated the presence of two pair of olefinic carbons [δ_{C} :144.43(C-3), 116.86(C-4) and 140.69(C-9), 127.72(C-10)], two methylene carbons with hydroxyl groups [δ_{C} :65.41(C-11) and 58.37(C-15)], four methylene carbons [δ_{C} : 31.38(C-5), 39.09 (C-7), 23.46(C-8) and 31.75(C-12)], two methyl carbons [δ_{C} : 17.50(C-13) and 23.03(C-14)], Two methylene [δ_{C} : 45.53(C-2) and 39.14(C-6)] and one quaternary carbon [δ_{C} : 41.30(C-1)]. By comparing the carbon data with the literature, it is similar to the carbon skeleton of α -trans-bergamotene^[3], and the difference is that the carbon data of C-11 and C-15 change. Through further literature comparison, it was found that the C-11 and C-15 positions may be changed from methyl to methylene with hydroxyl. To test this conjecture, a series of HMBC correlations from H₂-11 to C-9/C-10/C-15 proved and from H₂-15 to C-9/C-10 proved that C-10 was connected with two methylene with hydroxyl (Fig. 2). In the NOESY spectrum (Fig. 2), the correlation peaks of H₃-13/H-2/H-6 showed that H-2, H-6, and H₃-13 have uniform orientation in space, which are α -orientations. Finally, the structure of **1** was established as α -trans-bergamotene diol, named viscolterpene A.

The Ten known compounds were identified as 1,7-bis (4-hydroxyphenyl) heptane-4e, 6e-diene-3-one (**2**), (E)-1,7-bis(4- hydroxyphenyl)hept-1-en-3-one (**3**), (3S)-3-methoxy-1,7-bis(4-hydroxyphenyl)-6e-hepten-5-one (**4**), 5,6-dehydro-4"-de-O-methylcentrolobin (**5**), (3S,7R)-5,6-dehydro-1,7-bis(4-hydroxyphenyl)-4"-de-O-methylcentrolobine (**6**), scoparone (**7**), caffeic acid (**8**), coniferin (**9**), syringin (**10**), pinoresinol (**11**) (Fig. 1). Additional, compounds **3-7** and **11** were isolated from *V. coloratum* for the first time.

In a word, phytochemical investigation of the leaves, stems, and branches of *V. coloratum* led to the isolation of a new sesquiterpene [viscolterpene A (**1**)], together with five known diarylheptanoids (**2-6**) and five known Phenylpropanoids (**7-11**).

Acknowledgments

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Analysis of lignans and triterpenoids in different parts of *Schisandra chinensis*

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Abstract

There are two very representative components-dibenzocyclooctene lignans and nortriterpenoids in *Schisandra chinensis*. In this study, dibenzocyclooctene lignans and nortriterpenoids in different parts of *Schisandra chinensis* were analyzed. UPLC-Q-TOF-MS and UNIFI informatics platform were used to qualitatively and quantitatively analyze the dibenzocyclooctene lignans in fruit, fruit stalk, leaf, vine, and root of *Schisandra chinensis*. Then, the differences between different parts of *Schisandra chinensis* were analyzed by multivariate statistical analysis. In addition, an analytical method by Orbitrap Fusion Lumos system suitable for microscale nortriterpenoids in *Schisandra chinensis* is provided.

Key words

Schisandra chinensis; enrichment; UPLC-MS/MS; dibenzocyclooctene lignans; nortriterpenoids
Schisandra chinensis (Turczaninowia) Baillon, is a medicinal plant (of the Schisandraceae family), known for its ethnomedicinal applications^[1]. Widely distributed in China, plants of the *Schisandra* genus are extensively used in traditional Chinese medicine^[2]. The dibenzocyclooctene lignans (DL) and nortriterpenoids (NT) are the characteristic components in *S. chinensis*^[3]. In this experiment, DL in different parts of *S. chinensis* was analyzed, and the differences and content changes of DL in different parts were clarified. In addition, our laboratory found a suitable method for the analysis of NT in *S. chinensis*.

Objective

To explore the effects of different parts on the distribution and content of DL in *S. chinensis*. To provide an analytical method for minor NT in *S. chinensis*.

Materials and methods

DL analysis methods: Waters ACQUITY UPLC I-class system (Waters, USA) equipped with a binary solvent delivery system was used and the chromatographic separation was executed on an ACQUITY CSH C₁₈ (2.1 mm×100 mm, 1.7 μm) column. Mass spectra were recorded by a Xevo G2 SI Q-TOF (Waters, USA) mass spectrometer. The mass spectrometer with electrospray ionization (ESI) was used for the MS analysis in the positive mode.

NT analysis methods: Vanquish UHPLC system (Thermo Scientific, US) equipped by ACQUITY UPLC[®] HSS T3 (2.1 mm ×100 mm, 1.8 μm) column. Mass spectra were recorded by the Orbitrap Fusion Lumos system (Thermo Scientific, US) with heated electrospray ionization (HESI) as used for the MS analysis in the negative mode.

Results and discussion

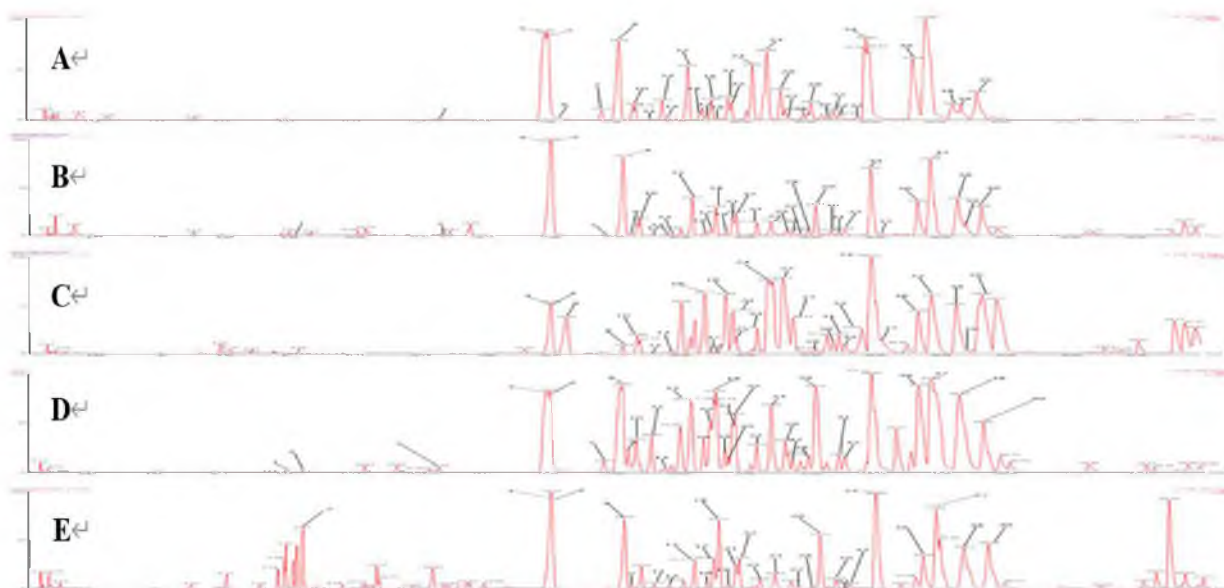


Fig. 1: Chemical profiles of *S. chinensis*, ion chromatogram of lignans.
(A: fruits; B: fruit stalks; C: roots; D: rattan stems; E: leaves)

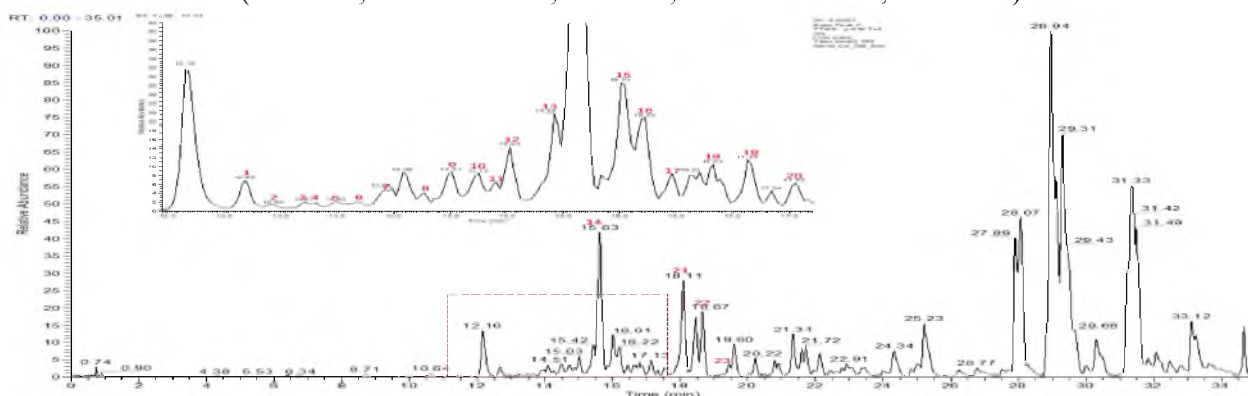


Fig. 2: Typical total ion current (BPI) chromatograms of substances in the *S. chinensis* extract, under negative ion mode.

By comparing with the database (Self built databases and Waters Traditional Medicine Library), references, and standards and analyzing by the UNIFI informatics platform, a total of 40 DL were preliminarily identified from the five parts of *S. chinensis*. Among them, 32 were identified from fruits (Fig. 1A), 35 from fruit stalks (Fig. 1B), 28 from roots (Fig. 1C), 31 from rattan stems (Fig. 1D), and 24 from leaves (Fig. 1E).

The DL characteristic peaks of different parts of *S. chinensis* were extracted and imported into SIMCA-P 13.0 software for multivariate statistical analysis. The results of HCA and PCA showed that the fruits and rattan stems of *S. chinensis* gathered into one class, the fruit stalks and leaves of *S. chinensis* gathered into one class, and the roots were significantly different from other parts. Further PLS-DA analysis showed that the components that produced significant differences in different parts (VIP>1.2) of *S. chinensis* were Schisandrastemoside A (peak 2), (+)-1-hydroxy pinoresinol-1-O- β -D-glucoside (peak 1), Benzoylgomisin Q (peak 17), Gomisin H (peak 25), Schisantherin D (peak 13), and Tigloygomisin H (peak 23) respectively.

The DL in different parts of *S. chinensis* were determined and analyzed by UPLC-Q-TOF-MS^E method and positive ion collection. The results showed that the content of lignans in different parts

of *S. chinensis*: rattan stems (26.7876 mg/g) > roots (17.6672 mg/g) > fruits (16.8269 mg/g) > leaves (4.4147 mg/g) > fruit stalks (2.7807 mg/g).

Through previous experiments, it was found that after ultrasonic extraction of the sample powders in different parts of *S. chinensis* in 80% methanol, 50%-95% of the components were enriched with SP850 macroporous adsorption resin as analytical samples, and then rich NT peaks could be obtained by using the mass spectrometry conditions in "**Materials and methods**". At present, 23 NT peaks have been identified from *S. chinensis* (Fig. 2), and found some characteristic precursor ions: 543.2197 [M-H]⁻, 589.2247 [M+HCOO]⁻, 559.2169 [M-H]⁻, 605.22 [M+HCOO]⁻, 527.2248 [M-H]⁻, 573.2297 [M+HCOO]⁻, 595.1940 [M+HCOO]⁻ and some characteristic fragment ions: 18 Da [M-H₂O], 28 Da [M-CO], 44 Da [M-CO₂], 60 Da [M-CH₂C(OH)₂], 62 Da [M-H₂O-CO₂], 74 Da [M-CH₃CH=C(OH)₂], etc. However, due to the lack of standards, the identification results need further research and supplement.

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Isolation and identification compounds from *Rhodiola crenulata*

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Abstract

To study the chemical constituents from the dried roots of *Rhodiola crenulata*. The compounds were separated and purified by solvent extraction, silica gel column chromatography, ODS column chromatography, and preparative HPLC. The structures of the isolated compounds were identified by NMR, HR-MS, and references. Nine compounds were isolated from *Rhodiola crenulata*. Among them, compound **1** was a new fatty acid, named mollisinol C.

Key words

Rhodiola crenulata, chemical constituents, new fatty acid.

Rhodiola crenulata (Hook. f. et Thoms) H. Ohba, as an important member of the Crassulaceae family, is mainly distributed in the high cold region of Yunnan and Sichuan province as well as the Tibetan Autonomous Region^[1]. As a functional food, *Rhodiola crenulata* is used for prevention against high-altitude illness and regarded by the tourists going to plateau as a traditional phyto-adaptogen to environmental challenges^[2]. Moreover, the extracts of *Rhodiola crenulata* have been made into pharmaceutical preparations and cosmetics with varied bioactivities. Modern pharmacological studies have demonstrated that the genus *Rhodiola crenulata* possessed the functions of reinforcing immunity^[3], antioxidant, immunomodulatory, anti-aging, anti-fatigue, neuroprotective, anti-inflammatory, antidepressive, anxiolytic, nootropic, life-span increasing and central nervous system (CNS) stimulating activities. Due to the diverse biological activities of *Rhodiola crenulata*, the chemical constituents of *Rhodiola crenulata* of the isolates were investigated by our research group.

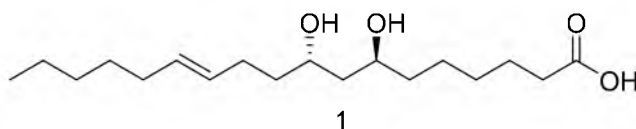
Objective

To isolate and identify the naphthoquinone constituents of dried roots of *Rhodiola crenulata*, and to provide a material basis for the subsequent research on its anti hypoxia activity and mechanism.

Materials and methods

NMR spectra were measured by a Bruker DPX-600 Superconducting NMR Spectrometer (Germany). Preparative HPLC was conducted on a Shimadzu CBM-20A (Japan). An AB SCIEX Triple TOF 5600 mass spectrometry (USA) was used to record HR-ESI-MS data. Column chromatography was carried out using silica gel (200-300 mesh, Qingdao, China), ODS (50 μm , Germany). The plant material was gathered from Heilongjiang Province, China. Prof. Rui-Feng Fan identified the plant as the rhizomes of *Rhodiola crenulata*.

Results and discussion



1

Compound **1** was obtained as a colourless oil. The molecular formula $\text{C}_{18}\text{H}_{34}\text{O}_4$ was established by HR-ESI-MS (m/z 337.2437 $[\text{M} + \text{Na}]^+$; calcd 314.2457). $^1\text{H-NMR}$ shows a Methyl signal at δ 0.91

(3H, t, $J=6.9$), two hydroxylated methines at δ 3.50 (1H, brd, $J=5.0$), 3.49 (1H, brd, $J=4.4$), and two olefinic H-atoms at δ 5.44 (1H, m), 5.50 (1H, m). The two degrees of unsaturation were due to the COOH and C=C moieties. The ^1H and ^{13}C NMR spectra of **1** closely resembled those of Mollisinol B^[5], except that the chemical shift of C-10 moved to the high field region. Combined with HR-ESI-MS analysis, it was speculated that the phenylamino of C-10 was not replaced by a hydroxyl group. The same hydrogen coupling constants at positions 7, 9 and 8 are 5.0 and 4.4 respectively. According to Karplus formula^[4], the dihedral angles are 127° and 57° respectively. It was determined that one of the hydroxyl configurations at positions 7 and 9 was R and the other is S. According to the reference 5, position 7 is S and position 9 was R. Therefore, compound **1** was determined to be (7S*,9R*,E)-7,9-dihydroxy octadecyl-12-enoic acid, named mollisinol C.

In addition, eight known compounds were identified as tyrosol, Salidroside, P-coumaric acid, (E)-creoside I, crenulatin, Caffeic acid, 7-hydroxy-6-methyl-hepta-5-en-2-one, Xylogranatinin.

In a word, one new fatty acid (**1**) and eight known compounds (**2-9**) were isolated and identified from the *Rhodiola crenulata*.

Funding

This work was financially supported by key Research and Development Projects of Heilongjiang Province [GA21D008] and heilongjiang Touyan Innovation Team Program.

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Triterpenoids isolated from the fruit of *Acanthpanax senticosus* (Rupr. & maxim.) Harms

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Abstract

A phytochemical investigation on the 70% EtOH extract of the fruit of *Acanthpanax senticosus* resulted in the isolation of two new triterpenoids, 3,4-seco-olean-12-en-4,23-diol-3,28-dioic acid (**1**) and hederagenin-3-O- β -D-glucuronopyranoside 6'-O-buthyl ester (**2**), together with six known ones (**3-8**). Structural elucidation of all the compounds were performed by spectral methods such as 1D or 2D (^1H - ^1H COSY, HSQC, and HMBC) NMR spectroscopy, in addition to high resolution mass spectrometry. Compounds **3**, **5**, **6**, **7** and **8** were first isolated from *A. senticosus* and compound **4** was isolated for the first time from Araliaceae.

Keywords

Acanthpanax senticosus, Araliaceae, triterpenoids, isolation

Acanthpanax senticosus, previously classified as *Eleutherococcus senticosus*, also called "Siberian ginseng" or "Ciwujia". After consulting the literatures, the roots, rhizomes, stems, leaves, and fruit of *A. senticosus* have been found to be medicinal parts. Many chemical compounds in *A. senticosus* have been isolated, including triterpenoid saponins, flavonoids, lignans, and so on. saponins and flavonoids are also been found to be the main active ingredients of *A. senticosus* for the central nervous system, including improving sleep quality, anti-depression, and anti-Parkinson, but interestingly, triterpenoid saponins were also can be isolated from the fruit of *A. senticosus* and had moderate inhibitory effects on neuroinflammation. Based on the interest in triterpenoids with structural and bioactive diversity, we investigated the n-butanol layer of 70% ethanol extract of *A. senticosus* fruits.

Objective

To save the resources of *A. senticosus*, isolate and identify triterpenoids of dried fruit of *A. senticosus*, and provide a material basis for the subsequent research on its central nervous system.

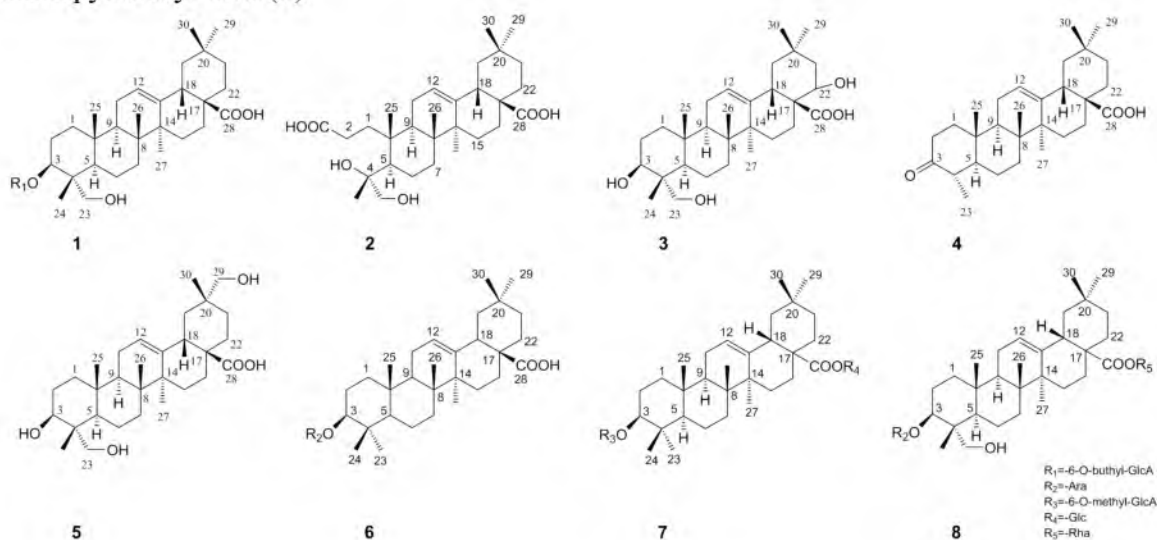
Results and discussion

Compound **1**: HR-ESI-MS at m/z 505.3520 $[\text{M}+\text{H}]^+$ (calcd for $\text{C}_{30}\text{H}_{50}\text{O}_6$, 505.3529). The ^1H -NMR and ^{13}C -NMR data of **1** were similar to those of 3,4-seco-olean-12-en-4-ol-3,28-dioic acid. The difference is that C-2 was replaced by a hydroxyl group, which was supported by the HMBC correlation of H-23/ C-4 and H-5/ C-23.

Compound **2**: HR-ESI-MS at m/z 705.4560 $[\text{M}+\text{H}]^+$ (calcd for $\text{C}_{40}\text{H}_{65}\text{O}_{10}$, 705.4578). One-dimensional NMR data of **2** resembled those of hederagenin-3-O- β -D-glucuronopyranoside 6'-O-methyl ester, and the major difference was the substituent C-23 is changed from methyl to n-butyl in compound **2**, which was supported by the ^1H - ^1H COSY correlation of H-1''/ H-2''/ H-3''/ H-4'', the DEPT 135 of C-1'', C-2'' and C-3'' are methylene groups, and the HMBC correlation of H-1''/ C-6'.

The structures of known compounds **3-8** were determined as Kalopanax-geninL1 (**3**), hederagonic acid (**4**), 29-hydroxyhederagenin (**5**), 3-O- α -L-arabinopyranosy-oleanolic acid(**6**),

chikusetsusaponin IVa methyl ester(7), 3-O- α -L-arabinopyranosyl hederagenin 28-O- α -L-rhamnopyranosyl ester(8).



Funding

This work was financially supported by Heilongjiang Touyan Innovation Team Program.

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Cytotoxic sesquiterpenoids from *Atractylodes chinensis* (DC.) Koidz.

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ABSTRACT

Two new sesquiterpenoids named atrchiterpene A-B (**1-2**), a new natural product (**3**) and ten known compounds (**4-13**) were isolated from *Atractylodes chinensis* (DC.) Koidz. Compound **1** was a rare N-containing eudesmane-type sesquiterpenoid. The spectroscopic techniques performed structure elucidation, including 1D, 2D NMR spectra and HRESIMS. All compounds were evaluated for their cytotoxic activity against HepG2 cancer cell line. Compound **13** showed a significant inhibitory effect on HepG2 cells with an IC₅₀ value of 5.81 ± 0.47.

Keywords

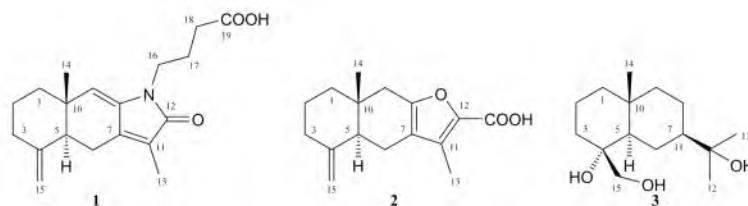
Atractylodes chinensis; sesquiterpenoids; cytotoxicity

Atractylodes chinensis (DC.) Koidz. is a perennial herb of *Atractylodes*, a natural medicinal material in northeast China. *A. chinensis* is rich in sesquiterpenes and polyethylenes, and so on. After consulting the literature, sesquiterpenoids have been found to show widespread biological activities, such as cytotoxicity, anti-inflammatory and so on. Based on the interest in sesquiterpenoids with structural and bioactive diversity, we separated the chemical components of the 70% ethanol extract of *A. chinensis*. Two new sesquiterpenes (**1-2**), a new natural product (**3**) and ten known compounds (**4-13**) were obtained and identified in this study. And all compounds were evaluated for their cytotoxic activity against HepG2 cancer cell line.

Objective

In order to isolate and identify sesquiterpenes from the rhizomes of *A. chinensis*, and provide material basis for further study.

Results and discussion



Compound **1** was isolated as a yellow amorphous solid, which was shown to have a molecular formula of C₁₉H₂₅NO₃, as deduced from positive HR-ESI-MS at m/z 316.1890 [M+H]⁺ (calcd for C₁₉H₂₆NO₃, 316.1907). Briefly, compound **1** verified the carbon skeleton similar to cespilactam A^[1]. The variation between them was that **1** had no hydroxyl group at position 17, and was linked to -CH₂-COOH. The NOESY correlations of H-1 β with Me-14 and H-1 α with H-5 identified Me-14 as the β conformation and H-5 as the α conformation. Finally, compound **1** was named atrchiterpene A.

Compound **2** was extracted as a yellow amorphous solid. The molecular formula was determined by [M+K]⁺ ion at m/z 299.1035 in HR-ESI-MS data as C₁₆H₂₀O₃ (calcd for C₁₆H₂₀O₃K, 299.1044). And the structure of compound **2** was similar to that of compound **4** in the literature^[2], except that the C atom at the 4 and 15 positions became a group of olefinic carbons, and the H-12 was replaced

by carboxyl. The NOESY correlations of H-1 β with Me-14 and H-1 α with H-5 identified Me-14 as the β conformation and H-5 as the α conformation. The CD spectrum of compound **2** was highly similar to that of kalshinoid A [3]. So the absolute configuration of **2** was determined as 5S, 10S. Finally, compound **2** was named atrchiterpene B.

Compound **3** was obtained as a yellow amorphous solid, shown to have a molecular formula of C₁₅H₂₈O₃, as deduced from positive HR-ESI-MS at m/z 274.2383 [M+NH₄]⁺ (calcd for C₁₅H₃₂NO₃, 274.2377). And the structure of compound **3** was consistent with that of eudesma-4 α ,11,15-triol [4], but it had been isolated from plants for the first time.

In addition, ten known sesquiterpenes (1 β ,4 α ,6 β)-gorgonane-1 β ,4 α ,11-triol (**4**), 4(15)-eudesmene-1 β ,7,11-triol (**5**), 3-eudesmene-1 β ,7,11-triol (**6**), (4 α ,7 β ,9 α)-farfugane-4,9,11-triol (**7**), (4 α ,7 α ,9 α)-farfugane-4,9,11-triol (**8**), atractylenolid III (**9**), 8 β -methoxyatra ctylenolide (**10**), 8 β ,9 α -dihydroyeudesman-4(15),7(11)-dien-8 α ,12-olide (**11**), atractylenolide I (**12**), hinesolone (**13**) were identified.

Funding

This work was financially supported by the Key Research and Development Projects of Heilongjiang Province [GA21D008], Heilongjiang Touyan Innovation Team Program.

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New dibenzocyclooctadiene lignans from leaves of *Schisandra chinensis*

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Abstract

Three new dibenzocyclooctadiene lignans, schinlignan H (**1**), schinlignan I (**2**) and schinlignan J (**3**), together with eleven known dibenzocyclooctadiene lignans (**4–14**) were isolated from the leaves of *Schisandra chinensis*. Their structures were elucidated by comprehensive analysis of spectroscopic data (MS, IR and NMR). The absolute configurations of the biphenyl ring in new compounds (**1–3**) were discerned by circular dichroism (CD) spectroscopy.

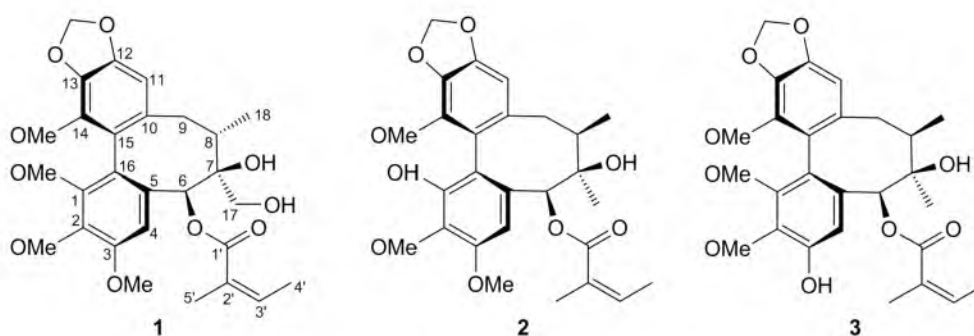
Keywords

Dibenzocyclooctadiene lignans; Leaves of *Schisandra chinensis*; Circular dichroism

Introduction

Schisandra chinensis (Turcz.) Baill. (*S. chinensis*), a climbing plant of Schisandraceae, was distributed in northeast China, Japan and Korea, and it has been widely used against hepatitis, diabetes, diarrhea and insomnia. *S. chinensis* has been extensively studied because of its high medicinal and health functions. In this study, eleven known dibenzocyclooctadiene lignans along with three new ones, schinlignans H–J (**1–3**), were isolated from the leaves of *S. chinensis* by different chromatographic methods.

Results and discussion



The structures of three new dibenzocyclooctadiene lignans (**1–3**).

Schinlignan H (**1**) is a white amorphous powder. The molecular formula of $C_{28}H_{34}O_{10}$ was determined by positive high-resolution electrospray ionisation mass spectrometry (HR-ESI-MS) (m/z 548.2490 [$M+NH_4$] $^+$, calcd for $C_{28}H_{38}NO_{10}$, 548.2490). And the 1D NMR spectra indicated that compound **1** highly resembled schisanwilsonin A except for the substituent at C-7, which was replaced by a hydroxymethyl group. It was verified by one methylene signal at H₂-17 (δ_H 3.25 and 3.74) in the ¹H-NMR spectrum, and the chemical shift of C-17 was shifted to the low field by 47ppm, as well as the observed HMBC correlation of H₂-17/C-6, H₂-17/C-7 and H₂-17/C-8, and the absent HMBC correlation of methyl with C-7. According to the molecular formula, the quaternary carbon at C-7 was substituted by a hydroxyl and a hydroxymethyl group. The absolute configuration of the biphenyl ring in a dibenzocyclooctadiene lignan can be discerned on the basis of their characteristic CD spectra, which is dominated by axial chirality of the restricted bond rotation of biphenyl ring. The CD spectra of *S*-biphenyl-configured lignan show a positive Cotton

effect around 220 nm, and a negative Cotton effect at 250 nm. Conversely, the lignans having *R*-biphenyl configuration show a negative Cotton effect at 220 nm, and a positive Cotton effect at 250 nm. In our study, the CD curve gave a strong negative Cotton effect at around 250-285 nm, which suggested that **1** possessed a *S*-biphenyl configuration. The NOESY correlations of H-4/H-6, H-6/H₂-17, H₂-17/H₃-18 and H-8/H-11 indicated a 'twist-boat-chair' (TBC) conformation for the cyclooctane ring, and H-6, H₂-17 and H₃-18 were in α -orientation, while OH-7 was in β -orientation. Finally, the structure of schinlignan H (**1**) was determined.

Schinlignan I (**2**) was obtained as a white powder, analyzed as C₂₇H₃₂O₉ by means of HRESIMS (m/z 518.2387 [M+NH₄]⁺, calcd for 518.2385). The comparison of **2** the NMR with those of schisanwilsonin A demonstrated quite similarities except that the methoxy group of C-1 in schisanwilsonin A was replaced by a hydroxyl group in **2**. This structural difference was confirmed by the HMBC correlations from H-4 (δ_H 6.60) to C-1 (δ_C 149.1), and the absent HMBC correlation of methoxy with C-1. Thus, the planar structure of **2** was elucidated. The CD spectrum of **2** displayed a negative Cotton effect at around 250-285 nm, indicating that **2** owns an *S*-biphenyl configuration. The observed NOESY correlations of H-4 with H-6, H-6 with H₃-17, H₃-17 with H-8 and H-8 with H-11 indicated that H-6, H₃-17 and H-8 were in α -orientation, while OH-7 and H₃-18 were in β -orientation. Consequently, the structure of schinlignan I (**2**) was identified.

Schinlignan J (**3**), a white powder, had the same molecular formula as **2** according to HR-ESI-MS (m/z 518.2387 [M+NH₄]⁺, calcd for 518.2385). Comparison of the ¹H and ¹³C NMR spectral data of **3** with those of **2** suggested that the structure of **3** was quite similar to **2**. The only difference was the position of the hydroxyl group, which was located at C-3 in **3** instead of C-1 in **2**. It was confirmed by the chemical shifts of the three methoxy groups above 56 ppm, as well as the observed HMBC correlation of the proton signal at δ_H 7.52 (H-4) with C-3 (δ_C 150.4) and the absent HMBC correlation of methoxy with C-3. Further spectrum analysis indicated that other substituents and the absolute configuration were identical to those of **2**.

Eleven previously reported compounds (**4-14**) were identified as schisantherin D (**4**), deoxyschizandrin (**5**), tigloylgomisin P (**6**), gomisin A (**7**), gomisin J (**8**), gomisin N (**9**), wuweizisu C (**10**), schinegllignan A (**11**), kadsuphilin B (**12**), gomisin G (**13**), sieverlignan C (**14**), respectively, by comparison their spectral data with those in the reported literatures.

Funding

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and structure determination of five new lignans, gomisin A, B, C, F and G, and the absolute structure of schizandrin[J]. *Chemical and Pharmaceutical Bulletin*, 1979, 27(6): 1383-1394.

Study on the Mechanism of Schisandra chinensis and Evodia rutaecarpa in Improving A β ₁₋₄₂ Induced Cognitive Impairment in Alzheimer's Disease Rats

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Abstract

Schisandra chinensis and Evodia rutaecarpa are both traditional herbal medicines widely used as supplements in China for many years. In our previous work, we have demonstrated that *Schisandra chinensis* - *Evodia rutaecarpa* (S-E) has a stronger ameliorative effect on cognitive impairment in Alzheimer's disease (AD) rats compared to single agent. The aim of this study was to investigate the effects of different ratios of Schisandra chinensis - Evodia rutaecarpa on learning and memory and cognitive impairment in AD rats and its possible mechanism. First, Morris' s water maze test showed that different proportion of Schisandra chinensis and Evodia rutaecarpa could improve the learning and memory ability and spatial exploration ability of A β 1-42-induced AD model in rats. Schisandra chinensis and Evodia rutaecarpa were then observed to have different intensities of action when acting on different pathways by western blot (WB) and reverse transcription-polymerase chain reaction (Rt-pcr). The results showed that when Schisandra chinensis content was dominant, the therapeutic effect of the drug pair focused on up-regulating BDNF/TrkB/CREB pathway activity and thus inhibiting A β aggregation, while when Evodia rutaecarpa was used as the main component, the therapeutic effect of the drug pair focused on down-regulating GSK-3 β /TAU pathway activity to prevent tau hyperphosphorylation. In conclusion, this study found that *Schisandra chinensis* - *Evodia rutaecarpa* may have different mechanisms of action on its two components during the treatment of AD and found the optimal ratio of the drug to treat AD, providing strong support and reference for the clinical application of *Schisandra chinensis* - *Evodia rutaecarpa*.

Keywords

Alzheimer's disease; *Schisandra chinensis*; *Evodia rutaecarpa*; Morris water maze; Learning and memory impairment;

Alzheimer's disease (AD) is the most common cause of dementia and is associated with aging and cognitive impairment. By the middle of this century, the number of Alzheimer's patients in the United States is expected to grow to 13.8 million. In 2019, over 16 million family members and other unpaid caregivers provided approximately 18.6 billion hours of care for people with Alzheimer's or other dementia. Total expenditures for health care, long-term care, and hospice services for people aged 65 years and older with dementia were estimated at \$305 billion in 2020. The above facts indicate that the treatment of Alzheimer's disease is urgent.

Schisandra chinensis, the dried and ripe fruit of Schisandra chinensis (Turcz.) Baill, a member of the Magnoliaceae family, has been found to act on the nervous system and enhance cognitive function by affecting BDNF/TrkB/CREB pathway activity and protecting against diseases mediated by various neuronal injuries[2]. Evodia rutaecarpa is the dried near-ripe fruit of Evodia ruticarpa (A.s.) Hook.f.& Thomson, a member of the Rutaceae family, and evodiamine in Evodia rutaecarpa

is able to downregulate GSK-3 β levels to exert anti-inflammatory and anti-oxidative stress effects, berberine is able to reduce the pathological damage of AD by inhibiting the hyperphosphorylation of tau protein[3] , therefore, in the current work, we investigated the effects of different ratios of Schisandra ruti-carpa drugs on cognitive impairment in A β 1-42-induced AD model rats and deeply analyzed the potential mechanisms of producing this effect.

Objective

To explore the effect of different proportion of Schisandra chinensis and Evodia rutaecarpa on learning and memory ability in AD rats and its possible mechanism.

Materials and methods

Morris water maze test was used to investigate the effect of S-E on learning and memory ability in AD rats, Congo red and immunohistochemical tests were used to observe the effect of S-E on pathological markers of AD, and WB and RT-pcr were used to analyze the mechanism of S-E in the treatment of AD.

Results and discussion

In Morris' s water maze test, S-E administration not only reduced the latency of AD rats, but also increased the number of crossing the original platform in AD rats compared with the model group, indicating that S-E administration could improve the spatial memory impairment induced by A β ₁₋₄₂ in AD model rats. In order to exclude the effect of the exercise ability of rats on the experimental results, we measured the mean swimming speed of rats and showed that there was no significant difference in the exercise ability of rats in each group ($p > 0.05$, Figure 1c), indicating that the difference in the previous experimental results was not caused by the different exercise ability of rats in each group.

In order to investigate the effects of different ratios of S-E on A β deposition in the brains of AD rat models, we performed Congo red and immunohistochemical experiments, and the experimental results showed that (Figures 2a and b), A β ₁₋₄₂ injected model groups had increased A β deposition in the cortex, while each ratio of S-E treatment effectively reduced the number of senile plaques and the average plaque occupation area in rats, with S-E4:1 and S-E2:1 groups with *Schisandra chinensis* as the main component showing a stronger performance than S-E1:2 and S-E1:4 groups with *Evodia rutaecarpa* as the main component, which indicated that S-E could inhibit A β accumulation and deposition in the brains of AD rats and *Schisandra chinensis* played a major role in it. Next, we investigated the effect of different ratios of S-E administration on BDNF/TrkB/CREB signaling pathway in AD rat brain. The results of WB experiments showed (Figure 2 c) that each proportion of S-E up-regulated the expression of proteins involved in the BDNF/TrkB/CREB signaling pathway compared with the model group. The results of RT-pcr assay (Figure 2 d) showed that each ratio was able to increase the expression of BDNF, TrkB, and CREB mRNA compared with the model group, however, we found that the therapeutic effects of S-E4:1 and S-E1:2 were still different, which indicated that *Schisandra chinensis* played a major role in the up-regulation of BDNF/TrkB/CREB signaling pathway activity.

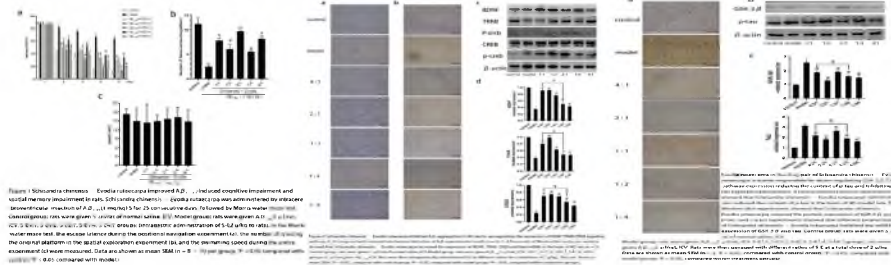
The results of immunohistochemical showed that the p-tau content in the brain of rats in the model group was significantly increased compared with that of rats in the control group, and the p-tau content was reduced after different ratios of S-E administration, and the S-E1:2 and S-E1:4 groups with *Evodia rutaecarpa* as the main component showed significantly stronger performance than the

S-E4:1 group, but there was little difference from the S-E2:1 group, which indicated that *Evodia rutaecarpa* played an important role in reducing the p-tau content by administration, while the special performance of the S-E2:1 group we speculated that it was due to other effects of *Evodia rutaecarpa*. Then we measured the content of GSK-3 β and p-tau protein and the expression of their related genes in rat brain by WB and RT-pcr experiments and found that each ratio of *S-E* significantly down-regulated GSK-3 β and p-tau protein and their related gene expression.

Table 1

RT-PCR

Forward primer: 5'-CTATACATAGGCTCTTCTTA-3'	Reverse primer: 5'-ATTGGTGGCTCTTGGATTGGA-3'
TauB	
Forward primer: 5'-TGGTGAACATTCAGGTTTCT-3'	Reverse primer: 5'-AGAGTATGCTGCTGCTGCTGCT-3'
CREB	
Forward primer: 5'-CTAAATATGAGTGGAGAGT-3'	Reverse primer: 5'-GAAAGTATGAGTGGAGAGT-3'
GSK-3β	
Forward primer: 5'-GGGCACCGAGCTGATCTTT-3'	Reverse primer: 5'-GCCAAAGACCTTCAGCA-3'
Actin	
Forward primer: 5'-CCAGGAGTCTTACCAAGGGAAGAC-3'	Reverse primer: 5'-TCTCTTCTTACGTTTAAACGATC-3'
GLAF1B	
Forward primer: 5'-AAGACCCCTTCATTCAC-3'	Reverse primer: 5'-TCCACGACCTACTACGCA-3'



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Mechanism of DangGui-KuShen herb pair on ischemia heart disease based on serum metabolomics in rats

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Abstract

To clarify the protective effect of Danggui (*Angelicae Sinensis Radix*, ASR)-Kushen (*Sophorae Flavescentis Radix*, SFR) herb pair on cardiac tissue and explore its mechanism in ischemic heart disease (IHD). Left anterior descending branch of coronary artery was used to establish the IHD model in rats, and explore the protective effect of ASR-SFR on heart was explored by the pathological tissue sections. Combined with UPLC-Q-TOF/MS technology, the untargeted metabolomics of rat serum samples was studied to obtain the biomarkers and metabolic pathways of IHD. Compared with the control group, the myocardial tissue of the model group was significantly abnormal. The results showed: compared with the control group, the myocardial tissue of the model group was significantly abnormal. It was found that 22 serum biomarkers were screened, and linoleic acid metabolism, arachidonic acid metabolism, glycerophospholipid metabolism, retinol metabolism, and sphingolipid metabolism may be related to IHD. In short, this research not only strongly supports and strengthens the current understanding of the synergistic effects of ASR and SFR in IHD, but also provided reference for the rational clinical application of ASR-SFR.

Keywords

Angelicae Sinensis Radix; *Sophorae Flavescentis Radix*; herb pair; metabolomics; biomarker; pathway analysis

Cardiovascular diseases (CVDs) have the characteristics of high morbidity and mortality. It is characterized by a sudden decrease in blood flow and oxygen supply to the heart, leading to cardiometabolic disorders, myocardial necrosis, arrhythmia, myocardial infarction, and sudden death^[1]. The molecular mechanism of myocardial ischemia is complex and involves the disorder of multiple metabolic pathways. Therefore, searching for effective drug targets and opening up new therapeutic approaches has become a research hotspot in ischemic heart disease^[2].

The research on herb pairs interaction has attracted Danggui (ASR), the dry root of *Angelica Sinensis* (Oliv.) Diels^[3]. It is considered to be good medicine for promoting blood circulation in East Asia and has been used historically to combat myocardial hypoxia damage, improve blood circulation, and enhance immunity^[4]. Kushen (SFR), the dry root of the legume *Sophora flavescens* Ait. It has a wide range of pharmacological activities, such as anti-inflammatory, anti-tumor, anti-bacterial, and anti-virus. The combination of DG and KS is common in many TCM prescriptions, such as Danggui Beimu Kushen Pills and Danggui Kushen Pills, but currently, there is no research on its anti-IHD metabolomic characteristics.

Objective

To explore the protective effect of ASR-SFR on IHD and its metabolomic mechanism, so as to provide new ideas for the development of clinical preparations.

Materials and methods

Hematoxylin-eosin (HE) staining was used to prove the protective effect of ASR-SFR on myocardial ischemia. The untargeted metabolomics of IHD rats was studied by UPLC-Q-TOF/MS technology, the different biomarkers between the sham operation group and model group were screened, and the related metabolic pathways were analyzed.

Results and discussion

In the sham operation group, the myocardial cells were arranged in order, with normal morphology, the round nucleus in the center, without lipofuscin deposition, obvious myocardial striation, uniform fiber staining, clear cell boundary, consistent shape, no abnormal stroma, and no obvious inflammatory changes. In the model group, more myocardial fibers were dissolved and replaced by proliferative connective tissue. There was significant improvement in ASR-SFR group. The results indicate that angelica and *Sophora flavescens* have a positive protective effect on acute myocardial ischemia (Figure 1).

In this study, the UPLC-QTOF-MS technology was used to compare the serum metabolic profiles of the sham operation group, the model group, and the administration group under the positive and negative ion modes. First, a principal component analysis score chart was established. In the positive and negative ion modes, a clear grouping trend was observed between the Sham, Mod, and DK groups (Figure 2A and B). Subsequently, the OPLS-DA supervised pattern recognition method was used to find the overall metabolic difference between normal rats and ischemic heart disease. There were separated clusters between the two groups, indicating that the coronary artery ligated IHD rats had metabolic abnormalities (Figure 2C, and D). Compared with the sham operation group, the endogenous metabolites in the serum of the model group rats increased, including citric acid, uric acid, glycocholic acid, cholic acid, L-arginine, cinnamoylglycine, 3-Oxo-octadecanoic acid, 12 (s) -HETrE, 12 HETE, lipoxin B4, thromboxane B2, butylenylcarnitine, pimelycarnitine, phosphorylcholine. Compared with the sham operation group, the endogenous metabolites in the model group decreased, including palmitic acid, 2-arachidonylglycerol, isoleucine, L-threonine, tyrosine, alanine, alanyl-valine. After administration, it was found that the increased endogenous substances in the model group had a callback trend.

Finally, to explore the potential pathways affected by metabolism-related proteins, the above 22 endogenous metabolites related to ischemic heart disease were imported into the MetScape database. In this study, the results indicate that the occurrence of IHD may be related to 5 pathways, including linoleic acid metabolism, arachidonic acid metabolism, glycerophospholipid metabolism, retinol metabolism and sphingolipid metabolism. The above results suggest that taking DK combination can change these biomarkers and related metabolic pathways, to exert the curative effect on IHD.

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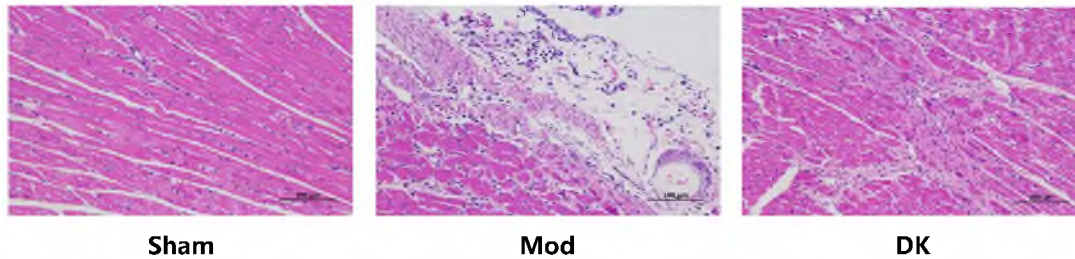


Fig. 1. Myocardial injury assessed by HE staining, scale bar, 100 µm.

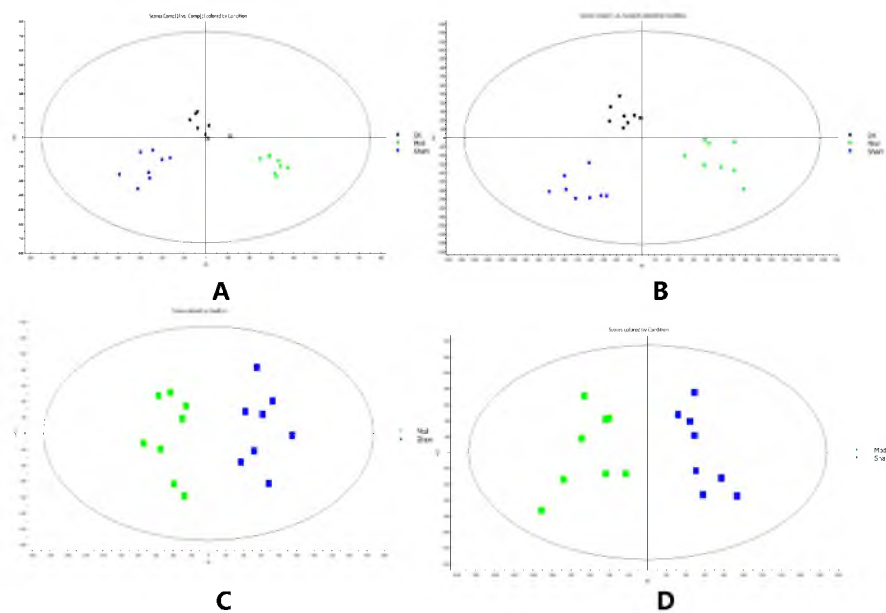


Fig. 2. PCA and OPLS-DA in serum positive (A and C) and negative (B and D) ion modes.

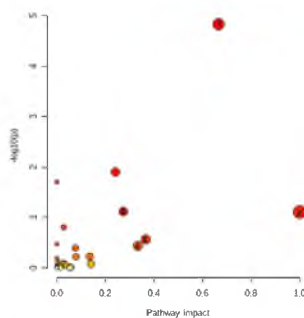


Fig. 3. Metabolic pathways are involved in potential markers in serum. (1. Linoleic acid metabolism; 2. Arachidonic acid metabolism; 3. Glycerophospholipid metabolism; 4. Retinol metabolism; 5. Sphingolipid metabolism)

Exploring the mechanism of panax notoginseng-drynaria fortunei in the treatment of femoral head necrosis based on network pharmacology

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Abstract

Osteonecrosis of The Femoral Head (ONFH), also known as ischemic necrosis of the femoral head, is an orthopedic disease that results in blood supply disorder of the femoral head, local tissue necrosis and structural change for various reasons, followed by dysfunction, with the main clinical manifestations of hip pain and dyskinesia^[1]. China has about 10 million patients with femoral head necrosis, accounting for about 50% of the worldwide incidence, and growing at the rate of about 100,000 to 200,000 cases per year^[2-4]. For the prevention and treatment of femoral head necrosis in the early and middle stages, traditional Chinese medicine has unique advantages in that it can not only effectively relieve hip pain, but also avoid the risks and costs brought by surgery, with significant efficacy^[5,6].

After data mining, Wang Dandan^[7], Gu Yong^[8] and Wang Ding^[9] et al. found that Notoginseng Radix and Rhizoma Drynariae appeared more frequently in Fang Yaozhong for the treatment of femoral head necrosis, and had strong correlation with other drugs, so they were often used as combination pairs for the treatment of femoral head necrosis. According to the Pharmacopoeia of the People's Republic of China, Radix et Rhizoma Notoginseng is effective for dispelling blood stasis, stopping bleeding, relieving swelling and pain, while Rhizoma Drynariae is effective for healing wounds, relieving pain, tonifying kidney and strengthening bone. They are also the core drugs that constitute common drugs such as Gubu Pill, Guyuling Capsule, and Guihong Zhuanggu Capsule. It can be seen that Notoginseng Radix et Rhizoma Drynariae medicine plays an important role in the treatment of femoral head necrosis with traditional Chinese medicine.

Keywords

network pharmacology; Notoginseng; Rhizoma drynariae; caput femoris necrosis

Objective

To explore the mechanism of Radix et Rhizoma Notoginseng-Rhizoma Drynariae in the treatment of femoral head necrosis based on network pharmacology.

Methods

The active components and component targets of Radix et Rhizoma Notoginseng-Rhizoma Drynariae pair were collected and screened using Chinese Medicine System Pharmacology Database and Analysis Platform (TCMSP), which were supplemented by CNKI and PubMed databases, and the targets were converted by UNIPORT database. The action targets of femoral head necrosis were collected through GeneCards and OMIM databases, and the intersected targets were obtained and imported into STRING database to generate PPI network, which was used to construct Chinese medicine-active ingredient-target network with Cytoscape 3.9.0 software. Enrichment analysis of GO function and KEGG pathway of core targets was conducted through DAVID database.

Results

A total of 20 active components and 229 potential targets, and 1386 targets for femoral head necrosis of the "Notoginseng Radix et Rhizoma Drynariae" drug pair were obtained. GO enrichment analysis mainly includes such functions as inflammatory response, apoptotic process, regulation of angiogenesis, and response to estrogen. The KEGG enrichment analysis mainly included lipid and arteriosclerosis, interleukin -17 signaling pathway, and rheumatoid arthritis signaling pathway.

Conclusion

"Notoginseng Radix et Rhizoma Drynariae" has the characteristics of multiple components, wide targets and complex pathways in the treatment of femoral head necrosis, and it may play a role in the treatment of femoral head necrosis through such targets as IL6, TNF, TP53, lipid metabolism, interleukin -17 and other signaling pathways.

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Microarray analysis of lncRNA and mRNA expression profiles in chronic salpingitis

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Abstract

The expression profiles of lncRNA and mRNA in chronic salpingitis and normal tubal tissues were screened by gene chip, the differentially expressed genes between the two groups were identified, and the function of these genes and relationship between altered lncRNAs and mRNAs were analyzed to explore the possible mechanisms of CS and search for the key genes in this study. As a consequence, 10 hub mRNAs and 1 lncRNA were identified as the most important genes in CS, and they play a key role in CS through the bioprocess and pathway of regulation of leukocyte differentiation and NF-kappa B signaling pathway.

Keywords

Chronic salpingitis, pelvic inflammatory disease, microarray analysis, lncRNA

Chronic salpingitis (CS), one of the pelvic inflammatory diseases (PID), is mostly developed from untimely treated acute pelvic inflammation or persistent asymptomatic infection, often causes complications such as infertility, ectopic pregnancy, and chronic pelvic pain, and seriously affects women's physical and mental health¹.

Antibiotics are premier drugs for salpingitis, but their therapeutic effects on this chronic infection are not ideal. Furthermore, many of the early infections are difficult to detect. It was reported that more than 70% cases of the Chlamydia trachomatis (CT) infection in reproductive tract are asymptomatic, and therefore, this infection is liable to develop into chronic PID, especially CS. Surgery for CS, such as salpingoplasty, adhesiolysis, and interventional therapy, usually has high risks of recurrence and ectopic pregnancy, in addition to intra- and postoperative and anesthesia complications.

Long noncoding RNAs (lncRNAs) are more than 200 nt in length, represent the most transcribed noncoding RNA group, and are the main transcriptional products of mammalian genomes. Due to lack of complete reading frame, lncRNAs cannot be translated into protein, but as the signal, decoy, guide, and scaffold, they could play a significant regulatory role in complex organisms. lncRNAs have been confirmed to be involved in inflammatory diseases, metabolic and autoimmune disorders, tumors, etc., and have been found to be a key regulator of gene expression in the defensive system by controlling differentiation of innate and adaptive immune cells, as well as inflammatory responses and resistance of pathogens in a highly lineage-specific manner. Mechanism studies have also proved that lncRNAs are important regulators of a wide range of biological processes under normal and disease conditions, such as cell proliferation, cell cycle, apoptosis, and cell migration. In view of the pervasiveness and prominence of lncRNAs in diseases, we hope to reveal the mechanism of CS and detect the key molecules in CS through transcriptomics study and found the new target for clinical treatment.

Objective

To explore the mechanism of CS and search for the hub genes which play a key role in CS and are

expected to be the new targets of clinical treatment.

Materials and methods

Gene chips were used to detect the expression of the genes in 4 CS and 4 normal tissue samples, and fold changes and p-value were utilized to filter the genes. Then we investigated the function of altered mRNAs by enrichment analysis through Gene Ontology (GO) and Kyoto Encyclopedia of Genes and Genomes (KEGG) databases. To understand the function of lncRNA in CS, co-expression analysis of differentially expressed lncRNAs (DELs) and mRNAs (DEMs) and prediction of cis and trans regulatory mechanism of DELs were carried out, followed by progress and pathway enrichment of DEMs regulated by DELs. After that, a protein-protein interaction (PPI) network for these DEMs was conducted, and hub genes in PPI network were searched using Cytohubba plugin of Cytoscape, the function of these hub genes was analyzed using CluoGO and Cluepedia plugin. The key lncRNAs that trans-regulate hub genes were also identified.

Results and discussion

1847 differentially expressed lncRNAs (626 upregulated and 1221 downregulated) and 757 mRNAs (480 upregulated and 277 downregulated) were obtained. For upregulated genes functional enrichment, immune response and TNF pathway were respectively the most significant GO and KEGG terms by p-value, and for downregulated genes functional enrichment, DNA binding and Glycosphingolipid biosynthesis-globo and isoglobo series were respectively the terms by p-value. We obtained 54 DELs and 232 their trans-regulated DEMs, and gathered top 20 functions, regulation of cell activation with the best p-value is their main function. Furthermore, we obtained 8 hub genes (ITGAX, LYN, SYK, NLRP3, IRF4, RIPK1, HMGB1, IL1R1) through PPT network construction and degree calculation. The terms with the best p-values were gathered by GO and KEGG enrichment respectively to understand the function of these genes, which are regulation of regulation of leukocyte differentiation and NF-kappa B signaling pathway. The 8 hub genes were trans-regulated by 33 DELs, and lnc-ENST00000641729.1 with the most connective degree was considered the most important DEL.

Thus, ITGAX, LYN, SYK, NLRP3, IRF4, RIPK1, HMGB1, IL1R1 and lnc-ENST00000641729.1 play a key role in CS, their significant dysregulation promotes the occurrence of CS through specific biological process and pathway of regulation of leukocyte differentiation and NF-kappa B signaling pathway.

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To explore the related mechanism and significance of sulforaphane in the treatment of diseases

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Objective

The study found that plant-derived chemicals are high in antioxidant, antimutagenic activities, low in toxic effects on mammals, and can help maintain medicinal properties on human health. Based on this background, in order to understand a kind of from the cruciferous vegetable family of isothiocyanates—sulforaphane, this article research its significance for the treatment of disease development from the aspects of sulforaphane related mechanism.

Materials and methods

Search CNKI, PUBMED and other large literature databases. The keywords include sulforaphane, cancer, liver injury, neuroprotective effect, antioxidation and so on. The detected literatures were classified, summarized and analyzed. And then summary the research progress on the related mechanism of sulforaphane in the treatment of various types of diseases.

Results

SFN is an effective activator of NRF2, and the improvement of most diseases begins with the activation of NRF2. (1) SFN is considered to be one of the most effective natural products in the prevention and treatment of cancer. It plays a multiple protective role by activating NRF2 to regulate cell dynamic balance at the molecular level, thus inhibiting various factors that affect the evolution of cancer cells. (2) SFN has antioxidant effect, and the antioxidant effect of SFN is mainly realized through Nrf2-ARE signaling pathway. In oxidative stress-related nervous system diseases, such as cerebral hemorrhage, cerebral infarction, brain injury, Parkinson's disease and other animal models, SFN has been proved to have a good neuroprotective effect, while HO-1 and NQO1 are relatively important antioxidant enzymes in this process. (3) In addition, SFN usually synergistic with antioxidant action in lipid metabolism to improve the occurrence and development of diseases. For example, in liver injury diseases, SFN can improve acute alcoholic liver injury by activating NRF2 and inhibiting SREBP-1c and other related factors. (4) SFN also had an anti-inflammatory effect in improving fibrosis inflammation. By lowering the expression of miR-155 through Nrf2 transcription, NOS2 could be reduced and the expression of Arg-1 could be significantly enhanced to achieve anti-inflammatory effect and inhibit acute colonic inflammation induced by DSS.

Discussion

SFN can affect multiple targets through the activation of NRF2 to achieve the effect of treating various diseases, which provides theoretical value for the research and development of specific drugs for SFN-related diseases. In this era of urbanization and environmental pollution, extracting substances with less toxic and side effects from food and medicinal plants to act on the human body's defense mechanism is of great significance for prevention and treatment of human health.

Research progress on bioactivity of metal complexes based on active components of tradition Chinese medicine

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Abstract

In order to provide a theoretical basis for the research and development of new drugs in traditional Chinese medicine, the relevant studies on the biological activities of metal complexes of active components in traditional Chinese medicine in recent years are reviewed. The complex of active components of traditional Chinese medicine, such as polyphenols and polysaccharides, with metal phases such as copper and zinc, has been studied comprehensively at home and abroad, and its antibacterial and anticancer biological activities have been measured. Studies have shown that the complexation of active components of traditional Chinese medicine with metals can significantly improve their related biological activities, which is an effective way to develop a class of new drugs in traditional Chinese medicine.

Keywords

TCM composition, Metal complex, Biological activity, review

With the development of big health industry in China and Russia, it is urgent to develop new drugs with better efficacy. It is an effective way to develop new drugs of TCM by complexing the effective components of TCM with trace metal elements to enhance their biological activities. Polyphenols, polysaccharides, saponins and other components of TCM were complexed with metal ions to exert synergistic effects. Not only the antitumor and hypoglycemic biological activities of the effective components of TCM were significantly improved. The biological activity of metal ions was also demonstrated. In this paper, by referring to the relevant research literature at home and abroad in recent years, the relevant research on the biological activity of metal complexes of effective components of TCM is summarized as follows.

Objective

In order to provide a theoretical basis for the research and development of new drugs in TCM, the relevant studies on the biological activities of metal complexes of active components in TCM in recent three years are reviewed.

Materials and methods

Through the search of China National Knowledge Infrastructure (CNKI) and the National Library of Medicine (MEDLINE), a total of 67,152 related studies were recorded in CNKI and 96,944 in MEDLINE as of 2022. The number of foreign related studies showed an increasing trend, with a new high of 4,574 in 2020. After screening the two databases, 2339 clinical medicine related research articles were collected, which showed that the metal complex has excellent medical application prospects.

Results and discussion

The active components of TCM have many excellent biological activities. After complexing with metals, they not only retain these excellent pharmacological effects, but also exert various biological activities of metals. Many studies have shown that the active components of TCM have

stronger biological activity than single active components when they are complexed with metal central atoms. The pharmacological activities of metal complexes of active components of TCM are mainly manifested in antioxidant, anti-tumor and other aspects. In recent years, they have been found to have hypoglycemic and lipid-lowering activities, as described below:

Antibacterial activity

The metal complex of active component of TCM has excellent antibacterial activity, and it has inhibitory effect on both Gram-negative and Gram-positive bacteria. GHOLAMI M et al. [1] measured the antibacterial effect of curcumin metal complex on *Pseudomonas aeruginosa* PAO1 flora, and the results showed that copper, zinc and iron complexes reduced the number of bacterial growth by 1.5%, 3.2% and 3.3%, respectively, indicating that they significantly inhibited bacterial growth. SAHA T et al. [2] measured the antibacterial efficacy of curcumin complex against *Staphylococcus aureus* ATCC29213 and *Escherichia coli* ATCC25922, and the experiment showed that 25 M of curcumin manganese complex could kill 92.90% of bacteria, while the double concentration could kill 95.58%.

Anti tumor activity

The effective component metal complexes of TCM have excellent anti-tumor effects. It is based on the discovery of anticancer activity of cisplatin that more and more scientists have been engaged in the anticancer research of metal complexes. GABER A et al. [3] studied the inhibitory ability of papaverine gold complex on human breast cancer cell McF-7 and human liver cancer cell HEPG-2, and the results showed that the anti-cancer activity of the metal complex was better than that of papaverine, and the 50% inhibitory concentration (IC₅₀) was significantly lower than that of papaverine. HALEVAS E et al. [4] synthesized three kinds of chrysin gallium complex and explored its cytotoxicity to a variety of cancer cells. The results showed that the anticancer activity of the three gallium complexes was better than that of chrysin itself.

Hypoglycemic activity

The effective component of Chinese medicine metal complex has better hypoglycemic effect than ligand. CHUKWUMA C I et al. [5] synthesized zinc acetate complexes of cinnamic acid and evaluated their anti-glycation and α -glucosidase and α -amylase inhibitory activities. After complexing metal ions, the anti-glycation activity of cinnamic acid was increased by 2 times, and the inhibitory effect on α -glucosidase was also increased by 2 times. Therefore, the effective component metal complex of TCM has great potential to develop new drugs for diabetes.

Other biological activities

In addition to the biological activities listed above, the metal complexes of the active components of TCM also have a variety of biological activities. JIA Y et al. [6] prepared three metal complexes of corn whisker polysaccharide and determined them by free radical scavenging experiments. Compared with the ligand of corn balsa, the Zn(II) complex showed enhanced antioxidant activity. Other studies have also shown that metal complexes, the active components of TCM, can also regulate immunity, promote bone and angiogenesis, and reduce blood lipids.

The biological activity of the active components of TCM was significantly enhanced after complexation with metals. As mentioned above, the antioxidant, antibacterial and anticancer activities of the metal complex were superior to those of the effective components. The synergistic effect of metal and ligand to enhance the biological activity of active components of TCM is one of

the effective ways to develop new drugs. The effective components of TCM, such as stars, terpenoids, alkaloids, etc., are expected to be more effective components of TCM for metal complexation research, so as to develop more metal complexation drugs with excellent biological activity for Chinese and Russian people.

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Clinical overview of acupuncture combined with medicine in treating menstrual headache

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Abstract

Menstrual headache is a common paroxysmal disease in women. It not only affects the physical and mental health of patients, but also seriously reduces their quality of life. Acupuncture combined with medicine is safe and efficient. This paper reviews the research reports of acupuncture combined with medicine in the treatment of menstrual headache in recent years, and summarizes and discusses the clinical classification and different treatment methods.

Keywords

acupuncture ; combination of acupuncture and medicine ; menstrual headache ; migraine ; summary
Menstrual headache is one of the syndromes before and after gynecological menstrual period, which is equivalent to menstrual migraine, and it is a headache with the rise and fall of menstruation. Contemporary women ' s social status is improved, social rhythm is accelerated, social pressure, family pressure increases, emotional changes and so on make the headache more intolerable. Literature^[1] shows that there are more than 95 % of women suffering from menstrual headache, of which 50 % are mild and 30 % are moderate. It seriously affects women ' s daily life and becomes an important problem in women ' s production and life.

In terms of treatment, the clinical efficacy of western medicine is obvious, but the recurrence rate is high, combined with long-term use often accompanied by adverse reactions of the digestive system, the long-term effect is not ideal. The combination of acupuncture and medicine is not only effective, but also safe without side effects of drug therapy. In recent years, the development of acupuncture combined with medicine therapy is changing rapidly. Therefore, the clinical research situation of acupuncture combined with medicine in the treatment of menstrual headache in recent years is summarized, according to the classification of ' TCM gynecology ' as follows.

1. Blood stasis type

Yue Chongwei^[2] et al. randomly divided 91 cases of menstrual headache with syndrome of blood stasis into two groups, 45 cases in the control group and 46 cases in the study group. Study group : Using Quyu Tongqiao Prescription (Chuanxiong 15g, Chishao 12g, Chaihu 9g, Taoren 10g, Dangshen 15g, Danggui 12g, Honghua 10g, Xixin 3g, Gancao 10g) one dose a day, decoction, morning and evening take, with acupuncture (Sanyinjiao, Taichong, Baihui) needle 20min, once a day. Start treatment 5 days before menstruation, lasting 10 days, continuous treatment of three menstrual cycles. Control group : take Sanyinjiao, Taichong, Baihui acupuncture treatment, line needle 20 min, 1 time a day, continuous treatment of 3 menstrual cycles. In the control group, 7 cases were cured, 10 cases markedly effective, 15 cases effective, 13 cases ineffective, the total effective rate was 71.11 %. In the study group, 11 cases were cured, 15 cases were markedly effective, 17 cases were effective, and 3 cases were ineffective. The total effective rate was 93.48 %. Compared with the two groups, Quyu Tongqiao Decoction combined with acupuncture can improve the TCM syndrome of patients with headache of blood stasis type, and has obvious curative effect.

2.Liver fire type

Ma Wenjun^[3] randomly divided 72 cases of headache due to hyperactivity of liver-fire syndrome into two groups, with 36 cases in each group. The control group was treated with Danzhi Xiaoyao Powder (basic prescription : 15 g, gardenia 10 g, bupleurum 15 g, angelica 15 g, paeoniae alba 15 g, poria cocos 15 g, jujube 10 g, licorice 10 g, uncaria 15 g, chrysanthemum 15 g). Add 500 ml water, boil 150 ml, 1 dose a day, 2 times in the morning and evening, for 7 days. Treatment group : on the basis of the control group plus acupuncture treatment. Acupuncture points : Taiyang (double), Fengchi (double), Touwei (double), Biangu (double), Qubin (double), Taichong (double), Xiashi (double). Needle retaining 30 min, once every 10 min, the above operation. Starting 1 week before menstruation, once a day for 7 days. Both groups were treated for 3 menstrual cycles. The total effective rate of the treatment group was 91.67 %, which was higher than 72.22 % of the control group, and the efficacy of the study group was significantly better than that of the control group. Danzhi Xiaoyao Powder combined with acupuncture in the treatment of meridian headache with hyperactivity of liver fire had obvious clinical effect.

3.Blood deficiency type

Xu Li^[4] et al. will dialectical belongs to liver stagnation and blood deficiency type menstrual headache in 35 cases, using black Xiaoyao powder addition and subtraction (Shudihuang 20 g, Dangguishen 20 g, Hangbaishao 20 g, Baizhu 15 g, Fuling 15 g, Chaihu 10 g, Zhigancao 10 g) per paying water decoction juice 300 ml, one dose a day, morning and evening warm clothes, since the date of treatment for three consecutive menstrual cycles, each from 7 days before menstruation, evening for 10 days. Combined with acupuncture (Baihui, Sishencong, Fengchi, Taiyang, Lieque, Xuehai, Taichong) 7 days before menstruation, daily filiform needle flat needling, Xuehai reinforcing and reducing method, Taichong reinforcing and reducing method, with a sense of qi after retaining needle 30 min, once a day, acupuncture to the end of the third day of the menstrual period, a total of 10 days, after 3 menstrual cycles, stop acupuncture observation. The results showed that 20 cases were cured, 9 cases improved, 4 cases markedly effective, 2 cases ineffective, the total effective rate was 94.29 %. There were significant differences in symptom scores before and after treatment. Black Xiaoyao Powder combined with acupuncture in the treatment of liver stagnation and blood deficiency type of menstrual headache is effective.

Discuss

In recent years, menstrual headache has become a common disease that plagues the lives of women. However, there are still few studies on menstrual headache, and there is no uniform standard for classification, which is very unfavorable for the study of this disease. Moreover, there are few studies on the deficiency syndrome of menstrual headache in clinic. Nowadays, due to physiological structure problems, women are easy to consume qi and blood, or due to improper diet, injury to spleen and stomach and other reasons, there are more and more menstrual headaches of blood deficiency type. It is also hoped that there are more and more treatment methods for the deficiency syndrome of menstrual headache in clinic.

The author believes that menstrual headache is a secondary disease of gynecological menstruation. It is important to alleviate headache and treat gynecological primary disease. A single acupuncture can only alleviate migraine symptoms, but cannot be cured. Headache is easy to recur. Or a single Chinese medicine treatment, for alleviating headache immediate problem solving is slow, so that

patients still suffer greater pain in the onset. The combination of acupuncture and medicine can play a synergistic effect, regulating qi and blood, promoting blood circulation and removing blood stasis, and dredging collaterals to relieve pain, to achieve the effect of treating both symptoms and root causes. It can not only alleviate the difficult headache symptoms at the onset, but also fundamentally solve the gynecological problems, which is worthy of clinical popularization.

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Research Progress on Central Mechanism of Acupuncture Regulating Chronic Fatigue Syndrome

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Abstract

Keywords: acupuncture, central mechanism, chronic fatigue syndrome, neuroimaging technology

Objective

By reviewing the published literature on the central mechanism of chronic fatigue syndrome and the intervention mechanism of acupuncture in the treatment of chronic fatigue syndrome in recent years, the research status of the central mechanism of acupuncture in the treatment of chronic fatigue syndrome was summarized and analyzed, and the direction for further research was prospected, which would provide ideas for the follow-up study on the central mechanism of acupuncture in the treatment of chronic fatigue syndrome and provide scientific basis for the clinical application of acupuncture in the treatment of chronic fatigue syndrome.

Methods

Seven databases, including China Journal full-text Database (CNKI), Wanfang academic Journal full-text Database (Wan fang), VIP Chinese Sci-tech Journals Database (VIP), China Biomedical Literature Database (Sino Med), PubMed, Cochrane Library and Embase database, were searched with the keywords of "chronic fatigue syndrome" AND "central mechanism", "acupuncture" AND "chronic fatigue syndrome" AND "mechanism" and corresponding Chinese. The search time limit was before June 2022. Included articles were summarized and analyzed.

Results

Chronic fatigue syndrome is a complex dysfunction syndrome characterized by long-term persistent or repeated fatigue, often accompanied by a variety of physical and mental symptoms. Although the etiology and pathogenesis are unclear, there are documented neurological symptoms such as central fatigue, sleep disorders, autonomic nerve function impairment, cognitive difficulties and pain changes, indicating that the occurrence and development of CFS is closely related to abnormalities of the central nervous system. Acupuncture has a significant effect on the treatment of chronic fatigue syndrome. In recent years, scholars in China and abroad have also conducted a large number of studies on the effectiveness and central mechanism of acupuncture in the treatment of chronic fatigue syndrome. In conclusion, the regulation of acupuncture on the brain of patients with chronic fatigue syndrome is multifaceted, and the treatment mechanisms are mostly concentrated on the regulation of oxidative stress and neuroinflammation, neurotransmitter levels, hypothalamic–pituitary–adrenal axis function, metabolite content in the brain, functional connection and activation of brain regions, mitochondrial energy metabolism and hippocampal function, etc. However, the results of this study are still controversial, and the mechanism of acupuncture treatment for chronic fatigue syndrome is still unclear, which needs further study.

Discussion

Acupuncture may improve the clinical symptoms of patients with chronic fatigue syndrome by regulating many central mechanisms. In future studies, multimodal neuroimaging technology should be used to analyze the subtypes of patients with chronic fatigue syndrome and verify the central mechanism of acupuncture in the treatment of chronic fatigue syndrome from the perspectives of structure, function and metabolism. In addition, acupuncture has the advantage of comprehensive regulation, and it is safe, convenient and without toxic and side effects, which is worthy of more extensive clinical application.

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Research progress of acupuncture therapy for scapulothoracic periarthritis

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Abstract

Periarthritis of shoulder refers to the unexplained aseptic inflammation of the soft tissues around the shoulder joint, which seriously affects the daily work and life of patients. Acupuncture of traditional Chinese medicine has outstanding effect in the treatment of this disease and is recognized by patients. Therefore, this article summarizes and summarizes the acupuncture treatment of periarthritis of shoulder in recent years from acupuncture combined with exercise therapy, special acupuncture method and special needling method, in order to provide reference for clinical diagnosis and treatment.

Keywords

Scapulothoracic periarthritis; Acupuncture therapy; review

Periarthritis of shoulder, also known as "shoulder coagulation", "50 shoulder", the disease belongs to the Chinese medicine "arthralgia" category. Patients often have shoulder pain and shoulder movement disorders. Traditional Chinese medicine believes that the cause of the disease is due to old age, qi and blood deficiency, blood does not nourish tendon-nourishing; Wind, cold and dampness invasion and shoulder strain lead to shoulder meridian stasis, impassability of tendons, and pain^[1]. There is no unified conclusion on the cause of this disease in Western medicine, and the theory of chronic inflammation and fibrous hyperplasia is the mainstream. Western medicine for the treatment of periarthritis of shoulder is mainly to relieve shoulder pain and symptomatic treatment of shoulder joint movement disorders, but the treatment effect is general and should not be used for a long time^[2]. Traditional Chinese medicine has excellent curative effect on this disease, which is summarized as follows.

1. Acupuncture combined with exercise therapy

"The Annals of Lv's Spring and Autumn Period" once said, "Running water is never stale, a dot-hinge is never worm-wormed", which explained to the world the importance of exercise to people by taking analogs of natural objects, and the present acupuncture therapy was inspired by this. Xu Senlei^[3]. 60 patients were randomly divided into acupuncture group (i.e., Chengshan acupuncture through the mouth of the healthy side) and moving acupuncture group (i.e., Chengshan acupuncture through the mouth of the healthy side combined with shoulder joint therapy of the affected side). After 2 courses of treatment, the effect of moving acupuncture group was more significant than that of acupuncture group ($P < 0.05$).

2. Special stabbing method

2.1 swollen thorn method

"Lingshu. Official Needle" once recorded: "the giant thorn, left to take right, right to take left." The giant thorn method is suitable for the treatment of pain^[4]. Reports^[5] using the swollen thorn therapy of acupuncture the contralateral hand six stitches (i.e., "yu ji", or valley, three rooms, si 3, eight evil will take 2 and 3 refer to the event webbed reason behind the red white meat, 3 and 4 refer

toement at the same time, the treatment is still in the stage of patients with peri-arthritis of shoulder pain, the curative effect is remarkable.

2.2 thrust method

"Neijing" once recorded, "Qi stab, straight into the one, the other into the two, in order to treat cold small deep. Or three thorns, three thorns, cure Bi qi small deep also." Jia Yanfei^[6] divided the patients into the treatment group (acupuncture stimulates the pain points and gives three acupuncture points, and the other acupoints are given conventional acupuncture) and the control group (conventional acupuncture), and the results showed that the treatment of scapulohumeral peri-arthritis with the same acupuncture is more effective.

3. Special needling method

3.1 Fire needle therapy

Fire acupuncture therapy refers to the method of treating diseases by rapidly piercing the needle body of a special needle tool into a certain part after burning it red, so as to give a certain warm stimulation to the part of the body^[7]. Lin Yujie^[8] divided 60 patients into 30 cases of needling tendon focal points (treatment group) and 30 cases of conventional needling group (control group), and the results showed that the needling group had better curative effect.

3.2 Floating needle therapy

Floating needle therapy is to Pierce a special floating needle needle into the loose connective tissue under the skin, and sweep it with a large area at the same time, so as to dreg the local tendons and improve the local blood supply. Ampen^[9] used floating needle to treat 22 cases of scapulohumeral peri-arthritis, and achieved good results, with an effective rate as high as 90.9%.

4. Discuss

In conclusion, acupuncture therapy has achieved significant clinical effects in the treatment of peri-arthritis of shoulder, but there are still shortcomings. 1) There are differences in the selection of acupoints, such as shoulder three needles in different papers have different records. 2) In clinical experiments, the comparison between various special treatment methods and conventional acupuncture is mostly carried out, and the comparison between special acupuncture methods is rarely carried out. 3) Insufficient sample size. 4) Lack of long-term follow-up in clinical trials. 5) Lack of clinical efficacy evaluation criteria. Because of the above problems in the treatment of peri-arthritis of shoulder by acupuncture nowadays, our clinical workers should strengthen the research efforts in order to relieve the pain and bring good news for patients with peri-arthritis of shoulder.

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Clinical research progress of acupuncture and moxibustion in the treatment of ophthalmoplegia

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Abstract

Ophthalmoplegia has the characteristic of diverse causes. Nowadays it's also a incurable diseases, which can cause a severe impact on people's life and study. This paper summarizes previous articles on acupuncture and moxibustion for ophthalmoplegia, and discusses the eye acupuncture, body acupuncture, electroacupuncture, filiform fire acupuncture and moxibustion.

Keywords

acupuncture, moxibustion, ophthalmoplegia

Ophthalmoplegia is currently common in the clinic and could be seen in neurology, surgery and endocrinology. Its etiology may involve stroke sequelae, intracranial tumor compression, brain trauma, diabetes, myasthenia gravis etc^[1]. Abnormal eye movement and re-examination as the main clinical symptoms. It has a great impact on the daily life of patients. Modern medicine is not clear about the treatment of this disease, mainly based on drug treatment and surgical treatment. In recent years, acupuncture therapy has played a huge role in the treatment of ophthalmoplegia and has achieved good clinical efficacy.

1. Eye acupuncture therapy

Yang Guannan and others applied acupuncture to deal with 38 patients with ophthalmoplegia, needled at EX-HN4, ST1, BL1, Ganqu(Liver area) and Danqu(Gallbladder area). The distance of diplopia were decreased significantly and the total efficacy rate was 94.74% after the treatment^[2].

Another 38 ophthalmoplegia patients were treated during the combination between eye acupuncture and acupoint injection. Acupuncture points on the side of the lesion were mainly selected included Shangjiaoqu, Piweiq, Xiajiaoqu. After two weeks of treatment, the total effective rate of the observation group(89.47%) was significantly higher than that of the control group(52.63%)^[3].

2. Body acupuncture therapy

Cai Yucui simultaneously selected body acupuncture(LI4, LR3, GB37, SP6) and eye acupuncture(Shangjiaoqu, Danqu, Piqu) to treat 58 patients with ophthalmoplegia after stroke. After one month of treatment, the total effective rate is 91.37%^[4]. Bai Xiaoming applied the principle of taking acupuncture points after following the scriptures to treat 52 patients and the main points included GB20, SJ5, GB34, BL62. The total effective rate was 98.1%^[5].

3. Electroacupuncture therapy

Zhang Xiaodong and others used electro-acupuncture for 30 patients. After taking the acupuncture points around the eye by means of penetration, then the doctor would connect related points with 6805-II type electro-acupuncture instrument at continuous waves. The total effective rate is 86.66%^[6]. Duan Chunxiao and others selected intraorbital electroacupuncture to treat 56 patients with

abducens nerve palsy following ischemic stroke. Among them, 34 cases were judged to be cured by the results of diplopia and the total effective rate was 79.47%^[7].

4. Filiform fire acupuncture therapy

Lu Jia and others treated 30 patients with filiform fire-needling at root-kont points(BL67, ST45, BL1, ST8). The total effective rate after three course of treatment was 93.33%^[8].

5. Moxibustion therapy

Yang Aiping and others applied the moxibustion at the acupoints of the eyes combined the ultrasonic wave on 31 diabetic ophthalmoplegia. Depending on the affected nerve, the corresponding acupuncture points were selected for moxibustion. The cure time was shorter than that of the control group. The total effective rate was 87.10%^[9]. Ding Li selected acupuncture points through dialectical acupuncture for 30 patients. Main points were Shangjiaoqu, Gandanqu, Shenqu, Piweiqu, BL1, EX-HN7. Yin deficiency and hyperdosity would add LR3 and sputum obstruction of spleen deficiency would add ST36, ST40. The total effective rate was 93.3%^[10].

Conclusion

Through the use of eye acupuncture, body acupuncture, electroacupuncture, moxibustion and other methods to treat ophthalmoplegia regardless of the Causative factors, has achieved nice curative effect. Traditional Chinese medicine believes that ophthalmoplegia is related to the unfavorable meridian of the liver and the insufficient metaplasia of the spleen and stomach, so through the acupuncturing the eye periphery and the part, the eye meridian qi will be stimulated, the meridian tendons would be nourished, the qi machine around the body will be adjusted. Acupuncture mainly combines traditional theory and anatomy to accurately treat ophthalmic paralysis. However, recent reseaches still have some shortcomings. For instance: 1) Large samples of clinical randomized controlled trials are lacking. 2) Acupuncture for the treatment of ophthalmoplegia has not been standardized. I believe that with our unremitting efforts, the efficacy of acupuncture in the treatment of ophthalmic paralysis will be even more significant.

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Simultaneous determination of four constituents in licorice by HPLC

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Abstract

To develop a method for determining the contents of glycyrrhizic acid, glycyrrhetic acid, liquiritin, and liquiritigenin in licorice by HPLC, and the sample was extracted with 70% ethanol by ultrasound for 45 min. The quantitative analysis was carried out on the Diamonsil C₁₈ chromatographic column (250 × 4.6 mm, 5 μm), using the mobile phase consisting of acetonitrile (A) and H₂O with 0.05% phosphoric acid (B) by a gradient elution program (0 to 10 min, 14% A→23% A; 10 to 24 min, 23% A→30% A; 24 to 30 min, 30% A→34% A; 30 to 35 min, 34% A→36% A; 35 to 42 min, 36% A→42% A; 42 to 48 min, 42% A→51% A; 48 to 53 min, 51% A→70% A; 53 to 75 min, 70% A→90% A) at a flow rate of 0.8 mL·min⁻¹ at 40 °C. The injection volume was 10 μL, and the detection wavelength was set at 250 nm. The results showed that the four constituents could be separated, and the regression equation of glycyrrhizic acid, glycyrrhetic acid, liquiritin, and liquiritigenin were in good linearity over 9.73 – 486.25, 0.30 – 14.75, 6.85 – 342.50, and 0.36 – 18.00 μg·mL⁻¹, respectively. The recoveries were 98.57%, 91.74%, 99.03%, and 95.44%, and the RSDs were in the range of 1.25% – 2.39% (n = 6). This method is proved by methodology validation that it is accurate, reproducible, stable, and easy to operate, and can be used for the control and evaluation of the quality of licorice.

Keywords

Licorice; HPLC; Constituent content; Simultaneous determination

Licorice, the root of *Glycyrrhiza uralensis* Fisch., contains triterpenoids, flavonoids, and other active constituents^[1], with various pharmacological effects like anti-virus, anti-oxidation, and detoxication, is used widely for medicine, food, chemical industry and so on, an annual demand reaches to 60 thousand tons, and known as "Ten prescriptions, nine licorices"^[2].

The "content determination" of licorice recorded in the Chinese Pharmacopeia (ChP, 2020) only takes glycyrrhizic acid and liquiritin as quantitative constituents^[3], and the quality control indicators are relatively single, which is difficult to reflect fully the quality of the herbal medicine. Therefore, in order to better control and evaluate the quality of licorice, a method for simultaneous determination of glycyrrhizic acid, glycyrrhetic acid, liquiritin, and liquiritigenin was established, which to provide a reference for further research.

Objective

To develop a method with the characteristics of strong accuracy, high stability, good repeatability, and convenient operation for determining simultaneously the contents of glycyrrhizic acid, glycyrrhetic acid, liquiritin, and liquiritigenin in licorice by HPLC.

Materials and methods

The 3-year-old *Glycyrrhiza uralensis* fresh roots were collected from the medicinal garden of the Heilongjiang University of Chinese Medicine, China, cleaned with water, dried at 55 °C for 48 hr, and pulverized by the pulverizer, and sifted through a 60-mesh sieve. Then, the 1.0 g fine powder of licorice was placed in the conical flask with a rubber stopper, 125 mL of 70% ethanol was added,

weighed, and then ultrasound-assisted extraction (power was 500 W, frequency was 40 kHz) for 30 min, weighed again and compensated with 70% ethanol for the inevitable solvent losses during extraction. Finally, the supernatant was filtered with a 0.45 μm millipore filter for the HPLC analysis.

Glycyrrhizic acid (1405-86-3) was obtained from Chengdu Maidesheng Technology Co., Ltd. (Chengdu, China); liquiritin (551-15-5) from Shanghai Jinsui Biotechnology Co., Ltd. (Shanghai, China); glycyrrhetic acid (471-53-4) and liquiritigenin (578-86-9) from Chengdu Zhibiao Chemical Pure Biotechnology Co., Ltd. (Chengdu, China).

The experimental samples were tested by dint of the Diamonsil C₁₈ chromatographic column (250 \times 4.6 mm, 5 μm). The column temperature, flow rate, injection volume, and detection wavelength were 40 $^{\circ}\text{C}$, 0.8 mL $\cdot\text{min}^{-1}$, 10 μL , and 250 nm, separately. The mobile phases consisted of acetonitrile (A) and H₂O with 0.05% phosphoric acid (B). The gradient program was as follows: 0 to 10 min, 14% A \rightarrow 23% A; 10 to 24 min, 23% A \rightarrow 30% A; 24 to 30 min, 30% A \rightarrow 34% A; 30 to 35 min, 34% A \rightarrow 36% A; 35 to 42 min, 36% A \rightarrow 42% A; 42 to 48 min, 42% A \rightarrow 51% A; 48 to 53 min, 51% A \rightarrow 70% A; 53 to 75 min, 70% A \rightarrow 90% A.

Referencing the above chromatographic conditions, take the mixed reference materials with different series of concentrations to calculate the linear regression equation and its related parameters; take the 1.0 g fine powder of licorice to carry out the tests of precision, stability, and repeatability, respectively; take the 0.5 g fine powder of licorice with known content and add the mixed reference materials equivalent to the content of the sample to carry out the tests of recovery.

Results and discussion

The chromatogram (Figure 1) revealed that four constituents in licorice could be separated effectively, with the resolution > 1.5 and the number of theoretical plates > 5000 , which showed that the method had good specificity.

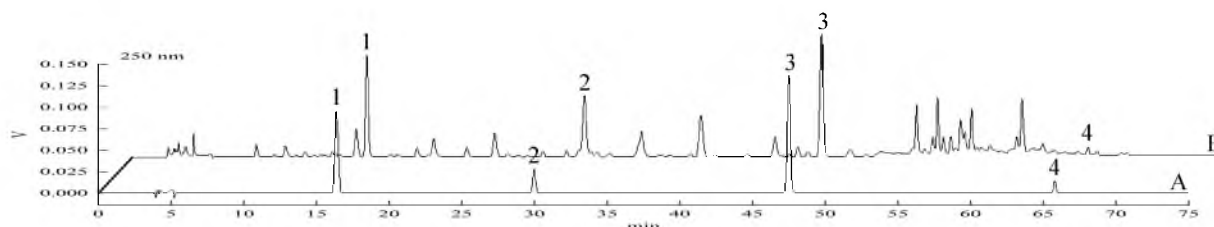


Figure 1. Chromatograms of four constituents in licorice. (A) reference material; (B) licorice; 1–liquiritin; 2–liquiritigenin; 3–glycyrrhizic acid; 4–glycyrrhetic acid.

The linear relationships of glycyrrhizic acid, glycyrrhetic acid, liquiritin, and liquiritigenin were good in the range of 9.73 – 486.25, 0.30 – 14.75, 6.85 – 342.50, and 0.36 – 18.00 $\mu\text{g}\cdot\text{mL}^{-1}$, separately, and the r was greater than or equal to 0.9995, as displayed in Table 1.

Table 1. Regression equations, correlation coefficients, and linear ranges of four constituents in licorice.

Ingredient	Regression equation	r	Linear range ($\mu\text{g}\cdot\text{mL}^{-1}$)
Liquiritin	$Y = 8.47 \times 10^3 X + 1.84 \times 10^4$	0.9998	6.85 – 342.50
Liquiritigenin	$Y = 2.44 \times 10^4 X + 6.23 \times 10^3$	0.9995	0.36 – 18.00
Glycyrrhizic acid	$Y = 9.26 \times 10^3 X + 2.16 \times 10^4$	0.9998	9.73 – 486.25

Glycyrrhetic acid $Y = 1.66 \times 10^4 X + 3.57 \times 10^3$ 0.9996 0.30 – 14.75

Note: Y–The areas of chromatographic peaks; X–The concentration of reference materials.

Besides that, the methodological investigation exposed that the RSDs were all less than 2.35%, indicating the precision of the instrument, the repeatability of the analytical method, and the stability of the sample within 24 hr after preparation were all good.

The recoveries of glycyrrhizic acid, glycyrrhetic acid, liquiritin, and liquiritigenin were 98.57%, 91.74%, 99.03%, and 95.44% in turn, and the RSDs also met the relevant requirements, implying that the detection method had good recovery and accuracy.

Taken together, the established HPLC for simultaneous determination of the contents of four constituents in licorice can reflect relatively comprehensively the quality of the herbal medicine. The method is simple, stable, reliable, accurate, repeatable, and has good applicability, and it can be used for the control and evaluation of the quality of licorice.

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Correlation study between exhaled nitric oxide level and TCM syndrome of upper airway cough syndrome

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Abstract

Objective To compare the distribution of UACS patients in general data, TRAF syndrome performance, TCM syndrome type and blood eosinophils with different FeNO value levels, and to explore the correlation between FeNO value level and UACS TCM syndrome. **Methods** The study cases were obtained from 100 UACS patients who met the inclusion criteria presented at the Respiratory Clinic of the First Affiliated Hospital of Heilongjiang University of Traditional Chinese Medicine between May 2021 and May 2022. All cases were divided into normal FeNO and elevated FeNO groups, including 45 in the normal FeNO group and 55 in the elevated FeNO group. Both groups were investigated with a clinical syndrome questionnaire, and the relevant ancillary examinations were recorded in detail, and a statistical analysis was performed using SPSS 22.0. **Conclusion** The FeNO value can reflect the TCM syndrome characteristics of UACS patients, and the percentage of blood eosinophils and the FeNO level can complement mutually to reflect the airway inflammation and clinical characteristics.

Keywords

exhaled breath nitric oxide level, TCM syndrome, UACS

Upper airway cough syndrome (UACS) is a syndrome caused by nasal disease to discharge back after the nose and pharynx, directly or indirectly stimulating cough receptors, resulting in cough as the main manifestation, previously known as "postnasal drip syndrome" (postnasal drip syndrome, PNDS). The pathogenesis of UACS is not clear in modern medicine, and most scholars at home and abroad believe that there are mainly the following categories: airway inflammation, theory of sensory nerve sensitivity, retronasal drip, nasal abnormal function and other. Regarding the treatment of the disease, there are etiological treatment and symptomatic treatment, such as antihistamines, glucocorticoids, decongestants for the relief of nasal symptoms, antibacterial drug for the treatment of bacterial sinusitis and other. However, there are still many problems, with complex etiology and long course. In clinical UACS patients often have onset or persistent cough is the primary cause of persistent pharyngeal itching. Once pharyngeal itching occurs, accompanied by cough, symptoms lasting for several weeks or even months, seriously affecting the quality of life of UACS patients. To this end, the study "comparing TCM clinical characteristics of UACS with normal FeNO values with UACS with rising FeNO levels" was conducted to provide further clues for TCM diagnosis and treatment of UACS.

Objective

The correlation between FeNO level and TCM syndrome of UACS was discussed by comparing the differences of general data, clinical manifestations and TCM syndrome distribution of UACS patients with different FeNO levels.

Materials and methods

The study subjects were UACS patients treated in the respiratory clinic of the First Affiliated Hospital of Heilongjiang University of Traditional Chinese Medicine from stage 2021.5 to 2022.5. There were 100 cases, 45 in the normal FeNO group and 55 in the elevated FeNO group. The sex, age, and disease duration of both UACS patients ($P > 0.05$) were comparable. All patients were divided into FeNO normal and elevated FeNO groups according to their FeNO level, the normal group with FeNO.

The study method is to conduct a self-drafted TCM syndrome questionnaire survey for all patients, including general data, detailed medical history, related examinations, pulmonary function, and exhaled gas nitric oxide examination.

The statistical method is to use Excel software for data entry of basic case data, including preliminary data integration and data reduction, and use SPSS 22.0 statistical software to preprocess the collected data, and gradually carry out statistical tests and analyze the results. When comparing two. Based on the results of the normal test, the measurement data obey the normal distribution and the variance is homogeneous. Two independent samples t-test was used for the comparison between the two groups. And expressed as mean \pm standard deviation; In case of non normal distribution or uneven variance, the non parametric Mann Whitney U test was used to compare the level differences between the two groups. The results were expressed in the median (interquartile range), and the rates were compared by chi square test with a four grid table. In all statistical results, $P < 0.05$ means the difference is statistically significant, and $P < 0.01$ means the difference is statistically significant.

Results and discussion

The distribution of syndrome type is to statistically analyze the FeNO value of the two groups and compare it with non parametric test. The average FeNO value of the normal group is (15.71 ± 5.41) ppb, and the average FeNO value of the FeNO increased group is (46.76 ± 14.10) ppb, $z = -8.576$, $p = 0.000$ (< 0.01). The FeNO value between the two groups has statistical significance. At the same time, the FeNO value levels among the three groups of syndrome types were compared. Using the nonparametric test of multiple samples, the results showed that $\chi^2 = 10.301$, $p = 0.016$ (< 0.05). The results showed that there was no statistical significance between yin deficiency and blood stasis syndrome and lung and spleen deficiency syndrome ($p = 0.72$, $p = 0.259$). There was a statistical difference between wind evil Fu Lung Syndrome and the other two syndrome types. The comparison between wind evil Fu Lung Syndrome and phlegm heat Yu lung syndrome $z = -2.10$, $p = 0.036$, The comparison between the syndrome of wind evil subduing the lung and the syndrome of lung and spleen deficiency $z = -2.079$, $p = 0.038$, $P < 0.05$ shows that the FeNO value of the syndrome of wind evil subduing the lung is significantly higher than the other two syndrome types. The clinical manifestations were statistical analysis. The results showed that there were statistical differences between the two groups in night cough, intermittent cough, cold, wind, odor stimulation and pharyngeal itching ($P < 0.05$).

Lung function is the lung function related index of UACS patients in the two groups included in this study, involving small airway function, lung ventilation function, etc., which has no statistical difference ($P > 0.05$).

A total of 43 of the 100 subjects in this study received EOS determination, including 18 cases in the FeNO normal group, with an average blood EOS of (2.46 ± 1.16)% and 25 cases in the FeNO

elevated group, with an average blood EOS of $(4.88 \pm 2.10)\%$. Statistical analysis of the differences between the two groups showed that there were statistical differences ($P < 0.05$).

As a result, the syndrome of apoplexy pathogenic to the lung in UACS TCM syndrome type is closely related to the increase of FeNO level. The symptoms closely related to FeNO level include odor stimulated cough, pharyngeal itch, night cough, dry cough, intermittent cough, etc., and the above clinical manifestations are basically consistent with the clinical manifestations of wind pathogenic to the lung syndrome diagnosed in TCM syndrome type. Exhaled nitric oxide shows higher sensitivity than lung function, can detect and diagnose diseases earlier, and can better reflect the TCM syndrome characteristics of patients with chronic cough. The percentage of eosinophils in peripheral blood of UACS was positively correlated with the increase of FeNO level.

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Discussion on schisandra in the treatment of type 2 diabetes based on the theory of “sour gram sweet” and “vinegar-processed the liver meridian” in Chinese medicine

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Abstract

Schisandra chinensis is a famous traditional Chinese medicine in China, which has a long medicinal history. The theory of Chinese medicine believes that type 2 diabetes (T2DM) belongs to the category of "Xiao Ke", the patient ate too much fat and sweet, The patient eats too much fat and sweet, resulting in the accumulation of sweet substances in the body to form the evil of sweetness and turbidity. In clinical compound, Schisandra chinensis "sour gram sweet" is often used to treat type 2 diabetes, and according to the processing theory, "vinegar-processed into the liver meridian", so that its vinegar products show better therapeutic effects. This study starts from the classic theory that vinegar making Schisandra enhances the "sour" taste and "vinegar enters the Liver Meridian", combined with the theory of five elements and five flavors of traditional Chinese medicine that "sour gram sweet, sour enters the liver and regulates stagnation". ”and aim at diabetes, the "evil of sweet turbidity" and "Liver failing in controlling dispersion" pathogenesis, the interpretation is based on the "sour gram sweet" five-flavor theory, and "vinegar-processed into the liver meridian" Traditional Chinese medicine processing theory to enhance the efficacy of Schisandrae Chinensis Fructus Processed with Vinegar in the treatment of diabetes, aiming to provide certain theoretical and clinical practical value for the treatment of diabetes.

Keywords

Schisandra chinensis; Type 2 Diabetes Mellitus; sour restrains sweet; vinegar-processed; Liver Meridian

Modern medical research shows that type 2 diabetes mellitus (T2DM) is now the third largest chronic non-communicable disease in humans after tumors and cardiovascular diseases, with more than 100 complications, which can endanger systemic vascular lesions and lead to brain, eye, heart, kidney, foot, peripheral nerve and other damage. Clinically commonly used biguanide, insulin and other drugs for treatment, although the hypoglycemic effect is obvious, but often appear liver and kidney dysfunction, gastrointestinal discomfort and other side effects. China's ancient famous old Chinese medicine for thirst quenching, that is, diabetes etiology and therapy of many understandings are very reasonable, pay attention to the overall concept, from the overall perspective of patients, the therapeutic effect is more relaxed and lasting, in view of the "evil of sweet turbidity" and "liver failure catharsis" of diabetes, the theories of "sour gram sweet" and "acid to supplement the liver, nourish the liver yin, and enhance the drainage of the liver" are used clinically, and the clinical application of "suan wei yu xiao soup", "sheng gan jiang tang fang" and "suan sheng gan" compound have remarkable efficacy. In the prescription, Schisandra chinensis is used as a king's medicine or a courtesy medicine, indicating that the treatment of diabetes by Schisandra is attributed to its "sour" taste, has astringent and astringent, and because of its "sour

gram sweet" effect after the vinegar system, and "vinegar-processed the liver meridian, and the liver governs catharsis" function is superior to raw products, and diabetes polydiuria evidence is more appropriate. Therefore, this paper explains that the use of Schisandra chinensis vinegar to treat type 2 diabetes under the guiding ideology of "sour gram sweet" and "vinegar-processed the liver meridian" will play a greater role in the clinical prevention and treatment of diabetes and related complications in modern medicine, in order to open up new ideas for medical treatment of diabetes.

Objective

Discussion on prevention and treatment of type 2 diabetes with Schisandra chinensis vinegar based on "sour gram sweet" and "vinegar-processed the liver meridian"

Materials and methods

This study starts from the classic theory that vinegar making Schisandra enhances the "sour" taste and "vinegar enters the Liver Meridian", combined with the theory of five elements and five flavors of traditional Chinese medicine that "sour gram sweet, sour enters the liver and regulates stagnation". "and aimat diabetes, the "evil of sweet turbidity" and "Liver failing in controlling dispersion" pathogenesis, the interpretation is based on the "sour gram sweet" five-flavor theory, and "vinegar-processed into the liver meridian" Traditional Chinese medicine processing theory to enhance the efficacy of Schisandrae Chinensis Fructus Processed with Vinegar in the treatment of diabetes

Results and discussion

In the clinical use of traditional Chinese medicine, Schizandra is often used to treat diabetes, of which vinegar Schisandra is superior to raw products, because it has the "sour" taste enhanced "sour kegan" effect, and "vinegar into the liver through the liver main drainage" function. Among them, the increase in sour taste is astringe yin and stop sweating of "acid over sweet", and the effect of shrinking urine and thirst is enhanced, while "vinegar-processed into the liver meridian" emphasizes the "liver main drainage" to regulate blood glucose homeostasis. Therefore, vinegar schisandra is a tonic, which is more appropriate to the diabetes mechanism proposed by Traditional Chinese medicine, and can alleviate symptoms such as thirst, hunger, frequent urination and weight loss. Therefore, it has certain theoretical and clinical practical value to explore the prevention and treatment of type 2 diabetes under the perspective of "sour gram sweet" and "vinegar-processed into the liver meridian".

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Discuss the effect connotation of "nourishing Yin and improving water" based on material and energy metabolism

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Abstract

According to the theory of traditional Chinese medicine, edema due to kidney yin deficiency belongs to the category of edema, the origin of which lies in the kidney [1-4]. The herb *Scrophularia ningpoensis* Hemsl is the dried root of *Scrophularia ningpoensis*, which is sweet, bitter and salty in taste and slightly cold in nature, and belongs to the lung, stomach and kidney meridians. It has the effect of clearing heat and cooling the blood, nourishing Yin and lowering fire, and detoxifying and dispersing nodules^[5-6]. In this experiment, we used urine metabolomics technology combined with pharmacodynamics and histopathology to investigate the efficacy of "nourishing Yin and promoting water" from the perspective of material and energy metabolism. To search for potential biomarkers and associated metabolic pathways through key targets, so as to further provide theoretical basis for the safe clinical application of "nourishing Yin and promoting water" effects of Xuan Ginseng. It provides theoretical support for the treatment or alleviation of such diseases by genistein, and also provides a strong scientific basis for the future development of new drugs and their safe clinical application.

Keywords

Radix scrophulariae; Material energy metabolism; Kidney-yin deficiency and nephrogenic edema; Urine metabolomics; Pharmacodynamics indicators

Objective

To explore the effect of radix scrophulariae and its effect on substance and energy metabolism in rats with renal Yin deficiency and edema, and to explain the function connotation of radix scrophulariae "nourishing Yin and benefiting water" through its expression on substance and energy metabolism.

Materials and methods

forty-eight male SD rats were randomly divided into blank group, Yin deficiency group, Yin deficiency recovery group, Yin deficiency edema group, furoxamil group and radix scrophulariae group, with 8 rats in each group. Except the blank group, the other groups were given the mixture of thyroxine and rexepin injection intragastric for 10 consecutive days to replicate the model of kidney-yin deficiency in rats. On the 11th day, the edema group and scrophulariae ginseng administration group were given intraperitoneal injection of aminoside purinomycin (PAN) solution to replicate the model of nephrogenic edema. The group was given water decoction of scrophulariae ginseng by intragastric administration from 12th. On the 18th day, kidney tissue was taken for light and electromicroscopic examination. Blood and urine were treated for Scr, BUN, T, T3, T4, T, E2, cAMP/cGMP, TP, ALB, UP and other relevant pharmacodynamics indicators. At the same time, the UPLC-Q-TOF-MS technique was used to analyze the urine of rats in each group to explore the potential biomarkers and the most correlated pathways of matter and energy metabolism.

Results and discussion

Pathological results showed that compared with the normal group, the kidney of all Yin deficiency groups had different degrees of pathological damage; Compared with the Yin deficiency groups, the scrophulariae group and furosemide group significantly improved the pathological injury degree of model rats; In terms of pharmacodynamics indexes, Scr, BUN, T, T3, T4, T, E2, cAMP/cGMP, TP, ALB and UP levels could be adjusted in Scr group. In addition, metabonomics results showed that scrophulariae group could ameliorate the deviation of metabolic trajectory in model rats. At the same time, 14 biomarkers with common differences with model and scrophulariae intervention were found, involving 15 related metabolic pathways, which were mainly enriched in energy metabolism and amino acid metabolism by analysis of related metabolic pathways.

Conclusion

It is speculated that radix scrophulariae can exert the functions of nourishing Yin and nourishing water by regulating the related indexes of material energy stage, urine metabolites and energy metabolism-related pathways, so as to achieve the therapeutic effect of diseases, thus further providing theoretical basis for the safe clinical application of the functions of nourishing Yin and nourishing water.

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Research Status and Prospect of Chinese Herbal Medicine Volatile Oil in the Prevention and Treatment of Depression

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Abstract

Depression is a common mental disease in the current society. Because its incidence rate is increasing year by year, it has become a hot social problem to be solved urgently. The existing clinical antidepressants have deficiencies in the onset time, treatment effect, side effects and other issues. Plant volatile oils, especially traditional Chinese medicine volatile oils, have become a new research hotspot because of their rapid onset, rapid metabolism in vivo, wide range of applications, and many action targets. By searching the relevant research on the treatment of depression with volatile oil of traditional Chinese medicine in recent years, this paper compares and analyzes the administration methods, effective mechanism and experimental results in relevant experiments, in order to provide reference for the research and application of volatile oil of traditional Chinese medicine in the treatment of depression, provide theoretical support for the development of traditional Chinese medicine volatile oil health products with antidepressant effect, and promote the development of traditional Chinese medicine health industry.

Keywords

depression; Chinese herbal medicine; volatile oil; Aromatherapy

Depression, also known as depressive disorder, is a common mental disease in current society. Depression will increase the risk of cardiovascular disease, metabolic syndrome and other chronic diseases [1-2], and serious cases can lead to suicide. According to the relevant statistics of the World Health Organization, by 2019, more than 300 million people in the world have suffered from depression [3], and depression has become a social problem that cannot be ignored. As a kind of effective component widely existing in Chinese herbal medicine, volatile oil of traditional Chinese medicine has the characteristics of rapid onset, multi-target effect, rapid metabolism in vivo and so on. Its treatment of depression has a broad research space. This paper analyzes the current research status of depression by sorting out the relevant research on the treatment of depression with volatile oil of traditional Chinese medicine in recent years, in order to provide reference for the application of volatile oil of traditional Chinese medicine in the treatment of depression.

Common ways of action of volatile oil of traditional Chinese Medicine

At present, the common ways of action of volatile oil are regulated by olfactory system, skin and mucosa, digestive tract, etc. Studies have shown that the volatile oil of traditional Chinese medicine can enter the brain quickly after nasal administration, and its bioavailability in brain tissue is significantly higher than that in other tissues and organs, with rapid effect and good targeting. Modern medical research has proved that volatile oil has a good penetration promoting effect. Its hydrophobicity and small molecular characteristics make it easy to be absorbed by skin and mucosal tissue, and then quickly enter the systemic circulation. In traditional Chinese medicine theory, traditional Chinese medicine containing volatile oil mostly has the nature and taste of Xinsan. Traditional Chinese medicine believes that Xinwei can open up the reason, so as to achieve

the effect of internal disease and external treatment. In recent years, most of the studies on the treatment of depression with volatile oil of traditional Chinese medicine still take effect by intragastric administration through the digestive tract.

Overview of research on the mechanism of volatile oil of traditional Chinese Medicine

As for the pathogenesis of depression, the current mainstream theories include monoamine neurotransmitter theory, neuroendocrine theory, inflammatory reaction theory, and neurotrophic factor theory. The existing treatment of depression is still based on Western medicine intervention, but western medicine treatment cycle is long, there is a risk of side effects, and it is also easier to relapse after withdrawal. Traditional Chinese medicine treatment has faster metabolism and fewer side effects, especially the treatment of aromatic drugs can reduce the stress sensitivity of patients, which is more helpful to relieve emotions and adjust mental state. Monoamine neurotransmitters are the most commonly used treatment entry point, and the research on the action mechanism of volatile oil of traditional Chinese medicine related to its content change is the most common. The volatile oil of traditional Chinese medicine, such as asarum, frankincense and *Lepidium indicum*, has been proved that its treatment mechanism of depression is related to the change of monoamine neurotransmitters .

Existing research problems

In recent years, most of the studies on the treatment of depression with volatile oil have taken the form of intragastric administration, as well as inhalation, sniffing and so on. Although different ways of administration can regulate depression, different pathways still need further comparative study in terms of onset speed, treatment effect, drug utilization efficiency and so on. In addition, whether the final effect will be affected by the same metabolic pathway, but different ways of administration, the different dosage per unit time, that is, the different intensity of administration, is worth studying after controlling the variables, in order to explore the possibility of using different ways of administration according to the different stages of patients in clinical treatment.

In the aspect of mechanism research, the mechanism of traditional Chinese medicine volatile oil in the treatment of depression is mostly verified by detecting the changes of monoamine neurotransmitter content. However, in recent years, in the field of depression research, there are increasing discussions about BDNF. In the field of traditional Chinese medicine, studies have proved that traditional Chinese medicine and traditional Chinese medicine preparations can regulate the growth and regeneration of neurons by regulating BDNF, so as to play a role in the treatment of depression. Then, as an important effective component of traditional Chinese medicine, whether the volatile oil of traditional Chinese medicine can also play a therapeutic role through the same mechanism, and because of its high fat solubility, strong volatility and other characteristics, it is worth further exploration and research.

Conclusion and Prospect

As a common mental disease in today's society, depression will not only bring economic burden, but also have a negative impact on people's daily life and even the progress and development of society. It is worth noting that in addition to depression, there are also some patients who have depressive symptoms but fail to meet the diagnostic criteria of depression. Patients in this situation can be diagnosed as depressed. Whether the intervention of depression can reduce the incidence of depression needs further clinical observation and research. As a kind of aromatherapy of traditional

Chinese medicine, volatile oil has less side effects on human body than drug treatment, and it is easier to be applied in people's daily life to relieve emotions and anxiety. The author believes that under the health centered medical development trend, the development of volatile oil of traditional Chinese medicine should have broad prospects for development. Further clarify the pharmacological mechanism of traditional Chinese medicine volatile oil in the treatment of depression, develop unique and advantageous aromatic preparations, give play to the unique "preventive treatment" diagnosis and treatment idea in traditional Chinese medicine theory, and widely apply traditional Chinese medicine volatile oil with antidepressant effect to people's daily life, which is of great significance to better maintain people's physical and mental health and promote the development of traditional Chinese medicine health industry.

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Research progress of pain treatment with traditional Chinese medicine based on TRPA1

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Abstract

Because of its wide distribution in many types of cells, TRPA1 can mediate the production of many pain diseases. This paper reviews the research situation of TRPA1 and pain related diseases in the treatment of traditional Chinese medicine in recent years.

Keywords

TRPA1; Traditional Chinese medicine; pain

Transient receptor potential ankyrin 1 (TRPA1) is a non selective cation channel in the trpa subfamily. TRPA1 participates in the transmission of various pathophysiological pain, and is the final pathway of a large number of chemically diverse pain agonists. It may be a potential target in the treatment of pain. ^[1]

Neuropathic pain

TRPA1 exists in dorsal of ganglia (DRG), spinal motoneurons, peripheral nerves, enteric myenteric plexus neurons, vagus nerve, trigeminal nerve and other neurons in the human nervous system. Astragaloside (Ag) is one of the main effective components of Huangqi Guizhi Wuwu decoction. Ag can significantly reduce the expression level of TRPA1 in DRGs of chronic restriction injury of the scientific nerve (CCI) rats, thereby improving the degree of cell vacuolation and degeneration in DRGs, reducing the proportion of DRGs neurons in the process of necrosis, and delaying the process of nerve necrosis. ^[2]

Intestinal bowel syndrome

Irritant bowel syndrome (IBS) is a highly common complex functional gastrointestinal disease. Tongxie Yaofang can significantly reduce the secretion of 5-hydroxytryptamine (5-HT) in RIN-m, reduce the expression of TRPA1 mRNA and protein in its cells, reverse the imbalance of intestinal endocrine cells by inhibiting the activation of TRPA1, regulate the expression of 5-HT, and reduce the secretion level of inflammatory factors, so as to achieve the purpose of treating IBS. ^[3]

Intestinal inflammation

Intestinal inflammation is a kind of intestinal inflammatory disease with chronic recurrence and remission of persistent abdominal pain. TRPA1 on the chromaffin cells in the intestinal wall is the detector of the stimulation signal in the intestinal cavity. When it is adversely stimulated, it will release 5-HT to promote the frequency of intestinal peristalsis to expel the irritants. Xiaojianzhong decoction can improve the pathological changes of inflammatory tissues in jejunum and colon, and reduce the expression of TRPA1, 5-HT and 5-HT specific receptors 5-HT_{3R}, 5-HT_{4R}. Thus, the intestinal peristalsis frequency and inflammatory reaction are regulated. ^[4]

Chronic pancreatitis

Chronic pancreatitis (CP) is a destructive disease characterized by persistent pain, inflammation and irreversible morphological changes, accompanied by partial or total loss of pancreatic function. Wuzhuyu decoction, Xiaojianzhong Decoction and Lizhong pill can reduce the expression of

TRPA1 in pancreatic tissue under CP, indicating that TRPA1 is the key target of CP treatment and analgesia. [5]

Migraine

At present, it is believed that the occurrence of migraine is mainly contributed by the calcitonin gene related peptide (CGRP) of trigeminal nerve. The activity of TRPA1 in trigeminal nerve is related to the release of CGRP. Such abnormal pain is often related to the neuronal phenomenon mediated by TRPA1 activation and subsequent oxidative stress. Qingnaozhitong capsule can effectively reduce the expression levels of TRPA1, CGRP and cyclooxygenase in brain tissue, and its mechanism may be to improve pain symptoms by reducing TRPA1 signal transduction. [6]

Expectation

The application of TRP family in the molecular mechanism of modernization of traditional Chinese medicine is still in its infancy. Traditional Chinese medicine has an amazing curative effect on the pain treatment of various diseases since ancient times, and the number of cured cases is invincible. The intervention of TRPA1 has brought a new target for the exploration of modern molecular mechanism of traditional Chinese medicine in the treatment of pain.

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Protective effect of Tianyang Pill on renal function of streptozotocin (STZ) - induced diabetic kidney disease mice

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Objective

To study the protective effect of Tianyang Pill on renal function in streptozotocin (STZ)-induced diabetic kidney disease (DKD) mice.

Keywords

Tianyang Pill; diabetic kidney disease; mice;Crea;Urea;ALB

Methods

The DKD model was established by intraperitoneal injection of STZ in the model preparation group, and the mice successfully replicated were randomly divided into model group, Tianyang pill group and metformin group. Tianyang pill was given intragastric administration according to 12.5g/(kg ·d), metformin was given intragastric administration according to 200mg/(kg ·d), and the control group and model group were given the same amount of normal saline every day for 3 weeks. After the last administration, the blood glucose level of mice was detected, the urine of mice was collected, the 24-hour urinary protein was measured by urine protein detection kit, the body mass and kidney wet weight of mice were measured, and the kidney coefficient was calculated. The levels of serum total cholesterol (TC), triglyceride (TG), creatinine (Crea), urea (Urea) and albumin (ALB) were detected by automatic biochemical analyzer. Serum AGEs, PCX and Nephritin protein levels were measured by ELISA kit, renal tissue PCX and Nephritin mRNA levels were detected by RT-PCR, and renal histopathological changes were observed by HE, PAS and Masson staining.

Results

Compared with the control group, the levels of 24-hour urinary protein, blood glucose, renal coefficient, serum Crea, Urea, ALB and AGEs in the model group were significantly higher ($p < 0.05$).

Compared with the model group, the levels of 24-hour urinary protein, renal coefficient, serum Crea, Urea and ALB in the Tianyang pill group were significantly lower ($p < 0.05$), while the levels of serum PCX, Nephritin protein and renal PCX and Nephritin mRNA in the Tianyang pill group were significantly higher ($p < 0.05$).

Conclusion

Tianyang Pill can significantly improve the levels of 24-hour urinary protein, renal coefficient, serum Crea, Urea, ALB, AGEs, PCX, Nephritin and renal tissue PCX and Nephritin mRNA in DKD mice, and significantly improve the renal function of DKD mice.

Effects of acupoint electrical stimulation on limb motor functional reconstruction after stroke

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Abstract

The aim of this study was to explore the effects of electrical acupoint stimulation on limb motor dysfunction after stroke. Patients who meet the inclusion criteria are randomly divided into two groups--acupoint electrical stimulation group and non-acupoint electrical stimulation group. The treatment duration was 8 weeks and follow-up was 3 months. Scale evaluation was compared before and after treatment.

Keywords

stroke, limb motor dysfunction, traditional Chinese medicine, functional electrical stimulation. Stroke is a devastating neurological disease with a high disability rate and mortality [1], with limb motor dysfunction left in most patients [2]. The rehabilitation of limbs is time-consuming [3]. It is a difficult point of stroke sequela, and a lot of exploration on different rehabilitation therapies have been conducted by domestic and foreign scholars. With the increasing recognition of traditional Chinese medicine (TCM), especially acupuncture, the therapies of stroke sequelae by integrated traditional Chinese and Western medicine have been widely used. In recent years, functional electrical stimulation (FES) has been concerned in rehabilitation field. Therefore, the combination of FES and TCM acupoint therapy on limb functional reconstruction after stroke is worth further study.

Objective

To explore the effects of acupoints combined with FES in the treatment of limb motor dysfunction after stroke and to compare the clinical effect difference between acupoint electrical stimulation and non-acupoint electrical stimulation.

Materials and methods

The patients were stroke inpatients meeting the inclusion criteria in the Second Affiliated Hospital of Heilongjiang University of Chinese Medicine, all of whom had imaging support. After signing the informed consent, all patients were randomized divided into two groups in a blind manner--acupoint electrical stimulation group and non-acupoint electrical stimulation group with 100 cases in each, and the treatment lasted for 8 weeks. Before and after the whole treatment, the outcome variables included MBI [4], CSS [5], FMA [6] and Brunnstrom [7] were evaluated. SPSS 26.0 statistical software were used for analysis.

Results and discussion

Patient demographics: age, gender, course of disease, functional damage and serious underlying diseases, date of admission. MBI, CSS, FMA and Brunnstrom were both improved after the two treatment and patients in the acupoint electrical stimulation group had more curative effects.

Stroke is a common complex nervous system disease with a rising prevalence and morbidity [8]. Abnormal movement patterns can affect the recovery of motor function and cause wrong posture, which needs to be corrected timely. By stimulating the corresponding acupoints of the limbs at low

frequency, the contractile ability of the muscles is enhanced, the relaxation and contraction function of muscle groups is coordinated, to effectively improve the motor function of the affected limb and promote the recovery of the central nervous system. Through the evaluation scales, the curative effects will be visualized and objectified for better interpreting the movement of the central nervous system control strategy, which may provide a new reference for integrated traditional Chinese and Western medicine in the treatment of motor function recovery after stroke.

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Inflammation and inflammation-targeting therapies in DR

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Abstract

Diabetes mellitus (DM) leads to a series of physiologic and metabolic alternations in the retina, but which of these changes is still unclear to acknowledged characteristics of diabetic retinopathy (DR). A number of the physiologic and molecular mechanisms that have been verified to underlie DR fit with inflammation. Furthermore, the progression of diverse aspects of DR has been apparently hindered in animal models by some anti-inflammatory treatments. Herein, we review the role of inflammation in DR and focus on the current inflammation-targeting treatments in DR.

Keywords

diabetic retinopathy, inflammation, anti-inflammation, therapy

Diabetic retinopathy (DR) is the chief reason for visual damage or loss in the diabetic population globally ^[1]. Among microvascular complications of DM, including diabetic cardiomyopathy and nephropathy, the prevalence rate of DR is very high. According to the latest systematic review and meta-analysis, the prevalence rate for DR and vision-threatening DR was 22.27% and 6.17% among DM patients in the global world ^[2]. The huge public health burden of DR worldwide underscores the significance of constantly seeking new strategies surpassing current standards of diabetes care. Many hypothetic mechanisms have been proposed to elucidate the pathogenesis of DR, including oxidative stress, advanced glycation end-products (AGE), vascular endothelial growth factor (VEGF), and others ^[3]. Among them, inflammation plays a significant role in DR as the chronic inflammatory state contributes to long-term complications of diabetes like DR and many of molecular changes consistent with the role of inflammation have been observed in DR animals and patients ^[4]. The detailed mechanisms remain to be clarified, but these inflammatory alterations seem to contribute to DR progression since their block has been observed to hinder retinal abnormalities in DM animal models ^[5]. In this review, we will first review the role of inflammation DR, and then highlight the current inflammation-targeting therapies in DR.

The role of inflammation in DR

Inflammation is a non-specific response to stress or damage via many molecular mediators, which is regarded as a subsequent event of disturbed glucose metabolism and elevating insulin resistance ^[6]. As we know, the pathological manifestation of DR (the chronic low-level inflammation situation) shares many similar features with chronic inflammatory ailments: elevated vascular permeability, edema, enhanced expression of angiogenic factors, and so on. In immune-dependent pathologies, the inflammatory course leads to a complicated cascade reaction that changes the physiological responses of the influenced eyes. Diabetes and other inflammatory stimuli may disturb the homeostasis of the eye, subsequently generating an “inflamed” phenotype. Thus, the expression of cytokines, including IL-1, VEGF, MCP-1, and so forth, is elevated, and the apoptotic phenomenon is enhanced which, taken together, result in the onset of DR. Inflammation may contribute to the destructive effects on vascular and neuronal sections of the retina mediated by DR ^[7].

Current inflammation-targeting therapies

Rigorous diabetic control is still the best-authorized strategy to restrain/prevent diabetic complications, but the block of inflammation might promote hindering DR even in the existence of hyperglycemia. Salicylates that curb COX enzyme-mediated leukostasis and ICAM-1 expression are worth discussing since their profitable effect has been suggested in research reporting decreased incidence of DR in patients administrating salicylates for rheumatoid arthritis [8]. However, contradictory conclusions were yielded in the prospective clinical human trials with some studies showing no benefit (or harm) of aspirin on DR, which may contribute to the dose of aspirin taken was not enough to have had anti-inflammatory actions [9]. Alternatively, due to the elevated incidence rate of stroke and heart attack, it is impossible to apply specific COX-2 inhibitors systematically [10], preclinical studies with topical administration were observed to alleviate signs of DR [11].

Inflammatory Molecules are also targeted to intervene in DR, including TNF α , IL-1 β , leukostasis, and so forth. For example, Infliximab (a TNF α neutralizing antibody) lessened macular thickness and ameliorated visual acuity in 4 sufferers who were unable to better respond to laser photocoagulation therapy [7, 12]. But more large-population trials are necessary to demonstrate the efficacy of these medicines in DR patients.

Besides, other inflammatory components could be the potential targets to treat DR as well. Angiopoietins stands for a family of inflammatory cytokines that combine with the receptor tyrosine kinase Tie2 and are significant modulators of angiogenesis. The recent research also declared that Ang-2 modulated the TNF- α -induced expression of ICAM-1 to promote the adhesion of monocytes and the subsequent tissue inflammation. Therefore, the Ang-2 pathway is currently being targeted in a recent ongoing clinical trial with a Tie-2 activator in patients with non-proliferative DR, where ameliorations in DR severity will be assessed.

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Research on the Discovery Strategy of Q-markers of Traditional Chinese Medicine——Chinmedomics

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Abstract

Quality markers(Q-markers) is a new concept of quality control for traditional Chinese medicine (TCM). Since its introduction in 2016, it has received extensive support and participation from researchers and manufactures of the entire industry. The core theories and research methods of quality markers are summarized from five aspects: “effectiveness”, “specificity”, “transfer and traceability”, “compatibility environment” and “measurability”. Chinmedomics, integrates serum pharmacochemistry and metabolomics technique, on the premise of corresponds of prescription-syndrome with therapeutic effect, it can not only find the material basis of the prescription efficacy, but can be applied to search Q-markers which are related to clinical efficacy, reflecting compatibility of prescriptions. Thus to solve the technical problems of finding and confirming Q-markers of TCM in a comprehensive way, and ensure the validity and safety of TCM.

Keywords

Q-markers, Discovery strategy, Chinmedomics, Quality control, Classical formula

Introduction

The Q-marker should be a chemical constituent that: (1) has clear chemical structure and biological activity; (2) chemical specific to a medicinal material (decoction pieces) but not from other medicinal materials; (3) is either intrinsic in herbs or formed during processing; (4) preferably represents the “king (Jun)” herb according to the principle of TCM compatibility, but also considering “minister (Chen), assistant (Zuo), guide (Shi)”;

(5) can be qualitatively identified and quantitatively determined [1,2]. In the latest Q-markers research of Sijunzi decoction (SJZD) conducted by the Chinmedomics method, researchers preliminarily determined malonyl-ginsenoside Rb₂ and ginsenoside Ro as the Q-markers of ginseng(*Panax ginseng* C. A. Mey.); dehydrotumulosic acid and dihydroxy lanostene-triene-21-acid as the Q-markers of poria(*Poria cocos* (Schw.) Wolf); glycyrrhizic acid, isoglabrolide, and glycyrrhetic acid as the Q-markers of licorice(*Glycyrrhiza uralensis* Fisch.); and 2-atractylenolide as the Q-marker of macrocephala(*Atractylodes macrocephala* Koidz.) [3].

Strategies for the discovery of Q-markers in classical formulas

Classical formulas are ancient prescriptions that are still widely used, have definite curative effects, and have obvious characteristics and advantages. For the development and research of classic prescriptions, researchers not only need to find Q-markers for final quality control, but also need to establish a full-process quality control system, including the source of medicinal materials, production, transportation, preparation, metabolic processes in the body, and the final expression of biological effects. Faced with the above problems, Chinmedomics is still a powerful research method, the specific research ideas has shown in Figure 1. Firstly, we need to conduct basic quality

inspections of medicinal materials and decoction pieces, which should at least meet the pharmacopoeia standards, and then conduct quality delivery inspections of intermediates. After ensuring that the quality of the raw materials is stable, the ancient books are further consulted to determine the dosage of the prescription, and then the decoction process is investigated, and the corresponding actual product is finally obtained. In addition to *in vitro* analysis of the corresponding actual product to determine which medicinal material each ingredient belongs to, an *in vivo* verification experiment is also carried out. Including animal modeling, model evaluation, finding biomarkers, then administering the model and evaluating the efficacy, analyzing the serum sample information, and combining the results of *in vitro* analysis to find the migrating constituents in blood. Correlation analysis (PCMS) of migrating constituents and biomarkers in blood is underway, combining the two requirements of specificity and transfer and traceability, and finally determine the Q-markers of the classic prescription. Based on the research results of Q-markers, further research on characteristic fingerprints and content determination is carried out, and a quality standard system for chemical components related to efficacy is established ultimately.

Results and discussion

Applying the above research strategies, Q-markers discovery study was carried out on the classical formula Guyinjian decoction (GYJ). GYJ is a traditional Chinese formula for the treatment of liver and kidney yin deficiency, which derived from the book "Jing Yue Quan Shu", Volume 51, written by Zhang Jingyue in the Ming Dynasty. Modern clinical studies have shown that GYJ has definite therapeutic effect for the treatment of gynecological diseases such as polycystic ovary syndrome, menopausal syndrome, kidney deficiency-type menorrhagia, intermenstrual bleeding, and functional uterine bleeding etc. The experimental results show GYJ can effectively intervene in functional uterine bleeding model rats, mainly through Morroniside, Schisandrin A, Catalpol, Glycyrrhizic acid, Liquiritin, Loganin, Hyperoside, Polygalaxanthone III, Rinsenoside Re, Liquiritin apioside, p-hydroxycinnamic acid, glycyrrhetic acid, 8-episoxylic acid, Glycyrrhizin, Cistanoside A, Licochalcone B, Dihydroferulic acid, Quercetin, Glycyrol, Cistanoside F, Schisandrin B, Protocatechuic acid-3-glucoside, Apigenin, 5-Hydroxymethyl-2-furancarboxylic acid, Sinapinic acid, key *in vivo* significant components, regulating tyrosine metabolism and steroid hormone biosynthesis, pentose and glucuronic acid biosynthesis, arachidonic acid metabolism, lipid metabolism, fatty acid metabolism, protein catabolism, ubiquinone and other terpene quinones biosynthesis play a role. Through PCMS correlation analysis, the final determination of Ginsenoside Re, Catalpol, Hyperoside, Schisandrin A, Polygalaxanthone III, 3',6-Disinapoylsucrose, Morroniside, Loganin, Glycyrrhizic acid, Liquiritin are the key components related to the efficacy of GYJ in the treatment of functional uterine bleeding, so these are determined as Q-markers. The above research results demonstrate that the Chinmedomics strategy can be perfectly applied to the discovery research of Q-markers, and it is worthy of further promotion and application, which will contribute to the innovation and development of the Sino-Russian health industry.



Figure 1. Strategies for the discovery of Q-markers in classical prescriptions using Chinmedomics.

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Uncovering traditional Chinese medicine with modern technology

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Abstract

Purpose and Significance: Traditional Chinese medicine (TCM) theory has been summarized by thousands of years of experience, and continues to use natural science culture to enrich and develop in practice, so that it has a unique scientific connotation, but traditional theory is difficult to be understood by modern society. Applying the modern technology to reveal and fully interpreting the TCM has become an urgent problem to be solved. **Method:** Summarize the application of modern technology in the quality control, effectiveness, pharmacodynamic material basis and mechanism of action of TCM. **Results and Conclusions:** The combination of TCM and modern technology promotes the inheritance, innovation and development of TCM, thereby promoting the modernization and internationalization of TCM.

KeyWords

Traditional Chinese medicine; Modern technology; Development;

Introduction

Traditional Chinese medicine (TCM) has received increasing attention in the international community because its treatment concept of syndrome differentiation and treatment coincides with the concept of precise treatment^[1]. The international status of TCM is increasingly important, which has broad prospects for the development of TCM. However, the unique scientific connotation and therapeutic theory of TCM are quite different from the modern medical expression system. Therefore, the use of modern technology to decipher and express the characteristics of TCM has become an important proposition in the field of modern life sciences. At present, many modern technologies play a role in the field of TCM research^[2].

1. Structural identification of compound

The analysis and identification of active components of TCM is the premise of elucidating its pharmacodynamic material basis, and it is also the basis and core of quality control of TCM. Nuclear Magnetic Resonance can be used for high-throughput, qualitative and quantitative analysis of the complex chemical composition of traditional Chinese medicine, and in the identification and structural identification of organic and biochemical molecules. Feng et al.^[3] used quantitative proton nuclear magnetic resonance spectroscopy (¹H-qNMR) to quantitatively and qualitatively analyze isoimperatorin columbia, and osthole in *Angelica sinensis*.

Capillary electrophoresis (CE) has become a component of modern Chinese medicine composition separation and identification technology because of its advantages of high efficiency, rapidity, accuracy and sensitivity, easy operation, less solvent consumption, low cost and less environmental pollution. Yang et al.^[4] based on a capillary electrophoresis-chemiluminescence method for the simultaneous determination of four phenolic acids found in Shuanghuanglian oral liquid.

2. Compatibility rule of TCM

Liquid chromatography-mass spectrometry Liquid chromatography-mass spectrometry (LC-MS) complements the superior separation performance of liquid chromatography with high selectivity

and sensitivity of mass spectrometry, and has the advantages of wide analytical range, strong separation ability, reliable qualitative analysis results, and high automation. Ren et al.^[5] revealed the attenuation mechanism of *Aconiti kusnezoffii* combined with Yunnan Baiyao based on UPLC-MS and found that 17 endogenous serum metabolites with potential toxicity were regulated to normal levels during compatibility. By comparing the number of protein expression, the compatibility of TCM can also be studied. Zhu et al.^[6] used proteomics to find that compared with decomposed recipe, the administration of Chaihu-Shugan-San increased the expression of 22 proteins.

3. Mechanism of action

TCM formula is composed of several herbs and dozens of components, which are decomposed into countless chemical molecules, so it is a very difficult thing to clarify the mechanism of action of TCM and an important issue that afflicts the internationalization of TCM. Yu et al.^[7] used a comprehensive strategy of qRT-PCR assay, Western blotting, and 16S rDNA high-throughput sequencing to find that Prim-O-glucosylcimifugin avoids the development and progression of ulcerative colitis by inhibiting ERK1/2, AKT, JNK1/2, I κ B- α , p38, and p65 phosphorylation and up-regulating the expression of occludin, claudin-3, and ZO-1 proteins. Yin et al.^[8] found based on serum medicinal chemistry of TCM that Dachengqi Decoction played a therapeutic effect on colorectal cancer Colorectal cancer by regulating PI3K-AKT, AGE-RAGE and IL-17 signaling pathways.

4. Target exploration

Many studies have shown that the main active components of TCM can target one or more specific molecules and thus exert many clinical therapeutic effects. Construct the network of "multi-component-multi-target" to lay a foundation for subsequent precise treatment of TCM. The emergence of gene chip solves the shortcomings of traditional nucleic acid blot hybridization technology, such as cumbersome operation, long sample determination cycle and low operation and determination efficiency. Gene chip can be the main tool to express the results of genomics research of TCM. Hu et al.^[9] showed that microRNA-7 was the most upregulated miRNA in gastric cancer cells after Curcumol treatment according to microarray analysis results.

5. Future perspectives

The booming development of modern instruments and analytical technology and the continuous emergence of research strategies provide strong technical support for breaking through the bottleneck of TCM research, making the development of TCM more closely related to modern medicine and helping to promote the modernization process of TCM. This article only summarizes the contribution of several modern technologies in deciphering the scientific connotation of TCM, and I believe that more modern technologies will be applied to TCM in the future to build a more stable bridge of "traditional Chinese medicine-modern medicine".

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Pathogenesis of diabetic peripheral neuropathy and effective ways of herbal medicine intervention

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Abstract

Diabetic peripheral neuropathy (DPN) is the most common complication of all types of diabetes and the main cause of disability in diabetic patients. The occurrence of early DPN starts from the feet of diabetic patients and is "sock-like". With the development of the disease, it gradually involves the upper limbs, and eventually amputation leads to disability and even life-threatening. Based on the results of pathological studies, it was found that the pathogenesis of DPN is complex, involving multiple mechanisms such as hyperglycemia, polyol pathway activation, and oxidative stress. Chemical drugs, including methylcobalamin, α -zinc sulfate, and pentoxifylline, are often used to inhibit the development of DPN, but chemical drugs have limitations. There are a great number of side effects, and drug dependence is easy to occur. Secondly, the target is single, and it is impossible to achieve multiple targets and multiple ways to improve the related symptoms of diabetic peripheral neuropathy. Herbal medicine has the incomparable advantages of chemical drugs, that is, multi-component, multi-target, multi-level overall effect. Consequently, this article reviews the pathogenesis of diabetic peripheral neuropathy and the effective ways of herbal medicine intervention.

Keywords

Diabetic peripheral neuropathy, herbal medicine, pathogenesis, effective ways

According to data released by the International Diabetes Federation (IDF), there are more than 537 million people with diabetes worldwide, Accounting for about 10.5% of the global population. there are about 130 million diabetic patients in China, and another about 50 million potential diabetic patients. In the past 10 years, the number of diabetic patients in China has increased by 56%. As the number of diabetic patients has skyrocketed, the number of diabetic peripheral nerve patients, a common complication of diabetes, was daily on the increase. Diabetic peripheral neuropathy (DPN) refers to the symptoms related to peripheral and central nervous system dysfunction in diabetic patients who have been in a state of metabolic disorder for a long time. This complication is the leading cause of disability and even the culprit of death¹. DNP has the characteristics of bilateral symmetry, the lower limbs are heavier than the upper limbs, and the nighttime is heavier than the daytime. Initially, lesions appeared in the distal end of the lower extremities, and as the disease progressed, it gradually developed upward, forming a typical "sock-like" and "glove-like" shape. In addition, the pathogenesis of DPN is complex, involving multiple mechanisms such as polyol pathway activation, oxidative stress, and microcirculation disorders².

In view of the pathogenesis, symptomatic medication, chemical drugs such as methylcobalamin, α -zinc sulfate, epalrestat and pentoxifylline are used to interfere with the occurrence and development of DPN. Compared with chemical drugs, traditional Chinese medicine has mild medicinal properties and fewer side effects. At the same time, traditional Chinese medicine has the characteristics of multi-component, multi-target and multi-channel, which can realize

multi-component cooperation and enhance the therapeutic effect.

Pathogenesis of diabetic peripheral neuropathy

Oxidative stress is a large amount of reactive oxygen species produced in the body when the body is in a high-sugar environment for a long time, resulting in a serious imbalance between the production of reactive oxygen species and the antioxidant system in the body, and the excess reactive oxygen species damages the body's tissues³. Oxidative stress in this high-glucose environment activates the polyol pathway, leading to peripheral nerve damage.

Polyol activation refers to the activation of aldose reductase in blood vessels and peripheral nerves when blood glucose is higher than normal and normal glucose metabolism pathway can no longer meet glucose metabolism, and a large amount of sorbitol is produced⁴. Sorbitol accumulates in blood vessels and peripheral nerves, causing peripheral nerve damage.

Effective ways of herbal medicine intervention

Herbal medicine is a complex complexus, containing a variety of chemical components, each component cooperates or restricts each other, and exerts a variety of pharmacological effects. The study found that the traditional Chinese medicine Jinmaitong and XiongShao Capsule capsules are typical prescriptions for the treatment of diabetic peripheral neuropathy. All of them are rich in flavonoids and their glycosides, which are mainly used to treat diabetic peripheral neuropathy by resisting oxidative stress^{5,6}.

Baimai ointment is a kind of Tibetan medicine. Some scholars have studied the mechanism and pharmacodynamics of Baimai ointment in the treatment of diabetic peripheral nerves on the premise that its chemical composition has been determined. It was found that curcumin in Baimai ointment is the main pharmacodynamic substance, which mainly acts on IL6, IL10, TNF, CCL2, CXCL12, EGF, VEGFA, BDNF, TGF β 1 and TNF, as well as PI3K-AKT and MAPK signaling pathways, thereby improving mechanical and thermal effects. Painful hypersensitivity reactions⁷.

Perspective

As China's influence on the world stage has zoomed, herbal medicines are also widely used around the world. More and more authoritative scientific research institutions have also proved the effect and safety of herbal medicines through a variety of experiments. Following the historical trend, for purpose of bringing down the side effects of chemical drugs on patients and improving the happiness index of diabetic patients, the application of herbal medicine should be vigorously promoted. Adhering to the idea of both internal and external treatment of traditional Chinese medicine, the application of traditional Chinese medicine in diabetes and its complications is rapidly promoted.

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Mechanisms of bile acid metabolism regulating cholestatic liver disease

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Abstract

Cholestatic liver disease (CLD) is a type of hepatobiliary system disease in which the production, secretion and excretion of bile inside and outside the liver caused by various reasons, so that bile cannot normally flow into the duodenum and enter the blood. Bile acids can act as signaling molecules and metabolic regulators to regulate host lipid, glucose and cholesterol homeostasis by activating nuclear receptor and membrane receptor. Bile acids alter the gut microbiota to promote the development of CLD. Bile acids form a complex molecular regulatory network through multiple receptors, multiple signals, and multiple pathways to regulate their own metabolism, inflammatory response, cytotoxicity, autophagy and other biological processes, thereby regulating the occurrence and development of CLD.

Keywords

Bile acids, Metabolism, Cholestatic liver disease

Introduction

In recent decades, with the development of qualitative and quantitative analysis methods for bile acids, more and more evidences have shown that bile acids, as endogenous signaling molecules, can regulate glucose metabolism, lipid metabolism, energy metabolism, etc. and play an important role in CLD.

1. Synthesis of bile acids

The synthesis of bile acids takes cholesterol as raw material, and a series of enzymatic reactions occur through the classical pathway and the alternative pathway to form bile acids. The classical pathway is also called the neutral pathway, because the intermediate product of this pathway is neutral cholesterol, and cholesterol 7 α -hydroxylase (CYP7A1) is the rate limiting enzyme of this reaction pathway; cholesterol in the classical pathway firstly hydroxylate from 7 α site, and then 12 α is hydroxylated, 27 α is hydroxylated, breaking the side chain to generate cholic acid and chenodeoxycholic acid (CDCA), respectively, and then combine with taurine and glycine to form a conjugated primary bile acid[1].

The alternative pathway is also known as the acidic pathway, because it produces acidic cholesterol, which is started by sterol 27 α -hydroxylase (CYP27A1) and sterol 12 α -hydroxylase (CYP8B1), and finally produces CDCA. At present, the significance of the acid pathway is unclear, and there is evidence that it is up-regulated when the classical pathway is disrupted.

2. Mechanisms of bile acids metabolism regulating CLD

2.1 Nuclear receptor

The nuclear receptor farnesoid X receptor (FXR) widely exists in the liver, intestine and other tissues rich in bile acids, and its endogenous ligands are CDCA, deoxycholic acid, lithocholic acid and so on. An important pathological feature accompanying CLD is the accumulation of bile, which inevitably leads to changes in the composition and concentration of bile acids. When the bile acid

content is abnormal, especially the bile acid that has a strong stimulating effect on FXR is reduced, it will lead to an imbalance in the synthesis and transport of bile acid regulated by FXR, and eventually lead to the accumulation of high concentration of bile acid and cause liver damage. The FXR signaling pathway mainly inhibits hepatocyte bile acid synthesis, absorption or promotion of bile acid secretion into bile by regulating rate-limiting enzymes and transporters related to bile acid metabolism, so as to alleviate the toxic damage caused by excessive bile concentration[2, 3].

2.2 Membrane receptor

The G protein-coupled receptor TGR5 is one of the members of the G protein-coupled receptor superfamily, is mainly expressed in the gallbladder, liver, intestine and other tissues. It is a membrane receptor for bile acids and is involved in the occurrence and development of various metabolic diseases. TGR5 is activated after binding with bile acids, and by activating downstream signaling pathways such as CAMP/PKA and AKT signaling pathways, regulating the formation of cytokines and inflammasomes, and playing an anti-inflammatory, anti-cholestasis and anti-apoptosis role[4]. As an important regulator of maintaining energy homeostasis and bile acid homeostasis and regulating glucose metabolism, TGR5 also plays an important role in regulating the body's inflammatory response. TGR5 can inhibit inflammation by inhibiting the activity of NLRP3 and regulating the NLRP3-Caspase-1 signaling pathway[5].

2.3 Gut microbiota

In CLD, bile acids accumulate excessively in the liver, gallbladder, and duodenum. Abnormal bile acids affect the homeostasis of intestinal flora through enterohepatic circulation. The gut microbiota decomposes bile acids through metabolism and affects bile acids composition and hydrophobicity. The imbalance of intestinal flora will affect the synthesis, reabsorption and excretion of bile acids, and play an important role in the metabolism of glycolipids[6].

In turn, the disorder of bile acid anabolism will destroy the intestinal barrier, cause bacteria to breed, promote bacteria and lipopolysaccharide to enter the blood, activate inflammatory reaction, and aggravate the destruction of intestinal liver circulation. In addition, macrophages can affect the composition of intestinal flora by increasing the activation of the inflammasome and destroying the intestinal permeability, and synergize with bile acids to promote liver cell damage and promote the development of cholestatic lesions.

Discussion

The main clinical manifestation of CLD is cholestasis in the liver. On the one hand, through the interaction of gut microbiota, the metabolism of hepatic bile acid is affected and the metabolic disorder of bile acid caused by excessive bile acid content is involved. On the other hand, excessive levels of bile acids in the liver can inhibit the pathological damage of CLD through bile acid metabolism-related rate-limiting enzymes and transporters, FXR, TGR5 and other receptors.

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Study on determination method of main constituents in Shengyu Decoction

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Abstract

Shengyu Decoction(SYD) is a well-known prescription for the treatment of “qi” and “blood” deficiency. Using ginsenoside Rg₁, ginsenoside Re, Verbascoside and calycosin 7-O-glucoside as indicator components, a method was established for the content determination of Shengyu decoction reference samples. This provides a scientific basis for its quality research, thereby contributing to the the innovation and development of the Sino-Russian health industry.

Keywords

Shengyu Decoction, content determination, HPLC-UV

Shengyu Decoction(SYD), a classic prescription for the treatment of “qi” and “blood” deficiency, was first described in "The Secret Collection of Lanshi" written by Dongyuan Li, a physician of the Jin Dynasty of China^[1, 2]. SYD is composed of six herbs: raw radix of *Rehmannia glutinosa* (Gaertn.) DC., prepared radix of *Rehmannia glutinosa* (Gaertn.) DC., rhizoma of *Ligusticum striatum* DC., radix of *Panax ginseng* C.A. Mey., radix of *Angelica sinensis* (Oliv.) Diels, and radix of *Astragalus membranaceus* Moench. Based on Chinmedomics strategy^[3-5], this study selected ginsenoside Rg₁, ginsenoside Re, verbascoside and calycosin 7-O-glucoside as indicators to establish a multi-component content determination method, which provides a scientific method for the quality control research of SYD .

Objective

Establish a reliable method for the content determination of SYD, so as to provide a scientific basis for the development and application of SYD in the future.

Materials and methods

Materials include the above 6 kinds of decoction pieces, ginsenoside Rg₁ standard, ginsenoside Re standard, verbascoside standard, calycosin 7-O-glucoside standard, acetonitrile, methanol, phosphoric acid, and n-butanol.

Chromatographic analysis of ginsenoside Rg₁ and ginsenoside Re were performed using an High Performance Liquid Chromatography (HPLC) equipped with a SHISEIDO CAPCELL PAK C18 column (4.6 mm×250 mm, 5 μm) with mobile phases acetonitrile (19%) and 0.1% phosphoric acid in water (81%). In addition, the column temperature was 30°C, the volume injected was 10 μl, the flow rate was 1 ml/min and the detection wavelength is 203 nm.

Chromatographic analysis of calycosin 7-O-glucoside was performed using an HPLC equipped with a SymmetryShield™ RP18 column (4.6 mm×250 mm, 5 μm) with mobile phases acetonitrile (13%)

and 0.1% formic acid in water (87%). In addition, the column temperature was 30°C, the volume injected was 10µl, and the flow rate was 1 ml/min and the detection wavelength is 260 nm.

Chromatographic analysis of verbascoside was performed using an HPLC equipped with a SHISEIDO CAPCELL PAK C₁₈ column (4.6 mm×250 mm, 5 µm) with mobile phases acetonitrile (18%) and 0.085% phosphoric acid in water (82%). In addition, the column temperature was 30°C, the volume injected was 10µl, and the flow rate was 1 ml/min and the detection wavelength is 332 nm.

Accurately weigh the appropriate amount of ginsenoside Rg₁, ginsenoside Re, verruscoside, and calycosin 7-O-glucoside reference substance, and add methanol to each to prepare a reference substance solution of appropriate concentration.

A reference sample with a weight of 1g was added to a volume of 50ml of methanol, and ultrasonically extracted for 30min. The solution was filtered, four-fifths of the filtrate was evaporated to dryness, and reconstituted with 10mL of water. Next, wash with water-saturated n-butanol 5 times, each with a volume of 25mL, and then wash with ammonia test solution 3 times, each with a volume of 20mL. Finally, the n-butanol layer was evaporated to dryness, and dissolved in methanol to a volume of 5mL to obtain one of the test solutions. Prepare negative control solution in the same way.

Add a reference sample with a weight of 1g into methanol with a volume of 20ml, and extract it by ultrasonic for 30min to obtain another test solution. Prepare negative control solution in the same way.

Results and discussion

Based on the above methods, we carried out methodological validation. The specificity test results show that the established method has good specificity; the linearity test results show that the established method has a good linearity, and the regression equation, linear range and correlation coefficient of each component are shown in Table 1; The stability, precision, repeatability and recovery rate were all good, and the specific results are shown in Table 2.

In conclusion, in this study, method for the content determination of ginsenoside Rg₁, ginsenoside Re, verbascoside, and calycosin 7-O-glucoside in the reference sample of Shengyu Decoction was established, which laid a solid foundation for the formulation of quality standards in the research and development of Shengyu Decoction. foundation, and contribute to the innovation and development of the Sino-Russian health industry.

Table 1 Regression equation, linear range and correlation coefficient of each component

indicator component	regression equation	linear range	R ²
ginsenoside Rg ₁	$Y=3.824 \times 10^3 x + 4.065 \times 10^4$	12.71-602.3 µg/mL	0.9992
ginsenoside Re	$Y=3.048 \times 10^3 x + 1.726 \times 10^4$	12.9-300 µg/mL	0.9990
verbascoside	$Y=1.661 \times 10^4 x - 3.863 \times 10^3$	1.34-21.4 µg/mL	0.9993
calycosin 7-O-glucoside	$Y=2.723 \times 10^4 x + 3.865 \times 10^4$	3.35-53.6 µg/mL	0.9990

Table 2 Results of methodology investigation for each component

indicator component	Precision RSD%	Repeatability RSD%	Stability RSD%	recovery rate%
ginsenoside R _{g1}	0.82	0.051	1.6	96.51
ginsenoside Re	0.67	0.041	1.3	95.60
verbascoside	0.67	0.63	2.1	100.8
calycosin 7-O-glucoside	0.33	1.50	1.5	105.3

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Studies on the Antithrombotic mechanism of SiMiao YongAn Decoction

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Abstract

Thrombus is a clinically common peripheral vascular disease, which is a cause of several serious complications and seriously endangers the development of a large health industry. The TCM formula SiMiao YongAn Decoction has definite efficacy in treating thrombus. In this research, the relevant mechanisms of action of SiMiao YongAn Decoction for the treatment of thrombosis were investigated to provide a reference for the further development of SiMiao YongAn Decoction.

Keywords

SiMiao YongAn Decoction, antithrombosis, mechanism

1. Introduction

Thrombus are small fragments formed by blood flow at the surface of exfoliated or patched cardiovascular system vessels, arterial thrombosis is responsible for myocardial infarction and stroke, while venous thrombosis can lead to venous thromboembolism and pulmonary embolism^[1]. It consists of insoluble fibrin, deposited platelets, accumulated leukocytes, and entrapped erythrocytes. There are three reasons for thrombus formation: damaged blood vessels, altered blood flow and stasis of blood flow.

SiMiao YongAn Decoction was first recorded in 《YAN FANG XIN BIAN》. It is now listed in the catalogue of ancient famous classical formulas (The First Batch), which is composed of four kinds of traditional Chinese medicines, namely Lonicerae japonicae Flos, Scrophulariae Radix, Angelicae sinensis Radix and Glycyrrhizae Radix et Rhizoma, which contain terpenoids, flavonoids, phenylpropanoid and organic acids. And it can obviously improve vascular status and exert an antithrombotic effect^[2].

2. Pathological change

An animal model of Thromboangiitis obliterans was created by injecting male SD rats with sodium laurate solution, and a series of ischemic symptoms occurred: swelling and lameness of the foot, deformation of the vascular endothelial cells, disarrangement of the endothelial and smooth muscle cells, massive inflammatory cell infiltration, and a large rise in blood viscosity and plasma viscosity, etc. After administration of SiMiao YongAn Decoction, the ischemic symptoms of the rats were strengthened: the temperature of the skin enhanced, the blood color was revived, and the swelling and lameness of the feet were alleviated. Microstructurally, it can be observed that the deformation of rat vascular endothelial cells was renewed, the arrangement of endothelial cells and smooth muscle cells was coordinated, and the infiltration of inflammatory cells was diminished. A large decrease in blood viscosity and plasma viscosity was also observed, and it was further observed that RBC specific volume, aggregation index and rigidity index were modulated.

3. Metabolomics studies

Using metabolomics method, 35 metabolites were selected as biomarkers and pathway analysis demonstrated 17 related metabolic pathways mainly involving vitamin B6 metabolism, cysteine and methionine metabolism, phenylalanine metabolism, and so on. After administration of SiMiao

YongAn Decoction, the rats showed reduced symptoms and the PCA results showed that the treatment group was located close to the control group. SiMiao YongAn Decoction could be adjusted to 22 biomarkers of 35 biomarkers; respectively including pyranosyl acid, p-ethylbenzenesulfonate and L-methionine, and so on. Pathway analysis identified cysteine and methionine metabolism, phenylalanine metabolism and vitamin B6 metabolism as key pathways^[3].

4. Discussion and conclusion

Antithrombotic effects of SiMiao YongAn Decoction is significant. Metabolomics was used to discover that SiMiao YongAn Decoction could regulate 22 metabolites and pathway enrichment analysis found that cysteine and methionine metabolism, phenylalanine metabolism and vitamin B6 metabolism were the key pathways. Oxidative metabolism of methionine contributes to diseases such as atherosclerosis and thrombosis^[4]; elevation of cysteine is also associated with thrombus formation; phenylalanine and tyrosine, as the precursors of catecholamines, are involved in the synthesis of substances such as norepinephrine, which play an important role in the regulation of vascular tone; vitamin B6 can be metabolized to p-ethylbenzenesulfonate, which increases vascular risk factors^[5]. Indicating that methionine, cysteine, phenylalanine, tyrosine and vitamin B6 might be the key metabolites for SiMiao YongAn Decoction to exert the therapeutic effects on thrombosis.

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Applied metabolomics in discovery of the active ingredients and molecular targets of traditional Chinese medicine

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Abstract

Traditional Chinese Medicine (TCM), which has a history of thousands of years of clinical practice, is gaining popularity and applicability around the world. However, due to the TCM's numerous ingredients and intricate interaction with the human body, it remains difficult to disclose its molecular mechanism, which substantially impedes TCM modernization and globalization. Metabolomics is a viable tool for investigating the active ingredients and molecular targets of TCM from a holistic perspective, which is congruent with the multi-components, multi-targets, and systematic regulatory characteristics of TCM. This article is to summarize and evaluate the studies of the metabolomics approach for delineating the active ingredients and molecular targets of TCM and provides new methods and ideas for the research and development of new drugs from TCM, as well as it aids TCM modernization.

Keywords

metabolomics, active ingredients, molecular targets, traditional Chinese medicine

Limitations for the study of TCM in the active ingredients and molecular targets

Traditional Chinese medicine (TCM) is a great treasure trove of practical clinical knowledge accumulated over thousands of years and an important contributor to global health care. However, A key obstacle involved in the process of TCM modernization and globalization lies in the dimness of the active ingredients and molecular targets, which largely restricts the investigations with respect to pharmacology, mechanism of action, and quality control. Since ancient times, much of what is known about how to identify the material basis of TCMs and understand the action mechanism of TCMs are derived from observations and experiences that lack a scientific basis in clinical practice. Modern analytical approaches for TCM active ingredients, such as serum pharmacochemistry and fingerprinting, are not based on TCM's underlying principle, which has certain inevitable limitations. Currently, studies of the molecular targets of TCM have limitations, since they are based only on a single mechanism pharmacological model, and there are also limited by modern molecular biotechnology studies, which do not reflect the holistic and systemic characteristics of TCM. Thus, to fully reflect the holistic view of TCM, there is an urgent need to establish a new technical means that not only meets TCM's characteristics but follows also the study of TCM modernization to clarify the active ingredients and molecular targets of TCM.

An overview of metabolomics technology

Metabolomics is a systemic method concerned with the comprehensive characterization of small molecule metabolites found in cells, tissues, biofluids, and organisms to pathophysiological stimuli and/or genetic modifications. Metabolomics is based upon the theories of system biology and is dependent on modern analytical methods including nuclear magnetic resonance (NMR) spectroscopy, gas chromatography coupled to mass spectrometry (GC-MS), and liquid chromatography-mass spectrometry (LC-MS) as the main technical means, and is the systematic

study of all small-molecule endogenous metabolites with molecular weights less than 1000, the ultimate goal of which is to provide more definitive data on the nature of the changes within a living body resulting from the imbalance of internal and external factors in the organism. Its holistic and comprehensive are similar to the multi-components, multi-targets and multi-pathways characteristics of TCM, which offers opportunities and challenges for TCM modernization and serves as a bridge between TCM and modern medical research.

Application of metabolomics technology in the active ingredients of TCM

Quality control of the main active ingredients is important for the safety, efficacy and consistency of TCM, and its research technical approaches are crucial for the development of TCM. Metabolomics could not only evaluate the metabolism of biological samples, and identify biomarkers, but also screen the active ingredients in TCMs based on the overall efficacy. ZhiziBaipi Decoction (ZBD) is a classic TCM formula consisting of *Gardenia jasminoides* Ellis, *Phellodendron amurense* Rupr. and *Glycyrrhiza uralensis* Fisch, and is effective at treating damp-heat jaundice syndrome (DHJS) and various liver diseases. However, its active ingredients remain unclear. Wei et al.^[1] performed MS-based metabolomics to screen bioactive ingredients, and found five prototype constituents and five metabolites were strongly associated with drug efficacy. Wutou decoction (WTD) is a TCM prescription for the treatment of rheumatoid arthritis (RA), and Li et al.^[2] analyzed the key pharmacodynamic components of WTD in RA rats by combining untargeted metabolomics and serum pharmacology of TCM to enrich the evidence of WTD quality markers (Q-markers) studies. The results showed that 12 compounds, including aconitine, L-ephedrine, L-methylephedrine, etc., are the key pharmacological components that regulate the metabolism of RA rats, and they are identified as Q-markers.

Application of metabolomics technology in the molecular targets of TCM

After entering the body, TCM usually exists and plays a role in the form of prototypes and metabolites, rather than as single chemicals, which can cause the concentration variations of endogenous metabolites and thus shift the fluxes of metabolic pathways. Metabolomics offers a rapid and efficient technology for screening the active ingredients of TCM and can provide insight into complex biochemical processes and enable the identification of biomarkers that may serve as therapeutic molecular targets. Si-Miao-Yong-An-Tang (SMYAT) is a classic prescription for the treatment of thromboangiitis obliterans (TAO). However, the mechanism are still unclear. Previous studies have evaluated the therapeutic effect and mechanism of SMYAT on TAO model rats using urine metabolomics. It is found that the therapeutic effect of SMYAT is closely related to 22 core biomarkers, such as normetanephrine and 4-pyridoxic acid, and preliminarily explored the therapeutic molecular targets of SMYAT^[3]. Yunnan Baiyao is a famous Chinese patent medicine in Yunnan Province. However, its mechanism for promoting blood circulation and removing blood stasis is not fully explained. In the work of Zhang et al.^[4], the authors used metabolomics technology to reveal the regulatory effect of Yunnan Baiyao on small molecular metabolites in promoting blood circulation and removing blood stasis, and exploring the related urine biomarkers. Finally, 28 urine biomarkers were identified, clarifying the relevant metabolic pathways that play a vital role in the Yunnan Baiyao treatment. These were used as the molecular targets for Yunnan Baiyao to promote blood circulation and remove blood stasis.

Perspective

Although metabolomics techniques have been widely used in the studies of active ingredients and molecular targets of TCM in recent years, it also faces many challenges and limitations. The main problems that face the impact of metabolomics on TCM are the detection and analysis technology and multivariate statistical methods challenges to improve coverage and the biological challenges to improve our understanding of active ingredient functions; Also, the continuous improvement of organism-specific metabolomics databases is absolutely critical to the field of metabolomics enhance data mining of metabolomics, and further insights into the regulation of metabolite biosynthesis will be obtained by facilitating the integration of metabolomics data with other omics data. According to the holistic philosophy of TCM, metabolomics has great potential to integrate ancient TCM with modern medicine, which can be used to interpret the active ingredients and molecular targets of TCM to a certain extent, and provides a promising path for the modernization of TCM.

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Progress on pharmacology research of Ciwujia injection

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Abstract

Ciwujia injection is a Chinese medicine injection, which has the effect of calming liver and kidney, invigorating essence and strengthening bone. It is used to treat cerebral hemorrhage, cerebral infarction, coronary heart disease, angina pectoris, diabetes and menopause syndrome. The pharmacological effects of Ciwujia injection on cardio-cerebrovascular system, renal ischemia, anti-tumor, anti-depression, anti-diabetes and improving learning and memory ability were briefly reviewed in this paper.

Key words: Ciwujia injection, pharmacological effects

1. Introduction

Ciwujia is the root and rhizome or stem of *Acanthopanax senticosus* (Rupr.etMaxim.)Harms. It was first found in Shennong's Herbal Classic and listed as top grade, and has the effect of tonifying deficiency and helping the weak. Ciwujia injection is extracted from the upper part of *acanthopanax senticosus* with modern scientific extraction technology. Although Ciwujia injection has entered clinical treatment, it is necessary to strengthen the research on the pharmacological mechanism of Ciwujia injection to provide scientific basis for its prevention and treatment of diseases.

2. Protective effect on the cerebrovascular system

Ciwujia injection can significantly regulate blood lipids, inhibit inflammatory reaction and improve endothelial cell function in patients with acute cerebral infarction, and can significantly improve the therapeutic effect of acute cerebral infarction, which may be related to the chemical components of Ciwujia injection including ketone compounds, polysaccharides and various saponins^[1].

3. Protective effect on the cardiovascular system

Some scholars^[2] have found that Ciwujia injection has a protective effect on myocardial cells injured by ischemia-reperfusion. Its protective mechanism may be through the activation of PI3K/AKT signaling pathway and AKT phosphorylation to effectively inhibit the occurrence of hypoxia-induced apoptosis of cardiomyocytes, and cardiovascular protective factors (insulin, NO, IGF-1, erythropoietin) play an important role. Several studies^[3-4] have shown that Ciwujia injection can protect the cardiovascular system by reducing levels of inflammation and oxidative stress.

4. Protective effect on renal ischemia-reperfusion

Studies have shown that Ciwujia injection has a protective effect on renal ischemia-reperfusion injury in rats, and the mechanism may be related to the activation of Nrf2/HO-1 pathway, inhibition of NF- κ B nuclear translocation, and further inhibition of oxidative stress and inflammatory response in renal tissues^[5].

5. Improvement on learning and memory ability

Zhang Yue^[6] found that Ciwujia injection could significantly improve the learning and memory ability of brain hypoxic rats. The mechanism was that Ciwujia injection could alleviate the damage of brain tissue caused by hypoxia, which was related to the increase of f-actin protein expression in brain tissue.

6. Antidepressant effect

Continuous administration of Ciwujia injection can significantly relieve symptoms of depression model rats, such as loss of appetite and decreased body mass. The levels of SS and NPY increased and the levels of SP decreased in plasma of rats after administration, indicating that Ciwujia injection can restore the function of neuropeptides in brain by regulating SS, SP and NPY^[7].

7. Antitumor effect

The apoptosis of human cervical cancer HeLa cells induced by Ciwujia injection may be realized through the caspase-dependent apoptosis pathway, among which the apoptotic proteases caspase-8 and caspase-3 play an important role^[8]. It was found that Ciwujia injection could inhibit the proliferation of McF-7 cells in vitro in the experimental study of inhibiting human breast cancer cells^[9].

8. Antidiabetic effect

Ciwujia injection can reduce the levels of blood glucose, Ins and NO, reduce the content of MDA and increase the activity of SOD in diabetic rats. The mechanism of action may be related to lowering blood glucose, improving insulin resistance (IR), increasing NO level and antioxidant capacity^[10].

9. Others

In addition, Ciwujia injection has strong or weak pharmacological effects on liver^[11], lung^[12] and nervous^[13] system.

10. Summary

The complex chemical composition of Ciwujia injection makes it difficult to study its pharmacological mechanism. After reviewing the relevant literature, it is found that many pharmacological studies remain superficial, and the exact mechanism remains to be further explored. This paper reviews the pharmacological studies of Ciwujia injection in recent years, in order to understand the more comprehensive pharmacological characteristics and mechanism of ciwujia injection, which will be helpful for the follow-up target study of its related mechanism.

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Research progress on pharmacological effects of plant polysaccharides of tonic Chinese medicine on enhancing body immune function

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Abstract

Tonic Chinese medicine is an important part of traditional Chinese medicine, especially tonic Chinese medicine polysaccharides, which have the functions of enhancing the body's immune function, antioxidant and anti-tumor, and has great research and development potential in the future. This paper summarized the role and mechanism of tonic Chinese medicinal plant polysaccharides in enhancing the body's immune function, aiming to provide some reference for the follow-up research and development of tonic Chinese medicinal plant polysaccharides drugs with strong body immune function.

Keywords: tonic Chinese medicine; plant polysaccharide; immunity function; health industry

In recent years, with the aggravation of the aging of our population and the increase of sub-healthy people, people's concept of health has gradually changed to the diagnosis and treatment of "cure without disease," hoping to maintain health by enhancing physical fitness and improving immunity. Under this background, tonic Chinese medicine has become an important part of the TCM health industry with its unique advantages, especially the tonic Chinese medicine plant polysaccharide component, which is effective for enhancing the body's resistance and improving immune function. Based on this, this paper summarizes the function and mechanism of plant polysaccharide in tonic Chinese medicine to enhance the body's immune function, discusses the existing problems in the study of plant polysaccharide components, and proposes solutions. In order to provide reference for further study and application of subsequent plant polysaccharides.

1. Introduction to tonic Chinese medicine

Tonic Chinese medicine is a kind of traditional Chinese medicine which is mainly used to help the deficiency of the human body, enhance disease resistance. It has the effects of tonifying Qi, nourishing blood, nourishing yin, and assisting yang, and are mainly used for treating various deficiency syndromes. Modern pharmacological studies have shown that plant polysaccharides, the key active components of tonic Chinese medicinals, can enhance the body's immune function and non-specific resistance to a variety of harmful stimuli through multiple pathways.

2. Pharmacological effects of plant polysaccharides from tonic traditional Chinese medicine on enhancing immune function

Ginseng polysaccharide can increase its phagocytosis by activating macrophages, and promote dendritic cell maturation, stimulate the complement system to play an immunomodulatory role^[1], promote NK cell activity in the spleen of mice, induce IFN- γ and IL-2 in the presence of ConA, and enhance resistance to viruses^[2]. Astragalus polysaccharide can enhance the humoral immunity of the host by stimulating the secretion of B cells, promoting B cell proliferation, increasing the number of T lymphocytes and increasing the immunoglobulin in serum, and it can also activate TLR4-MyD88-dependent signal transduction pathway, promote the expression of NF- κ B nuclear translocation and transcription level, and activate macrophages to exert the immune enhancement

effect^[3]. Angelica polysaccharides can enhance immunity by promoting lymphocyte proliferation, stimulating the secretion of certain cytokines and increasing the proportion of CD³⁺, CD⁵⁶⁺ cells^[4]. Radix rehmanniae preparata polysaccharide can significantly promote the proliferation of T lymphocytes stimulated by ConA, activation of human and mouse dendritic cells, induction of mLNT cells to produce IFN- γ and TNF- α , activation of immune response^[5]. Cordyceps polysaccharide can stimulate the secretion of cytokines IL-12, IFN- γ , IL-4, IL-6 and the production of transcription factors T-bet, GATA-3, ROR γ t, and Foxp3, and up-regulate the key proteins of NF- κ B pathway (p-I κ B- α , NF- κ B p65), thereby reducing the side effects of cyclophosphamide on intestinal mucosal immunity and intestinal microflora^[6]. Polygonatum polysaccharide can improve spleen and thymus index in mice with low immunodeficiency caused by cyclophosphamide, increase spleen and thymocyte proliferation capacity, increase macrophage ability, enhance IL-6 and TNF- α secretion, and alleviate immunodeficiency in mice with cyclophosphamide^[7].

3. Discussion

As an important active component of plants, plant polysaccharides have significant effects in promoting the secretion of cytokines, activating the complement system of NK cells and T/B lymphocytes, and promoting the production of antibodies. In conclusion, plant polysaccharides, as the material basis for enhancing the immunity of the body, play an extremely obvious role in promoting and recovering the immune function of the body, and are immune modulators with great development potential.

Although the tonic Chinese medicinal plant polysaccharides have a significant effect on enhancing the immune function of the body, there are still many problems in their development, for example, it is difficult to obtain a single polysaccharide with high purity by the existing extraction and separation methods, the structure confirmation is difficult due to the complexity of the polysaccharide molecule, and it is difficult to accurately learn the absorption, distribution, metabolism and excretion rules of the polysaccharide molecule to be tested in vivo. To solve these problems, new extraction and separation technologies should be innovated and developed in clinic to increase the concentration of single polysaccharide, new methods for polysaccharide structure analysis should be deeply studied, and the action rules of polysaccharides should be explored from multiple levels and multiple pathways such as cells and molecules, so as to more comprehensively clarify the mechanism of tonic Chinese medicinal plant polysaccharides in enhancing the body's strong immune function. We will vigorously support and develop the research and development of polysaccharide components of tonic Chinese medicine so that they can play a better role in maintaining human health and fully escort the health of the Chinese nation.

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Recent progress of multi-omics technology in early biomarker screening of colorectal cancer

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Abstract

Colorectal cancer is a common digestive tract malignant tumor that seriously threatens human health. It is one of the malignant tumors with high morbidity and mortality. At present, the incidence of colorectal cancer in the world is the fourth among all cancers, and the mortality rate is the second, and it is on the rise. Thus, the need for non-invasive, specific, and accurate screening methods for the early identification of colorectal cancer has prompted many researchers to turn to molecular techniques such as genomics, proteomics, and metabolomics. This paper discusses the application of multi-omics technology in the screening of early markers of colorectal cancer and provides a reference for the early identification and diagnosis and treatment of colorectal cancer.

Keywords

Multi-omics techniques; colorectal cancer; biomarker

Multi-omics technology is an emerging interdisciplinary discipline that studies the composition of genes, mRNAs, proteins, metabolites, and other components of a biological system and the interrelationship of these components under specific conditions, and its core is the integration of different kinds of components in biological systems, from genes to cells, to tissues, to individuals at all levels. The core of the discipline is the integration of different components of biological systems, from genes to cells to tissues to individuals. The technology platforms include genomics, transcriptomics, proteomics, metabolomics, and microbiomics.

1. Epigenetics

Epigenetics is the study of the effects of physical, chemical, biological, and other environmental factors and dietary habits on genetic factors, and this effect causes changes in genetic material other than DNA sequences. Epigenetic modifications mainly include DNA methylation, histone modification, and non-coding RNA regulation (such as miRNAs and lncRNAs). Since abnormal changes in epigenetic regulation usually occur in the early stages of malignant tumors, they can be used as molecular markers for early diagnosis to improve the accuracy of diagnosis. Abnormal DNA methylation at gene CpG sites is the most common molecular alteration in colorectal carcinogenesis, some abnormally methylated genes with different specificities and sensitivities are detected in blood or feces, and abnormal genes in serum/plasma Methylation, including SEPT9, p16, HPP1/TPEF, RUNX3, TMEFF2, NGFR, APC, MGMT, RASSF2A, THBD, and C9OFR50, has been shown to have potential to detect or monitor colorectal cancer^[1].

2. Proteomics

Proteomics is an extension of the concept of the proteome, which refers to the analysis of the composition and activity of dynamically changing proteins in cells from an overall perspective with the proteome as the research object. Proteomics can be used in many aspects of cancer research. The most common and convenient proteomic strategy to discover cancer biomarkers involves the identification of differentially expressed proteins and peptides. by comparing the proteomes of

cancerous and non-cancerous tissues, protein biomarkers are proteins that are significantly up-regulated or down-regulated in the cancer proteome compared to the normal proteome and can be used as potential protein biomarkers. The researchers isolated stromal cells from colon adenocarcinoma mucosal tissue and compared the protein content of stromal cells with the protein content of healthy colonic mucosal tissue to identify stromal differentially expressed proteins such as DCN, FN1, PKM2, HSP90B1, S100A9, MYH9, TUBB and YWHAZ as potential targets for colon cancer prevention, diagnosis, and treatment^[2].

3. Metabolomics

Metabolomics is a promising approach to detecting biomarkers with high diagnostic performance, and metabolites are closely related to phenotypes, reflecting processes occurring in cells or organisms. The most accessible biological samples, such as feces, urine, and blood, hold great potential for detecting early-stage cancer biomarkers. 1H-NMR metabolomics was used to analyze the metabolic changes in the serum of colorectal polyps, colorectal cancer patients, and healthy control volunteers. The main abnormal metabolic pathway in colorectal cancer is glycolysis; glycine, serine, and threonine metabolism; glutamine and glutamate metabolism; and alanine, aspartate, and glutamate metabolism. Isoleucine, Alanine, Choline, Serine, Glycerin, Succinic Acid, Polyunsaturated Fatty Acids, N-Acetyl Cysteine, Glucose, Lactic Acid, Glycine, Valine, Glutamic Acid, Glutamine and Metabolites of aspartate are potential biomarkers^[3].

4. Microbiome.

Microbiome refers to the study of symbiotic or pathological microbial ecological groups on animals and plants. The microbiome includes bacteria, archaea, protozoa, fungi, and viruses. The human body has more than 1 trillion species of microorganisms, including a variety of symbiotic microorganisms, which play a vital role in individual health. The human colon is estimated to contain 10¹⁴ bacteria, the densest and metabolically active microbial community in the human body. Analysis of 16S rRNA genes or whole-genome metagenomic sequencing showed that the distribution of microbiota in the gut of CRC patients and healthy people was very different, Lower bacterial diversity and abundance in stool samples and intestinal mucosa from colorectal cancer patients compared to healthy individuals In colorectal cancer patients, *Bacteroides fragilis*, *Fusobacterium nucleatum*, *Enterococcidae*, *Streptococcus digestive*, *Enterococcus faecalis*, *Escherichia coli*, *Shigella* and *Streptococcus hemolyticus* increased significantly, while *Bifidobacterium faecalis*, *Brucella*, *Clostridium*, *Bifidobacterium* and *Rosella* decreased significantly. Differences in gut biota may serve as non-invasive CRC biomarkers^[4]

Discussion:

Multi-omics techniques can help us more easily understand the complex process of colorectal cancer from precancerous state to a cancerous state. The combination of high-throughput data at the epigenomics, proteomics, metabolomics, and microbiome levels with bioinformatics will help to discover more early-stage colorectal cancer biomarkers and improve its early screening. rate. This article reviews the current status of omics research in colorectal cancer, focusing on biomarker discovery. A large number of potential biomarkers related to the pathophysiological state of colorectal cancer have been identified. However, studies so far have focused on smaller populations and smaller sample sizes. Future follow-up studies in larger populations and larger samples are needed to confirm the validity of the current findings.

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Structural properties and anticancer mechanism of pectic polysaccharides

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Abstract

The anticancer activity of pectic polysaccharides (PPs) was proved by numerous studies, and the bioactivity of PPs was closely related to its complicated structures. Based on the summary and analysis about structure characteristics of the reported PPs, the anticancer mechanism and related structural features were systematically clarified. It was found that not only the direct effects on the cancer cells by proliferation inhibition or apoptosis, but also the regulation of immune system, gut microbiota and gut metabolism as indirect effects, jointly played important roles in the anticancer of PPs. Nevertheless, during the study of PPs as promising anticancer components, the exact structure-function relationship, digestion process *in vivo*, and comprehensive action mechanism are still not well understanding.

Keywords: Pectic polysaccharides, Structural properties, Anticancer mechanism

Cancer is mainly caused by the high metastasis and unlimited proliferation of cancerous cells, which possesses a high fatality rate and ranks second in the cause of death in the world [1]. In generally, the disorder of internal environment is seen as the main etiology for the outbreak of cancer, such as long-term disorder of the immune system, intestinal microbes and glucolipid metabolism, as well as the grave harm of the body caused by radiation, toxic chemical reagent and other poisonous substance in a short term. Besides some intestinal flora increasing with the severity of cancer, the reduction of the microflora diversity and intestinal homeostasis also accelerates the development of cancer. PPs are a class of complex plant polysaccharides composed of galacturonic acid (GalA) backbone and neutral sugar side chains, which are the main component of plant cell wall with abundant resources for the amounts and categories [2]. Meanwhile, PPs can directly act on the immune system. In addition, PPs can be fermented in intestinal and furtherly regulated the complex intestinal microbial and metabolism. It was found that the metabolites originated from PPs, such as butyric acid, propionic acid and other short chain fatty acids (SCFAs), showed the mitigation of cancer.

Structure-anticancer activity relationship

Extensive studies have reported various kinds of PPs with anticancer activity, which were prepared from different resources by multiple methods. Based on the comparative analysis, the probably functional structure domains or the specific structure units of PPs were speculated and summarized, which will be beneficial for the direction preparation of functional PPs, as well as the further study and commercial development. In the present study, the possible functional structure regions of anticancer PPs were summarized, analyzed and classified according to the action mode of anticancer activity.

It has been widely proved that the anticancer activity of PPs is related to the binding or expression inhibition of Gal-3. The possible functional structure regions of PPs as the Gal-3 inhibitors were summarized: (1) Charged residues attached in the RG-I backbone; (2) High GalA content; (3) Aromatic ring hydroxyl, which was mainly come from the interaction between polyphenol and PPs

during the extraction with high temperature; (4) The cooperation between short side chains of 1,4-galactan. Although the possible functional domains which can bind to Gal-3 have been reported, the specific structure of PPs relating to the binding sites of Gal-3 was still unclear, as well as the further action mode of anticancer.

The immunity activation caused by PPs was verified to show a positive effect on cancer therapy. For example, RG-II improved immune response of Dendritic cells (DCs) by activating the Toll like receptor 4 signaling pathway, which inhibited the proliferation of cancer cells. In addition, macrophages, NK cells and lymphocytes could be activated by HG structure with high content of methoxy group, and which furtherly inhibited the proliferation of lung cancer [3].

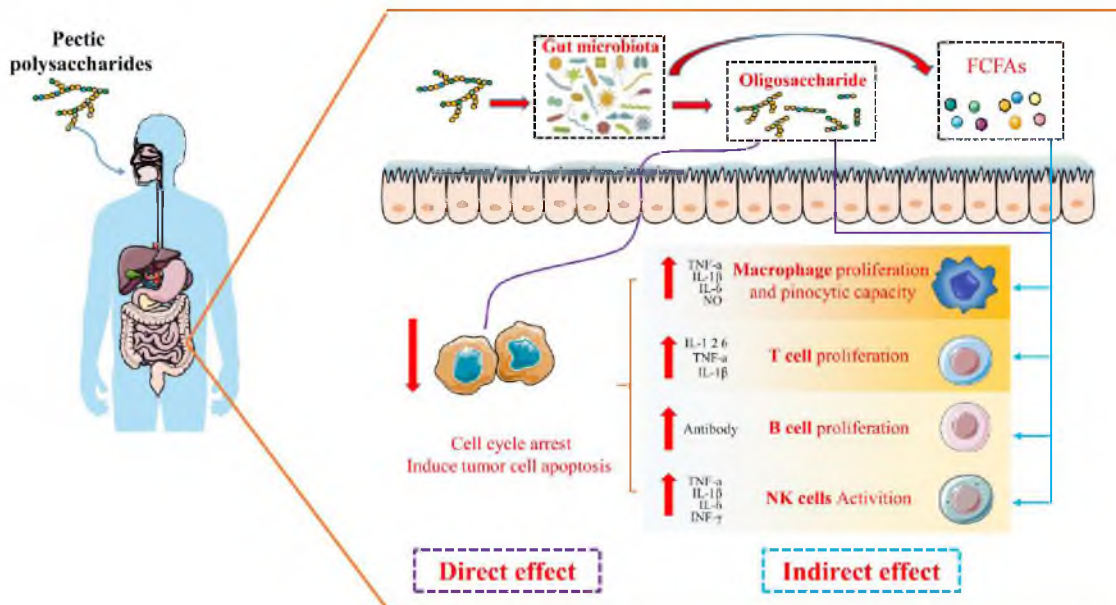


Fig. 1. The anticancer mechanism of pectic polysaccharides

anticancer mechanisms of PPs

As an immune activator, PPs can enhance immunological activities by activating immune cells and inducing cytokines production to affect the progression of cancer [4], which also can combine with anticancer drugs to overcome or alleviate the drug resistance and side-effects; Inflammation inhibition of PPs is also regarded as an important way for the cancer therapy, because long-term inflammation is a general sign during tumor progression. Various PPs were reported to perform anticancer activity by activating immune cells and related proteins. For example, IL-10 and IL-1 receptor antagonist released from mouse macrophages inhibit colon cancer growth by inhibiting signal transducer and activator of transcription 3.

Based on the studies in recent years, a close correlation between the gut microbiota variation and tumorigenesis was verified. Therefore, PPs are potential to regulate the gut microbiota composition and metabolism. In addition, mounting evidence from histochemical data suggests that the intestines of cancer patients are generally characterized by the reduction of microbial diversity and beneficial metabolites, as well as the enrichment of certain specific gut microbiota and harmful metabolites. Therefore, it can be speculated that the intervention of PPs in microbial composition may be an effective strategy to prevent cancer progression and improve the efficacy of cancer treatment. In addition, PPs with different structures will lead to significant differences in the influence on gut

microbiota composition, which may be caused by the diversity of arbohydrate enzymes encoded by gut microbiota.

This review discussed the direct and indirect effects of PPs anticancer activity, which mainly focus on two aspects: Directly inhibit the proliferation or lead to the apoptosis of cancer cells through the interaction with specific proteins; Indirectly act on cancer by the regulation of immune system and intestinal microecosystem to maintain homeostasis.

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Study on characteristic chromatogram of *Curcumae Rhizoma* based on UPLC-UV method

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Abstract

In this study, UPLC-UV characteristic spectrum of *Curcuma* was established, which provided a new method for the quality control of *Curcuma* medicinal materials. Use waters acquity UPLC HSS T3 column (2.1 mm×100 mm, 1.8 μm), the mobile phase was acetonitrile-0.1% phosphoric acid aqueous solution linear gradient elution, the column temperature was 35 °C, the flow rate was 0.3 mL/min, the detection wavelength with 270 nm at 0~6.5 min and 240 nm at 6.5-12 min was set. The chromatograms of 9 batches of *Curcumae Rhizoma* were determined to screen the common peaks as the characteristic peaks and calculate their similarity. The UPLC-UV chromatograms of 9 batches of *Curcumae Rhizoma* were collected, and 15 common peaks were determined as the characteristic peaks, and the similarity was more than 0.9.

Keywords

Curcumae; UPLC-UV characteristic chromatogram; Quality Control

Rhizoma Curcumae was first recorded in the theory of medicinal properties, which was the dry rhizomes of *Curcumae Cuecuma. phaeocaulis* Val, *Curcumae kwangsiensis* S. G. Lee et C. F. Liang or *Cuecuma. wenyujin* Y. H. Chen et C. Ling from *Curcumaeaceae*, *Curcumae* Guangxi, which were recorded in the previous editions of Chinese Pharmacopoeia^[1]. At present, the 2020 edition of ' Pharmacopoeia of the People 's Republic of China ' (I) of *Curcuma* medicinal materials only under the character, microscopic and thin layer identification, the determination of volatile oil content, the lack of specific quality evaluation method, can not comprehensively and reasonably evaluate the quality of *Curcuma* medicinal materials and decoction pieces^[2]. In this study, the chromatographic separation and UV detection conditions of *curcuma zedoary* were systematically investigated, in order to provide reference for the comprehensive quality control of *curcuma zedoary*.

Objective

Ultra performance liquid chromatography-ultraviolet spectroscopy (UPLC-UV) was used to establish the characteristic chromatogram of chemical constituents in *Curcumae Rhizoma*, improve the quality standard of *Curcumae*.

Materials

Ultra performance liquid chromatography system (including binary ultrahigh pressure pump system, sample management system, PDA detector, column temperature box, Empower chromatographic workstation) (Acquity UPLC, Waters, USA). Curcumenone (PS220509-03, content ≥ 90%), Curzerenone (PS012809, content ≥ 98%), Furanodienon (PS000318, content ≥ 98%), Germanone (batch number RFS-J02501901011, content ≥ 98%), Furanodiene (PS220510-03, content ≥ 95%), purchased from Chengdu Ruifensi Biotechnology Co., Ltd. The origin of nine batches of *curcuma zedoary* is Yunnan Kunming, and the batch numbers are 180201, 180202, 180205, 180206, 180207, 190301, 190201, 180601 and 181001, respectively, which are provided by Harbin Traditional

Chinese Medicine Fourth Factory Co., Ltd.

Methods

Take 1.0 g of curcuma zedoary powder, precise weighing, placed in a plug cone bottle, adding methanol 25 mL, ultrasonic extraction 45 minutes, shake, through 0.22 μm microporous membrane, the sample solution.

Chromatographic column : Waters ACQUITY UPLC HSS T3 column (2.1 \times 100 mm, 1.8 μm); mobile phase A: acetonitrile, mobile phase B: 0.1% phosphoric acid aqueous solution; gradient elution (0 – 2 min, 35% – 55% A, 2 – 4 min, 55% – 60 % A, 4 – 5 min, 60% – 60% A, 5 – 7 min, 60% – 80% A, 7 – 12 min, 80% – 100% A) detection wavelength was 270 nm in 0 – 6.5 min and 240 nm in 6.5 – 12 min ; column temperature is 35 $^{\circ}\text{C}$; the flow rate was 0.3 mL /min.

The test solution of Curcumae Rhizoma was taken and injected for six consecutive times. The relative retention time and relative peak area of each common peak were calculated to investigate the consistency of chromatographic peak retention time and relative peak area.

Six parallel prepared test solutions were taken and analyzed according to chromatographic conditions. The relative retention time and relative peak area of each common peak were calculated to investigate the consistency of the retention time and relative peak area of chromatographic peaks. The relative retention time and relative peak area of each common peak were calculated after 0, 2, 4, 6, 8, 10, 12 h, respectively, and the consistency of chromatographic peak retention time and relative peak area was investigated.

Results and discussion

The results of methodological investigation showed that the RSD values of the relative retention time of each common chromatographic peak were all less than 1.0%, and the RSD of the relative peak area of each common peak was less than 1.0%. The similarity between the measured chromatographic characteristic map and the obtained common pattern map was 1.000 calculated by similarity evaluation software, indicating that the instrument was stable and the precision was good. The extraction and detection methods had good reproducibility, and the test solution was stable within 12 h.

UPLC chromatograms of nine batches of Curcumae Rhizoma and their reference solutions were determined. The similarity evaluation system of chromatographic fingerprint of traditional Chinese medicine (2012 edition) was used for analysis, and the corresponding similarity evaluation calculation of curcuma zedoary samples was carried out. The similarity between the characteristic map and the control map of each batch of Rhizoma Curcumae was 0.993, 0.992, 0.978, 0.989, 0.983, 0.991, 0.997, 0.997 and 0.97, respectively, indicating that the stability between batches of nine batches of Rhizoma Curcumae was good, as shown in Fig. 1. By comparing the UV spectra of the reference substance, it was determined that peak 6 was curcuma dicycloenone, peak 9 was curcuma ketone, peak 11 was curcuma furandienone, peak 14 was gemarone, and peak 15 was curcuma furandiene, as shown in Fig. 2.

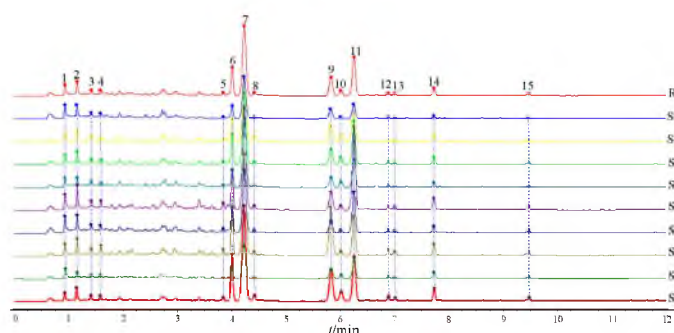


Fig. 1 UPLC-UV chromatogram (S1-S9) and control chromatogram (R) of 9 batches of *Rhizoma Curcumae*

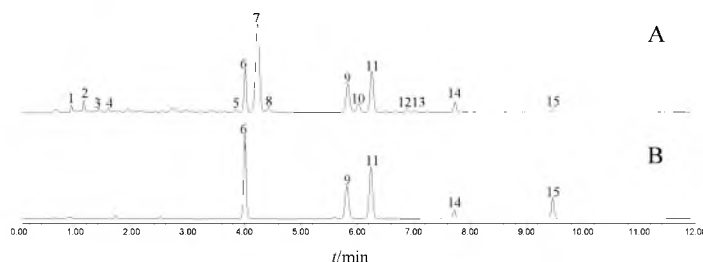


Fig. 2 UPLC-UV characteristic spectrum (A) of *Rhizoma Curcumae* and chromatogram of mixed reference solution (B)

Note: 6. Curcumenone; 9. Curzerenone; 11. Furanodienon; 14. Germacrone; 15. Furanodiene.

In this study, the UPLC-UV characteristic spectrum detection method of *Rhizoma Curcumae* was established, and 15 characteristic peaks were determined. The characteristic peaks of *Rhizoma Curcumae* dicycloenone, *Rhizoma Curcumae* ketone, *Rhizoma Curcumae* furandienone, Gemperidone and *Rhizoma Curcumae* furandiene were identified. This characteristic spectrum more comprehensively characterized the main chemical components of *Rhizoma Curcumae*, and provided a new method for the quality control of *Rhizoma Curcumae*.

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Progress in diabetic retinopathy treatment with traditional Chinese medicine

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Abstract

Diabetic retinopathy (DR) is one of the most common microvascular complications in diabetic patients, which poses a great threat to human vision health. Due to changes in lifestyle and dietary habits, the incidence of metabolic diseases such as diabetes is increasing year by year, and the number of DR patients in various countries is also increasing. Traditional treatment and prevention methods can no longer meet the health needs of DR patients. In order to find new safe and effective methods for the treatment of DR, traditional Chinese medicine (TCM) as an alternative therapy for DR has received extensive attention from researchers, providing more possibilities for effective treatment.

Key word: Diabetic Retinopathy, Traditional Chinese Medicine

Diabetic retinopathy (DR) is a common microvascular complication of diabetes, which can cause severe visual impairment. Its pathological manifestations are retinal vascular hyperplasia, basement membrane thickening and retinal neuropathy^[1]. Due to the increasing prevalence of diabetes, the incidence of DR is increasing year by year. According to statistics, there will be about 103 million adult patients with DR in 2020, and this number will grow to 160 million by 2045^[2]. DR has become the main cause of acquired blindness in adults worldwide, seriously threatening people's physical and mental health. At present, the main treatment methods for DR include retinal laser photocoagulation, vitrectomy, intraocular injection of steroids, and anti-vascular endothelial growth factor drugs. However, these methods are costly, difficult to operate, difficult to recover after surgery, and have serious side effects. It cannot be used as an effective treatment for DR patients widely^[3]. In recent years, researchers have conducted a lot of research on the use of traditional Chinese medicine (TCM) to treat DR, and its safety and effectiveness may have found a new and effective way for the drug treatment of DR^[4].

Therapeutic effect of TCM on DR

The TCM treatment of diabetic retinopathy has a long history. With the promotion of the modernization of TCM, modern pharmacology and clinical medicine continue to develop it. The clinical use of TCM for DR is mainly based on TCM formula, TCM extract and TCM monomer.

TCM Formula

The TCM formula focuses on overall changes, and the combined use of multiple drugs affects each other to reduce toxicity and enhance efficacy. Keluoxin capsule could affect adenosine phosphate-activated protein kinase (AMPK), extracellular signal-regulated protein kinase 1/2 (ERK1/2), phospholipid Metabolic pathways, such as acyl-inositol 3-kinase (PI3K), recall the levels of 51 biomarkers in the blood of DR mice by Chinmedomice research^[5]. Fufang Xueshuantong could improve the pathological structural changes and excessive apoptosis of the rat retina, and affect the complement and coagulation cascade and PPAR signaling pathway to alleviate streptozotocin-induced DR rat ^[6]. Yiqi Tongluo Fang could improve dyslipidemia and retinal

structural changes during the development of DR, which may be related to its anti-inflammatory and antioxidant effects by reducing cytokine expression^[7]. Bushen Yiqi Huoxue prescription also exerted anti-inflammatory and anti-angiogenic effects by reducing serum IL-1 β , IL-6, TNF- α and VEGF concentrations in rats^[8].

TCM extract

The aqueous extract of *Euonymus alatus* (Thunb.) Siebold had a significant inhibitory effect on the migration and generation of vascular endothelial cells, which could affect the DR process by slowing down angiogenesis^[9]. Astragalus membranaceus injection could inhibit the pro-inflammatory response of lipopolysaccharide (LPS)-induced macrophages by activating the AMPK-mTOR pathway and reduce the production of IL-6^[10].

TCM monomer

The monomer of TCM is a single component separated from Chinese herbal medicine. Artesunate could significantly inhibit retinal cell autophagy and inflammatory cytokine production, and protect blood retinal barrier by activating AMPK^[11]. Astragaloside IV could inhibit the overexpression of miR-138-5p and ROS and protect retinal pigment epithelial cells from iron death induced by high glucose level^[12].

Results and discussion

DR is a disease for which no effective and complete cure has been found, causing great suffering to patients. TCM has great advantages in the treatment of DR. The method of administration is simple and inexpensive, and it can also be precisely prescribed for the different symptoms of each patient. TCM formula, extract and monomer can exert anti-inflammatory, anti-oxidative and anti-apoptotic effects to hinder the development of DR. However, the complexity and diversity of TCM bring great potential for development, but also increase the difficulty of drug screening. There are still insufficient clinical trials on the safety evaluation and adverse drug reactions of TCM for DR.

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Research progress in the mechanism of Polygalae Radix for improving sleep disorder

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Abstract

Due to the gradual increase of external pressure, sleep disorder has become a common disease in modern people. As a traditional means to improve sleep, the clinical effect of Traditional Chinese medicine has been recognized by the majority of patients, and Polygalae Radix (PR), as a sedative and hypnotic drug commonly used in clinical Chinese medicine, has attracted the attention of sleep researchers because of its compatibility in the prescription. In this paper, we summarize the pharmacological effects of PR on sedation and hypnosis, and find that its mechanism of improving sleep is related to regulating neurotransmitters in sleep-wake regulatory nucleus, changing GABA system, regulating the synthesis of dopamine and adrenalin, and then playing a role in improving sleep by affecting sleep-related neurotransmitters in the brain.

Key words: sedative-hypnotic, Sleep disorders, Polygalae Radix, neurotransmitter

Sleep disorder is a frequent manifestation of the brain's regulatory function, which is the spontaneous hyperactivity of the brain that is not controlled by consciousness. Therefore, the "disease location" of sleep disorders in the brain, often without clear pathological changes, more belong to functional disorders, manifested as one or more difficult to fall asleep characteristics: difficulty falling asleep, sleep maintenance difficulties, wake up early, no comfortable sleep^[1]. Insomnia also includes daytime effects such as fatigue, lack of energy, lack of concentration, and decreased arousal.

Guided by the holistic view and dialectical treatment, TCM has definite clinical efficacy and is widely used in various sleep disorders. In traditional Chinese medicine, Onji (Polygalae Radix, roots of *Polygala tenuifolia* WILLD) has been used for the treatment of insomnia, palpitations with anxiety, restlessness and disorientation. A modern population-pharmacoepidemiology survey reported herbal remedies for insomnia, and it has been reported that PR has so far been a common individual herbal remedy for improving sleep^[2].

By reviewing the latest articles on improving sleep, the results show that the mainstream hypotheses that produce sleep disorders are: hypothalamic-pituitary-adrenal axis dysfunction hypothesis, 3P hypothesis, and central neurotransmitter disorder hypothesis. Modern molecular biology studies have shown that the neurotransmitters associated with sleep system include γ -aminobutyric acid (GABA), 5-hydroxytryptamine (5-HT), dopamine (DA), norepinephrine (NE) and their metabolites 5-hiAA. The active ingredient in Chinese traditional medicine PR can regulate neurotransmitters and play a sedative and hypnotic role, thus improving sleep^[3].

Results

1. Regulates of neurotransmitters in the sleep-wake regulatory nucleus

The sleep-wake modulating system is consisted of the sleep-promoting and wake-promoting neurons. The neurons responsible for the sleep-wake regulatory system have gabaergic-VLPO, orexinergic-Pef, noradrenergic-LC, serotonergic-DRN and hitaminergic-TMN. The VLPO is the

major sleep-promoting nucleus. The NA-containing neurons in LC, 5-HT-containing raphe neurons in DRN, histamine-containing neurons in TMN and orexin-containing neurons in Pef compose the ascending arousal systems as wake - promoting neurons to promote and maintain the wakefulness^[4]. The sleep-wake state is regulated by the inhibitory interaction between sleep-promoting and sleep-promoting neurons. Some animal studies have shown that PR can prolong sleep time and shorten sleep latency, thus enhancing the sedative- hypnotic effect induced by pentobarbital. After taking RP, it was found that the sleep-promoting neurons in VLPO were activated while the sleep-promoting neurons in LC and Pef were inhibited. Meanwhile, PR significantly increased the levels of GABA, the sleep-promoting modulator, in VLPO, LC and Pef and decreased the levels of wake-promoting neurotransmitter NA in LC, VLPO, PPT and LDT. From the data of the present study, it should be presumed that PR may inhibit the arousal NA neuron” s activity in LC and reduce the levels of NA in LC and VLPO, and weaken the regulating ability of LC on VLPO. On the other aspect, PR may activate the sleep-promoting GABAergic VLPO neurons, increase the levels of GABA in VLPO, LC and Pef, thereby inhibiting wake- promo -ting nuclei LC and Pef, then promote the occurrence of sleep, achieve the purpose of improving sleep.

2. Altering sleep structure by changing the gamma-aminobutyric acid (GABA) system

Gamma-aminobutyric acid, also known as GABA, is an amino acid in the human brain and an important inhibitory neurotransmitter in the nervous system. When the human body needs to rest and sleep, the brain will release the neurotransmitter GABA, so that the nervous system excitation is reduced, slowly into the state of sleep. Studies have shown that GABA levels in brain tissue can drop by as much as 15 percent during sleep compared to waking.

3,4,5-trimethoxycinnamic acid (TMCA) is one of the constituents derived from *Polygalae Radix*, enhances pentobarbital-induced sleeping behaviors, and to alter sleep architecture through the c-aminobutyric acid (GABA)ergic systems in mice^[5]. TMCA decreased the locomotor activity. TMCA prolonged total sleep time, and reduced sleep latency induced by pentobarbital, similar to muscimol, a GABA_A agonist. From the electroencephalogram recording for 6h after TMCA administration, the number of sleep/wake cycles were reduced by TMCA. TMCA also increased the total sleep time and non-rapid eye movement (NREM) sleep. In addition, TMCA increased Cl⁻ influx in primary cultured cerebellar granule cells of mice. TMCA increased the activation of glutamic acid decarboxylase (GAD) and the expressions of c-subunit of GABA_A receptors in the cerebellar granule cells. However, and b-subunits proteins of GABA_A receptors were not increased. Therefore, TMCA would increase pentobarbital induced-sleep and NREM sleep in mice. These results indicate that TMCA may enhance sleep and alter sleep architecture through GABA_A ergic systyems.

3. Regulates the synthesis of dopamine (DE) and norepinephrine (NA)

The neurotransmitter Norepinephrine (NE) and Dopamine are key neurotransmitters that cause insomnia, and THE NE neurotransmitter is mainly related to fast wave sleep and wakefulness, and regulates sleep-wake cycle. The DA neurotransmitter plays an extremely important role in arousal. When DA neurons fire in the brain, arousal increases and vice versa.

NE and DA can be converted from phenylalanine through tyrosine produced by phenylalanine hydroxylase^[6]. Studies have shown that in a sleep disorder model of p-chlorophenylalanine (PCPA) production, phenylalanine metabolism is disrupted, leading to increased tyrosine production in the

nervous system, which in turn leads to increased NA and DA levels. After yuanzhi treatment, the content of phenylalanine in brain tissue was significantly reduced, and the symptoms of sleep disorder in model rats were relieved.

Discussion

Sleep is crucial for all living things, as it makes up about a third of our lives, and when disrupted or disrupted, it can have serious negative effects on quality of life and daytime functioning, and can even affect physical health. The traditional Chinese medicine PR has the effect of sedation and hypnosis, which can improve sleep from a variety of nerve aspects. It provides new thinking for the treatment of various diseases caused by sleep disorders.

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Progress in the research on prevention effects of tonic herbal medicines for Alzheimer's disease

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Abstract

The prevalence of Alzheimer's Disease (AD) is increasing year by year, but there is still no effective treatment. Therefore, it is particularly important for its early intervention and new drug development. Traditional Chinese medicine believes that AD is mostly caused by kidney deficiency and is mostly treated with tonic drugs in clinical. The research on tonic drugs such as nourishing qi, nourishing yang, nourishing blood, and nourishing yin in the prevention of AD were summarized to enrich the scientific connotation of traditional Chinese medicine in the treatment of AD, and to provide reference for the further research and development of AD drugs.

Key words: Alzheimer's disease, tonic medicine, traditional Chinese medicine

1. Introduction

Alzheimer's Disease (AD) is a brain disease with progressive lesions of the nervous system. and is dependent on multiple factors, such as A β protein deposition, Tau protein phosphorylation, cholinergic system, oxidative stress, neuroinflammation. With the aging of the population, the incidence of AD is on the rise. A survey in 2020 showed that among the elderly over 60 years old in China, the number of AD patients reached 9.83 million, with a prevalence rate of about 3.9%. But there is currently no drugs to cure AD. In view of the complex pathogenesis and high prevalence of AD, early intervention of traditional Chinese medicine with multiple targets and low side effects has become a hot spot in AD drug research and development. Tonic medicine with nourishing effect is a good choice for the prevention of AD.

2. qi-invigorating medicines

Qi-invigorating medicines can replenish Qi to tranquilize mind and improve brain learning and memory ability, represented by Panax ginseng, Astragalus membranaceus, Eleutherococcus senticosu. Panax ginseng has great nourishment of renal qi to tonic five viscera. Kwan demonstrated that its main components ginsenosides could protect A β -induced oxidative stress in PC12 cells, and its action mechanism was related to the reduction of reactive oxygen species and the improvement of related parameters of mitochondrial bioenergetics, mitochondrial membrane potential and mitochondrial morphology^[1]. With the effect of tonifying Qi and lifting yang, Astragalus membranaceus can improve brain learning and memory ability. A research reported that Astragalus polysaccharide could activate the Nrf2 pathway, relieve oxidative stress, reduce the level of A β ₁₋₄₀ and A β ₁₋₄₂ in APP/PS1 mice, and significantly improve the cognitive function of mice^[2]. Astragaloside IV could inhibit the activity of neuroinflammatory factors, protect neurons from damage, and improve cognitive impairment in mice^[3]. Eleutherococcus senticosu replenishes Qi and nourishes blood to protect nerves. A new study suggested that its active ingredients such as

ciwujianoside C3, eleutheroside M, and ciwujianoside B could penetrate the blood-brain barrier and enhance memory ability^[4].

3. yang-invigorating medicines

Yang-invigorating medicines can invigorate kidney-yang and improve learning and memory ability, such as *Epimedium brevicornu Maxim.*, *Cistanches Herba*. Relying on strengthening yang and tonifying the kidney, *Epimedium brevicornu Maxim.* can be used to treat dementia caused by kidney deficiency. The study found that icariin in *Epimedium brevicornu Maxim.* improved cognitive dysfunction in AD rats by activating autophagy-lysosomal system and reducing the accumulation of amyloid A β protein^[5]. *Cistanches Herba* has the function of invigorate the kidney-yang and its active ingredient can exert anti-AD effect. Yang et al. proved phenylethanoid glycosides in *Cistanches Herba* could attenuate the cognitive dysfunction features of the APP/PS1 transgenic mice^[6].

4. yin-invigorating medicines

Yin-invigorating medicines can replenish vital essence and nourish the marrow to cultivate the mind. *Lycium barbarum* is a kind of medicine and food homologous supplement medicine and food homology, which can tranquilize mind and benefit intelligence by nourishing yin. The research found that *Lycium barbarum* polysaccharides exerted neuroprotective effect on L-glutamate-damaged PC12 cells through mitochondrial pathway, and significantly increased the levels of acetylcholine and choline acetyltransferase in AD mice, and improved cognitive dysfunction^[7]. *Polygonatum chinensis* plays a role in preventing AD by nourishing kidney and nourishing yin. A monomeric polysaccharide from *Polygonatum chinensis* was proved to improve cognitive impairment in 5xFAD mice, which was related to the regulation of gut microbiota^[8].

5. blood-invigorating medicines

Blood-invigorating medicines can nourish heart and soothe the nerves by tonifying blood. Mulberry has the function of tonifying blood and reinforcing kidney. It has been shown that mulberry could reduce astrocytes in the cerebral cortex and hippocampus, relieve neuroinflammatory stress, clear A β protein deposition, and improve their learning and memory abilities of APP/PS1 mice^[9]. *Angelica sinensis* has the effect of nourishing and activating blood, and is mainly used for vascular dementia. Du et al. found that *Angelica* polysaccharide regulated neurotransmitters, free radicals and inflammatory factors by activating the BDNF/TrkB/CREB pathway, to protect neurons in the hippocampus, and to improve memory impairment in AD rats^[10]. The processed *Rehmannia glutinosa* has stronger nourishing-yin effect, so as to better play the role of improving AD. Modern research shown that oligosaccharides of prepared *Rehmannia Radix* enhanced antioxidant capacity and reduced A β toxicity on Transgenic *Caenorhabditis elegans* Models for AD^[11].

6. Discussion

Studies have shown that nourishing qi, strengthening yang, nourishing yin, and nourishing blood can regulate the heart and kidney, improve learning and memory ability, and the mechanism of action is related to the improvement of nerve function and oxidative stress and other factors. However, most traditional Chinese medicines have complex components, and the mechanism of action to improve AD has not been fully elucidated; Single herbs mostly stop at the experimental stage and lack clinical data. Therefore, it is necessary to formulate a program for the prevention and

treatment of AD according to the theory of traditional Chinese medicine, and to actively carry out clinical research, to provide strong evidence for AD new drug development.

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Pharmacological effects of Shen Bai formula on myocardial injury based on serum metabolomics coupled with UPLC-Q-TOF/MS/MS

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Abstract

Adriamycin was injected intraperitoneally to replicate the myocardial injury rat model which was evaluated by detecting the contents of serum myocardial zymogram, cTn-I, ATP etc., ECG, cardiac histopathological changes and recording the energy metabolism of rats. After that, metabolite profiling of myocardial injury was performed through ultra-high performance liquid chromatography combined with triple TOF mass spectrometry (UPLC-TOF/MS/MS) combined with pattern recognition approaches and pathway analysis. The results showed that Shenbai formula improved the detection indexes of rats in varying degrees. Through metabolomics, we found that 16 blood biomarkers were closely related to myocardial injury and 14 metabolites may correlate with the regulation of Shen Bai formula treatment. This study has revealed the potential biomarkers and metabolic networks of myocardial injury, illuminated the biochemistry mechanism of myocardial injury and the metabolic pathways influenced by Shen Bai formula.

Key words

Viral myocarditis, Myocardial injury, Shen Bai formula, Metabolomics, Biomarker, Promethion metabolic measurement system

Viral myocarditis (VMC) is the focal or diffuse myocardial cell degeneration and necrosis, accompanied inflammatory cell infiltration by virus, which leads to the myocardial injury, cardiac dysfunction, and arrhythmia. Nowadays, the academic circles generally believe that there are three distinct phases in the pathogenesis of viral myocarditis [1-4].

Shen Bai formula (SBF) is a TCM formula consisting of the herbs, such as Astragalus membranaceus, Ginseng, Radix bupleurum, Sophora flavescens, etc., which is the main therapy of viral myocarditis sequelae in clinical. According to TCM theory and treatment after more than 5000 cases of clinical observation, it found that SBF has a good effect of eliminating and improving the arrhythmia and myocardial injury and prevents the development of viral myocarditis from chronic phase to sequela. Furthermore, recent research had discovered that a lot of chemical constituents of the herbs in SBF were confirmed as being able to treatment of viral myocarditis, myocardial injury, and other cardiovascular diseases [5-8].

Objective

To lay a foundation for the research on the pharmacodynamic material basis of traditional Chinese medicine in the treatment of myocardial injury and the development of new traditional Chinese medicine.

Methods

After a week of adaptive feeding, rats were randomly divided into 8 groups: control groups 1 and 2, model groups 1 and 2, Shen Bai formula treatment groups at high dose (SBFH), medium dose (SBFM), low dose (SBFL) and captopril group. In addition to the control groups, the rats with intraperitoneal injection of Adriamycin solution once every other day, every time 2.5mg/kg, for 6

consecutive times. At the beginning of the 12th day, rats from control group 1 and model group 1 were sacrificed to collect biological samples for myocardial injury model evaluation and biomarker assay. At the same time, treatment groups were in accordance with the 15.3g/kg of high dose, 7.65g/kg of medium dose, 3.825g/kg of low dose and 2.25mg/kg of captopril were administered orally, once a day, treatment for a month.

Collect rat blood and prepare serum analysis samples with appropriate methods. The electrocardiogram, liver, heart and spleen index, serum CK, LDH, α -HBDH, AST, cTn-I, SOD, MDA, ATP and BNP contents and myocardial pathological changes and the metabolic measurement system record were evaluated to evaluate the myocardial injury model. After that, imported the data collected by mass spectrometry into Progenesis QI software, selected ions with VIP value greater than 1 or S-plot absolute value greater than 0.85, but must also meet the requirements of P value less than 0.05, Max fold change greater than or equal to 2, and Minimum CV value less than or equal to 30 as analysis conditions, to identify biomarkers accurately, we need to combine peak view 2.1 and Master view software, KEGG and HMDB database.

Results

Based on the established metabolomics techniques, the structures of a total of 16 blood potential biomarkers were identified: Deoxyadenosine, 9'-Carboxy-gamma-tocotrienol, Sphingosine 1-phosphate, cis-4-Hydroxy-D-proline, 9-cis-Retinoic acid, Norvaline, 2-Methylbutyryl Glycine, Leukotriene B4 etc. and these blood biomarkers involve seven metabolic pathways, which are Sphingolipid metabolism, GPI biosynthesis, Retinol metabolism, Glycerophospholipid metabolism, Biosynthesis of unsaturated fatty acids, Arginine and proline metabolism, Purine metabolism. It can be clearly found from metabolic profiles that after the SBF treatment of Adriamycin induced myocardial injury, the metabolic profile of rats has changed, which indicates that drugs have a strong effect on metabolites. To determine whether SBF was possible to influence the metabolic pattern of rat myocardial injury, the intensities of the metabolites were compared. SBF high and medium dose groups can reverse biomarkers close to the control group, 14 biomarkers were statistically significant reversed by the high dose and 13 biomarkers were statistically significant reversed the medium dose, besides, captopril group can reverse 12 biomarkers while the low dose reversal effect was not good.

Conclusions

To our knowledge, we established metabolomics to approach to elucidate metabolic characters of the myocardial injury model rats induced by Adriamycin and therapeutic effects of SBF at the global metabolomics platform. This is the first study that reports UPLC-TOF/MS/MS to detect the blood metabolic profile and biomarkers in rat model of myocardial injury and potential targets of SBF and its effects on myocardial injury based on a metabolomics strategy. We have successfully replicated a doxorubicin-induced rat model of myocardial injury and detected 16 potential biomarkers and predicted the major metabolites network of myocardial injury. Taking these biomarkers as possible drug targets, it is revealed that SBF could reverse the pathological process of myocardial injury through regulating the perturbed metabolism pathways. Serum metabolomics provides the basis for discovering the mechanism of SBF treatment of myocardial injury.

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Application of metabolomics technology on toxicity and detoxification mechanism of traditional Chinese medicine

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Abstract

Traditional Chinese medicine (TCM) is a unique healthcare resource in China and an economic resource with great potential. With the development of China's economy and society, the demand for healthcare services has been growing rapidly. TCM healthcare services mainly include health preservation, healthcare, medical treatment, and rehabilitation, and the core of herbal medicine is the supply of healthcare services based on TCM products. With the advancement of the TCM modernization process, the progression of the TCM healthcare industry has been promoted. Meanwhile, the toxicity and safety of TCM are the critical issues hindering the progression of TCM. Metabolomics can promptly analyze multiple metabolic pathways and show great advantages in the research on the efficacy and toxicity of herbal medicine. Based on the background of comprehensive healthcare, this paper briefly reviews the research progress of metabolomics technology in the toxicity and detoxification of TCM, in hope of assisting the development of the TCM healthcare industry with Chinese characteristics and serving the construction of healthy China.

Keywords: comprehensive healthcare; traditional Chinese medicine (TCM); toxicity; detoxification; metabolomics

1. Introduction

With the advent of the aging population society, the changing of people's lifestyles, and the continuous progression of the social economy, people's need for healthcare is becoming immediately urgent. Chinese medicine is an asset accumulated by the Chinese nation for thousands of years, and has made great contributions to human health. With the progression of the modernization and internationalization of herbal medicine, an increasing number of people have known and used it. However, Chinese medicine's ingredients are complex, and its safety has always been a concern, especially the safety of toxic herbal medicine. [1] Therefore, the toxicity of herbal medicine needed systematic and serious research. In the current research, acute and long-term toxicity, biochemical index detection, and histopathological observation are often used to evaluate the mode of herbal medicine toxicity. With the advancement of modern technology, the introduction of metabolomics technology has greatly contributed to the elucidation of the toxicity nature of Chinese medicine. To use high-throughput and high-sensitivity technology to conduct targeted and untargeted analysis of small molecules in organisms, monitor the whole process of toxicity occurrence and development [2], and identify potential toxicity biomarkers and related metabolic pathways to further clarify the mechanism of toxicity and detoxification, which enriches the research connotation of the toxicity of TCM.

2. Application of metabolomics in the research of toxic traditional Chinese medicine

Researchers have carried out a lot of studies on the metabolomics of the toxicity of herbal medicines and conducted in-depth discussions on the basis of toxic substances of Chinese

medicines, the mechanism of toxic action and the scientific connotation of changes in the toxic effects of Chinese medicines.

Cui et al [3] used metabolomics to research the reproductive toxicity of aristolochic acid I and identified 30 biomarkers of testicular toxicity caused by aristolochic acid I, including glycerol, creatinine, sphingosine, etc. Aristolochic acid I can induce pathological and physiological changes in testis by inhibiting amino acid metabolism, fatty acid absorption, and oxidative decomposition in mouse testis cells. Zhu[4] et al used metabolomics combined with traditional toxicity evaluation methods to systematically study the hepatotoxicity of cantharidin, identified 54 potential toxicity biomarkers, and found that the toxicity of cantharidin may be related to glutathione metabolism, taurine acid and hypotaurine metabolism, etc. He et al [5] used gas chromatography-mass spectrometry to detect and analyze the metabolic characteristics of rat plasma and urine samples after oral administration of periplocin and Panax notoginseng saponins, as well as the different compatibility ratios of Panax notoginseng saponins and Panax notoginseng saponins. A total of 49 potential biomarkers associated with periplocin-induced cardiotoxicity were identified. Seven pathways were identified by metabolomic pathway analysis. Through the analysis of related metabolic pathways, Panax notoginseng saponins can effectively reduce the cardiotoxicity of periplocin by affecting the tricarboxylic acid cycle, energy metabolism, and arachidonic acid metabolism.

Metabolomics technology can quickly analyze multiple metabolic pathways, and efficiently study the toxicity and detoxification of Chinese medicines. The mechanism of target organ toxicity can be comprehensively studied by analyzing endogenous metabolites. The introduction of metabolomics has transformed the traditional evaluation based on experience into a modern evaluation based on scientific methods and standards, making the research of TCM more scientific, normative and standard. However, with the deepening of research, it is found that the types of differential metabolites and the database required for metabolomics research are still limited, and the experimental results cannot be unified, and the integration of data obtained by different experimental methods needs to be improved.

3. Discussion

Due to the lack of scientific research on the pharmacodynamic material basis and mechanism of Chinese medicine, and the incomplete understanding of the toxicity and adverse reactions of Chinese medicine, it is challenging to evaluate its clinical value and safety. Solving the toxicity of traditional Chinese medicine and making it more widely used in clinical practice is the purpose of traditional Chinese medicine to treat diseases. The emergence of metabolomics technology may provide a more effective research model for the toxicity and detoxification of traditional Chinese medicine. Nevertheless, it is important to establish reliable, reproducible analytical methods that integrate metabolomic techniques with clinical questions and turn clinical questions into scientific questions. Solving the above problems will ensure the rationality and safety of traditional Chinese medicine, as well as promoting the globalization of traditional Chinese medicine. Furthermore, it is of great significance to develop the traditional Chinese medicine health industry, to further strengthen the research and development of modern traditional Chinese medicine, and to promote its standardization, scientificization and internationalization process, and it is more conducive to benefiting the cause of human health.

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Research progress on effective components of traditional Chinese medicine Astragalus under the background of general health

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Abstract

With the continuous progress of science and technology and the continuous improvement of health cognition, people have also put forward newer and higher requirements for the scientific and technological innovation and development of the medical and health industry; and the traditional Chinese medicine Astragalus has become a major medicine because of its ability to treat or affect some common diseases. One of the most popular herbal medicines in the world in the context of health, the active ingredients in it have always been in the spotlight. Therefore, this paper mainly reviews the bioactive substances of Astragalus, to pave the way for deepening the industrial development of Astragalus in the medical field and promoting the development of traditional Chinese medicine in a large health environment.

Key words: Astragalus, chemical constituents, medicinal value

Introduction

Health is the foundation and necessary condition for the all-round development of human beings. The cause of health is linked to people's well-being and economic development. With the progress of society, people's demand for health is increasingly urgent, which provides a huge impetus for the development of a large health environment. In this context, the development and utilization of traditional Chinese medicine has also ushered in a great opportunity for development. As a medicinal and edible variety of traditional Chinese medicine, astragalus has a large annual demand and is showing a steady upward trend. In the context of the continuous development of the big health industry and people's increasing awareness of health care, medicines using astragalus as raw materials are becoming more and more abundant^[1]. With the continuous deepening of research on Astragalus by domestic and foreign scholars, the chemical constituents of Astragalus have been continuously discovered. Studies have shown that the chemical components of Astragalus are mainly saponins, polysaccharides and flavonoids^[2]. This article will describe its chemical composition to provide a theoretical basis for the sustainable development of traditional Chinese medicine Astragalus in a large health environment.

Various chemical constituents in Astragalus

1. Saponins in Astragalus

Astragalus saponin is the main active ingredient in Astragalus. Since the 1970s, due to the progress of separation technology, more than 40 kinds of triterpenoid saponins have been isolated from Astragalus membranaceus and related plants of the common genus. Among them, 4 new saponins have been discovered one after another 2 species were also shown to stimulate splenocyte proliferation in mice, and cytotoxicity was not evident^[3].

2. Flavonoids in Astragalus

One of the beneficial components of the biological activity of astragalus is flavonoids. Since people have isolated formononetin and isoflavones from Astragalus membranaceus, more than 60

flavonoids have been isolated and identified, such as flavonoids, isoflavones, flavonols, isoflavones and dihydroisoflavones, etc^[4].

3. Polysaccharides in Astragalus

The molecular structure of astragalus polysaccharide (APS) is relatively complex, and separation, purification and characterization are difficult. Therefore, more than 30 astragalus polysaccharide molecules have been isolated so far. , further studied the effect of different temperatures on the structural characteristics and activity of astragalus polysaccharides^[5].

4. Other ingredients

There are also some trace elements in astragalus, such as magnesium, barium, molybdenum, silver, etc.; and organic substances such as betaine, choline, glutamic acid, proline, arginine, beta sitosterol, etc.; also contains 25 kinds of amino acids such as asparagine, aspartic acid, glutamic acid, etc., of which threonine, lysine, phenylalanine, isoleucine, methionine, leucine and valine are essential amino acids^[6].

Discussion

As a commonly used bulk traditional medicinal material, Astragalus enjoys the status of "Ten Medicines and Eight Qi" in the field of traditional Chinese medicine. This paper reviews the chemical constituents of Astragalus that have been discovered, and lays the groundwork for promoting the continuous role of traditional Chinese medicine Astragalus in the health industry.

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Progress on anticancer activity and mechanism of natural flavonoid compounds for nasopharyngeal carcinoma

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Abstract

Nasopharyngeal carcinoma (NPC) is one of the common human malignant diseases all over the world especially in southern China and South East Asia which is typically treated with radiotherapy and chemotherapy. However, the survival and life quality of NPC patients are still very poor. Therefore, novel and selective antitumor agents are pressingly needed. Herbal medicines have been used for many centuries to treat patients with malignant tumors. In recent years, the role of flavonoid compounds in maintaining normal physiological functions and preventing diseases has received wide attention. To provide more information for the research and development of anti-NPC drugs, we reviewed and summarized the progress in the discovery of natural flavonoid anti-NPC compounds and their mechanism of action. The research shows that natural flavonoid compounds have showed potential activities on NPC in vitro or in vivo and also are worthy of further study and application in NPC treatment.

Key words: nasopharyngeal carcinoma, natural flavonoid, anticancer activity, mechanism

Nasopharyngeal carcinoma (NPC) is a characteristic tumor displaying epidemiological, genetic and regional distribution properties and is unique by its natural behavior and therapy. Although radiotherapy can achieve a high cure rate in early stage NPC, the treatment outcome for the advanced stage is still unsatisfactory. Cisplatin and paclitaxel have been two of the most active cytotoxic chemotherapeutic drugs in NPC. Despite an aggressive approach combining both chemotherapy and radiotherapy, about 25-30% of patients still fail with local recurrence and/or distant metastases. The prognosis for patients with metastatic disease is poor. Therefore, new therapeutic strategies need to be explored in order to further improve the treatment outcome.

The chemical structure of natural products was rich, which could not only be used in combination with chemotherapy drugs to reduce the drug resistance of tumor cells to chemotherapy drugs, but also be used alone in some advanced cancer patients with poor physique and unable to tolerate large doses of anticancer drugs. Therefore natural products played an increasingly important role in the development of new anti-cancer drugs and natural flavonoid compounds were one of them. In the present study, we reviewed the chemical structure, anticancer activity, anticancer mechanisms for NPC. We provided new perspectives and possibilities for discovering lead compounds for NPC treatment, and also provided ideas for the mechanistic study of natural compounds against NPC.

Objective

To review and summarize the progress in the discovery of natural flavonoid anti-NPC compounds and their mechanism of action.

Results and discussion

In recent years, flavonoids that had been found with anti-NPC activity were quercetin(1), baicalin hydrate(2), isoliquiritigenin(3), pectolarigenin(4), galangin(5) and garcinone C(6).

Quercetin(1), the most abundant flavonoid found in Traditional Chinese Medicines, fruits, vegetables and in beverage such as tea and red wine. Quercetin inhibited both proliferation and angiogenesis in nasopharyngeal cancer through suppression of VEGF and NF- κ B activity^[1]. Baicalin hydrate(2) is a flavonoid with anti nasopharyngeal carcinoma activity extracted from *Scutellaria Baicalensis georgi*. Baicalin hydrate inhibits NPC cell growth in vivo and in vitro by inducing apoptosis and cell cycle arrest. Baicalin hydrate significantly induced cell cycle arrest at the G2/M phase by affecting the cyclin-related proteins level and induced cell apoptosis in a p53-dependent manner in vivo and in vitro^[2]. Isoliquiritigenin(3) can inhibit the migration and invasion of nasopharyngeal carcinoma cells by down regulating the expression of MMP-2 and MMP-9^[3]. And inhibit the proliferation and induce apoptosis of nasopharyngeal carcinoma cells by regulating mir-32/lats2/wnt. Pectolinarigenin(4) is a flavonoid derived from the medicinal plant *Eupatorium odoratum L.* Pectolinarigenin inhibited cell viability and cell migration of NPC C666-1 cells in concentration- and time-dependent manner which was associated with the activation of mitochondrial-related apoptosis and the accumulation of reactive oxygen species (ROS). Pectolinarigenin also activated caspase signaling pathway^[4]. Galangin(5) is a flavonoid derived from the roots of the *Alpinia galanga (L.) Willd.* Galangin induces apoptosis and S-phase arrest by attenuating the PI3K/AKT signaling pathway. Silencing of p53 did not block the anti-cancer activity of galangin on NPC cells. Galangin effects on apoptosis and S-phase arrest in NPC cells are mediated via interfering with the PI3K-AKT signaling pathway in a p53-independent manner^[5]. Garcinone C(6), a natural compound isolated from *Garcinia oblongifolia* Champ., is a flavonoid derivative with potential cytotoxic effects on NPC which significantly inhibited cell viability of the human NPC cell lines CNE1, CNE2, HK1 and HONE1. Garcinone C stimulated the expression levels of ATR and 4E-BP1, while efficiently inhibiting the expression levels of cyclin B1, cyclin D1, cyclin E2, cdc2, CDK7 and Stat3^[6]. The anticancer activity and mechanism of natural flavonoid compounds for nasopharyngeal carcinoma were in Fig. 1.

To sum up, at present, there are more and more studies on the anti nasopharyngeal carcinoma effect of natural flavonoid compounds, but most of them remain at the level of activity research, and the mechanism research is not deep enough. Further exploring its mechanism of action is of great significance to the study of anti nasopharyngeal carcinoma effect of natural compounds.

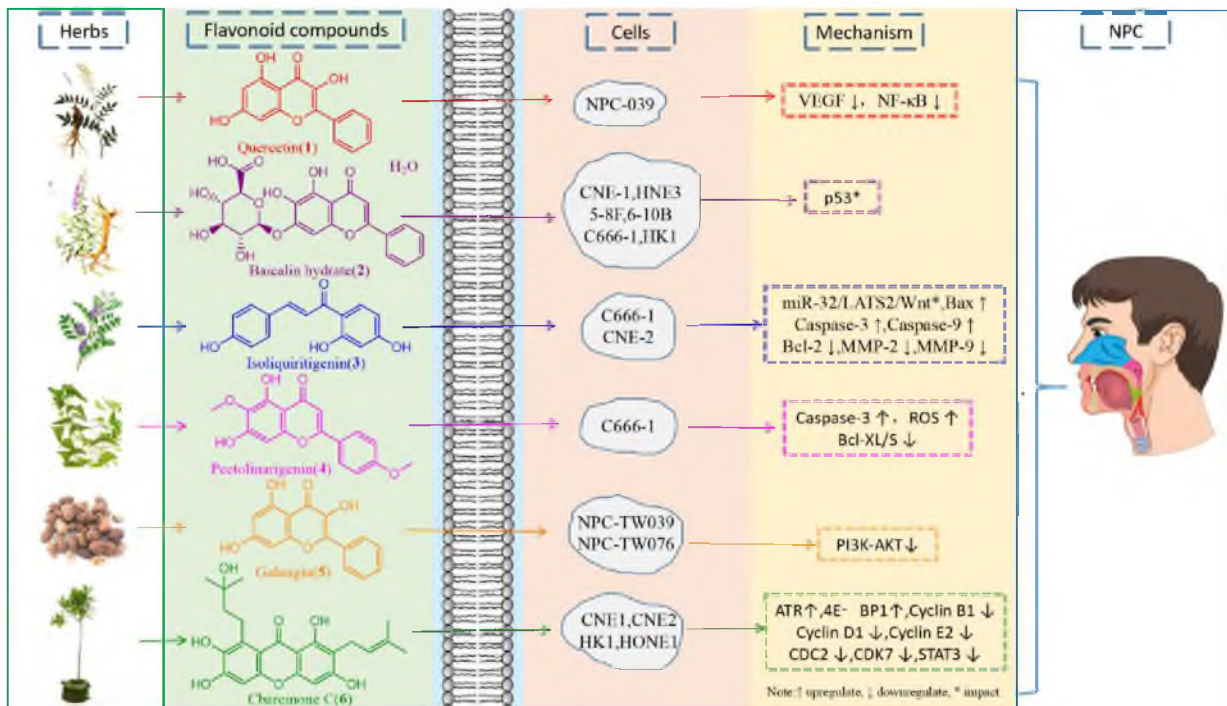


Fig. 1. The anticancer activity and mechanism of natural flavonoid compounds for nasopharyngeal carcinoma

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Research progress on the in vivo constituents and pharmacokinetics of *Acanthopanax Senticosi Radix Et Rhizoma Seu Caulis*

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Abstract

By reviewing the relevant literature records on the pharmacokinetic research of *Acanthopanax Senticosi Radix Et Rhizoma Seu Caulis* (ASR) in recent years, the pharmacokinetic processes of the active components of ASR in vivo, such as absorption, distribution, metabolism and excretion laws, were analyzed, thus this paper summarizes the ASR in vivo constituents and reviews the effects of pharmacokinetic parameters and mode of administration on pharmacokinetics, in order to provide effective reference and help for the further development and application of ASR.

Keywords: *Acanthopanax Senticosi Radix Et Rhizoma Seu Caulis*, pharmacokinetics, Isofraxidin, Eleutheroside

ASR is the dried root and rhizome or stem of *Acanthopanax senticosus*. It is a widely used Traditional Chinese Medicine that could invigorate qi, strengthen the spleen, and nourish kidney in the theory of Traditional Chinese Medicine. In recent decades, a great number of chemical, pharmacological, and pharmacokinetics studies on ASR have been carried out worldwide. Several kinds of chemical compounds have been reported, including triterpenoid saponins, lignans, coumarins and flavones. Besides, a growing number of pharmacokinetics researches of ASR also have been conducted. However, no review of pharmacokinetics of ASR has been published by now, so the aim of present review is to give a comprehensive summary and analysis of the pharmacokinetics of ASR by consulting currently available literatures.

Constituents in vivo of ASR

Wang et al.^[1] identified 27 prototype ingredients and 20 metabolites were detected in the plasma of rats after oral administration. From the analysis of the metabolites detected in the plasma, the metabolic reactions of flavonoids include hydroxylation, deglycosylation, glucuronide conjugation and demethylation. The metabolic reactions of coumarins include hydroxylation and hydrolysis. In the end, 10 drug prototype ingredients and 7 metabolites were found in the drug-containing rat brain tissue, and the main constituents in vivo are eleutheroside B, E and isofraxidin.

Pharmacokinetics of Isofraxidin

Isofraxidin^[2], 7-Hydroxy-6,8-dimethoxycoumarin, is a major active component of ASR, commonly used in anti-tumor^[3], anti-oxidation, antibacterial and anti-inflammatory treatment. Sun et al.^[4] determined the pharmacokinetic parameters of isofraxidin in ASE or pure compounds by solid phase extraction and high performance liquid chromatography. The results showed that the process of pure isofraxidin accorded with the two compartment model, the absorption was very rapid with the maximum concentration existing approximately 0.19 h which is not significantly different from the published data (T_{max} is about 0.236 h), it was cleared slowly from rat body ($T_{1/2\beta}=7.91\pm 1.03$ h). Contrastively, the plasma concentration of isofraxidin after oral administration of ASE showed two time courses; the first course is from 0 to 4h, the data fitted two compartment models, The second course of ASE, from 4 to 24 h, fit the one compartment model. Consequently the elimination time

of isofraxidin in rats after oral administration of ASR extract was longer than that after oral administration of isofraxidin.

Pharmacokinetics of Eleutheroside B and Eleutheroside E

Eleutheroside B, eleutheroside E are the main pharmacologically active components of the roots. Eleutherosides stimulate excitement, relieve fatigue, improve agility and learning ability, and extracts have been used in remedies for recovery after serious illness.

Ma et al.^[5] compared the pharmacokinetics of single drug (eleutheroside B and E) and water extract. In addition, the absolute bioavailability of eleutheroside B and eleutheroside E after oral and intravenous administration was also studied. The data showed that the AUC_{0-t} of eleutheroside B was found to be significantly increased after oral administration of ASR aqueous extract compared with oral administration of a single substance ($P=0.034$). No significant difference was observed in C_{max} of eleutheroside B and eleutheroside E in rat plasma for an aqueous extract of ASR and single substances. Moreover, enterohepatic circulation was found in eleutheroside E after oral administration an aqueous extract of ASR. Hence notable differences in the pharmacokinetic behavior and enterohepatic circulation were found after oral administration of an aqueous extract of ASR compared with the single substances.

Conclusions

ASR was widely adapted as a nourishment treatment in Chinese folk medicine. It gained considerable advocacy and use among a fairly broad Soviet population after its introduction to the general Soviet medical community. The Chinese Pharmacopeia recorded it as a formula agent, used widely in Traditional Chinese Medicine. To date, a large number of compounds have been isolated and identified from ASR and various biological activities of the compounds have been confirmed. Among them, Isofraxidin, syringin, eleuthroside E, ASP, sesamin, and flavonoids are the active compounds the main types of active compounds responsible for the pharmacokinetics of ASR. The pharmacokinetic characteristics of these active components provide an effective basis for the material basis and mechanism of action of ASR in vivo. However, more studies are still needed to demonstrate more knowledge to allow a better understanding of this herb.

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Research progress in rheumatoid arthritis treatment of traditional Chinese medicine

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Abstract

Rheumatoid arthritis (RA), a common inflammatory disease of the immune system. The pathogenesis of RA is complex, which is one of the main diseases leading to pain and disability, and affects the quality of life of patients. The incidence rate is also increasing year by year. Many reports on the treatment of RA with Traditional Chinese Medicine (TCM) have been published, and have attracted more and more attention from doctors all over the world.

Keywords: Rheumatoid arthritis(RA); Traditional Chinese Medicine

Introduction

Rheumatoid arthritis (RA) is a common inflammatory disease of the immune system, such as delayed diagnosis and treatment, joint synovitis and formation of pannus in the joint, and then continuously invade the cartilage and bone of the joint, resulting in the destruction of the joint deformity fusion, and ultimately loss of function. Disability due to loss of the ability to work seriously affects health and the quality of life of patients^[1]. Disabled as a result of the loss of the Labour force, the quality of life of patients is severely reduced. At the same time, it also brings a huge burden to patients and society. Therefore, many methods for the treatment of RA have been proposed. The commonly used drugs for RA in western medicine mainly include steroids and non-steroidal anti-inflammatory drugs, anti-rheumatism drugs, biological agents, analgesics and hormones, but none of them can achieve a complete cure. And the above drugs have stomach irritation, renal toxicity, heart and liver damage, affect the endocrine system and other serious adverse reactions, so as to bring unnecessary pain to patients^[2]. The treatment mechanism of traditional Chinese medicine in the treatment of rheumatoid arthritis has the characteristics of rich layers, multiple targets, stable efficacy and high safety, especially in terms of symptom improvement. great significance.^[3]

Treatment of RA with monomer of TCM

With the development of traditional Chinese medicine, more and more anti-RA monomers are extracted from Traditional Chinese medicine. Studies have shown that quercetin can induce the apoptosis of fibroblast synovial cells and inhibit the proliferation of fibroblast cells by activating p53, reducing the release of cytochrome C, inhibiting the expression of Bcl-2, Bax and interleukin 1 β ^[4]. It can also activate osteoclasts and inhibit cartilage degradation by reducing interleukin-1 β and tumor necrosis factor- α levels^[5]. Baicalein can significantly improve oxidative stress, inhibit p38 phosphorylation caused by nuclear translocation of CFA and P65, and induce changes in oxidative protein products and inflammatory cytokine levels^[6]. β -Sitosterol has an effect on the polarization of macrophages, can induce macrophages to secrete more interleukin 10, and significantly inhibit the infiltration of inflammatory cells.

TCM extract for RA Treatment

The extract of Cortex cercis significantly improves RA patients by reducing serum levels of

inflammatory factors such as TNF- α , IL-1 β , IL-6 and IL-10. The swelling degree of the hind paw in mice and the writhing response in mice have obvious anti-inflammatory and analgesic effects^[7].

The extract of Ashwagandha Ethanol inhibits the activity of NF- κ B signaling pathway by reducing the phosphorylation levels of nuclear factor kappa B (NF- κ B), nuclear factor kappa B inhibitor- α , (I κ B- α), thereby reducing serum TNF- α , IL-1 β , and IL-6 and other inflammatory factors, play a significant anti-RA effect^[8].

TCM prescription

Different from a single traditional Chinese medicine prescription, many kinds of traditional Chinese medicines are organically combined according to the compatibility to improve the curative effect or reduce the side effects. Ermiao San is the water extract of Cork and Atractylodes. At present, it has been proved in clinical application that Ermiao Powder has a good curative effect in the treatment of rheumatoid arthritis^[9]. At the same time, modern animal experiments have also explained that Ermiao Powder can activate nuclear transcription factor κ B and promote the phosphorylation of mitogen-active protein kinase (MAPK), thereby relieving joint congestion and edema in rheumatoid arthritis rats, and reducing synovium. Extent of tissue proliferation and articular cartilage destruction^[10].

Treatment of RA with external treatment of TCM

External treatment of traditional Chinese medicine is an effective method for the treatment of RA, and its treatment is worthy of clinical promotion, including external application of traditional Chinese medicine, traditional Chinese medicine fumigation and washing, bee acupuncture, moxibustion and other external treatment methods of traditional Chinese medicine for the treatment of RA. External treatment of traditional Chinese medicine or combined oral administration of traditional Chinese medicine, the control group was only given oral administration of traditional Chinese medicine, and the treatment group was given both oral administration of traditional Chinese medicine and external treatment of traditional Chinese medicine. Significant improvement, the total effective rates were 68% and 95%, the differences were statistically significant. The results of this study suggest that TCM external therapy is a safe and effective treatment method, and provides an option for improving the compliance of RA patients.

Discussion

This paper reviews the current situation of TCM in the treatment of RA from four aspects: traditional Chinese medicine monomer therapy, traditional Chinese medicine extract therapy, traditional Chinese medicine prescription therapy and traditional Chinese medicine external treatment. The literature reviewed in this paper shows that traditional Chinese medicine has a certain role in the prevention and treatment of RA. Although the preventive effect of traditional Chinese medicine on RA patients and RA animal models has been confirmed, there are still some problems, such as the insufficient number of subjects and the inability of animal models to fully reflect the characteristics of RA patients. Therefore, further clinical trials, especially randomized controlled trials, are needed to confirm the efficacy and safety of traditional Chinese medicine in the prevention and treatment of RA. At the same time, in addition to the above-mentioned traditional Chinese medicine treatment, exploring other Chinese herbal medicines and traditional Chinese medicine prescriptions may lead to new breakthroughs in the prevention and treatment of RA.

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Pathological mechanism of diabetic peripheral neuropathy

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Abstract

Diabetic peripheral neuropathy (DPN) is a common complication of both type 1 and 2 diabetes. It is a leading cause of lower-limb amputation and disabling neuropathic pain. DPN is a culmination of a complex interaction of several causatively linked pathophysiological processes, many of which are not fully understood. Persistent hyperglycemia, neurotrophic deficiency, thalamic dysfunction, oxidative stress, and metabolic and autoimmune disorders accompanied by glial cell activation, have been suggested as possible mechanisms that may contribute to the pathogenesis of DPN. Based on the pathogenesis, improve the understanding of DPN, and promote the development of the big health industry with characteristic medical culture.

Key words: Diabetic peripheral neuropathy (DPN); Hyperglycaemia; Neurotrophic factor deficiency; Inflammation; Oxidative stress

Health is the foundation and necessary condition for the all-around development of human beings, and the development of the health industry is also the common pursuit of the general public. DPN is the most common complication of both type 1 and 2 diabetes and occurs in more than half of affected individuals. Unfortunately, the early manifestations of this insidious disease are often missed until the disease is well established, at which point it seems to be irreversible. Importantly, most DPN-related amputations are preventable. With the help of "Healthy China" and the construction of the big health industry, this paper discusses diabetic peripheral neuropathy and provides a theoretical reference for the clinical application of DPN prevention and treatment according to its pathogenesis.

1. Hyperglycaemia

Chronic hyperglycaemia has a key role in the pathogenesis of DPN. Through several disturbances in metabolic pathways, hyperglycaemia leads to abnormalities in nerve polyol, hexosamine, and protein kinase C pathways. These abnormalities trigger the release of proinflammatory cytokines, accumulation of advanced glycation end products, and generation of reactive oxygen species^[1]. Simultaneously, the function of vascular endothelial cells is damaged and the nerve microcirculation is abnormal, the blood is in a hypercoagulable state, the vascular lumen is narrowed or even blocked, microcirculation disorders, nerve ischemia, hypoxic damage, and destruction of the continuity of myelin^[2]. Separately and in concert, these glucotoxicity metabolic and ischaemic changes lead to DPN by producing nervous system oxidative stress and apoptosis of both neurons and supporting glia.

2. Neurotrophic factor deficiency

Growth factors have the effect of promoting the growth and survival of neurons, and can also promote the growth of neuronal axons. As a special protein factor in the body, the neurotrophic factor plays an important role in maintaining the function of neurons and nerve fibers. The lack of neurotrophic factors will lead to the decline of neural tissue physiological function and self-healing ability. Some data show that nerve growth factors, brain-derived neurotrophic factors, and

insulin-like growth factors among neurotrophic factors are involved in the occurrence and development of DPN^[3].

3. Inflammation

The stimulation of non-neuronal cells (astrocytes, microglia, and immune cells) has a significant character in the growth of neuropathic pain. Activated microglia in the spinal cord are demonstrated in several studies to have a critical aspect in neuropathic pain by releasing proinflammatory cytokines, that are frequent intermediaries of allodynia and hyperalgesia. Pro-inflammatory cytokines are produced by glia and immunological cells have been implicated in various studies as a mechanism for neuropathic pain of various roots. Painful neuropathy in rats is connected to the liberation of pro-inflammatory cytokines such as IL-1, IL-6, and TNF^[4].

4. Oxidative stress

Oxidative stress is an imbalance between oxidation and anti-oxidation in the body, and it is a negative effect of free radicals in the body^[5]. The production of free radicals causes diabetic neuropathy. Increased glycolytic activity is a primary contributor process. In reality, multiple studies in experimental diabetes have depicted tissue injury induced by oxidative stress in the peripheral nerve. Mitochondrial damage also impairs neurotrophic support, resulting in lower levels of nerve growth factor (NGF) and neurotrophin-3 (NT-3). In the state of oxidative stress, on the one hand, peripheral nerves are damaged and the secretion of neurotrophic factors is reduced; on the other hand, continuous oxidative stress can induce nerve cell damage and even apoptosis, and the intracellular neurotrophin will be reduced accordingly, and vice versa. Not conducive to the body's self-compensatory repair of damaged nerves.

DPN is a common complication of diabetes, and its pathogenesis is very complex, including factors such as hyperglycemia metabolism, vascular damage, and lack of growth factors. These mechanisms work together to eventually lead to DPN. At the same time, there are still different opinions on its etiology and pathogenesis in the field of motherland medicine. Therefore, further research on its various factors will help people to have a more comprehensive understanding of painful diabetic peripheral neuropathy, to achieve the purpose of prevention and treatment.

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Metabolomics Advancing Effective Components Discovery from Traditional Chinese Medicine

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Abstract

Background Traditional Chinese medicine, a long history in China, has helped humans fight diseases and protect life, health, and reproduction. However, it has not been recognized internationally owing to the effective components are ambiguity. The emergence of metabolomics promotes the effective components discovery from traditional Chinese medicine. **Objective** To provide reference for the study of effective components of traditional Chinese medicine based on metabolomics. **Methods** Metabolomics, effective components and traditional Chinese medicine are used as keywords for literature retrieval through the pubmed platform, and the relevant literatures are summarized. **Results** This review introduces the research strategy based on metabolomics and its application in the discovery of effective components. **Conclusions** At present, the research on effective components from traditional Chinese medicine has made great achievements based on metabolomics.

Key words: metabolomics, chinmedomics, effective components, biomarkers, molecular targets
Traditional Chinese medicine (TCM) is a big complex system. A single herb has multiple components, and each components can interact with other components. In addition, the components in the same TCM from different habitats are also different. However, most of the TCMs used in clinical practice are formulae^[1]. The single herb contains many components, formulae become a very complex system. Therefore, it is extremely difficult to indentify the effective components of TCM. The proposal of precision medicine requires that TCM has clear effective components and action mechanism, etc.^[2], which needs a systematic approach / strategy to solve this problem. Metabolomics can characterize the effects of external factors on organisms from the molecular level - endogenous metabolites changes, for example, capture how circadian rhythms shift the types and levels of metabolites an organism produces, reveal transitions between health and disease in people or model organisms^[3]. Its systematicness and integrity coincide with the theoretical system of TCM^[4]. Therefore, metabolomics are widely used in the field of TCM research, for example, biomarker identification, effective components discovery and target exploration by mass spectrometry(MS)-based metabolomics^[5].

1 Metabolomics as drivers for biomarkers identification

The metabolome, the entity of metabolites, has become widely accepted as the dynamic and sensitive measure of the phenotype at the molecular level, placing metabolomics at the forefront of biomarker and mechanistic discoveries related to pathophysiological processes^[6]. The endogenous metabolites are identified by high-throughput analysis technology, and screening of syndrome / disease biomarkers by data analysis approach. He Yanmei et al screened out 25 potential urine biomarkers of Dampness-heat Jaundice Syndrome (DHJS) model rats by urine metabolomics based on UPLC / MS combined with pattern recognition, including Arachidonic acid, Phenylpyruvic acid, L-Urobilin and so on^[7].

2 Metabolomics:Advancing effective components discovery

Biotransformation of traditional Chinese medicine through metabolic enzymes in vivo, before the therapeutic effect, is proceed. Therefore, in vivo and in vitro chemical components analysis is the basis to find active ingredients^[5]. Preliminary discovery of potential effective components by linking syndrome / disease biomarkers to chemical components from blood, urine, tissue fluid, et. Liu Shaobo et al, with chinmedomics as the core, used high-throughput UPLC-MS technology to analyze the biomarkers in the rat model of kidney-yin deficiency syndrome. In the state of marked effect, the constituents absorbed into blood of Zhibai Dihuang Pill (ZBDH) were identified. Through the establishment of the correlation between biomarkers and blood transitional components, the effective components of ZBDH in the treatment of kidney-yin deficiency syndrome were determined, including Jatrorrhizine, 24-Deacetylalisol O, Armeparine metabolites, Ipolamiide, etc^[8].

3 Target exploration towards metabolomics

Deciphering the molecular targets is important, and metabolomics have achieved a breakthrough in target exploration, for instance, metabolomics can indicate potential targets for therapeutic intervention, especially promising enzymatic targets^[9]. Wei Wenfeng et al identified 42 differential metabolites in rats with damp-heat jaundice syndrome (DHJS) by chinmedomics, and found that Zhizibaipi Decoction (ZBD) could significantly reverse 29 differential metabolites, including chenodeoxycholic acid sulfate, bilirubin, D-urobilinogen, estrone glucuronide, 3-oxo-4,6-choladienoic acid, which participate in linoleic acid metabolism, glycerol phospholipid metabolism, and ascorbic acid and aldose metabolism^[10].

4 Future perspectives

Nowadays, metabolomics still has some limitations, and it needs to be combined with other omics (genomics, transcriptomics, proteomics, etc.), gut microbiota research, and network pharmacology to make the research results more comprehensive. It is believed that with the continuous improvement of modern analytical instruments, data processing methods and metabolic databases, metabolomics has made greater contributions to the development of traditional Chinese medicine.

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Progress of systems biology in the research of traditional Chinese medicine for coronary heart disease treatment

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Abstract

Systems biology systematically interprets the potential therapeutic mechanisms of traditional Chinese medicine via multi-component, multi-level, multi-target, and multi-path on the overall level, which is helpful for the research on the mechanism of traditional Chinese medicine for prevention and treatment of coronary heart disease(CHD). The applications of omics strategies for CHD research have been a hot topic. This paper discusses the ideas and progress of transcriptomics, proteomics, metabolomics and Microbiomics integration technology in the research of traditional Chinese medicine for prevention and treatment of CHD. This review provides a reference for the application of multi-omics technology in the in-depth study of traditional Chinese medicine for prevention and treatment of CHD.

Key words: systems biology; CHD; traditional Chinese medicine; omics

Introduction

Systems biology is a discipline that studies the composition of various components such as mRNAs, proteins, metabolites and microorganisms in a biological system and the interrelationships of these components under specific conditions, corresponding with its technology platform includes transcriptomics, proteomics, metabolomics, and microbiomics.

According to the China Cardiovascular Health and Disease Report, the number of patients with CHD in China is as high as 11.39 million, and the overall mortality rate is on the rise. Traditional Chinese medicine has definite curative effect on CHD and has its unique advantages. Using the technology and methods of system biology to study the treatment and prevention of CHD with traditional Chinese medicine has become a research hotspot of many scholars. The integrity and multi-level expression of system biology can better explain the mechanism of traditional Chinese medicine in treating coronary heart disease.

This paper summarizes four systems biology technologies and their applications in the treatment of CHD with traditional Chinese medicine, providing a technical platform for the mechanism of action in the treatment of CHD.

The applications of Systems biology

1 Transcriptomics

Transcriptomics is a discipline that studies the transcription of all genes in cells and their regulation of transcription at the overall level. The analysis of the whole situation of cell function, etc., common transcriptomic research technologies include gene chip, high-throughput sequencing and single-molecule sequencing, which can be used to sequence mRNA, lncRNA, circRNA and other genomes in samples. Berberine attenuated cardiomyocyte enlargement and stress overload myocardial hypertrophy by enhancing autophagy and downregulating the expression of lncRNA myocardial infarction-associated transcript (MIAT). Xiangdan injection can improve endothelial function in patients with CHD with blood stasis syndrome by regulating the expression of ET-1 and

eNOS mRNA.

2 Proteomics

Proteomics refers to the complete set of proteins expressed by the complete genome of a cell, tissue or organism. Separation techniques in proteomic studies include two-dimensional gel electrophoresis (2DGE), fluorescent two-dimensional differential gel electrophoresis (2D DGE), multidimensional liquid chromatography (MDLC), and capillary electrophoresis (CE). The proteomics method was used to study the changes of the protein profile of the body before and after the intervention of traditional Chinese medicine, which can evaluate and characterize the target and pharmacodynamic mechanism of traditional Chinese medicine from the molecular level, and provide a theoretical basis for the clinical diagnosis and treatment of traditional Chinese medicine. Liquiritin plays a protective role in CHD by regulating the proliferation and migration of hVSMCs by increasing SIRT1 protein expression^[1]. Catechins have anti-inflammatory effects by activating farnesoid X receptor, signal transducers and activators of transcription (STAT)-3 and protein kinase B (PKB/ Akt), thereby treating CHD^[2].

3 Metabolomics

Metabolomics is the study of the metabolic regulatory network of the body by studying the dynamic changes of the body's metabolites and disease processes. Metabolomics is widely used in the study of the pathophysiological changes of diseases, evaluating the functional status and changes of the living body as a whole to provide more information on disease diagnosis and drug efficacy. Metabolomics has the characteristics of integrity and system, which is consistent with the idea of "diagnosis and treatment" and "holistic view" of traditional Chinese medicine theory. By studying the change characteristics of endogenous metabolites caused by traditional Chinese medicine, it provides information of targets and mechanism to clarify the effective materials and action mechanism of traditional Chinese medicine on the prevention and treatment of CHD. Using UPLC-Q-TOF/MS technology research and analysis, Danlu Tablets can inhibit the expression of EGFR and activate MAPK signaling by regulating glycerophospholipid metabolism (LPCs) and energy metabolism (linoleic acid and γ -linolenic acid) in the serum of model rats. pathway, decreased the expression of TNF- α , IL-6, MMP9, ox-LDL and MDA, increased the expression of SOD, and then treated CHD^[3]. Xuefu Zhuyu Decoction can play a therapeutic effect on CHD by regulating lipid metabolism, amino acid metabolism and bile acid metabolism^[4].

4 Microbiomics

Microbiomics refers to the study of symbiotic or pathological microbial ecological groups on animals and plants. The microbiome includes bacteria, archaea, protozoa, fungi and viruses. The gut microbiota is directly related to human health. Traditional Chinese medicine and its active ingredients play a very important role in the treatment of CHD, which can maintain intestinal microecological balance, protect intestinal mucosa, and adjust the structure of intestinal flora. The main research techniques in microbiomics are 16S rRNA gene sequencing and metagenomic sequencing analysis. Baoyuan decoction can effectively improve the abnormal metabolism of intestinal flora Firmicutes and Bacteroidetes in rats with myocardial hypertrophy, thereby inhibiting pro-inflammatory and pro-oxidant signaling pathways, thereby protecting the myocardium^[5].

Conclusion

Systems biology adopts high-throughput technology to obtain complete information of organisms at

the transcript level, protein level, metabolite level and microbial level, and uses bioinformatics and data analysis techniques to characterize, which can deepen the understanding of traditional Chinese medicine. The overall understanding is consistent with the "multi-component, multi-effect, multi-target, and overall regulation" characteristics of traditional Chinese medicine. Therefore, systems biology technology can provide strong support for the application research of traditional Chinese medicine in the treatment of CHD, and will certainly promote the modernization process of traditional Chinese medicine.

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Research progress of danggui sini decoction in the treatment of primary dysmenorrhea

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Abstract

Danggui Sini decoction (DSD) has the effects of warming meridians, dispersing cold, nourishing blood and dredging pulse. It is widely used in clinical practice, and has a significant effect on the treatment of primary dysmenorrhea (PD). Research shows that DSD mainly plays its role in the treatment of PD by regulating inflammatory factors, spasmolysis and antioxidation. Modern clinical practice has adopted the methods of addition and subtraction and combined treatment, which has innovated the application of this prescription. This article will analyze and summarize the mechanism and clinical research of DSD in the treatment of PD.

Key words: Danggui Sini decoction, primary dysmenorrhea

Introduction

Dysmenorrhea is classified into primary dysmenorrhea (PD) and secondary dysmenorrhea based on whether the reproductive organs are pathological. PD is the most common type of dysmenorrhea, which is mainly caused by the increased content of prostaglandins (PG), oxytocin (OT), endothelin (ET) and other hormones [1], stimulating the contraction of myometrium or vascellum. Secondary dysmenorrhea is often seen in patients with endometriosis, adenomyosis and pelvic inflammation. DSD is widely used in modern clinical practice, mainly for peripheral neuropathy, dysmenorrhea and Raynaud's disease. This paper mainly reviews the research of DSD in the treatment of PD in recent years.

Pharmacological study on DSD

DSD mainly treats PD through anti-inflammatory, antispasmodic and anti-oxidative stress effects. Han Ying et al. [2] found through animal experiments that the extract of *Angelica sinensis* (Oliv.) Diels/*Paeonia lactiflora* Pall. in this prescription can reduce $PGF_{2\alpha}$ in rat endometrium, the total acid of *Angelica sinensis* (Oliv.) Diels can enhance the activity of macrophages and have anti-inflammatory effect. *Angelica sinensis* (Oliv.) Diels/*Paeonia lactiflora* Pall. extract can reduce the contents of vasopressin (OT) and oxytocin (OXT) in rat serum, alleviate the spasm of vascellum and myometrium, have antispasmodic effect, reduce the content of malondialdehyde (MDA) in serum, and have anti-oxidative stress effect. Que Danhua [3] and others applied network pharmacology and found that quercetin, kaempferol, isorhamnetin and other components may be the effective components of this prescription for the treatment of PD, and arachidonic acid metabolism, MAPK and NOD pathways may be the key pathways. Combined with animal experiments, they found that the level of writhing and uterine index decreased, uterine contraction decreased, vascular endothelial growth factor (VEGF) and cyclooxygenase 2 (COX-2) gene expression decreased, the level of IL-1, IL-6 and TNF- α were significantly reduced, which can verify that the prescription has antispasmodic and anti-inflammatory effects. Relevant literature [4,5,6]

also confirmed that quercetin, kaempferol and isorhamnetin can reduce PGs, TNF- α and other inflammatory factors to alleviate dysmenorrhea.

Clinical study on DSD

The curative effect of DSD was enhanced and the application of traditional prescriptions was innovated through the addition and subtraction of medicine, the change of administration method and the combination treatment with other methods. DSD combines with thermal moxibustion [7], compared with DSD alone, the VAS score is significantly reduced ($P < 0.05$). Plus modified DSD combines with acupoint sticking [8], the drug can reach the focus directly by selecting Qihai, Guanyuan and Shenque acupoints for sticking. After long-term medication, compared with DSD alone, the level of PGE₂ and PGF_{2 α} in serum were significantly reduced ($P < 0.05$), the VAS score was significantly reduced, and the effective rate was 95%, higher than 85% of the control group ($P < 0.05$). DSD combines with the specific electromagnetic wave therapeutic instrument (TDP)[9], due to electromagnetic wave can generate heat, the treatment can expand capillaries, improve microcirculation, improve uterine blood flow, and alleviate uterine spasm. After long-term medication, compared with ibuprofen treatment, the levels of serum high-sensitivity-c-reactive protein (hs-CRP) and IL-6 are significantly reduced ($P < 0.05$), the VAS score is significantly reduced ($P < 0.05$), the effective rate is 93.33%, higher than 73.33% of the control group ($P < 0.05$), the recurrence rate is 16.67%, lower than 53.33% of the control group ($P < 0.05$).

Discussion

A large number of clinical studies have proved the effectiveness and safety of DSD in the treatment of dysmenorrhea. And compared with routine western pharmaceuticals treatment such as ibuprofen, DSD has its own advantages, for example, the recurrence rate is lower ($p < 0.01$) and the symptoms keep improving despite withdrawing this prescription, indicating that this prescription can settle the root cause of the disease [10,11], which is of great significance for women who have suffered from dysmenorrhea for a long time. In the future, the combined application of DSD and other treatment methods has great potential and is worthy of further research. However, at present, there is little research on the effective components and action pathways of DSD. In the future, the combination of network pharmacology and experiments, and the technology of Chinmedomics can be applied to explore the effective components and action targets or pathways of DSD, providing scientific evidence for the clinical application of DSD.

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Research progress on pharmacological action of *Allium macrostemon*

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Abstract:

Allium macrostemon Bunge is a commonly used Chinese herbal medicines, which is mainly used to treat chest stuffiness and pains, abdominal distension, diarrhea and dysentery. Because of its high medicinal value, there have been many reports on the pharmacological effects of *Allium macrostemon*. In this paper, the current information concerning the pharmacological actions and the acting mechanism of *Allium macrostemon* is summarized comprehensively through reviewing relevant at home and abroad, intending to provide a critical appraisal of current knowledge for future in-depth study and rational development and utilization of *Allium macrostemon*.

KEY WORDS : *Allium macrostemon*; pharmacological actions; mechanism

Allium macrostemon Bunge (AMB), is a dry bulb of liliaceous plant (*A. macrostemon* Bge. or *Allium chinensis* G. Don. AMB), a well-known traditional Chinese medicine. It tastes pungent, bitter and warm in nature. Entering Lung, large Intestine meridian, has actions of promoting Qi circulation, activating Yang and removing stagnation inducing. It is an important traditional Chinese medicine for treating thoracic obstruction, diarrhea and dysentery. It mainly contains steroidal saponins, volatile oils, polysaccharides, nitrogen-containing compounds, phenylpropanoid compounds, flavonoids and other components¹. pharmacological studies showed that AMB possess a wide range of bioactivities such as anti-platelet aggregation, anti-atherosclerosis and blood lipid reduction, cardiovascular protection, spasmolysis and asthma relief, antioxidant, antidepressant, antibacterial and anti-tumor, suggesting that AMB are of important medicinal value. However, there is a lack of systematic review of pharmacological action and mechanism of AMB. In this paper, the pharmacological action and mechanism of AMB in recent years are reviewed, intending to provide a deeply understanding of the current research situation and scientific gap to promote future research and applications.

Antiplatelet aggregation activity

It is found that the mainly active ingredient of ABM is *Allium macrostemon* saponin, which can inhibit platelet aggregation. *Allium macrostemon* saponin can significantly inhibit the platelet aggregation induced by arachidonic acid (AA), adenosine diphosphate (ADP) and platelet activating factor (PAF) in vitro and in vivo. and the rosette test showed that the saponins in *Allium macrostemon* can effectively inhibit the combination of neutrophils and platelets.² *Macrostemon A* inhibits platelet aggregation by activating the protein downstream of CD40 pathway, thus affecting the ubiquitination degradation related to traf2 and leading to antithrombotic effect.

Anti-atherosclerosis and hypolipidemic effect

ABM has significant anti-atherosclerosis and lipid-lowering activities. The experimental results showed that the serum triglyceride, total cholesterol and low-density lipoprotein levels decreased significantly, while the high-density lipoprotein level increased significantly after continuous intragastric administration of *Allium macrostemon* extract from hyperlipidemic rats for 34 weeks.

As well as the results of histological studies, the area of atherosclerotic plaques decreased³.

Cardiovascular protective effects

Allium macrostemon extract can relax vascular smooth muscle by blocking calcium channel⁴. Furthermore, it can protect the vascular endothelial function of rats, and its mechanism is to increase the expression of 5-HT_{1D}mRNA and protein with vasodilating effect and decrease the expression of 5-HT_{2A}mRNA and protein with vasoconstricting effect. In addition, through the combination of nuclear magnetic resonance spectroscopy and multivariate statistical method, the metabonomics changes of myocardial ischemia before and after treatment were analyzed, which confirmed that ABM can treat myocardial ischemia through energy metabolism and amino acid metabolism.

Antispasmodic antiasthmatic activity

Comparing the therapeutic effects of positive control group and ABM treatment group on asthmatic guinea pigs with histamine phosphate spray, the results show that ABM extract can obviously prolong the incubation period of asthma in guinea pigs⁵. In addition, ABM extract can also inhibit the expression of IL-6 and TXB₂ factors and promote the expression of 6-keto-PGF_{1α} in asthmatic guinea pigs, and its mechanism may be related to controlling inflammatory reaction and inhibiting bronchial smooth muscle spasm.

Antitumor activity

According to research reports, studies have shown that AMB has significant anti-tumor effect. Total glycosides of ABM can reduce the mitochondrial membrane potential of HeLa cells, inhibit the proliferation of HeLa cells and promote their apoptosis. Total saponins of AMB. In addition, the volatile oil from ABM has inhibitory effect on S180 and H22 in vivo and in vitro, which indicates that the volatile oil from ABM has significant antitumor effect.

Other functions

AMB also has antioxidant, antidepressant, antibacterial and other pharmacological effects. Ding⁶ found that ABM extract can scavenge hydroxyl free radicals. Through the forced swimming experiment and tail suspension experiment, it is concluded that AMB can shorten the immobility time of mice, indicating that ABM has antidepressant effect, and promoting nerve regeneration and BDNF release is its potential mechanism. Guan Feng and others concluded that Allium macrostemon saponins have bacteriostatic effect on Escherichia coli, Staphylococcus aureus, Bacillus subtilis, Saccharomyces cerevisiae, Aspergillus Niger and Penicillium citrinum. In addition, Allium macrostemon saponin has antibacterial effect on Escherichia coli, Staphylococcus aureus, Bacillus subtilis, Saccharomyces cerevisiae, Aspergillus Niger and Penicillium citrinum.

Conclusion

This review gives an overview of the research status of pharmacological action and mechanism of ABM Bunge. It is now well recognized that ABM has the pharmacological effects of anti-platelet aggregation, anti-atherosclerosis and blood lipid lowering, cardiovascular protection, antispasmodic and antiasthmatic, anti-tumor, anti-oxidation, anti-depression and antibacterial. Many pharmacological effects were summarized, but the mechanism of action was not perfect. For example, the elucidation of the mechanism of action only stays at the level of efficacy or a few pathways and a few targets. And the verification of pharmacological action is only through the animal model. Therefore, future research should focus on the research to clarify the specific targets

and pathways of the effective components of various pharmacological actions of ABM, to provide the basis for the medicinal value of ABM and the development of new drugs.

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Research progress on molecular mechanism of anti-inflammatory effect of Zexie decoction

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Abstract: The study of classic recipe is a key step for the innovation and development of massive health industry. As a classic recipe, zexie decoction has a good research value. Zexie decoction is composed of *Alisma orientalis* and *Atractylodes*, which is a classic prescription with a long history of use. Modern research has found that it has a good anti-inflammatory effect. Zexie decoction mainly affects the interleukins(ILs), nuclear transcription factor-KB (NF-KB) and TLR/MAPK pathways. Through extensive review of Chinese and foreign literature, the paper reviews the molecular mechanism of the anti-inflammatory effects of Zexie decoction, in order to promote the in-depth research and clinical application of Zexie decoction, and contribute to the development of the modernization of traditional Chinese medicine.

Keyword: Zexie decoction; Anti-inflammatory; Molecular mechanism; Interleukin; Nuclear transcription factor-KB

1. Introduction

With the increasing influence of traditional Chinese medicine in the world of medicine, the innovation and development of the massive health industry of traditional Chinese medicine are gradually on the agenda. The study of classic recipes is a key step for the innovation and development of the health industry, among which zexie decoction is a classic recipe with a long history. Zexie decoction comes from "*Synopsis of Golden Chamber*", which consists of *Alisma orientalis* and *Atractylodes*. Modern research has found that Zexie decoction has a good anti-inflammatory effect. With the deepening of the anti-inflammatory effect of Zexie decoction, research teams have carried out a detailed study on how Zexie decoction affects the anti-inflammatory effect. The paper will explain the molecular mechanism of the anti-inflammatory effect of Zexie decoction from the aspects of interleukin level, affecting the nuclear transcription factor-KB (NF-KB) pathway and inhibiting TLR/MAPK pathway, so as to promote the in-depth research and clinical application of Zexie decoction and contribute to the development of the modernization of Traditional Chinese medicine.

2. Anti-inflammatory effect of Zexie decoction

2.1 Lower the ILs level

ILs is an important inflammatory factor that plays a role in the maturation, activation and proliferation of immune cells. IL-6 and IL-1 β are representatives of ILs. It has been found that Zexie decoction can down-regulate the mRNA expression of IL-6 and IL-1 β . Components such as *Alisol A 24-acetate*, *Alisol F* and *Atractylodes olactone* contained in Zexie Decoction play a major anti-inflammatory effect. The mechanism of action may be related to the stimulation of hepatic stellate cells through AMPK/mTOR/ULK1 pathway^[1].

2.2 Affect the nuclear transcription factor-KB (NF-KB) pathway

NF-KB is a protein complex with five subtypes, which plays an important role in the response to various immune responses. It has been found that Zexie decoction can block the nuclear transfer of

NF-KB and activating protein in LPS-stimulated mouse monocyte-macrophage leukemia cells, thereby blocking the expression of inflammatory genes in the cells [2].

2.3 Inhibition of TLR/MAPK pathway

TLR/MAPK signaling pathway is also important pathway involved in inflammatory response. Studies have found that Zexie decoction can inhibit myeloid differentiation factors in TLR4/NF-KB and MAPK signaling pathways and improve inflammation. Among them, atractylodes olactone I, atractylodes olactone II and atractylodes olactone III play an important role in inhibiting TLR/MAPK pathway [3].

3. Conclusion

The molecular mechanism of Zexie decoction against inflammation is mainly realized by down-regulating THE level of ILs, affecting NF-KB pathway and inhibiting the TLR/MAPK pathway. In addition to the above research mechanisms, there are still many possible mechanisms to be discovered. In the future, in-depth research on Zexie decoction can focus on a more comprehensive explanation of how the pharmacodynamic substances of Zexie decoction act on cytokines and receptors in various signaling pathways. Therefore, it can promote a deeper understanding of the pharmacological action of Zexie decoction, and then promote innovation and development of the massive health industry.

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Research progress of traditional Chinese medicine for treatment of insomnia

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Abstract

Insomnia is a sleep disorder characterized by difficulty in falling asleep, difficulty in maintaining sleep and dissatisfaction with sleep. Traditional Chinese medicine (TCM) has a unique therapeutic effect in treating this disease. The treatment methods include Chinese medicinal herbs and formulas and non-drug treatment. This paper will discuss the research progress of TCM in the treatment of insomnia from the causes of insomnia, the treatment of insomnia and the mechanism of TCM in the treatment of insomnia.

Key words: Insomnia; Traditional Chinese medicine; Research progress

1 Introduction

Insomnia is the most common sleep disorder in the clinic marked by difficulty initiating or maintaining sleep. Insomnia seriously damages the physical and mental health of patients, affects their quality of life, contributes to irritability, depression, anxiety and endangers personal and public safety^[1]. Benzodiazepine (BDZ) is widely prescribed for insomnia. However, long-term use of BDZ can lead to physiological dependence and adverse reactions. Patients with insomnia need other safer and more effective treatments. TCM is one of the most sophisticated and integrated traditional medicine system and has accumulated valuable clinical experience in thousands of years of applications^[2], which includes Chinese medicinal herbs and formulas and non-drug treatment. This paper will analyze the mechanism of TCM in the treatment of insomnia and summarize the existing treatment methods by reviewing the papers in this area.

2 Study on pathogenesis of insomnia in TCM

Insomnia in TCM is also called "eyes not dim", "not sleep", "not lie". TCM believes that insomnia is mainly due to emotional disorders, or too much exertion, which leads to dysfunction of viscera, deficiency of Qi and blood, imbalance of yin and Yang, resulting in failure to get normal sleep. TCM treatment of insomnia mostly follows the principle of 'toning up its deficiency, resolving its rest, and regulating its nihilism'.

3 TCM treatment for insomnia

3.1 Single Chinese herbal medicine

Ziziphi spinosae semen (ZSS), a traditional Chinese medicine, is used in clinics for the treatment of insomnia in China and other Asian countries^[3]. A study revealed that ZSS aqueous extract increased the content of serotonin(5-HT), gamma-aminobutyric acid(GABA) and dopamine(DA), decreased noradrenaline(NE) and glutamic acid(Glu) in the brain of insomnia model rats, and thus produced a sedative hypnotic effect^[4]. Acanthopanax senticosus is a genuine medicinal material in Northeast China. Its roots, seeds, and leaves can be used as medicine^[5]. Acanthopanax senticosus can replenish qi, strengthen spleen, invigorate kidney and tranquilize mind. Schisandra chinensis is mainly produced in Northeast China^[6]. The fruit of Schisandra chinensis contains schisandrin, vitamin C, resin, tannin and a small amount of sugar. A study demonstrated that Schisandrin B was able to improve PCPA-induced insomnia in rats, which may be partly associated with its ability to

elevate the levels of 5-HT and GABA in the hypothalamus^[7].

3.2 Traditional Chinese medicine compound formulas

Suan-Zao-Ren decoction (SZRD) is used traditionally as a sedative and hypnotic in Chinese medicine^[8]. According to a study about the holistic anti-insomnia mechanism of SZRD through herbal targeting and network pharmacology, the ingredients of *Ziziphi spinosae* semen can target multi-neurotransmitter receptors at synapse interface, which was reported to be associated with sedative and hypnotic effects, while the four additional herbs can hit multiple pathways downstream of membrane neurotransmitters^[9]. Shuang-Xia decoction (SXD) has been used to treat insomnia in oriental countries for more than thousands of years and it presents remarkable clinical effects. A study showed that SXD water extract compared to ethanol extract possessed better sedative effects on locomotion activity in normal mice and increased sleep duration in subhypnotic dose of sodium pentobarbital-treated mice^[10].

3.3 Non-drug treatment for insomnia

Acupuncture is one of the safest therapies in China and it has been used to treat insomnia since antiquity. Acupuncture balances the body and restores its physiological function by inserting thin needles at specific acupoints^[11]. A study revealed that by evaluation using ActiSleep-BT wireless sleep monitor, acupuncture treated insomnia after ischemic stroke; the effect is better than usual care^[12]. Compound essential oil consists of 7 essential oils, including sandalwood, aloe, rose, and lavender essential oils. The targets of the main active components of compound essential oil are distributed in different pathways, and the mutual regulation of multiple components and targets is a possible mechanism of action in the treatment of insomnia^[13].

4 Discussion

To date, many basic and clinical studies have promoted our understanding of the treatment of insomnia with TCM. Although some data only come from animal models, this will enable us to better understand the mechanism of TCM in the treatment of insomnia. In the future, it is warranted that more high-quality pharmacological research and clinical trials to reveal the mechanism of TCM in the treatment of insomnia.

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Research progress of traditional Chinese medicine in regulating intestinal flora

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Abstract

Recently, studies have found that intestinal flora is a new field in which traditional Chinese medicine (TCM) play therapeutic role. After oral administration, certain components derived from TCM can regulate the structure and metabolism of intestinal flora through contacting and interacting with the gut microbiome, and achieve the effect of treating diseases related to intestinal flora, which promotes the research and application of traditional Chinese medicine resources on human health.

Key words: intestinal flora, traditional Chinese medicine

Introduction

The intestinal microbiota, a neglected organ, impacting on health and disease is increasingly emerging. Gut microbiota could metabolize intestinal contents and generate a wide variety of metabolites, with its metabolites performs some basic physiological functions in the immunological, metabolic and neurological system of the human body^[1]. Normally, the gut microbiota maintains a homeostasis in the gut of healthy persons. Conversely, disease involving cardiovascular and metabolism may occur when this balance is disrupted. With successful discovery of some powerful compounds derived from traditional Chinese medicine (TCM), such as artemisinin, arsenic, and huperzine A, it is increasingly found that TCM can not only complement the drawbacks of western medicine, but play more and more important role in the combat against diseases^[2]. Recent studies have found that TCM can modulate the composition and metabolism of gut microbiota, thereby affecting the occurrence and development of diseases^[3]. Considering the pivotal role of TCM in gut microbiota homeostasis, an increasing number of TCM studies have paid attention to the treatment of diseases related to intestinal flora and have yield a broad platform for the utilization and the development of TCM.

Effect of TCM on intestinal diseases

Imbalances in the homeostasis of gut microbes can directly trigger increased gut inflammation, leading to gut disease. *Abelmoschus manihot* extracted from *Flos Abelmoschus manihot* that restored intestinal immunity in colitic mice by elevating the abundance of SCFAs-producing microbiota and further increasing the concentration of butyrate and acetate in the gut^[4]. Qingchang Huashi Formula (QHF) mainly is consisted of *Pulsatilla chinensis*, *Radix Angelicae Dahuricae* and *Astragalus membranaceus*. The research demonstrated that the alleviation of colitis by QHF was related with the restoration of gut microbiota^[5]. Inflammatory bowel disease can deteriorate to colon cancer, which is one of the malignant tumors that seriously affects human health. Berberine played a role in treating colon cancer by reversing the disturbance of intestinal flora and further improving glucose metabolism, SCFAs biosynthesis and fatty acid metabolism^[6].

Effect of TCM on metabolic diseases

Obesity, type 2 diabetes mellitus, and hyperlipidemia are the common metabolic diseases associated with the dysfunction of gut microbiota. *Ganoderma lucidum* and its high molecular weight

polysaccharides can reverse the decreased Firmicutes-to-Bacteroidetes ratios and endotoxin-bearing Proteobacteria levels, which maintained intestinal barrier integrity and reduced body weight, inflammation and insulin resistance in mice fed a high-fat diet^[7]. MDG-1, a water-soluble β -d-fructan extracted from the roots of *Ophiopogon japonicus*, can be degraded and utilized by some gut microbiota and adjust the abnormal gut microbiota and alter its Metabolites, that can be assimilated and used by the host, exerting weight loss effects, energy metabolism promotion^[8]. *Polygonatum kingianum* has been used in treating diabetes and related diseases in China for centuries. Its total saponins and total polysaccharides can improve type 2 diabetes mellitus by significantly increasing the abundance of Firmicutes Ruminococcus and Ruminococcus in the gut of diabetic rats^[9].

Effect of TCM on cardiovascular diseases

Cardiovascular disease is another problem affecting human health related to gut microbiota. Zhou et al. found that Dingxin Recipe can alter lipid metabolism by increasing the relative abundance of Muribaculaceae and Ruminococcaceae and decreasing the abundance of Erysipelotrichaceae, thereby improving atherosclerosis in mice^[10]. Gastrodin is the most abundant glucoside extracted from the *Gastrodia elata*, which is a traditional Chinese herbal medicine for cardiac-cerebral vascular disease. In a mouse model of early atherosclerosis, it remodeled the disorganized gut microbiota at the phylum and genus levels, and the intestinal mucosa damage and permeability were reversed, accompanied with the disease improvement^[11]. A variety of cardiovascular diseases eventually develop into heart failure. The study found that Ginseng Dingzhi Decoction had the effect of protecting cardiomyocytes and reducing heart failure, and the mechanism was related to increasing the proportion of short-chain fatty acids and anti-inflammatory bacteria and reducing conditioned pathogens in the intestine^[12].

Summary and Outlook

The gut microbiota is involved in immune responses and metabolic pathways associated with intestinal inflammatory and metabolic diseases. Various chemical components derived from Chinese medicine can play a pivotal role in treating multi-factor diseases by regulating the composition and metabolites of intestinal flora in multiple targets and multiple ways. At present, with the acceleration of the modernization process of TCM, the research and development of traditional Chinese medicine has been improved to a certain extent, simultaneously multiple modern science and technology such as Chinmedomics and metagenomics should also be applied in the research field of TCM, which will further promote the development of TCM, and provide new therapeutic avenues for more diseases treatment.

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Advance in the biomarkers discovery of viral myocarditis

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Abstract

Viral myocarditis is an acute or chronic inflammatory change of the myocardium caused by a viral infection, whose incidence has significantly increased in recent years and is life-threatening in severe cases. At present, the specific pathogenic mechanism of viral myocarditis has not been fully elucidated, and the common clinical diagnostic methods are lack of specificity, and there is no specific agent for treatment. This paper mainly expounds the research progress of viral myocardial biomarkers in recent years, providing a new direction for the future clinical diagnosis and treatment of diseases.

Key words: viral myocarditis; biomarkers; research progress;

1. Introduction

Viral myocarditis (VMC) refers to the local or diffuse non-specific inflammatory lesions of the myocardium caused by viral infection, and some patients repeatedly further develop into chronic myocarditis, dilated heart disease (DCM), heart failure and even sudden cardiac death^[1]. In recent years, the incidence of viral myocarditis has been gradually increasing, and the pathogenic viruses are also increasing with the research, enterovirus, adenovirus, parvovirus B19 (PVB19), human herpes virus 6 (HHV6), hepatitis virus and so on are pathogenic viruses, and the pathogenic viruses in different regions are also different^[2,3]. At present, there are many studies and statistics on pathogenic viruses in the United States and Europe, and there is a lack of specific studies in Asia and other places. In clinical diagnosis, serological tests such as reactive C protein, myocardial troponin, and creatine phosphate kinase are often performed, but the C reactive protein and erythrocyte sedimentation rate are only markers of inflammation, and they cannot clearly point to viral myocarditis^[4]. Searching for more targeted diagnostics has become a new research direction.

2. VMC-related biomarkers identified by molecular biology

Wang X et al^[5] modeled viral myocarditis in mice by Coxsackie virus CVB3 and compared Latency associated peptide in blood and liver cells (LAP) and total Treg, it was found that compared with the control group, there was almost no difference in total Treg amount in the viral group, but the total Treg amount in the LAP+ group was significantly reduced, which proved that the total Treg in the LAP+ group was more stable and sensitive than the total Treg and more suitable as a biomarker of viral myocarditis. Chen J et al^[6] selected children as VMC group and healthy children as control group for serum analysis respectively, and concluded that CK-MB, TNF- α and VMC can be used as diagnostic biomarkers of acute and restorative VMC, TNF- α and VMC can be used as a serum marker to assess the severity and progression of VMC. Marketou M et al^[7] found that the contents of miR, miR-21-5p and miR-1-3p were higher in the blood samples of VMC patients. miR-21-5p was positively correlated with GLS and closely correlated with left ventricular systolic dysfunction, while miR-1-3p was positively correlated with troponin I and correlated with the degree of myocardial injury.

3. VMC-related biomarkers identified by metabolomics

Metabolomics mainly studies small molecules as substrates and products of various metabolic pathways, and the pathways of viral myocarditis, Tan G et al^[8]Through cross-platform metabolomics and computer platform, 48 metabolites, such as caruline, such as valine, were selected by et al.Kong Q et al^[9]By establishing the model of viral myocarditis and dilated cardiomyopathy, they conducted metabolomic analysis of the components in serum, and identified the important metabolic pathways mainly responsible for metabolic differences: taurine and subtaurine metabolism; pyruvate metabolism; glycine, serine and threonine metabolism, and glycerol metabolism. And some potential metabolic biomarkers, such as taurine, valine and acetate for acute viral myocarditis, glycerol, valine and leucine for chronic toxic myocarditis, and citrate, glycine and isoleucine for dilated heart disease.

4. Discussion

Viral myocarditis still faces many challenges in the process of diagnosis and treatment, and there is no unified international diagnostic standard. Finding more and more accurate diagnostic markers can provide better help for patient detection and treatment.

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Research progress of targeted drug therapy with APC gene for colorectal cancer

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Abstract

Colorectal cancer (CRC) is a common malignant tumor in the digestive tract, and its incidence rate increases every year. Adenomatous polyposis coli (APC), is a tumor suppressor gene, and 80% of colorectal cancers have abnormal deletion or inactivation of the APC gene. At present, the mechanism of action of the APC gene on colorectal cancer is still unclear in China and abroad, and its expression in colorectal cancer deserves further study. In recent years, APC gene-targeted drug therapy has developed rapidly and become a research focus in this direction in the clinical treatment of colorectal cancer. In this paper, the development of targeted therapy with the APC gene as a target for colorectal cancer is reviewed and indicates the opportunities and challenges faced in this area.

Keywords: colorectal cancer, APC, targeted therapies

1. Introduction

Colorectal cancer (CRC) is one of the common malignant tumors in the digestive system. According to the global cancer statistics report released by the International Agency for Research on Cancer in 2020, the incidence of colorectal cancer is currently the third among all cancers and the mortality rate is the second in the world [1]. The treatment of colorectal cancer is dominated by surgery, but patients have a worse prognosis and have serious side effects and damage. Mutations in the tumor suppressor gene, APC are found in 80% of sporadic CRC tumors. Moreover, in the initial stage of CRC, APC mutates earlier than other genes, serving as the "gatekeeper gene" of colorectal cancer. In recent years, Targeted therapy has become a new therapeutic strategy for colorectal cancer, and the search for new APC-targeted drugs has become a hot topic of current research. This article reviews the potential of the APC gene as a therapeutic target.

2. Study on targeted drug therapy with APC gene for colorectal cancer

2.1 Traditional Chinese medicine treatment

Zhenqi Fuzheng formula (ZQFZ), of which the main ingredients are Astragalus membranaceus and Ligustrum lucidum, has potential anti-tumor bioactivity. Meng W et al. [2] found that ZQFZ exhibited anti-inflammatory activity by decreasing the phosphorylation of nuclear factor-kappa B (NF- κ B) pathway-related proteins in lipopolysaccharide-induced RAW264.7 cells. After 56 days of treatment, ZQFZ alleviated the progression of colorectal cancer (CRC) and increased the body weight and thymic index values of the Apc^{Min/+} mice. Evodiamine (Evo) is an alkaloid that can be extracted from the berry fruit *Evodia rutaecarpa* and has antidiarrheal, antiemetic, and antiulcer effects. Zhang Y et al. [3] discovered Evo suppressed the degree of weight loss and colon shortening induced by DSS in ApcMinC/Gpt mice and decreased the disease activity index value. In addition, Evo decreased the number and size of colonic tumors in ApcMinC/Gpt mice.

2.2 Chemosynthetic drug treatment

The statin family of drugs (Lovostatin, Mevastatin & Simvastatin) could potentially be exploited

for the treatment of a specific subset of APC mutated cancers. Shailes H et al. [4] adopted mechanistic analysis that indicated activation of Rac1, followed by a decrease in Wnt signaling, and a decrease in the level of survivin expression, a Wnt target protein, upon statin treatment in the APC-mutant cells only. Therefore, it can be used as an effective targeted therapy drug for colorectal cancer. Metformin, a clinically available AMPK activator can overcome this limitation that niclosamide effectively suppresses Wnt, it also inhibits Hippo, limiting its therapeutic potential for CRC. Kang HE et al. [5] found combinatory oral administration suppressed in vivo tumorigenesis and the cancer progression of APC-MIN mice models and inhibited YAP activity in CRC cancer cells and patient-derived cancer organoids through the suppression of cancer stemness.

2.3 Small molecule inhibitor treatment

TASIN-1 (Truncated APC-Selective Inhibitor 1), is a potent small molecule that selectively kills CRC cells with truncated APC protein. Wang W et al. [6] based on serum and sterol rescue experiments, discovered that TASIN-1 exerted its cytotoxic effects through inhibition of cholesterol biosynthesis at the level of Emopamil Binding Protein (EBP) and significantly reduced the number of polyps and tumor size in the APC mice model. The tankyrase inhibitors, G007-LK and G244-LM, reduce Wnt/b-catenin signaling by preventing poly (ADP-ribosyl) ation-dependent AXIN degradation, thereby displaying approximately 50% inhibition of APC mutation-driven signaling in most CRC cell lines. In the xenograft model most sensitive to tankyrase inhibitor, Ted Lau et al. [7] found that COLO-320DM and G007-LK inhibited cell-cycle progression, reduced colony formation, and induced differentiation, suggesting that b-catenin–dependent maintenance of an undifferentiated state may be blocked by tankyrase inhibition. These results established proof-of-concept antitumor efficacy for tankyrase inhibitors in APC-mutant CRC models.

3. Results and discussion

In recent years, the incidence of CRC has increased year by year. This article reviews the new direction of targeted therapy of CRC with the APC gene as a target in recent years and indicates the treatment of colorectal cancer into a new era of personalization. Preliminary results have been obtained in some clinical trials, which confirm that targeted therapy can improve patients' response rates and survival prognosis. However, issues related to the specific mechanism of APC gene-driven malignant tumor formation, the optimization and rational application of detection technology, and further treatment after drug resistance mutation require further research, and clinical trials with larger samples are required for further research in the future.

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Research progress of serum metabolomics in different animal models of blood deficiency

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Abstract

In this paper, the research progress of serum metabolomics in the changes of metabolic pathways in different blood deficiency animal models is classified. Blood deficiency syndrome is a common clinical syndrome in traditional Chinese medicine, and its pathology is very complex, and the general research methods have certain limitations. Through high-throughput detection and screening of small molecule metabolites in the serum of organisms, metabolomics can reflect the changes in the metabolite spectrum of the body with blood deficiency syndrome as a whole. With the rapid development of metabolomics, metabolomics has been widely used in the study of blood deficiency syndrome.

Keywords: serum metabolomics; blood deficiency syndrome; animal model; metabolic pathway
Metabolomics is used to detect changes in small molecules (≤ 1 kDa) produced by biological processes between normal and abnormal cells and is an important way to discover biomarkers of biological systems [1-3]. With the maturity of metabolomics, more and more scholars apply it to the research on the blood-enriching effect of traditional Chinese medicine. At present, the commonly used methods for replicating animal models of blood deficiency include the blood loss method, chemical injury method, radiation injury method, and other modeling methods. Numerous studies have shown that these modeling methods have an impact on the metabolites of body fluids or tissues. The author summarizes the research progress of metabolomics in studying the changes of endogenous metabolites in serum samples from animal models of blood deficiency syndrome as follows.

1 Serum metabolomics study on animal models of blood deficiency caused by cyclophosphamide or acetyl phenyl hydrazine

Wang Mu used an intraperitoneal injection of cyclophosphamide (CTX) to replicate the blood deficiency syndrome mouse model and used NMR technology to study the changes of small molecule metabolites in the serum of the normal control group and blood deficiency syndrome model group. The results showed that the low-density lipoprotein and leucine/isoleucine ratio in the serum of mice increased, while the content of lactic acid and choline decreased significantly. The changes of the above metabolites indicated that the blood deficiency caused by CTX may be related to energy metabolism, lipid metabolism, and glycolysis dysfunction. Zhang ZZ [4] replicated the rat model of blood deficiency syndrome by subcutaneous injection of acetyl phenyl hydrazine (APH) and used NMR analysis to compare the differences in plasma endogenous metabolites between the normal control group and the model group. The results showed that the plasma levels of lactic acid and nicotinamide in the model group increased, while the levels of leucine, choline, creatine, and glucose decreased.

2 Serum metabolomics study on an animal model of blood deficiency caused by chemical drug combination

Li WX^[5] used APH and CTX double-induced blood deficiency to replicate the blood deficiency model and used UPLC-TOF/MS to analyze the changes of plasma endogenous metabolites in the blood deficiency model group and the normal control group. The results showed that the blood levels of lysophosphatidylcholine, sphingosine, and niacin in the model group were significantly increased, while the levels of oleic acid and ceramide were significantly decreased. Analysis of related metabolic pathways showed that energy metabolism disorder in blood deficiency syndrome rats was related to the compensatory increase of thiamine pyrophosphate content and the decrease of oleic acid content; Li SJ^[6] found that the blood sphingosine in the blood deficiency model group. The content of alcohol and niacin increased significantly, and the content of serotonin decreased significantly. Li PL and Sun Hongguo^[7] used GC-MS technology to study the changes of metabolites in the blood of mice with blood deficiency caused by APH and CTX. The results showed that the levels of palmitic acid, arachidonic acid, and L-lactic acid in the blood of blood deficiency mice were significantly higher than those of normal mice, and the level of L-proline was significantly lower than that of normal mice.

3 Serum metabolomics study of blood deficiency animal model induced by 60Co γ radiation

Gamma-ray radiation mainly causes leukopenia, inhibition of bone marrow hematopoiesis, etc. It is one of the commonly used methods for establishing animal models of blood deficiency syndrome. Huo Chao used 60Co γ ray to replicate the radiation-injured mouse model of blood deficiency syndrome and applied 1HNMR technology to detect the changes of serum endogenous metabolites in the normal control group and the model group. The results of the study showed that the serum levels of phosphorylated choline, creatine, and low-density fatty acids in the model mice increased, while the levels of glucose, choline, and lactate decreased, and the above six endogenous metabolites could be used as biomarkers in mice with blood deficiency syndrome. group of things.

4 Serum metabolomics study of blood-deficiency animal models caused by blood loss

Huo Chao used chronic bloodletting combined with swimming fatigue to make the blood biochemical source insufficient to establish a near-clinical mouse model of blood deficiency syndrome and used NMR to detect the changes of small molecule metabolites in serum. The content of β -hydroxybutyric acid in the serum of blood-deficiency model mice caused by blood loss combined with the fatigue method was higher than that of normal mice, and the content of lactate and choline was lower than that of normal mice.

5 Discussion

In summary, many differential metabolites related to blood deficiency syndrome have been detected in animal models of blood deficiency by metabolomics, such as amino acids, fatty acids, sphingolipids, lactic acid, taurine, creatinine, Phosphorylcholine, etc. Because the body's metabolism is interfered with by multiple factors, such as age, gender, diet, drugs, and the environment. Therefore, how to eliminate the influence of these interfering factors and how to effectively screen metabolites related to blood deficiency syndrome is the current research direction of blood deficiency syndrome metabolomics. In recent years, metabolomics has become increasingly mature, a relatively complete metabolomics database has been formed, and metabolomics analysis technology has also been further developed.

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Research progress on anti-tumor effect of *Sophorae Tonkinensis Radix et Rhizoma*

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Abstract

As a traditional Chinese medicine, *Sophorae Tonkinensis radix et rhizoma* (ST) is derived from the dried roots and rhizomes of *Sophora tonkinensis* Gagnep., which is known as “Shan-Dou-Gen” and is a well-known regional drug of Guangxi in China. Many chemical components are found in ST, pharmacological studies have shown that alkaloids, flavonoids and polysaccharides from ST are the main anti-tumor active ingredients, and have good anti-tumor effects, the extract from ST also possess anti-cancer activities against various tumor cells, including cancer of the liver, lung, cervix and breast. In recent years, the anti-tumor effect of ST has attracted attention of some scholars, a large number of studies have shown that ST could exert an anti-tumor activity by inhibiting proliferation, adhesion, invasion and metastasis, promoting apoptosis and autophagy, triggering cell cycle arrest and improving immunity. It is of great scientific and practical value. This article focuses on the research progress of the anti-tumor effects and mechanisms of ST.

Key words: *Sophorae tonkinensis radix et rhizoma*, chemical composition, anti-tumor effect
Sophora tonkinensis Gagnep. is widely distributed in China, Korea, and Vietnam. ST was first written in Kaibao Bencao in Song Dynasty, and also recorded in many ancient books of traditional Chinese medicine. It has a long history of medicine, complex chemical components and diverse pharmacological effects. ST is traditionally used for clearing away heat and toxic materials, reducing swelling and relieving sore throat as recoded in Chinese Pharmacopoeia^[1]. Cancer is a leading cause of death worldwide, traditional Chinese medicine has unique advantages in fighting tumors. A variety of chemical constituents from ST have shown activities in anti-tumor, which has been proved to be able to against many kinds of malignant tumors with good anti-cancer effect.

1. Anti-tumor effect of ST extracts

ST extract and its multiple components have anti-cancer activity. Experiment shows that Studies indicated that the aqueous extract of Vietnamese Sophora Root could inhibit the proliferation of melanoma B₁₆BL₆ cells, as well as their adhesion and movement^[2]. Chloroform extract of *Sophora Tonkinensis* Gagnep. inhibited cell viability, clonal growth and induced cell apoptosis in a dose-dependent manner by silencing the PI3K/AKT/mTOR signaling pathway, arrested cell cycle in the G1/S phase, decreased cell migration and invasion, and significantly inhibited the tumor growth without toxicity^[3].

2. Anti-tumor effect of the bioactive compound of ST

Emerging evidence suggests that matrine from ST possesses anti-cancer properties, many findings indicate that matrine inhibits the growth of various cancer cells and regulates the expressions of genes and proteins associated with apoptosis, autophagy, cell invasion, metastasis, and cell cycle arrest^[4]. Cytotoxicity assay showed that tonkinensine B from ST decreased mitochondrial membrane potential, ATP synthesis, elevated ROS generation, up-regulated Bax/Bcl-2, caspase-3 and caspase-9, and reduced AKT phosphorylation levels in triple negative breast cancer

MDA-MB-231 cells, tonkinensine B induces apoptosis through mitochondrial dysfunction and inactivation of the PI3K/AKT pathway in triple-negative breast cancer cells^[5].

3. Anti-tumor effect of the mixed compounds of ST

In a novel strategy for computer-aided herbal medicine research based on omics and bioinformatics, ST had a significant inhibitory effect on the H226 cell line (lung squamous cell carcinoma), which ranks first in morbidity and mortality among lung cancers in China. Additionally, five biolabels (CPS1, CKM, CPT1B, COX5B, and COX4I1) were involved in the anti-lung cancer mechanism of ST and 3 compounds (gallic acid, betulinic acid, and caffeic acid)^[6].

4. Discussion

Malignant tumors are a global health problem, and ST may be a hopeful candidate for human cancer. Several chemical constituents of ST have shown good anti-tumor activity, but the specific mechanism of its anti-tumor action is not well explained, there is still worthwhile to further investigate its anti-cancer potential under a safety toxicological precaution at the molecular level, to promote the research and development of new anti-cancer drugs and new varieties of ST as well as their safe and effective clinical application, to provide more effective treatment methods for malignant tumor diseases. It has important reality significance for giving full play to the advantages of traditional Chinese medicine.

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Exploring the anti-inflammatory mechanism of baicalin based on NF- κ B signaling pathway

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Abstract

Baicalin is the main active component of the Chinese herb *Scutellaria baicalensis*, with a wide range of pharmacological activities, and is widely used clinically to treat neuroinflammation, enteritis, pneumonia and secondary inflammation with remarkable efficacy. The anti-inflammatory mechanism of baicalin has been studied in depth in recent years. One of the mechanisms by which baicalin exerts its anti-inflammatory effect is by attenuating the activity of NF- κ B and inhibiting the expression of inflammatory cytokines and other inflammatory mediators. In this paper, we have reviewed the domestic and international literature to summarize the regulatory effects of baicalin on NF- κ B and the anti-inflammatory effects based on this signaling pathway.

Key words: Baicalin, NF- κ B, inflammatory

Introduction

Baicalin, one of the active ingredients of the Chinese medicine *Scutellaria baicalensis*, is a natural flavonoid with the molecular formula $C_{21}H_{18}O_{11}$ and has a wide range of pharmacological activities with antibacterial, anti-inflammatory, antioxidant, diuretic, antitumour and hypocholesterolemic effects. In recent years, the anti-inflammatory mechanism of baicalin has been intensively studied and has significant anti-inflammatory activity in the treatment of neuroinflammation, enteritis, rheumatoid arthritis, autoimmune hepatitis and chronic liver disease.

Inflammation is a physiological response to external stimuli. Nuclear factor- κ B (NF- κ B), one of the key regulators mediating the inflammatory response, plays a key role in processes such as the inflammatory response and immune response. Upregulation of NF- κ B promotes the transcription of the inflammatory factors interleukin-6 (IL-6), interleukin-1 β (IL-1 β) and tumour necrosis factor- α (TNF- α). Both in vitro and in vivo experiments revealed that baicalin inhibited microglia activation and pro-inflammatory factor secretion, with the main mechanism of action being the inhibition of NF- κ B-related pathways. In this paper, we review the anti-inflammatory mechanisms of baicalin based on NF- κ B and its related pathways.

1. Inhibition of lipopolysaccharide (LPS)-induced inflammation

Fu et al.^[1] found that baicalin could prevent LPS-induced activation of the TLR4/NF- κ B p65 pathway and suppress inflammation in vitro and in vivo by inhibiting the expression of CD14 molecules. Yan et al.^[2] established a RAW264.7 cell model of LPS-induced inflammation and exposed them to various baicalin concentrations (0.1-1.0 μ mol/L) and found that baicalin inhibited the HMGB1/TLR4/NF- κ B pathway mediated by HMGB1 and suppressed the levels of factors such as TNF- α , IL-6, IL-1 β , Cox and iNOS by promoting the expression of miR-181b in the cells, and baicalin at 1.0 μ mol/L had a good anti-inflammatory effect.

2. Inhibits chronic inflammatory diseases

Zhang et al.^[3] found that baicalin significantly ameliorated cigarette smoke (CS)-induced airway inflammatory infiltration in rats, decreased PAI-1, significantly inhibited the levels of TNF- α and

IL-1 β in CS-exposed rats and cells, enhanced HDAC2 expression, and suppressed NF- κ B and PAI-1 expression. Zheng et al.^[4] found that baicalin alleviated thrombin-induced atherosclerosis (AS) inflammation and inhibited thrombin-induced activation of NF- κ B p65 and ERK1/2 signalling pathways in human umbilical vein endothelial cells (HUVECs).

3. Inhibition of microbial-induced inflammation

Ishfaq et al.^[5] showed that baicalin could prevent mycoplasma gallisepticum (MG)-induced inflammation and oxidative stress by activating autophagy and inhibiting the TLR-2-NF- κ B pathway and NLRP3-inflammatory vesicles. Zhang et al.^[6] showed that baicalin protected against RAW264.7 by inhibiting Salmonella typhimurium (S typhimurium)-induced ROS production in cells and inhibited TLR4/MAPK/NF- κ B signaling pathway to exert protective effects. Wu et al.^[7] showed that baicalin inhibited inflammation caused by MG and E. coli co-infection in the lungs and trachea of chickens, and showed that baicalin and NF- κ B docking showed the highest fitness scores and interactions by molecular docking techniques. Fan et al.^[8] found that baicalin inhibited the TGF- β 1 / TGF- β R1 / NF- κ B signalling pathway in activated PSCs, reducing the secretion of MCP-1 and further reducing the infiltration of macrophages and inflammatory cells in the local microenvironment of the pancreas.

4. Inhibits inflammation of intestinal damage

Using a piglet model of DON-induced intestinal inflammatory injury, Liao et al.^[9] found that baicalin could modulate the downstream inflammatory and oxidative responses following DON excitation by inhibiting NF- κ B and increasing mTOR signaling, thereby reducing intestinal inflammation and oxidative injury.

Discussion

In this paper, we summarize that baicalin directly or indirectly inhibits NF- κ B-related signaling pathway and reduces the production and release of inflammatory cytokines such as TNF- α , IL-1 β and IL-6 to exert anti-inflammatory activity. However, there are limitations in our current research on the anti-inflammatory activity of baicalin. The anti-inflammatory mechanism of baicalin can be studied from multiple targets and multiple pathways to provide a basis for baicalin to become a new anti-inflammatory drug.

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Research progress of *Trichosanthes* in the treatment of coronary heart disease with heart-yang deficiency

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Abstract:

Trichosanthes is a traditional Chinese medicine contained in the 2020 edition of Chinese Pharmacopoeia. It has a significant effect on the treatment of heart-yang deficiency coronary heart disease. This paper will briefly review the mechanism and the clinical application of *Trichosanthes* in the treatment of coronary heart disease with heart-yang deficiency. It also discusses the current research status of *Trichosanthes* in the treatment of heart-yang deficiency coronary heart disease, which provides a certain theoretical basis for the future research direction of new drugs and the innovation and development of great health.

Keywords: *Trichosanthes*; Heart Yang deficiency; Coronary Heart Disease

Introduction:

Trichosanthes is the dry ripe fruit of *Trichosanthes kirilowii Maxim.* or *Trichosanthes rosthornii Harms.* It has a certain protective effect on respiratory system, immune system and cardiovascular system. *Trichosanthes* is cold in nature and sweet in taste. It can dissolve phlegm and remove heat, moisturize the intestines and relieve defecation. It is especially suitable for patients with symptoms such as lung heat, phlegm stickiness, heartache and chest arthralgia^[1]. In traditional Chinese medicine, *Trichosanthes* is often used in compatibility with *Allium macrostemon*, *Pinellia ternata*, aconite and so on. The classic prescriptions of *Gualou Xiebai Liquor decoction* and *Gualou Xiebai Banxia decoction* are used in combination with other drugs for relieving yang and dispelling phlegm to treat coronary heart disease of heart-yang deficiency^[2]. *Trichosanthes* can regulate the yang-qi of the heart and promote the blood to run and nourish the whole body, regulate the beating of the heart and keep the veins unobstructed; it also helps to warm the water in the body and prevent congestion from blocking the chest^[3].

Mechanism of action

Trichosanthes is rich in flavonoids, polysaccharides, amino acids and proteins, which can play a multi-target and overall synergistic role and has great advantages in the treatment of coronary heart disease. Lei X et al.^[4] used the dual fluorescent pigments reporter gene detection line system to determine that the extract of guar can significantly inhibit the activation of NF- κ B to achieve anti-inflammatory effects and treat coronary heart disease. Yang G et al.^[5] found that the melon peel can inhibit the activation of Caspase-3 to inhibit the apoptosis of cardiomyocytes and thus prevent heart damage caused by coronary heart disease central muscle infarction. Hou Z^[6] verified that the combined administration of *Trichosanthes* seed oil and flavonoids decreased the levels of serum TC,

TG and LDL-C, thus reducing the coronary heart disease induced by hyperlipidemia. Wang Zhaobo^[7] found that quercetin, an important active ingredient in *Trichosanthes*, may play a key role in *Gualou Xiebai Banxia decoction* in the treatment of heart-yang deficiency coronary heart disease by regulating the PI3K-Akt pathway.

Clinical application

Trichosanthes has the effect of relaxing the chest, reducing phlegm and resolving masses. In the prescription, it is often combined with *Allium macrostemon* to activate yang and disperse accumulation of pathogen, conduct qi and eliminate phlegm to treat coronary heart disease with heart yang deficiency^[8]. In the synopsis of the *Jin Kui Yao Lue* written by Zhang Zhongjing, two classic prescriptions for the treatment of chest arthralgia, *Gualou Xiebai Liquor decoction* and *Gualou Xiebai Banxia decoction*, were recorded. Up to now, the clinic of traditional Chinese medicine still uses them as the basic prescription for the treatment of coronary heart disease with heart yang deficiency. Guo Hongwei et al.^[9] divided 80 patients with heart-yang deficiency coronary heart disease into two groups and compared them with the flavor of *Gualou Xiebai Banxia decoction*, and found that the treatment efficiency of the drug group was as high as 90%, and the number of onset and incidence was less than those in the control group. Cao Hongxin^[10] treated three patients with heart-yang deficiency coronary heart disease with the modified version of *Gualou Xiebai Banxia decoction* and found that the conditions of the three patients improved and the indexes gradually returned to normal.

Discussion

At present, more and more scholars carry out a more in-depth exploration of *Trichosanthes*, and the clinical application of *Trichosanthes* is becoming more and more common. However, most of these studies focus on the compatible prescriptions of *Trichosanthes*, the study on the specific functional components and mechanism of *Trichosanthes* single medicine in the prescription is not clear enough. In the future way of scientific research, we can consider the application of molecular biology technology, proteomics technology and other technologies to explore the specific mechanism of *Trichosanthes* in the prescription.

Conclusion

Trichosanthes has a very positive role in the treatment of the heart-yang deficiency subtype of coronary heart disease, our more in-depth exploration of *Trichosanthes* in the treatment of heart-yang deficiency coronary heart disease will have a very profound significance for the future research and development of new drugs and the search for new drug treatment targets.

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Metabolomics exploring therapeutic substance and mechanism of traditional Chinese medicine against diabetic retinopathy

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Abstract

Diabetic retinopathy is a common microvascular complication of diabetes, involving a series of complex pathogenesis, which has not yet been fully elucidated. Metabolomics is an attempt to qualitatively or quantitatively analyze all metabolites in biological matrices, and is a promising tool for early disease diagnosis and therapeutic drug screening. The multi-target and multi-way action mechanism of traditional Chinese medicine in the treatment of diabetic retinopathy has obvious advantages. However, the interpretation of its action mechanism and therapeutic substances is still insufficient. Therefore, this article reviews the application of traditional Chinese medicine anti-diabetic retinopathy treatment substance screening and mechanism interpretation based on metabolomics method.

Key word: Diabetic retinopathy, traditional Chinese medicine, metabolomics, therapeutic substance, therapeutic mechanism

Diabetic retinopathy is a serious public event that causes visual impairment and blindness in diabetic patients¹. Current evidence suggests that the global prevalence of diabetic retinopathy is increasing year by year, although improved ability to control blood glucose levels in diabetic patients can reduce the incidence of diabetic retinopathy². The clinical diagnosis and treatment of diabetic retinopathy has the characteristics of strong concealment, and the diagnosis and treatment effect is not good in the stage when the eye disease is obviously visible. Early eye screening and treatment for diabetic retinopathy have a good cost-effectiveness ratio for avoiding vision loss. Hitherto, new technologies such as retinal imaging and artificial intelligence have been developed and applied to effectively screen and diagnose diabetic retinopathy^{3,4}. Treatments such as calcium dobesilate and anti-vascular endothelial growth factor have obvious effects. However, the therapeutic benefit of a single target is greatly weakened with the prolongation of the course of diabetic retinopathy. Traditional Chinese medicine in the treatment of diabetic retinopathy has obtained good therapeutic benefits in clinical practice, and can effectively improve the microcirculation disorder of diabetic retinopathy⁵. However, the effector substances and mechanism of action of traditional Chinese medicine in the treatment of diabetic retinopathy are still unclear, and it needs to be explained by using modern analytical techniques. Metabolomics is a powerful omics tool that provides an informative phenotypic dimension that can be used to define various metabolic disorders and changes in metabolism after TCM treatment. Metabolomics has been used as a promising strategy for evaluating natural product efficacy and potential targets⁶.

Mechanism study based on metabolomics

Traditional Chinese medicine has a good effect on the prevention and treatment of diabetic retinopathy, but the relevant mechanism of action is not completely clear. Metabolomics research provides a theoretical basis for the mechanism of traditional Chinese medicine and traditional

Chinese medicine prescriptions in the treatment of diabetic retinopathy. The research strategy integrating metabolomics and network pharmacology provides an effective means for the mechanism interpretation of commonly used traditional Chinese medicine preparations in clinical practice⁷. The study firstly evaluated the pharmacodynamics of traditional Chinese medicine prescriptions, and then, on the basis of comprehensively characterizing the active ingredients of the prescriptions, used the traditional Chinese medicine serum medicinal chemistry method to identify the components absorbed into the blood. Metabolomics and correlation analysis were then used to find differential metabolites. Finally, the proteins in the common pathway of network pharmacology and metabolomics were screened to screen the key targets, so as to clarify the potential mechanism of the therapeutic effect of traditional Chinese medicine prescriptions. Urine of rats treated with Bushen Huoxue Prescription was subjected to metabolomic analysis using ultrahigh-performance liquid chromatography coupled with Q-exactive quadrupole-electrostatic field Orbitrap mass spectrometry, and a total of nine potential biomarkers were found⁸. Further metabolic pathway analysis showed that diabetic retinopathy was closely related to gut microbial metabolism, lipid metabolism and tryptophan metabolism.

Screening of therapeutic substances based on metabolomics

Chinmedomics is an effective means of combining TCM serum medicinal chemistry and metabolomics to discover bioactive components in TCM⁹. The researchers performed non-targeted analysis of blood samples from a mouse model of diabetic retinopathy using the Chinmedomics strategy that combines traditional Chinese medicine serum medicinal chemistry with metabolomics¹⁰. The results showed that Keluoxin, an effective prescription for the treatment of diabetic complications, can alleviate retinal dysfunction and pathological changes, regulate 51 blood biomarkers including leukotriene D4, A4 and L-tryptophan through phenylalanine metabolism, steroid biosynthesis, sphinolipid metabolism and other metabolic pathways. Therapeutic material basis research using Chinmedomics strategy provides a sufficient theoretical basis for the development of innovative drugs for diabetic retinopathy.

Prospects

At present, the metabolomics research of traditional Chinese medicine in the treatment of diabetic retinopathy mainly focuses on pharmacodynamic evaluation and biomarker screening. Metabolic flux analysis using stable isotope tracing will provide new explanations for the mechanism of diabetic retinopathy from the perspective of dynamic networks. Spatial metabolomics based on mass spectrometry imaging technology will also provide a new supplement to interpret the mechanism of traditional Chinese medicine and its metabolites in the treatment of diabetic retinopathy in situ from biological tissues. Traditional Chinese medicine omics is an increasingly popular method for evaluating the efficacy of traditional Chinese medicine prescriptions, and it is expected to be applied to the interpretation of more traditional Chinese medicine prescriptions for anti-diabetic retinopathy treatment substances and mechanisms.

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Application of UPLC-MS-based metabolomics in colorectal cancer

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Abstract

Metabolomics, one of the most modern omics technologies, has recently gained considerable attention in discovering novel biomarkers. It has been used to identify metabolic changes in the body, gain a better knowledge of disease processes, and accounting statements for preventative diagnosis and drug targeting. Dysregulation of cellular metabolism plays a key role in cancer development. Therefore, metabolomics can be invaluable in early cancer diagnosis, medical intervention, and cancer treatment evaluation. Many metabolomics research relies on highly sensitive platforms and throughput mass spectrometry platforms. The development of several mass spectrometry (MS) methodologies in recent years has contributed to discovering metabolites associated with cancer. Colorectal cancer (CRC) is the most diagnostic cancer around the world. It ranks 3rd in China in terms of incidence. This paper summarizes recent progress of mass spectrometry (MS)-based metabolomics in CRC.

Keywords Metabolomics, Colorectal cancer, Mass spectrometry, Biomarkers.

Introduction

Colorectal cancer (CRC) is common cancer as well as the third leading cause of mortality around the world, and its incidence is increasing in China [1]. CRC is a multifactorial disease with several associated risk factors, including genetics, environment, and lifestyle [2]. The average incidence of CRC is still quite high, despite advances in understanding mechanisms. A more precise mechanism analysis is required for screening methods and drug treatment in CRC research [3]. The use of metabolomics can thus be an integral part of the discovery of useful biomarkers and the investigation of accurate treatments for CRC.

Metabolomics is a new research area in omics science that employs advanced analytical techniques to monitor and evaluate metabolite alterations in patients following medical/external treatment or disease conditions [4]. Metabolomics technologies comprehensively analyzed low molecular weight compounds, such as small peptides, vitamins, and protein cofactors generated by metabolism in biological fluids. Recently metabolomics gained more attention in the field of biomarker discovery; however, unlike other omics technologies, such as transcriptomics, genomics, and proteomics. It could be more accurate in describing multifactorial disease because it illustrates gene-environment interactions [5]. MS techniques are widely used for both target and untargeted metabolomics research. MS technologies can identify organic and inorganic molecules using high sensitivity and specificity while requiring small specimens [6].

Tan and colleagues analyze serum metabolite profiles using GC-TOF-MS and UPLC-Q-TOF in patients with colorectal carcinoma and healthy individuals. In contrast to healthy individuals, colorectal patients showed distinctive metabolic signatures in the urea cycle, TCA cycle, fatty acids, glutamine, and gut flora metabolism. A different profile of differential metabolites was identified from OPLS-DA

results in which 2-hydroxybutyrate, 2-oxobutyrate, and 2-aminobutyrate, showed increased levels. In contrast, levels of indoxyl, indoxyl sulfate, and N-acetyl-5-hydroxytryptamine decreased in colorectal cancer patients [7]. Another UPLC-MS-based study by Clos et al. Showed differences in sphingolipids and cholesteryl esters in patients with CRC stool samples [8]. Another research study reported 154 metabolites such as amino acids glycolysis, urea cycle, tricarboxylic acid (TCA) cycle, and polyamine pathways; with the progression of cancer, the concentration of these metabolites gradually increased [9].

Discussion

Numerous research has been conducted to investigate the molecular mechanism of CRC from the perspective of intestinal flora and the compounds they produce, such as (glycolysis, tricarboxylic acid (TCA) cycle, amino acids, bile acids, urea cycle, and polyamine pathways) for drug target intervention. According to various studies, CRC is linked to inflammation and an alteration of the gut flora. Many microbiota-derived metabolites have been associated with CRC, and the discovery of biomarkers derived from microbiota metabolomes is a hot area of Research. Existing research has been focused on discovering new biomarkers. While the complete mechanism for the generation of markers and their diagnostic value still remains unclear. A combination of different experimental techniques such as Multiomics technologies, for example, genomics, proteomics, and metabolomics, are helping us to gain deeper insight into cancer and accelerate antitumor drug development

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Progress of metabolomics application in traditional Chinese medicine research

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Abstract

With the development of the times, changes in social needs and disease spectrum, the concept of comprehensive health has emerged as the times require. The ambiguity of the active ingredients and the treatment mechanism of traditional Chinese medicine in the pharmaceutical industry restricts it from making further contributions to the development of the comprehensive health industry. As an emerging research technology, metabolomics has shown broad application prospects. This review summarizes the application of metabolomics in revealing the effective components and therapeutic mechanisms of traditional Chinese medicine, in order to provide research ideas for the development of traditional Chinese medicine.

Key words: metabolomics, traditional Chinese medicine, effective components, treatment mechanism, comprehensive health

Traditional Chinese medicine is widely popular for its unique theory and thousands of years of clinical experience. However, the complexity of its chemical composition and the ambiguity of its therapeutic mechanism limit its further development. Metabolomics is an important part of systems biology. By analyzing thousands of small molecules in cells, tissues, organs or biological fluids, it can reflect the impact of stimulation on the metabolic function of organisms. In order to promote the development of traditional Chinese medicine and improvement of the comprehensive health industry, this review summarizes the application of metabolomics research technology in revealing the effective components and treatment mechanisms of traditional Chinese medicine.

1. Introduction to Metabolomics

Metabolomics technology mainly includes three parts: data collection, data analysis and data functional interpretation. Data collection is commonly done by ultra-high performance liquid chromatography, gas chromatography combined with mass spectrometry or nuclear magnetic resonance; data analysis mainly includes some of the preparing steps, deconvolution of overlapping peaks, peak picking, integration, alignment, data cleanup, normalization, as well as metabolite identification and Unsupervised learning and supervised learning; functional interpretation of data is mainly achieved through database, through pathway mapping and visualization and enrichment analysis^[1]. Its development has gradually transitioned from non-targeted metabolomics to targeted metabolomics^[2].

2. Application of metabolomics in traditional Chinese medicine

Xiong Hui et al used a chinmedomics research strategy combining metabolomics and serum pharmacology of Chinese medicine to determine the pseudoginsenoside F11 and ginsenoside Rd as the effective components of American ginseng^[3]. Similarly, Li Xianna et al used the above research methods to discover ten active components of *Phellodendri Amurensis* cortex in the inhibition of prostate cancer^[4].

Based on the UHPLC/Q-TOF-MS metabolomics approach to study the anti-hyperthyroidism effects of *Radix Scrophulariae*, it was found that compared with the control group, 44 metabolites in the

model group changed significantly, and the levels of these biomarkers were significantly decreased after treatment with *Radix Scrophulariae*. These metabolites involved in signaling pathways, including the biosynthesis of unsaturated fatty acids, primary bile acid biosynthesis and sphingolipid metabolism, with linoleic acid metabolism and sphingolipid metabolism identified as the most relevant metabolic pathways. It is suggested that *Radix Scrophulariae* can play a role in the anti-hyperthyroidism effects by affecting the metabolism of linoleic acid and sphingolipid^[5].

3. Discussion

The unique theory of traditional Chinese medicine and thousands of years of clinical experience, its effectiveness is beyond doubt, but it is not easy to be accepted by modern medicine, because the material basis and mechanism of its therapeutic effect are not clear. Therefore, it is urgent to apply modern science and technology to explain. As an emerging research technology, metabolomics is similar in concept to the holistic view of traditional Chinese medicine, and is very suitable for the study of traditional Chinese medicine. At the same time, it can also be combined with other research methods, such as serum pharmacochimistry of Chinese medicine, network pharmacology, proteomics, genomics, etc, to interpret traditional Chinese medicine at a deeper level and promote the development of the traditional Chinese medicine industry, so as to play a wider role in the development and improvement of the comprehensive health industry.

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Anti-HBV proteomic study of syringoside based on HBV transgenic mouse model

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Abstract

Using HBV transgenic mice as a model, TMT quantitative proteomics method was used to detect the proteins in liver tissue, and the proteins affected by syringumarin on the callback were mined, and the corresponding pathways were matched to clarify the anti-HBV mechanism of syringumarin. The results showed that after syringoside treatment, 12 HBV-related proteins were recalled in the liver, 5 were up-regulated, 7 were down-regulated, and 175 biological processes (BP) were involved in the GO function enrichment analysis. There were 22 points (CC) and 34 molecular functions (MF), and the KEGG pathway enrichment results showed that a total of 49 pathways were involved.

Key words:Syringopicroside, HBV, metabolomics

According to statistics from the World Health Organization, about 250 million people are chronically infected with HBV worldwide, resulting in nearly 1 million deaths each year. At this stage, the treatment of HBV infection is still a major problem to be solved urgently in the medical field.

Syringoside is a monomeric compound extracted and isolated from clove leaves. Syringoside has significant and safe anti-HBV effects, and is expected to be one of the ideal anti-HBV drugs, but its mechanism of action is unclear, which limits the development of new anti-HBV drugs.

This research group carried out proteomic research on liver tissue samples of HBV transgenic mice, excavated biological information related to HBV disease, and explored the mechanism of syringoprein intervention, so as to provide a scientific basis for the research of syringoprein anti-HBV drugs.

Objective

To explain the mechanism of syringoside against HBV, and to provide scientific basis for the research of new anti-HBV drug of syringoside.

Materials and methods

Selecting HBV transgenic mice as a model, using TMT quantitative proteomics method to detect the proteins in liver tissue, mining the proteins that syringoside affects the callback, matching the corresponding pathways, and clarifying the anti-HBV mechanism of syringoside¹

Results and discussion

After proteomic analysis, 55 HBV-related differential proteins in the liver were finally obtained, including 19 down-regulated differential proteins and 36 up-regulated differential proteins. GO functional enrichment analysis showed that HBV-related proteins were mainly involved in biological processes (BP) There are 229, 27 for cellular component (CC) and 58 for molecular function (MF). KEGG pathway enrichment results showed that a total of 147 pathways were

involved. After syringopic treatment, 12 landmark proteins showed benign callbacks, making them close to the expression level of the blank group, 5 were up-regulated, 7 were down-regulated, and 175 biological processes (BP) were involved in the GO functional enrichment analysis. There were 22 cellular components (CC) and 34 molecular functions (MF), and the pathway enrichment results showed that a total of 49 pathways were involved.

The seven down-regulated proteins affected by syringin included D3Z9J8, A0A0G2K2M9, A0A0G2JXM2, P62078, F1M8B7, Q5M7T5, and P62997. The five up-regulated proteins included Q9JI66, D4AA47, Q4KLI0, Q5PPG2, and P62142. The 49 pathways involved include glycosylphosphatidylinositol (GPI)-anchored biosynthesis, proximal tubule bicarbonate regeneration, amphetamine addiction, ferroptosis, autophagy-other, chronic depression, TGF-beta signaling, arginine and proline metabolism, long-acting potentiation, antigen processing and presentation, complement and coagulation cascades, Chagas disease, pancreatic secretions, alcoholism, bile secretion, dopaminergic synapses, inflammatory mediator modulation of TRP channels, oocyte meiosis, vascular smooth muscle contraction, adrenergic signaling in cardiomyocytes, lysosomes, amebiasis, transcriptional dysregulation in cancer, sphingolipid signaling, hippo signaling, cGMP-PKG signaling pathway, cAMP signaling pathway, mRNA monitoring pathway, oxytocin signaling pathway, hepatitis C, insulin resistance, cellular senescence, platelet activation, AMPK signaling pathway, hepatocellular carcinoma, herpes simplex virus type 1 infection, insulin signaling pathway, autophagy- Animals, tight junctions, focal adhesions, regulation of actin cytoskeleton, PI3K-Akt signaling pathway, spliceosome, thermogenesis, proteoglycans in cancer, human papillomavirus infection, endocytosis, metabolic pathways, etc. The mechanism of the effect of syringoside at the serum protein level is revealed, and it is explained from a deeper level that syringoside plays an anti-HBV effect by affecting the related marker proteins in the above protein pathways.

Through research, it was found that glycosylphosphatidylinositol (GPI)-anchored biosynthesis may be the key pathway of syringoside against HBV (Figure 5-25). The protein involved is Q5PPG2, and the corresponding gene is PIG-K. Cell surface proteins can attach to cell membranes through glycolipid structures called glycosylphosphatidylinositol (GPI) anchors. Hundreds of GPI-anchored proteins have been identified in many eukaryotes, from protozoa and fungi to mammals. All protein-linked GPI anchors share a common core structure characterized by the substructure Man (α1-4)GlcN (α1-6) myo-inositol-1P-lipid. Biosynthesis of GPI anchors occurs in three stages: pre-assembly of GPI precursors in the ER membrane, GPI attachment to the C-terminus of newly synthesized proteins in the ER lumen, and lipid remodeling and/or lipid remodeling in the endoplasmic reticulum and Golgi apparatus or carbohydrate side chain modifications. Defects in GPI-anchored biosynthetic genes may contribute to inherited diseases.

To sum up, the HBV-related proteins regulated by syringumarin were excavated by proteomics, and the mechanism of syringumarin against HBV was expounded, which also provided the basis for the wide application of syringumarin.

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Anti-HBV metabolomics study of syringopicroside based on HepG 2.2.15 cell model

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Abstract

This experiment was based on UPLC-MS metabolomics to clarify the effect of syringopicroside on endogenous metabolites in HepG2.2.15 cells. UPLC-MS technology was used to identify biomarkers in intracellular fluid, and to search for the biological effects of syringopicroside on callback. Through the analysis of relevant metabolic pathways, the key pathways of syringopicroside in its anti-HBV effect were explored, to explain the mechanism of action of syringopicroside against HBV.

Key words: Syringopicroside; HBV; metabolomics

Hepatitis B is an inflammatory disease of the liver caused by long-term infection with the hepatitis B virus. HBV is a hepatotropic DNA virus. Long-term human infection with HBV can cause chronic hepatitis B. If not treated in time, it may develop into liver fibrosis, liver cirrhosis and hepatocellular carcinoma^[1,2]. At this stage, the treatment of HBV infection is still a major problem to be solved urgently in the medical field. Currently, hepatitis B can be treated with medication. The drugs used are interferon (IFN) and nucleoside drugs (NAs)^[3,4]. However, these drugs have serious side effects and resistance^[5]. Therefore, traditional Chinese medicine, which is safe and effective in the treatment of HBV, has attracted more and more attention from researchers. As a monomeric compound extracted and isolated from clove leaves^[6], syringopicroside have a significant and safe effect in anti-HBV, and is expected to become one of the ideal drugs for anti-HBV. However, due to the unclear mechanism of action, the development of new anti-HBV drugs of the drug is limited. In order to clarify the mechanism of action of syringopicroside anti-HBV, our research group used UPLC-MS technology to explore the mechanism of syringopicroside's intervention, so as to provide a scientific basis for the research on new syringopicroside anti-HBV drugs.

Objective

Based on UPLC-MS metabolomics, the effect of syringopicroside on endogenous metabolites in HepG2.2.15 cells was clarified, to explain the mechanism of action of syringopicroside against HBV.

Materials and methods

UPLC-MS technology was used to identify the biomarkers in intracellular fluid, to find the biomarkers that syringopicroside affects the callback, and to explore the key pathways of syringopicroside to exert its anti-HBV effect through the analysis of related metabolic pathways.

Results and discussion

In this experiment, HepG 2.2.15 cells transfected with HBV virus were used as the research object, and human hepatoma cells HepG2 cells were used as blank control. UPLC-MS technology was used to detect HBV disease-related and intracellular endogenous metabolites after administration. Principal component analysis, orthogonal partial least squares discriminant analysis (OPLS-DA) multivariate statistical analysis and t-test were used to analyze the syringopicroside group,

lamivudine group, model group and blank control group. By analyzing the cellular endogenous metabolites in the blank and model groups, we found 255 HBV-related biomarkers, involving a total of 41 metabolic pathways. After syringopicroside treatment, 77 metabolites reverted to the blank group, involving a total of 8 metabolic pathways. After lamivudine treatment, 105 metabolites were affected to return to the blank group, involving a total of 32 metabolic pathways.

After cross-comparing the metabolic pathways affected by the two, it was found that the metabolic pathways affected by lamivudine were more diverse than those affected by syringopicroside, and the metabolic pathways affected by syringopicroside were relatively concentrated. Biosynthesis, glycerophospholipid metabolism, drug metabolism-other enzymes, aminoacyl-tRNA biosynthesis, and ether lipid metabolism. The specific metabolic pathways of syringopicroside are sphingolipid metabolism, glycine, serine, threonine, arginine and proline metabolism. It revealed the similarities and differences of the influence mechanism of syringopicroside and lamivudine on the cellular metabolism profile, and explained from a deeper level that syringopicroside plays an anti-HBV role by affecting the relevant biomarkers in the metabolic pathways of the above-mentioned cellular metabolome.

Through metabolomic studies, it was found that arginine biosynthesis is the key pathway of syringopicroside against HBV, and the main metabolites involved are L-arginine and N-acetylmethionine. Arginine is currently the most studied semi-essential amino acid. It can produce a variety of biologically active molecules through enzymatic reactions. It is mainly involved in three processes: urea cycle, nitric oxide synthesis and polyamine metabolism. It is used for hepatic coma and viral liver disease. Abnormal alanine aminotransferase. L-arginine is a semi-essential basic amino acid in the body, and it is one of the important metabolites in the urea cycle. It can convert high concentrations of ammonia into urea and excrete it with the urine. It is associated with hyperammonemia caused by liver disease. related. In addition, it is also a natural precursor of nitric oxide, which has the effect of relaxing vascular smooth muscle.

Therefore, in this experiment, metabolomics technology was used to explain the mechanism of action of syringopicroside against HBV. The research of this experiment can lay a foundation for the development of new anti-HBV drug of syringopicroside.

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Innovation and development of the health industry in China and Russia

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Abstract:

The large health industry aims to maintain, improve and promote health, improve people's physical and mental health and subjective feelings as the service standard, and provides a collection of production activities of all health-related products and services. The sustained and stable development of the large health industry not only improves the health level and quality of life of the Chinese people, but also adds bricks and tiles to China's opening up to the outside world. At the same time, we will cooperate more closely with Russia, and from the perspective of traditional Chinese medicine, we will join the excellent achievements of traditional Chinese medicine. Through the innovation of cooperation methods, we will further promote the development of the large health industry of China and Russia, bringing more significant advantages to industrial innovation and technological progress.

Key words: Big health industry, Cooperation between China and Russia, Innovation and development

According to the Outline of the Healthy China 2030 Plan, the large health industry can be divided into four sectors: medical care, medicine, health services, and fitness, leisure and sports. Since 2020, the COVID-19 epidemic has swept the world. Residents' health care awareness has been sharply improved, and the demand for health products and services has increased explosively, bringing new opportunities to the development of the large health industry. At present, the large health industry has developed into one of the largest and fastest emerging industries in the world.

Objective

Unlike the traditional pharmaceutical industry, the large health industry aims to maintain, improve and promote health, improve people's physical and mental health and subjective feelings as the service standard, and provides a collection of production activities of all health-related products and services. It is closely related to human health. In 2013, General Secretary Xi Jinping put forward the Belt and Road Initiative. In May 2014, President Putin clearly announced Russia's support for China's Belt and Road Initiative. Adhere to the concept of openness, pragmatism and win-win results to achieve common development between China and Russia.

Materials and methods

Affected by the COVID-19 epidemic in 2020 (home fight against the epidemic and fewer outdoor activities), the per capital medical care consumption expenditure of Chinese residents fell to 1,843 yuan. However, from the perspective of the overall trend, with the effective control of the epidemic in China, urban and rural residents gradually returned to normal work and life order. It will continue to grow.

In 2021, Russia's Business Consulting Daily said that the latest survey data released by the Russian International Audit and Network Consulting Agency showed that Russia was hit hard by the COVID-19 epidemic in 2020, and the number of Russian residents adhering to a healthy lifestyle decreased by about 3.7 million. According to the "Population Status" national plan

implemented by the Russian government, the proportion of residents maintaining a healthy lifestyle should reach 12% by 2024, while increasing the healthy life expectancy of the population from the current less than 60 years to 67 years. In addition, Russian social experts believe that Russians, especially in big cities, do not realize the importance of maintaining a healthy lifestyle. Russian President Vladimir Putin has always advocated a healthy lifestyle for residents. He has repeatedly said that sports and the values of a healthy lifestyle should be popularized in Russian society.

Through the integration and development of traditional Chinese medicine germplasm resources industry, traditional Chinese medicine cultivation industry, traditional Chinese medicine processing and processing industry, traditional Chinese medicine manufacturing industry and traditional Chinese medicine storage and circulation industry, such as the Belt and Road Initiative international industrial chain of traditional Chinese medicine, traditional Chinese medicine and characteristic towns. It has been integrated and developed into a small town with traditional Chinese medicine characteristics and a cultural industrial chain of traditional Chinese medicine.^[5]

Russia has strong research and development ability, and has achieved great results in the research and development of drugs for chemotherapy, depression and cardiovascular diseases in recent years. In 2019, President Putin signed Presidential Decree No. 254 approving the Health Development Strategy of the Russian Federation until 2025. China has always been Russia's largest trading partner. The COVID-19 epidemic in 2020 further accelerated the development of China and Russian medical trade, and also reflected the strong complementary of the medical industries and markets of China and Russia.

Results and discussion

Driven by multiple favorable factors such as policy support, demand brought about by population aging, and health awareness to stimulate consumption, China's large health industry has ushered in the development. At present, although the development of China's large health industry is still in the primary stage, the market potential is huge and the scale is constantly increasing. According to accounting, the total scale of the national health industry in 2018 was 6.42 trillion yuan, an increase of 12.43% over 2017, accounting for 7.08% of GDP, and the total scale of the national health industry in 2021 was 7.25 trillion yuan, an increase of 12.93% over 2018. Relevant institutions predict that the scale of China's large health industry will reach 14.48 trillion yuan in 2023.

With the in-depth promotion of the Belt and Road strategy and the continuous implementation of the mutually beneficial policy of industrial cooperation between China and Russia, more and more Chinese enterprises have begun to enter the Russian market. Through investment and trade cooperation in Russia, Chinese enterprises are becoming a new force in the development of Russia's big health industry. According to the health goal of the Russian people's livelihood, the average life expectancy of the Russian population will increase to 78 years by 2024. Industry analysts pointed out that alcohol consumption and high-calorie diets increase the health risks of Russians in the middle-aged and elderly, and cardiovascular and cerebrovascular diseases, diabetes, tumors, and excessive obesity are increasing. Under the background of the gradual docking between China's Belt and Road Initiative and Russia's Eurasian Economic Union, we are very optimistic about the development of Russia's health industry. Russia's natural health products can also "feed back" the Chinese market and serve the 'Healthy China' strategy. Industry analysis pointed out that with the improvement of people's living standards, health awareness and the advent of the era of global

aging, the health industry is becoming one of the important engines of global economic recovery.

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Thoughts on promoting the development of TCM health industry in Heilongjiang Province

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Abstract

With the introduction of the 14th Five-Year Plan for TCM Development in Heilongjiang Province and other related policies, actively promoting the high-quality development of TCM and health industry has become an important strategy to promote the economic and social development of Heilongjiang Province.

Key words: traditional Chinese medicine,big health industry,industrial development

The historical opportunity to promote the development of TCM health industry in Heilongjiang Province

The Central Committee of the Communist Party of China has raised the inheritance and development of TCM and healthy China as a national strategy, providing policy support for the development of TCM and health industry in Heilongjiang Province^[1].

The Heilongjiang Provincial Party Committee and the Provincial Government attach great importance to the role of TCM in the revitalization of Longjiang, which provides an inexhaustible impetus for the development of the TCM health industry in our province.

Heilongjiang Province has strong scientific and technological strength in TCM, which provides strong technical support for the development of TCM health industry.

TCM has a lofty position in the masses of the people, providing a good mass foundation for the development of the TCM health industry in Heilongjiang Province.

Some understandings on the development of the large health industry of TCM in Heilongjiang Province

Accelerate the construction of TCM think tanks and form a joint force in the development of TCM health industry.

Pay attention to key groups of TCM health services and improve the credibility of the government.

Quickly develop the "Northern TCM" industry with regional characteristics and start the Longjiang brand.

Strive to give full play to the academic advantages of the "Longjiang School of TCM", inherit and promote Longjiang TCM.

Introduce, cultivate and retain high-quality talents in TCM, and provide the first driving force for healthy Heilongjiang Province.

Build a smart platform for TCM health services to promote the construction of a healthy Heilongjiang Province.

With the help of the "One Belt, One Road" international exchange, promote Heilongjiang Province's TCM to go global.

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Analysis on difference of biochemical index changes in experimental streptozotocin-induced diabetic animal model

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Absrtact

Continuous high concentration of blood glucose can cause systemic vascular damage and affect the function of heart, eyeball, kidney and nerve. At present, diabetes is mainly prevented, so early recognition and diagnosis are of great significance for patients with diabetes. In its related research, the disease trend can be determined by detecting biochemical indicators, so as to achieve the purpose of timely medication intervention. The application of biochemical indicators in clinical and animal research of diabetes is not the same. This article reviews the differences of high-frequency biochemical indicators in the application of diabetes and its complications, so as to provide reference for relevant experiments in the future.

Key words: diabetes, biochemical indicators

Diabetes is a series of metabolic disorder syndrome including protein, fat, water and electrolyte due to the insufficient absolute or relative secretion of insulin and the reduced sensitivity of target tissue cells to insulin. This article mainly reviews the changes of biochemical indicators of diabetes. Required articles were collected from HowNet, Wanfang, and pubmed.

Biochemical indicators commonly used in clinical and animal experiments were fasting blood glucose (FBG), low density lipoprotein cholesterol (LDC-C), high density lipoprotein cholesterol (HDL-C), triglycerides (TG), and total cholesterol (TC). Compared with clinical trials, biochemical indicators used in animal trials were relatively few. In addition to the biochemical indicators used in previous trials, body weight, food consumption and water consumption were mostly selected as investigation indicators in animal trials. Table 1 shows the change range of biochemical indexes of high frequency application of diabetes.

Table 1 Change range of biochemical indicators for high-frequency application of diabetes

Biochemical indicator	Clinic	Rat	Mouse
FBG(mmol/L)	Normal 5.00 ± 1.10	Normal 5.55 ± 1.55	Normal 7.00 ± 2.00
	Diabetes ≥ 7.00	Model ≥ 11.10	Model ≥ 11.10
TC(mmol/L)	Normal 4.45 ± 1.55	Normal 2.50 ± 1.50	Normal 4.50 ± 3.50
	Diabetes > 6.00	Model 6.50 ± 2.50	Model 9.50 ± 5.50
TG(mmol/L)	Normal 1.61 ± 1.07	Normal 0.88 ± 0.53	Normal 1.25 ± 0.75
	Diabetes > 1.69	Model 3.20 ± 1.80	Model 1.90 ± 1.60
HDL-C(mmol/L)	Normal 1.30 ± 0.30	Normal 1.50 ± 0.90	Normal 2.05 ± 0.95
	Diabetes < 1.00	Model 0.82 ± 0.79	Model 4.50 ± 1.50
LDL-C(mmol/L)	Normal 1.70 ± 1.70	Normal 6.50 ± 4.50	-----
	Diabetes > 3.40	Model > 1.10	-----

Objective

In diabetes-related trials, the prevalence trend can be determined by detecting biochemical indicators, and timely medication can be applied. This paper reviews the changes of high-frequency biochemical indicators in different diabetic animal models, hoping to provide reference and help for

relevant experimental research.

Materials and methods

Relevant experimental articles on "diabetes" and "biochemical indicators" were searched through HowNet and pubmed, and summarized and elaborated.

Results and discussions

In this study, the FBG values of both clinical patients and animal models in the diabetes group were greater than those of the normal control group. In animal experiments, in order to ensure the stability of the model, the molding standard is elevated. The researchers have found that when $FPG \geq 16.70$, the diabetic model is relatively stable and can be tested well. Therefore, FPG in model group is generally higher than that in clinical patients in animal experiments. As shown in the table, the change ranges of biochemical indicators for other high-frequency applications of diabetes were not significantly different, which should be due to individual differences. In this paper, we selected the related literature on diabetes intervention and treatment, and selected the biochemical indicators with higher application frequency to be combined with clinical application to summarize the change law, hoping that this article can provide a valuable reference for the majority of researchers.

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Research progress of special acupuncture in the treatment of lateral femoral cutaneous neuritis

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Abstract

Lateral Femoral Neuritis is a common neurological disease in which patients perceive abnormal sensations such as thigh skin pain and burning. Traction, compression, and cold are the triggering factors, which affect the daily activities of patients. The disease affects the patient's daily activities. At present, there is no specific treatment method in Western medicine, and the advantages of acupuncture are obvious. This article discusses the clinical practice and mechanism of treatment of lateral femoral cutaneous neuritis with special acupuncture methods such as floating needle, fire acupuncture, and cutaneous acupuncture. It is found that compared with simple acupuncture, the treatment efficiency of special acupuncture is higher and the clinical efficacy is better, but there are still some problems that need to be improved.

Key words: Lateral Femoral Cutaneous Neuritis; Lateral Femoral Cutaneous Nerve Entrapment Syndrome; special acupuncture; acupuncture treatment.

Lateral femoral cutaneous neuritis (LFCN) is a common peripheral nervous system disease caused by the compression of the lateral femoral cutaneous nerve, which is distributed under 2/3 of the anterolateral thigh, so it is also called lateral femoral cutaneous nerve compression syndrome. The lateral femoral cutaneous nerve is a sensory nerve, and most of the clinical symptoms are pain, tearing, numbness, ant sensation, burning sensation and other abnormal feelings in the local skin of the thigh, of which the incidence of abnormal pain is the highest[1]. Modern medicine often uses neurotrophic drugs, anti-inflammatory drugs, local blocking and other basic conservative treatment. In addition to the above treatment, nerve decompression and neurolysis are the preferred treatment methods[2]. Traditional Chinese medicine classifies LFCN into the category of "Pi Bi" according to its clinical symptoms and pathogenesis, and mostly applies acupuncture treatment. In addition to ordinary acupuncture and electroacupuncture, some special needling methods have also been widely used and achieved good curative effects because of their convenient operation, safety and accuracy.

1 Action mechanism and clinical application of special acupuncture

1.1 Floating needle therapy

Floating needle therapy is a characteristic acupuncture therapy invented by doctor Fu Zhonghua, which combines traditional medicine with modern medicine. The doctor selects the special needle for floating needle to stab the patient's "affected muscle" horizontally or obliquely, and can use auxiliary methods such as sweeping and dispersing to arrival of Qi, and then enable the patient to move the affected part actively or passively, so that the blood in the affected part can be reperfused, so as to improve the situation of local ischemia. Liu P gave floating needle treatment to patients with LFCN, and the effect was excellent. Sweeping movement can make the needle body widely contact with loose connective tissue, produce piezoelectric effect, and then enhance the excitability of ion channels. Combined with reperfusion movement, it can increase vascular pressure and blood flow rate, reduce the role of inflammatory factors, and improve symptoms[3].

1.2 Fire acupuncture therapy

Yang Yi[4] treated LFCN patients, and the treatment effect was significantly better than that of electroacupuncture group ($P < 0.05$). The operator burns the needle body of the special high-temperature needle until it turns red, and quickly pricks the affected part or acupoints of the patient. The unique warm force can quickly reach the subcutaneous skin. It is often used in the treatment of arthralgia or coldness with its function of warming meridians and dispersing cold, activating blood circulation and dredging collaterals. In addition, studies have shown that fire acupuncture can promote the differentiation of endogenous neural stem cells into neurons and oligodendrocytes in SCI rats, inhibit the apoptosis of neurons in rats, improve their survival rate, and thus improve the motor sensory function of rats[5].

1.3 Cutaneous acupuncture therapy

Cutaneous acupuncture is a special needling technique evolved from the "half needling" of the "five needling" and the "burr" of the "nine needling" in ancient China. Yang Min[6] used percussopunctator to tap the patient's affected skin to micro bleeding, 5~8ml blood was drawn by cupping and treated once every 3 days, relieve the pain in the affected area. Cutaneous needle therapy can significantly reduce the content of inflammatory pain factors in patients' serum, promote blood circulation, improve neurotrophic status, and alleviate the abnormal feeling caused by nerve compression.

2 Discussion

The most fundamental cause of LFCN is the damage of lateral femoral cutaneous nerve. From the perspective of Western Medicine Anatomy, the lateral femoral cutaneous nerve originates from the L2-L3 spinal nerve, starts from the psoas major muscle, passes through the anterior superior iliac spine and the inguinal ligament, and is divided into anterior and posterior branches at the distal end of the inguinal ligament, respectively controlling the sensory function of the anterolateral and posterolateral thigh skin. Its unique anatomical position lacks the buffer of adipose tissue, and it is easy to cause the lateral femoral cutaneous nerve to be damaged when performing improper hip joint activities or being squeezed by external forces, resulting in abnormal skin sensation at the part^[7-8]. Traditional Chinese medicine believes that the etiology is mostly fatigue or lack of healthy qi. The pathogenic wind cold and dampness took the opportunity to invade the defensive Yang, and the yang-qi was blocked, resulting in the blockage of the meridians and the stagnation of qi and blood. Insufficiency of qi and blood leads to pain and numbness. Floating needle, fire acupuncture and cutaneous acupuncture for LFCN can not only reduce the sensory abnormalities caused by lateral femoral cutaneous nerve compression, but also repair nerves and reduce the recurrence rate. It can also regulate blood with Qi, strengthen the body's healthy qi, and thus improve the quality of life of patients.

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Research on technology of new beverage rosehip fruit vinegar based on the background of "China-Russia Great Health"

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Abstract

Purpose: Combining Heilongjiang's authentic medicinal material, rosehip, with the concept of "China-Russia Great Health", a new type of rosehip vinegar was developed based on the safety and health issues of the local Russian people, aiming to improve the physical quality of the Russian people. Accelerate the cooperation, exchanges, and development of traditional Chinese medicine between the two countries. **Methods:** The rose fruit vinegar is obtained by processing the rose fruit with yeast and acetic acid bacteria and through a series of treatments. **Conclusion:** The fruit vinegar is dark red in color and pure in color. Uniform; with the aroma of fruit vinegar and rose hip; moderate acidity, good taste; good stability, and no visible impurities.

Keywords: rose hip; Sino-Russian health; fruit vinegar;

The report of the 19th National Congress of the Communist Party of China clearly stated that a "Healthy China" should be regarded as an important part of the basic strategy of national development. With the acceleration of my country's population aging and people's pursuit of a better life, the big health industry has nurtured a market of over 10 trillion yuan and has become the industry with the most development potential today. The big health industry can further promote the implementation of the Healthy China strategy and build a global big health display and interaction platform.

A study demonstrating the prevalence of overweight and obesity in a representative adult population sample of 12 regions of the Russian Federation showed that [1] the prevalence of overweight and obesity in Russian adults (30.3%) is higher than in most OECD countries. According to statistics, obesity in Russia increased by 33% between 1995 and 2004 [2], and the increasing trend of the obesity rate in recent years has continued [3]. The steadily increasing obesity rate every year leads to more people suffering from obesity complications, such as hypertension, hyperlipidemia, and fatty liver, which seriously threaten people's health. In the treatment of obesity complications, traditional Chinese medicine has shown its unique charm and is gradually being accepted by the world. It cannot be ignored that in 2019, the scale of Chinese medicine products exported to Russia increased by more than 20% year on year, proving that there is still great potential for Chinese medicine products to be exported to Russia. Among them, Longjiang authentic Chinese medicinal materials, with their unique growth environment, rich wild resources, and first-class medicinal properties, have driven the new rise of the Longjiang Chinese medicinal materials industry.

Rosehip is a perennial deciduous shrub of the genus Rosaceae. It often grows in the mountains and forest margins in northern my country [4]. It is mainly distributed in the virgin forests of the Greater and Lesser Xing'an Mountains in China. It is an authentic medicinal material in Heilongjiang Province. According to research, rosehip extract can promote the decomposition and metabolism of triglycerides, and effectively reduce the content of triglycerides in liver cells [5], revealing its great potential in preventing and treating obesity complications. And as a medicinal and edible rose fruit,

there is an opportunity to enter the Russian market in the form of food or medicine. As a new type of drink that is easy to carry, rosehip fruit vinegar is more suitable for contemporary fast-paced life and can be displayed in the hot food window of the workplace, reducing the frequency of employees eating fast food and increasing healthy eating. The efficacy of preventing obesity and complications [6]. Based on this, we designed a process for making rosehip fruit vinegar, which provides a reference for the idea of Heilongjiang authentic medicinal materials to the Russian market.

Materials and Instruments

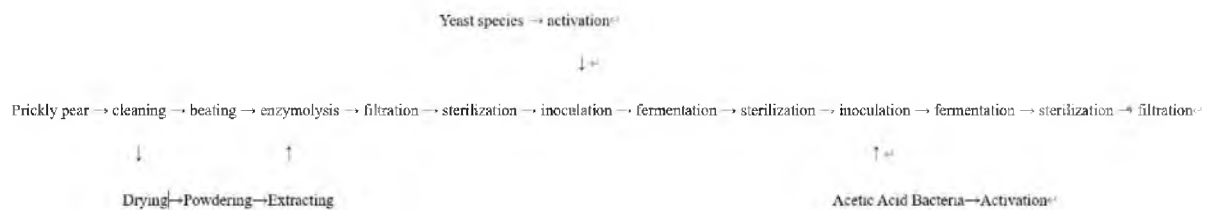
Prickly pear fruit (produced in Daxinganling); acetic acid bacteria (Yantai, Shandong); yeast (Yantai, Shandong); glucose (analytical pure, Aladdin); pectinase (Xiasheng Bio); juicer.

Experiment process

According to the raw materials, thorn rose fruit is divided into two ways: the whole fruit of thorn rose fruit vinegar and the thorn rose fruit juice vinegar.

The fresh rose fruit is used for extracting juice or the dried rose fruit is crushed and then extracted with distilled water, and the fruit juice is processed through alcohol and acetic acid fermentation to obtain fruit vinegar.

The fruit vinegar is obtained from the freshly squeezed or boiled rose juice through alcohol and acetic acid fermentation.



Washing: Wash the fresh rose hips and remove the stems.

Beating and enzymatic hydrolysis: Beat the rose fruit with a juicer for 20 s, add pectinase at a ratio of 0.5%, temperature 40 °C, and enzymatic hydrolysis for 45 min.

Filtration and sterilization: filter with 6 layers of gauze, add glucose to adjust the sweetness, and maintain sterilization at 75°C for the 30s.

Yeast strain activation and inoculation: Weigh an appropriate amount of yeast, add ten times the mass of distilled water, add one-tenth of the mass of glucose, activate at 35°C for 45 minutes, and inoculate 5% activated yeast liquid into the rosehip pulp.

Alcohol fermentation: measure the alcohol concentration of the fermentation liquid with an alcohol meter every 4 hours, obtain the rose fruit wine after the alcohol concentration remains unchanged, and proceed to the next step.

Activation and inoculation of acetic acid bacteria: Weigh an appropriate amount of acetic acid bacteria, add ten times the mass of 5% ethanol, activate at 30°C for 60 minutes, and inoculate the 5% activated acetic acid bacteria liquid into rose fruit wine.

Filtration: filter with 6 layers of gauze and continue to filter with a Buchner funnel to obtain rosehip vinegar.

Results

The obtained rosehip fruit vinegar was subjected to sensory evaluation.

The color is dark red, the color is pure and uniform; it has the aroma of fruit vinegar and thorn rose fruit; the acidity is moderate, the taste is good; the stability is good, and there are no impurities visible to the naked eye.

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Research on the development of health food from Longjiang authentic medicinal materials under the background of "China-Russia Great Health"

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Abstract

Objective: Combining the core concept of "China-Russia Great Health", using the authentic medicinal material - thorn rose fruit, to develop thorn rose fruit jam that conforms to the Russian flavor, improve the physical quality of the Russian people and improve the quality of life. Promote the common development of the traditional medicine industry in China and Russia; **Method:** Remove the core and burr of the rose hips, soak them in 1.0% salt water for 15 minutes to protect the color, and boil them in boiling water for 10 minutes to soften them. Put the softened rose hips in a beater to make a fine homogenate, add sugar, citric acid, and xanthan gum in turn, and stir well to dissolve them. Boil, stir, and concentrate on low heat until the jam is thick, canned, sealed, sterilized, and sterilized to obtain thorn rose fruit jam; **Conclusion:** Based on the sensory evaluation method, the rose fruit jam with the brown-red body, viscous, delicate and shiny, no particles and no flow, moderately sour and sweet, and rich and no peculiar smell is selected as the superior product. The optimal ratio obtained by Design-Expert software is: the addition of white sugar is 37.82%, the addition of citric acid is 0.27%, and the addition of xanthan gum is 0.20%. The introduction of rosehip health food can effectively promote the industrial development and innovation of "China-Russia Great Health".

Keywords: rose hips; Sino-Russian health; health food;

The construction and promotion of the "China-Russia Great Health" system are inseparable from the close communication between Chinese and Russian cultures and industries. As a unique health resource in China, traditional Chinese medicine plays a huge advantage and role in Sino-Russian cultural exchanges. Many Russian scientific research teams are increasingly considering the integration of traditional Chinese medicine in the research and development of medical devices, clinical rehabilitation therapy, and discovery of botanical medicines, and have gradually begun to have the ability to independently use the theory of traditional Chinese medicine for research and treatment. And in practice, more and more Russians truly feel the charm of traditional Chinese medicine. In the first quarter of 2022, the export value of traditional

Chinese medicines in the Sino-Russian medical product trade statistics table reached 11.1628 million US dollars, an increase of 82.70% year on year. At the same time, the export value of traditional Chinese medicine health products increased by 133.80% year on year. It can be seen that traditional Chinese medicine has an indispensable position in Sino-Russian trade exchanges. The Russian people's recognition of traditional Chinese medicine has gradually increased, and the concept of traditional Chinese medicine health care has also deepened [1].

Among the most common diseases promulgated by the Russian government in 2013, the first is endocrine gland diseases, the second is cardiovascular and cerebrovascular diseases, and the second is gastrointestinal diseases. According to incomplete statistics, the prevalence of the cardiovascular disease among the 39-60-year-old Russian population is as high as 68.03 person-times per 1,000

people. The Russian government also attaches great importance to improving the health of residents. Based on this phenomenon, combined with the cooperation prospect of "China-Russia Great Health", rational use of the advantages of traditional Chinese medicine health care function will lay the foundation for Russia to develop and introduce the health food of Longjiang genuine medicinal material - *Rosa japonica*.

The thorn rose fruit is the fruit of the genus *Rosaceae*, which is widely distributed in Northeast, North China, and other regions. It is rich in output and is a valuable wild resource in Northeast China. Its properties are sour, bitter, and warm. The ripe fruit tastes sour and sweet and is rich in various vitamins, of which the content of vitamin C is the highest. After testing, each 100g of fresh rose fruit contains more than 6810 mg of edible vitamin C, and the content of other vitamins is also very high, so the rose fruit is called a natural multivitamin concentrate[2]. Russia is the fifth largest fruit consumer and the third largest fruit importer in the world. The Russian people have a high demand for fruit, and Russia's terrain factors have led to a shortage of fruit production. While thorn rose fruit meets the needs of the Russian people for vitamin intake by its vitamin content, thorn rose fruit can digest food and accumulate, strengthen the spleen and regulate qi, and has a good health care effect on the third most common gastrointestinal disease of the Russian people. At the same time, its own has the effect of protecting the liver and protecting the liver. According to the research of Wei Ying and others, it has a good preventive effect on the fatty liver and can reduce the necrosis and fibrosis of liver cells. Long-term use of rose hips has certain preventive and therapeutic effects on alcoholic fatty liver or obese fatty liver caused by alcoholism or long-term consumption of high-calorie food in Russia. What is more worth mentioning is the health care effect of rosehip on the cardiovascular system. The polyphenols of rosehip can effectively inhibit the abnormal proliferation of VSMC and increase the production of NO, which indicates that rosehip can prevent atherosclerosis, and its total flavonoids It can be used for the production and preparation of anti-myocardial ischemia, hypolipidemic and antiarrhythmic drugs. To sum up, the introduction of rose hip health food can effectively promote the industrial development and innovation of "China-Russia Great Health", and improve the physical quality and living conditions of the Russian people [3].

Purpose:

The innovation and development of the "China-Russia Great Health" industry, highlight the geographical advantages of cooperation with Russia, use the authentic medicinal material - thorn rose fruit, and develop the thorn rose fruit jam that conforms to the Russian flavor, to improve the physical quality of the Russian people and improve the quality of life, Promote the common development of the traditional medicine industry in China and Russia, benefit the people, and open up new thinking and approaches for the country's "One Belt, One Road" initiative.

Materials and Methods:

Choose mature, plump, non-rotten rose hips, remove the core and burrs, soak them in 1.0% salt water for 15 minutes to protect the color, and boil the rose hips in boiling water for 10 minutes to soften them. Put the softened rose hips in a beater to make a fine homogenate, add sugar, citric acid, and xanthan gum in sequence [4], and stir well to dissolve them. Then, it is boiled, stirred, and concentrated in a small fire until the jam is thick, canned, sealed, sterilized, and sterilized to obtain thorn rose fruit jam.

Results and discussion:

Based on the sensory evaluation method, the rose fruit jam with a brownish red body, viscous, delicate, and shiny, no particles and no flow, moderately sour and sweet, and a strong fragrance and no peculiar smell, was selected as an excellent product. The optimal ratio obtained by Design-Expert software is: the addition of white sugar is 37.82%, the addition of citric acid is 0.27%, and the addition of xanthan gum is 0.20%. The Russian diet is inseparable from bread, and the development and promotion of rose fruit jam are in line with the tastes and daily needs of the Russian people. Its consumption method can be matched with bread or reconstituted drinks or supplemented with seasoning, etc. It can play a role in health care from the fundamentals of life[5] and effectively improve alcoholic fatty liver and obesity caused by alcoholism and a high-calorie diet. The production of the liver, spleen, and digestion reduces digestive system diseases, softens blood vessels, and supplements vitamins to delay the development trend of cardiovascular and cerebrovascular diseases.

To promote the collaborative innovation of industry, universities, and research institutes to promote the industrial upgrading of "China-Russia Great Health", we should establish an overall concept, and promote the revitalization and development of the industry with a higher pattern and stronger responsibility. As an authentic medicinal material in Northeast China and North China, *Rosa japonica* has the advantages of abundant real estate and high nutritional value and is an ecological resource with great potential. Combining the rational use of "China-Russia Big Health" can create a deep integration platform, effectively promote the collaborative innovation of production, education, and research, promote the structural reform of the supply side of traditional Chinese medicine, increase the health and well-being of the people of Longjiang, and at the same time enable the Russian people to improve their physical fitness and life. Quality, promote the big health industry with Longjiang characteristics and achieve better and higher quality development.

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Clinical observation on the treatment of post-herpetic neuralgia by collateral-pricking and blood-letting cupping combined with surrounding needling technique electroacupuncture

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Abstract

Objective: To explore the clinical efficacy of collateral-pricking and blood-letting cupping combined with surrounding needling technique electroacupuncture in the treatment of post-herpetic neuralgia (PHN). **Methods:** 60 patients with PHN were randomly divided into observation group and control group, 30 cases in each group. The control group was treated with pregabalin capsule for 20 days. The observation group was treated with puncture and bloodletting cupping combined with electroacupuncture on the basis of pregabalin capsule, once every 2 days, 10 days as a course of treatment, a total of 2 courses. The real-time visual analogue scale (VAS) before and after treatment was observed, and the clinical efficacy was compared between the two groups. **Results:** VAS scores of PHN patients in 2 groups after treatment were lower than before ($P < 0.01$), and the observation group was lower than the control group ($P < 0.05$). The total effective rate of observation group was 86.7%, higher than that of control group 73.3%. **Conclusion:** Acupuncture and bloodletting cupping combined with electroacupuncture peri-acupuncture is effective in the treatment of PHN.

Key words: Post-herpetic neuralgia; Collateral-pricking and blood-letting cupping; Surrounding needling technique electroacupuncture;

Post-herpetic neuralgia (PHN) refers to the pain left over after the healing of herpes zoster, and it usually lasts for more than one month^[1]. As a kind of sequela, PHN is the most common complication of herpes zoster, which tends to occur in middle-aged and elderly people and those with relatively low immunity, and the incidence of which is higher in men than in women. Modern medical treatment of PHN mainly through oral drugs, physical therapy, nerve block, surgical treatment, psychological intervention, etc. Although drug therapy has a certain effect, patients have great differences in pain relief, drug dependence and large side effects, long-term use will cause peripheral edema, dizziness, drowsiness, and seriously affect the endocrine system^[2]. Studies have found that acupuncture combined with cupping therapy has a significantly higher effect on PHN than conventional western medicine, and can significantly prevent the occurrence of PHN^[3]. Acupuncture can promote blood circulation and metabolism, regulate the function of neuro-endocrine-immune system, stimulate nerve regeneration and repair ability, relieve abnormal blood flow, reduce the occurrence of inflammatory reaction, cupping therapy can promote local microcirculation, reduce the concentration of pain-causing substances, effectively relieve pain. Therefore, this study used collateral-pricking and blood-letting cupping combined with surrounding needling technique electroacupuncture for the treatment of PHN.

Objective

To explore the clinical efficacy of collateral-pricking and blood-letting cupping combined with surrounding needling technique electroacupuncture in the treatment of post-herpetic neuralgia (PHN).

Materials and Methods

A total of 60 PHN patients admitted to the Eighth Acupuncture and moxibustion Clinic of the Second Affiliated Hospital of Heilongjiang University of Chinese Medicine from September 2019 to March 2021 were selected. The patients were divided into observation group and control group by random number table method, with 30 patients in each group. The control group received pregabalin capsule (produced by chongqing saiwei pharmaceutical co., LTD., SFDA approval no. H20130073, 75 mg/tablet) twice a day, 75 mg/tablet at the beginning and increased to 150mg/tablet 3 days later. Take it daily, 10 days as a course of treatment, 2 courses in a row. (1) Collateral-pricking and blood-letting cupping: Patients were placed in lateral decubitus position, and the skin of the painful part was disinfected. Three-edge acupuncture was used for 3-5 times, with a depth of 2mm. Cupping and flash method of appropriate size was selected according to the size of herpes zoster area, and the cupping was left for 10-15 minutes. Blood volume 2 mL-3mL. 2 days once, 10 days as a course of treatment, continuous 2 courses. (2) Electroacupuncture: the patient was in lateral decubitus position with the affected area fully exposed. The skin of the infected area was disinfected with 75% alcohol cotton ball. Hua tuo brand 0.30mm×40mm needle needle. The needle was inserted 30 mm away from the PHN skin lesion at a horizontal Angle of 15°, with the tip pointing at the painful site. First, one needle was used in the head and the other needle was used in the tail to penetrate into the skin lesion with a depth of 10mm. Then, the peripheral puncture was carried out at a distance of 15-20mm around the lesion. Four groups of needles were cross-connected to the KwD-808 electroacupuncture instrument of the Great Wall, which adopted a dense wave of 100Hz and a current of 2mA and lasted for 30 minutes. Once every 2 days, 10 days as a course of treatment, a total of 2 courses. Observation indicators: Visual analog scale (VAS) of herpes zoster in "Standard for Diagnosis and Treatment of TCM Diseases and Syndromes"; Curative effect standard: Curative effect standard of Syndrome differentiation and diagnosis of TCM.

Results and Conclusions

Before treatment, there was no significant difference in VAS scores between the observation group and the control group ($P>0.05$), indicating comparability. After treatment, VAS scores in 2 groups were lower than before, with statistical significance ($P<0.01$). The VAS score of the observation group was lower than that of the control group, and the difference between the two groups was statistically significant ($P<0.05$). The total effective rate of the observation group was 86.7%, and the total effective rate of the control group was 73.3%, and the difference was statistically significant ($P<0.05$). The results of this study showed that the clinical efficacy and pain grade of the observation group in the treatment of PHN were significantly better than that of the control group. PHN can be alleviated by acupuncture and bloodletting cupping combined with electroacupuncture. During treatment, no obvious adverse reactions occurred in 2 groups. In conclusion, collateral-pricking and blood-letting cupping combined with surrounding needling technique electroacupuncture in the treatment of PHN has obvious efficacy and is worthy of wide clinical application.

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Clinical progress of acupuncture in the treatment of neuronal tinnitus

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Abstract

Neuronal tinnitus refers to the absence of external sound stimulation, with conscious ringing in the ear as the main symptom, ringing sound can be such as cicadas, tide, wind, electric current sound, etc., on and off, even continuous. Its etiology and influencing factors are complex and diverse, and its pathogenesis is still unclear. Modern medicine believes that it is related to inner ear microcirculation disorder, insufficient blood supply and oxygen supply, nerve conduction pathway lesions and other factors. At present, modern medical treatment is mainly to improve local blood circulation, nutrition nerve, improve nerve block and anti-anxiety. TCM treatment of tinnitus is mainly based on syndrome differentiation of channels and collaterals and viscera. Traditional Chinese medicine, warm acupuncture, electroacupuncture, combination of acupuncture and medicine and other therapies have good clinical efficacy. This article only reviews the clinical research of acupuncture therapy on neuronal tinnitus in order to find a better method to improve tinnitus.

Keywords: acupuncture, electroacupuncture, neuronal tinnitus, review

1 Acupuncture treatment methods

1.1 Electric acupuncture at four points of the mastoid process

Professor Gao Weibin, famous Traditional Chinese medicine in Heilongjiang Province, second prize winner of National Scientific and Technological Progress, using traditional Chinese medicine acupuncture method, combined with acupoint theory and neuroanatomical knowledge, innovation of four mastoid points (mastoid 1: 0.4 inches behind auricle groove, flat upper edge of external auditory meatus; Mastoid 2: 0.4 inches after auricle groove, flat lower margin of external auditory canal; Mastoid 3: after the auricle groove 0.8 inches, flat upper edge of the external auditory canal; Mastoid 4: 0.8 inches behind auricle groove, flat lower margin of external auditory meatus), proposed the theory of electromagnetic wave bone conduction. Select the four points of the mastoid process, Ermen point, Tinghui point, Fengchi point, Gongxue point, electroacupuncture instrument select continuous wave of dense wave, dense wave current is large, can produce an electric field, Fengchi point, Gongxue point can improve vertebrobasilar artery and labyrinth artery blood flow increase, Ermen point, Tinghui point can improve labyrinth artery and blood circulation around the ear. This method is a new method to treat ear disease and has good clinical effect in improving tinnitus and deafness. Wang Chunying et al. used this method to treat 30 cases of neuronal tinnitus, the course of disease ranged from 3 to 32 (16.4±10.5) months, with a total effective rate of 96.7%, high improvement rate [1]. For young patients, Professor Gao also emphasized the screening of congenital vascular structure abnormalities, so as to predict the treatment effect.

1.2 Cervical jiaji point combined with ear three needles

There are sympathetic ganglia at cervical jiaji point (C3~5), and the auricular branch of vagus nerve innervates the external auditory canal. Electroacupuncture may regulate autonomic nerve function, relieve vasospasm, and thus improve the blood circulation of the inner ear [2]. Some studies have

compared the cervical jiaji point (C3~6) combined with three ear needles (Tinggong point, Tinghui point, wangu point) and traditional acupuncture points Ermen point, Tinggong point, Tinghui point and Yifeng point. The results showed that both methods could effectively relieve the severity of tinnitus and reduce the amount of tinnitus disability, but acupuncture at cervical Jiaji point combined with three ear needles had better clinical efficacy in the treatment of neuronal tinnitus [3].

1.3 Acupuncture at Shenguan point of Dong shi Qi Point

Shenguan acupoint is located in the depression below the medial condyle of tibia 1.5 inches straight down, between the posterior edge of tibia and soleus muscle. It is one of Dong's Qi acupoints. It is the key point for tonifying kidney, and it is effective for all kinds of symptoms caused by kidney deficiency. According to clinical observation, took the Shenguan point, Tinggong point, Tinghui point, Yifeng point and Hegu point, Taichong point, treated 32 cases of neuronal tinnitus caused by kidney-essence deficiency caused by overwork and staying up late, and the healing rate was 75.0%. This method of tonifying kidney and nourishing qiao acupuncture has good efficacy and high acceptance among patients [4].

1.4 Screw acupuncture

The method of screw acupuncture refers to that the needle body is inserted and fixed in the skin or subcutaneous acupoint for a long time to retain the needle, and the stimulation quantity is accumulated for a long time to accumulate the quantity effect in order to achieve the purpose of treating diseases. This method has certain advantages in the treatment of chronic diseases. A clinical observation took the Ermen point, Tinggong point, Tinghui point, Yifeng point, Neiguan point, Shenmen point, Anmian point, and to compare the efficacy of screw acupuncture with ordinary acupuncture. After 4 weeks of treatment, the total effective rate of screw acupuncture was 64.28% in the observation group and 41.46% in the control group. The effect and long-term efficacy of screw acupuncture were better for tinnitus patients [5]. There is a lack of clinical studies on the treatment of neuronal tinnitus by pure screw acupuncture, and more clinical and basic studies are needed to add conviction.

2 Summary

In this paper, four clinical acupuncture methods for the treatment of neuronal tinnitus were reviewed: electroacupuncture at the four points of the nipple, cervical jiaji point combined with the three points of the ear, acupuncture at The Shenguan point of Dong Shi qi point, and press acupuncture. Among the simple acupuncture therapy, the author believed that electroacupuncture was more effective, especially professor Gao Weibin's four points of the mastoid process and electric finger acupuncture. Clinical studies on the treatment of tinnitus by electroacupuncture have found that tinnitus is accompanied by cervical spondylosis in the largest number of patients, followed by sleep disorders and hypertension, respectively. Electroacupuncture can improve the vertebra-basilar artery blood flow velocity of tinnitus patients [6]. For neuronal tinnitus, especially for those with a long course of disease, there is currently no targeted treatment to achieve the purpose of cure. No matter in Traditional Chinese medicine or Western medicine, more treatment can only improve symptoms. There are relatively few clinical and basic researches on TCM. In addition to single acupuncture treatment, there are also combined therapies such as acupuncture combined with moxibustion, bloodletting therapy, cognitive behavioral therapy, drugs, and percutaneous electrical stimulation of the vagus nerve. Guard against disease before you become

ill .In life, especially young people should pay attention to regular work and rest, adjust mental stress, reduce the frequency of earphone use, etc., and form good living habits.

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Research progress of acupoint catgut embedding in treatment of chronic urticaria

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Abstract

Acupoint catgut-embedding, as a common treatment in Traditional Chinese medicine, has been widely used in clinical practice, especially in the treatment of chronic urticaria (CU), which has the advantages of small adverse reactions and low price. In order to further explore the effectiveness of acupoint catgut-embedding in the treatment of CU, the advantages and existing problems of acupoint catgut-embedding in the treatment of CU were summarized through retrieval of relevant literatures from China National Knowledge Infrastructure (CNKI), VIP, WANFANG DATA and PubMed in recent five years. In order to provide a reference for the clinical treatment of the disease, the relevant research ideas and prospects were put forward.

Key words: Acupoint catgut embedding; chronic urticaria; Review;

Chronic Urticaria (CU) is a common clinical allergic skin disease. The main symptoms are temporary inflammatory hyperemia and tissue edema caused by various causes in blood vessels, mucous membrane and skin, namely the so-called "wind mass". According to the interpretation of Chinese Urticaria Diagnosis and Treatment Guidelines (2018 edition), when the wind mass occurs daily or intermittently and the course of disease exceeds 6 weeks, it can be diagnosed as chronic urticaria ^{[1][2]}. CU can occur in all ages, with young and middle-aged women accounting for the majority (female/male ratio, 1.46:1) ^[3], and the course of the disease can be delayed for months or even years ^[4], The quality of life of patients is seriously affected. Second-generation antihistamines are often used as first-line drugs in western medicine to treat CU, but there are many adverse reactions, and the overall therapeutic effect is not very ideal ^[5]. This paper retrieves relevant researches in recent five years and summarizes them as follows.

1. Acupoint catgut embedding therapy

Acupoint embedding is developed by retention needle and embedding needle therapy, Zhang Jingyue said: "long disease..... Therefore, early acupoint catgut embedding is often used in the treatment of chronic diseases and refractory diseases ^[6]. Acupoint catgut embedding is a comprehensive treatment method including acupoint sealing, acupuncture, pricking of blood, retention of needles and embedding of needles, tissue therapy and other effects ^[7]. For patients with long-term illness and weakness, it can balance the qi of zang-fu organs, harmonizing Yin and Yang, activating channels, regulating qi and blood, tonifying deficiency and eliminating solid, invigorating positive and dispelling evil.

2. Application of acupoint catgut embedding in clinical treatment of CU

2.1 Catgut embedding monotherapy at acupoints

With the gradual deepening of people's understanding of CU, most of the three causes of "blood deficiency produces wind, blood stasis produces wind, and blood hot wind is filled" to select acupoints based on syndrome differentiation. The clinical symptoms of CU patients were significantly improved and the curative effect was better than western medicine.

2.2 Acupoint catgut embedding combined with other therapies

2.2.1 Acupoint catgut embedding combined with Traditional Chinese medicine

Under the guidance of the basic principle of syndrome differentiation and treatment of CU, TCM decoction can increase the effect and shorten the course of treatment, which has certain advantages.

2.2.2 Acupoint catgut embedding combined with Western medicine

Acupoint catgut embedding combined with Western medicine treatment can, on the one hand, increase the therapeutic effect of traditional Chinese and Western medicine, on the other hand, reduce the dosage of Western medicine to a certain extent, reduce the occurrence of adverse reactions^[8], and play a role of reducing toxicity and enhancing efficacy.

2.2.3 Acupoint catgut embedding therapy combined with autologous blood therapy

Self-blood therapy is a non-specific stimulation therapy combining the theory of menstrual blood in modern medicine and Chinese medicine. It integrates acupuncture, bloodletting and acupoint injection, and activates the immune function of the body by prolonging the time of acupoint treatment to produce anti-inflammatory and desensitization effects, so as to achieve the functions of harmonizing ying and protecting and relieving muscle penetration^[9]. It has certain clinical value in the treatment of CU.

2.2.4 Acupoint embedding combined with puncture cupping method

Puncture and bloodletting in puncture and cupping therapy can make blood vessels unblocked, the so-called "blood flow wind self-elimination", thus dispelling wind and relieving pruritus, and cupping has the function of warming meridian, dispersing cold, nourishing and dispelling evil, so puncture and cupping therapy can not only remove external evil, but also regulate the function of viscera, thus effectively treating urticaria^[10].

Discussion and outlook

As the inheritance and innovation of traditional acupuncture techniques, catch-embedding at acupoints is characterized by "staying quiet for a long time", and its unique "long-term mechanism" has been widely applied in clinical practice, especially for chronic diseases^[11].

It is hoped that in the future clinical studies on acupoint catgut embedding treatment of CU, the diagnosis and efficacy evaluation criteria can be standardized, a relatively perfect long-term follow-up system can be established, the long-term efficacy of acupoint catgut embedding treatment of CU can be clarified, and the rigor and credibility can be increased. Clarify the relevant theoretical research on acupoint catgut embedding treatment of CU, clarify and simplify the research on acupuncture point selection, improve the catgut embedding techniques and tools to highlight the characteristics, and provide more reference for clinical work.

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Changes in the sex hormones level in using cyclic chemotherapy

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Abstract

The toxicity associated with the use of polychemotherapy can cause late and long-term side effects, one of such effects is infertility. Improving the quality of life of people cured of a malignant neoplasm is possible by reducing the toxic effect of drugs. In this regard, the purpose of our study is to research changes in the level of sex hormones occurring in the body after the double administration of a complex of drugs for the treatment of hemoblastosis according to the CHOP program. As an experimental material, 50 sexually mature male Wistar rats were used. The first experimental group was administered intraperitoneally a complex of drugs to the CHOP program: The second experimental group, after the introduction of CHOP, the next day an antioxidant, dehydroquercetin, was added to the feed. Polychemotherapy-induced testicular lesion leads to a violation of the reproductive function of men on the "pre-testicular", "testicular", "post-testicular" levels of the reproductive system. So, understanding the patterns of the processes of reparative regeneration of damaged tissues is important for the development of rehabilitation programs, preservation of reproductive function and quality of life in patients who have undergone cytostatic therapy, especially in young people.

Keywords: toxicity, cyclic chemotherapy, male Wistar rats, sex hormones, hemoblastosis, infertility.

In recent years, there has been an increase in the incidence of oncological neoplasms, both among adults and among children. According to the statistics of the Federal State Budgetary Institution "NMIC of Radiology" of the Ministry of Health of Russia, in 2017, 3.63 million cases of cancer were recorded in the country, in 2018 – 3.76 million cancer patients, in 2019, 640 thousand new cases of malignant neoplasms were detected, which is why the total number of registered oncologists amounted to 3.92 million patients.

Unfortunately, children's morbidity has also increased. Every year, up to 20 thousand cases of cancer are detected in children under the age of eighteen, and if you pay attention to the age category of 1-5 years, then they account for about 15 thousand cases. Thus, in childhood, the highest incidence of oncological diseases falls on lymphoblastic leukemia and is equal to 29%, followed by tumors of the central nervous system – 23%, lymphomas – 12%.

However, to date, the possibility of curing most malignant neoplasms has already been proven through the introduction of proven antitumor treatment regimens, including a combination of drugs with various toxic effects and mechanism of action: steroid hormones, antimetabolites, antitumor antibiotics, cytostatics. The breakthrough made in the quality of diagnosis and treatment of malignant neoplasms led to the initiation of therapy in the early stages, as well as to a decrease in the mortality of the population from oncological processes. And yet, despite the decrease in mortality, modern anticancer drugs are characterized by a high degree of aggressiveness. Drugs of this group have an effect not only on areas of malignancy, but also on healthy tissues. This is due to the fact that the mechanism of action of antitumor drugs is aimed at blocking the rapid growth and division of tumor cells.

In addition to tumor cells, there is also damage to the cells of the mucous membranes of the oral cavity and gastrointestinal tract, bone marrow, reproductive system and hair follicles, in addition, damage to almost all normal structures of the body is possible. The toxicity associated with the use of polychemotherapy can cause late and long-term side effects, one of such effects is infertility. Improving the quality of life of people cured of a malignant neoplasm is possible by reducing the toxic effect of drugs. This is becoming one of the main public health problems. The purpose of our study is to research changes in the level of sex hormones occurring in the body after the double administration of a complex of drugs for the treatment of hemoblastosis according to the CHOP program.

Materials and methods

As an experimental material, 50 sexually mature male Wistar rats, aged 2.5 months, weighing 200 g were used. The animals were kept under normal vivarium conditions: under a certain lighting mode for the experiment: 12 hours under artificial lighting, 12 hours in the dark, at a temperature of 20 C. The experimental animals were housed in standard plastic cages, measuring 60×40×30 cm, with 10 mice in each cage. All experimental animals received balanced nutrition and water without restrictions. The animals were kept, all experimental manipulations and the killing of animals were carried out in accordance with the rules adopted by the European Convention for the Protection of Vertebrates Used for Experimental and Other Scientific Purposes (Strasbourg, 1996).

During the experiment, 50 rats were divided into two groups of 25 rats in each group. On the first day of the experiment, a blood sample was taken to determine the level of hormones: LH, FSH and testosterone. The first experimental group was administered intraperitoneally twice (with an interval of 7 days) a complex of drugs for the treatment of hemoblastosis in the clinic according to the CHOP program: cyclophosphane (21 mg/kg), adriamycin (2.1 mg/kg), vincristine (0.04 mg/kg) and prednisolone (2.1 mg/kg). The selected dose is 1/5 LD50. The second experimental group, after the introduction of CHOP, the next day an antioxidant, dehydroquercitin, was added to the feed. The choice of this scheme of polychemotherapy was due to the fact that these drugs are basic and are included in most modern treatment regimens for malignant diseases.

On the seventh day after the administration of the drugs, blood was taken from each experimental group in both experimental groups for further study of hormonal changes. After that, the complex of drugs was re-administered according to the SNOP program. In the second experimental group, dehydroquercitin was added to the feed.

On the 7th, 14th, 30th, 45th day after the repeated administration of the CHOP complex, blood was taken from rats in both experimental groups.

The experiment was conducted in accordance with the moral requirements for working with experimental animals "Rules for carrying out work using experimental animals" (Order of the Ministry of Health of the USSR No. 755 of 12.08.1987), the Federal Law on the Protection of Animals from Cruel Treatment of 01.01.1997, "On approval of the rules of laboratory practice" (order of the Ministry of Health of the Russian Federation of 19.06.2003, No. 267) and approved by the Local Ethics Committee of the Amur State Medical University. Gonad sampling is planned during the autopsy study of rats. After sampling, the gonads will be fixed in a 10% formalin solution and a series of micro-preparations will be made for subsequent study of the histological

structure of the gonads. Blood sampling was carried out posthumously, followed by centrifugation and determination of the level of FSH, LH, testosterone on ELISA test systems.

Results

Treatment of malignant neoplasms is often accompanied by side effects that directly depend on the patient's age, type of cancer, treatment regimen and doses, which has put forward a new urgent problem – the state of health and quality of life during remission of cancer or after recovery from it. So cytostatically induced testicular lesion leads to a violation of the reproductive function of men on the "pre-testicular" (CNS, PNS, pituitary gland), "testicular" (gonads), "post-testicular" (epididymis, etc. organs of the genitourinary system involved in spermatogenesis) levels of the reproductive system, which is especially important against the background of sharply declining fertility of the modern male population.

So, understanding the patterns of the processes of reparative regeneration of damaged tissues is important for the development of rehabilitation programs, preservation of reproductive function and quality of life in patients who have undergone cytostatic therapy, especially in young people.

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Laser Doppler Flowmetry in the diagnosis of community-acquired pneumonia

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Abstract

Currently, the method of Laser Doppler Flowmetry (LDF) for the study of microcirculatory disorders of various origins is becoming increasingly widespread in clinical practice. To study the state of the microcirculatory bed, a laser analyzer of capillary blood flow – LAAK-02 (Russia) was used. 140 patients with community-acquired pneumonia (VP) aged from 18 to 66 years (average age – 41.5 ± 8.4 years) were under observation: control (40 people) and main (100 people). Comparing the values of tissue perfusion in the control group with the values of perfusion in patients with moderate-severity VP, it was revealed that the blood flow in the tissue of patients with moderate-severity VP was significantly reduced and at the same time statistically significantly differs from the blood flow in the control group. Thus, taking into account the data we have obtained, we can conclude that it is possible to use laser Doppler flowmetry as a method of non-invasive diagnosis of VP for accurate lifetime diagnosis of the severity of this disease.

Keywords: Laser Doppler Flowmetry, microcirculatory disorders, non-invasiveness method, pneumonia

Currently, the method of Laser Doppler flowmetry (LDF) for the study of microcirculatory disorders of various origins is becoming increasingly widespread in clinical practice. LDF is a relatively new method of assessing the state of microcirculation, the main advantages of which are non-invasiveness, safety and simplicity of research, the possibility of both single and repeated measurements, rapid response to vascular disorders and high sensitivity of the equipment [1, 2]. The results of the LDF provide a basis for a deeper understanding of the pathogenesis of emerging microcirculation disorders and objective control of therapeutic measures. Thanks to the LDF method, it became possible to determine the contribution of individual mechanisms regulating blood flow in the microcirculatory bed. In this regard, the aim – to study the possibilities of laser Doppler flowmetry in the diagnosis of microcirculation disorders in patients with VP, depending on the severity.

Materials and methods

140 patients with community-acquired pneumonia (VP) aged from 18 to 66 years (average age – 41.5 ± 8.4 years) were under observation, of which 96 people (68.6%) were men, 44 people (31.4%) were women. The diagnosis was verified by the results of an X-ray examination. Patients with severe concomitant pathology were excluded from the study

All patients were divided into 2 groups: control (40 people) and main (100 people): 2 groups of mild and moderate severity were identified.

To study the state of the microcirculatory bed, a laser analyzer of capillary blood flow – LAAK-02 (NPP "Lazma", Russia) was used. The study was conducted in patients in a state of complete physical and mental rest after preliminary adaptation to the room temperature (20-22 °C) in the patient's supine position. The intranasal region was used to assess the state of peripheral blood flow. The blood flow was recorded at rest for 5 minutes. The following parameters were determined: P –

the level of microcirculatory perfusion expressed in relative perfusion units (tpu), $\pm p$ – the mean square deviation P, Kv – the coefficient of variation of tissue perfusion on the LDF gram, expressed as a percentage).

Results

Comparing the tissue perfusion data obtained in persons with mild VP with the results in the control group, it can be noted that the average level of tissue perfusion is slightly lower in the group of patients with VP than in the control group, however, this difference is statistically insignificant ($T_{tbl}=0.525$, $T_{tbl}=1.98$, $T_{nabl}<T_{abl}$, $P>0.95$). Comparing the values of tissue perfusion in the control group with the values of perfusion in patients with moderate-severity VP, it was revealed that the blood flow in the tissue of patients with moderate-severity VP was significantly reduced and at the same time statistically significantly differs from the blood flow in the control group ($T_{nabl}=2.036$, $T_{tbl}=1.98$, $T_{nabl}>T_{abl}$, $P>0.95$).

Thus, taking into account the data we have obtained, we can conclude that it is possible to use laser Doppler flowmetry as a method of non-invasive diagnosis of VP for accurate lifetime diagnosis of the severity of this disease.

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Comparative characteristics of the physicochemical properties and architectonics of gelatin scaffolds

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Abstract

Using the skin tissue engineering approach is a way to help the body to recover its lost skin in cases that the spontaneous healing process is either impossible or inadequate, such as severe wounds or burns. In the present study, gelatin-based scaffolds were made using cross-linking agents ribose and a leaching component sodium chloride to compare with scaffolds cross-linked by glutaraldehyde. Different methods were utilized to characterize the specimens, including SEM imaging, ethanol displacement method, method of scaffold dissolution in distilled water and in a 0.25% trypsin solution. The results indicated that the physicochemical properties and morphology of scaffolds made of gelatin with ribose and sodium chloride in a ratio of 1:2 by weight are comparable with the physicochemical properties and morphology of scaffolds modified with glutaraldehyde.

Keywords: scaffold, gelatin-based scaffolds, tissue engineering, scanning electron microscopy.

Various tissue analogs have been developing in tissue engineering for many years ^[1], including scaffolds made from natural polymers, which are a kind of extracellular matrix for cell cultivation. In regenerative medicine, a scaffold with cells is considered as a substitute for a lost skin area. Compared with such methods of influencing skin regeneration as antioxidant therapy ^[2], hyperbaric oxygenation ^[3], preference is given to scaffolds populated with cells due to a lower risk of developing fibrotic complications ^[4]. As cases of thermal damage to the skin become more frequent, there is a growing need to develop a biocompatible, affordable and hypoallergenic tissue-engineered product. One of the most promising materials for scaffolds is natural polymer gelatin, which is a collagen hydrolysate and widely used in tissue engineering due to the preservation of collagen properties ^[6]. Due to the weak physical properties as a one-component framework (dissolution in water at $t = 37^{\circ}\text{C}$, instability to hydrolysis), pure gelatin is unstable and unsuitable for cultivating cell cultures ^[7, 8]. But due to the presence of functional groups, to which free groups of crosslinking agents are attached, it is possible to supplement it with substances that compensate for these limitations ^[9]. The need for modification is due to the characteristics of the damaged tissue area: the temperature is more than 37°C , the action of proteolytic enzymes, and a number of others. The architectonics of the scaffold is also important for intercellular interactions ^[10]. Due to communicating pores, scaffolds imitate the extracellular matrix of cells, provide transport of nutrients, metabolic products, and growth factors, and promote cell adhesion and proliferation ^[11]. The purpose of the study was to compare the physicochemical properties and morphology of gelatin scaffolds obtained by cross-linking with glutaraldehyde and ribose and modified with sodium chloride.

Materials and methods

The scaffolds were prepared by pouring gelatin using cross-linking agents glutaraldehyde and ribose and a leaching component sodium chloride. The purpose of adding glutaraldehyde to gelatin is to improve the mechanical properties of the latter. At the same time, certain concentrations of glutaraldehyde are cytotoxic ^[12], in connection with which we searched for safe crosslinking

components, the most accessible of them was ribose. Ribose is a crosslinking agent from the group of sugars that increases the strength of the framework and is not toxic to cells ^[13]. The method of scanning electron microscopy and the ethanol displacement method were used to study the architectonics of scaffolds. The time of onset and complete dissolution of the samples in distilled water and in a 0.25% trypsin solution at a temperature of 37°C were compared to assess the physical properties of the scaffolds. The scaffold preparation method was patented ^[14].

Results

Gelatin scaffolds with glutaraldehyde showed the highest thermal stability and enzymatic stability. According to the results of scaffold morphology assessment in the sample with ribose and salt in the ratio of 1:3 by weight, numerous pores with an average size of $63.7 \pm 20.1 \mu\text{m}$ with a porosity of $22.9 \pm 1.8\%$ by the ethanol displacement method were revealed, in a sample with ribose and salt in pores with an average size of $75.5 \pm 12.4 \mu\text{m}$ with a porosity of $34.7 \pm 2.3\%$ by the ethanol displacement method were detected in a 1:2 ratio by weight; pores with an average size of $72.8 \pm 21.7 \mu\text{m}$ and with a porosity of $29.3 \pm 1.5\%$ according to the ethanol extraction method. Evaluating the physicochemical properties of scaffolds with ribose and salt in a ratio of 1:2, the time for complete decomposition of the samples in distilled water was 11520 ± 30 min, in a solution of 0.25% trypsin - 69 ± 20 min. Assessing the physicochemical properties of scaffolds, the time for complete decomposition of gelatin samples with ribose and salt in a ratio of 1:3 in distilled water was 11520 ± 30 min, in a solution of 0.25% trypsin, the time was 37 ± 10 min. Assessing the physicochemical properties of scaffolds with glutar and salt in a ratio of 1:9, the time for complete decomposition of the samples in distilled water was 12960 ± 30 min, in a solution of 0.25% trypsin, the time was 1455 ± 20 min.

Based on the results of the study, it can be concluded that the physicochemical properties and morphology of scaffolds made of gelatin with ribose and sodium chloride in a ratio of 1:2 by weight are comparable with the physicochemical properties and morphology of scaffolds modified with glutaraldehyde.

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Oxidative stress and inflammation in COVID-19 in neurological patients

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Abstract

83 neurological patients (43 with COVID-19, and 40 SARS-Cov2 negative) and 44 healthy people were involved in the study. In patients with neurological diseases, the content of oxidized forms of lipids and pro-inflammatory interleukins in the blood was increased relative to healthy people. With the addition of COVID-19, the content of oxidized lipid forms practically does not change, but pro-inflammatory IL-6 significantly increases, and anti-inflammatory IL-10 decreases. In patients with ischemic stroke, the content of oxidatively modified lipids in the blood is higher than in other neurological diseases.

Keywords: inflammation, oxidative stress, COVID-19, neurological patients, pro-inflammatory cytokines, IL-6, IL-8, IL-18.

Inflammation and oxidative stress are considered important pathogenetic mechanisms in the development of COVID-19 ^[1]. Neurological complications often accompany COVID-19 ^[2]. In this regard the aim of the our study – to find out the intensity of oxidative stress and inflammation in neurological patients on the background of COVID-19.

Materials and methods

The study involved 83 neurological patients with ischemic strokes, encephalopathy, radiculopathy, polyneuropathy, paraplegia, lumboischialgia. Among them 43 were with COVID-19, and 40 were SARS-Cov2 negative (control group). Also examined were 44 healthy people without clinical signs of acute and chronic diseases comparable in age and sex. The content of oxidized lipid forms was determined in blood plasma based on UV registration - absorption spectra of lipid extracts, namely diene conjugates (DC) by absorption at 233 nm, conjugated trienes and ketodienes by absorption at 278 nm. Relative indicators were calculated: the ratio of absorption of oxidized forms of lipids to unoxidized E_{233nm}/E_{204nm} and $278nm/E_{204nm}$ ^[3]. Lipid hydroperoxides (HL) according to the ability to oxidize Fe^{2+} ions ^[4]. The content of interleukins was determined by ELISA using diagnostic kits from Vector Best.

Results and discussion

The results of determining the content of lipid oxidation products in blood plasma in the examined groups are shown in Table 1. The content of non-oxidized forms of lipids, which have an absorption maximum at 204 nm, did not differ in the examined groups. In contrast, the content of all oxidized forms of lipids in patients with neurological diseases, regardless of SARS-Cov2 infection, was significantly higher compared to the group of healthy people by 1.7-2 times. Lipid hydroperoxides in the groups of patients were increased by more than 2.5 times. At the same time, no significant differences were found between neurological patients with and without COVID-19 (Table 1).

Significant sharp increase in pro-inflammatory IL-6, IL-8, IL-18 and anti-inflammatory IL-10 in the blood of patients with neurological diseases in relation to healthy people was established (table 2).

Table1. Indices of blood plasma lipid oxidation in the examined groups

Группы	№ п/п	204нм	233нм	233/204	278нм	278/204	DC (nmol/ml)	HL (nmol/ml)
Healthy people (n=26)	1	0,586± 0,046	0,030± 0,035	0,057± 0,0076	0,013 ±0,002	0,0212± 0,0025	5,69± 0,665	27,5± 1,73
Neurological patients SARSCov2 negative (Control) (n=40)	2	0,583± 0,034 P _{2,1} = 0,243	0,063± 0,0071 P _{2,1} < 0,001	0,109± 0,0087 P _{2,1} < 0,001	0,023± 0,0025 P _{2,1} < 0,001	0,044± 0,0036 P _{2,1} < 0,001	12,0± 1,36 P _{2,1} < 0,001	74,8± 10,4 P _{2,1} < 0,001
Neurological patients COVID-19 (n=43)	3	0,542± 0,0026 P _{3,1} = 0,585 P _{3,2} = 0,262	0,053± 0,006 P _{3,1} = 0,002 P _{3,2} = 0,281	0,099± 0,0078 P _{3,1} < 0,001 P _{3,2} = 0,441	0,020± 0,0021 P _{3,1} = 0,006 P _{3,2} = 0,350	0,039± 0,0032 P _{3,1} < 0,001 P _{3,2} = 0,607	10,1± 1,71 P _{3,1} =0,002 P _{3,2} =0,281	70,7± 3,54 P _{3,1} <0,001 P _{3,2} =0,705

Table2. The content of interleukins and CRP in blood plasma in the examined groups(pg/ml)

Группы	№	IL-6	IL-8	IL-10	IL-18
Healthy people(n=44)	1	2,36±0,33	4,30±0,67	4,23±0,67	157±16
Neurological patients SARSCov2 negative (Control) (n=15)	2	18,6±5,7 P _{2,1} =0,014	24,9±5,12 P _{2,1} =0,0012	16,1±2,7 P _{2,1} <0,001	445±102 P _{2,1} =0,0025
Neurological patients COVID-19 (n=17)	3	66,7±14,7 P _{3,1} =0,0013 P _{3,2} =0,014	20,7±0,97 P _{3,1} <0,001 P _{3,2} =0,428	8,90±1,41 P _{3,1} =0,0067 P _{3,2} =0,030	357±57 P _{3,1} =0,0033 P _{3,2} =0,228

The content of IL-6 was especially sharply increased - from 2.36 ± 0.33 pg / ml in the group of healthy people to 18.6 ± 5.7 pg / ml in SARS-Cov2 negative neurological patients (8 times) and up to 66 .7±14.7 pg/ml in SARS-Cov2 positive patients (28 times). Significant differences in the content of interleukins were also established between the two groups of neurological patients. In particular, in patients with COVID-19, the content of pro-inflammatory IL-6 was 3.6 times higher, and anti-inflammatory IL-10 was 1.8 times lower when compared with SARS-Cov2 negative neurological patients.

The content of oxidized forms of lipids and interleukins in the blood of patients depended on the nosological form of the disease and was higher in patients with ischemic stroke in comparison with other neurological diseases. In particular, in the group of SARS-Cov2 positive patients with stroke, it was 86.0 ± 5.05 nmol/ml, and in other neurological diseases it was 68.3 ± 4.87 nmol/ml. In the SARS-Cov2 group, the values were 81.4 ± 10.4 nmol/ml and 69.8 ± 10.1 nmol/ml, respectively. Oxidative stress and inflammatory response were particularly pronounced in two patients who developed sepsis. In one of them, the content of diene conjugates reached 46 nmol/ml, lipid hydroperoxides 409 nmol/ml, IL-6 50.4 pg/ml, and IL-18 887 pg/ml. Thus, in patients with neurological diseases, the content of oxidized lipids and pro-inflammatory interleukins in the blood was increased relative to healthy people. With the addition of COVID-19, the content of oxidized lipid forms practically does not change, pro-inflammatory IL-6 significantly increases, and anti-inflammatory IL-10 decreases. In patients with ischemic stroke, the content of oxidatively modified lipids in the blood is higher than in other neurological diseases.

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Analysis of long-term results of treatment of induced keratopathies by a combined energy method, including corneal collagen crosslinking in combination with phototherapeutic keratostromectomy

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Abstract

The method combines phototherapeutic keratostromectomy with corneal collagen cross-linking allows to reduce the phenomenon of corneal syndrome, reduce edema and indirectly increase visual acuity. The purpose is to analyze the long-term results of the use of corneal collagen crosslinking in combination with phototherapeutic keratostromectomy in the treatment of patients with advanced endothelial-epithelial corneal dystrophy. We observed 30 patients (30 eyes) with advanced stage of endothelial-epithelial corneal dystrophy. The first (control) group consisted of 15 people (15 eyes) who underwent corneal collagen crosslinking. The second (main) group included 15 people (15 eyes). In patients of the second group, corneal collagen crosslinking was combined with phototherapeutic keratostromectomy. After 1 month in the control group there were 20.1% more patients with corneal syndrome than in the main group, and after 24 months it was 33.5% higher, respectively. Patients who have undergone combined intervention significantly improve their quality of life while waiting for radical treatment.

Keywords: phototherapeutic keratostromectomy, corneal collagen cross-linking, endothelial-epithelial corneal dystrophy, long-term results.

Secondary endothelial-epithelial dystrophy (EED) of the cornea is one of the formidable complications of injuries, surgical interventions on the eyeball and severe inflammatory diseases of the cornea. [5, 6] Crosslinking of corneal collagen, phototherapeutic keratostromectomy are pathogenetically targeted methods of treatment of induced EED. [1-4] It is assumed that the combined use of these techniques can increase the effectiveness of each method and lead to an increase in the therapeutic effect.

The positive therapeutic effect of the method is associated with the formation of a fibrocellular membrane in the surface layers of the cornea and the compaction of existing collagen molecules in the stroma of the cornea, the appearance of new bonds between them, as well as the effect of "pulling" the cornea resulting from crosslinking, by reducing the hydration of the cornea. The method allows to reduce the phenomenon of corneal syndrome, reduce edema and indirectly increase visual acuity.

The purpose of this work is to analyze the long-term results of the use of corneal collagen crosslinking in combination with phototherapeutic keratostromectomy in the treatment of patients with advanced endothelial-epithelial corneal dystrophy.

Materials and methods

We observed 30 patients (30 eyes) with advanced stage of endothelial-epithelial corneal dystrophy. Of these, 17 men (17 eyes) and 13 women (13 eyes). In all patients, EED developed after cataract extraction by various methods with implantation of different IOL models. We assessed the severity

of dystrophy in patients according to the classification of V.V. Volkov and M.M. Dronov in 1978, it corresponded to the III stage of EED. At the time of admission, all 30 patients had severe pain and corneal syndrome, corneal tissue hydration, bullous changes in the epithelium, and recurrent corneal erosions. Of all patients, two groups were formed, initially comparable in terms of gender, age, and comorbidities. The first (control) group consisted of 15 people (15 eyes) who underwent corneal collagen crosslinking. The second (main) group included 15 people (15 eyes). In patients of the second group, corneal collagen crosslinking was combined with phototherapeutic keratostromectomy. The criteria for the effectiveness of treatment in the groups were indicators of pachymetry, the timing of the completion of epithelialization, the timing of relief of the corneal syndrome, visual acuity, and transparency of the cornea. The studies were carried out before surgery and after surgery, until complete epithelialization. Then at 1, 3, 6, 12 and 24 months. In the event of a recurrence of the disease, patients were prescribed standard local anti-inflammatory, keratoplastic therapy.

Results

The obtained results indicate that in patients of the main group the completion of epithelialization, relief of corneal syndrome, a decrease in pachymetry occurs at an earlier time and compared with the control group. These circumstances lead to a more pronounced increase in the transparency of the corneal tissue due to a decrease in hydration of the cornea. At the same time, it should be noted that according to the results of treatment, visual acuity in the main group also exceeded similar indicators in the control group of patients. In addition, after the combined energy intervention of crosslinking + PTK, a more stable clinical effect is observed, expressed in a lower percentage of relapses of the corneal syndrome in comparison with patients who underwent only corneal collagen crosslinking. After 1 month in the control group there were 20.1% more patients with corneal syndrome than in the main group, and after 24 months it was 33.5% higher, respectively.

Thus, combined intervention, including the use of corneal collagen crosslinking and phototherapeutic keratostromectomy, is an effective treatment for EED in stage 3 of the disease. In comparison with isolated crosslinking, the combined technique allows to reduce the time of corneal epithelialization (by 2 days on average), the time of relief of corneal syndrome (by 1 day on average), to achieve more stable and high functional results (an increase in visual acuity by an average of 0.02) and throughout the observation period, to reduce the percentage of relapses. Patients who have undergone combined intervention significantly improve their quality of life while waiting for radical treatment.

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Oxidative stress and the possibilities of succinate-containing pharmacocorrection

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Abstract

The possibility of correcting the processes of lipid peroxidation induced by the action of a low-frequency alternating magnetic field and the introduction of cytoflavin has been investigated. It was found that daily exposure to a low-frequency alternating magnetic field for 21 days for three hours contributes to an increase in the content of lipid hydroperoxides by 14-20%, diene conjugates by 13-17%, malondialdehyde by 44-47% against the background of a decrease in the activity of the main components of the antioxidant system in the blood of experimental animals ($p < 0.05$). Administration of cytoflavin to rats at a dose of 100 mg / kg intraperitoneally daily for 21 days immediately before magnetic induction contributes to a significant decrease in the concentration of lipid hydroperoxides in the blood by 9-18%, diene conjugates – by 10-12%, malondialdehyde – by 21-32% compared with control group rats ($p < 0.05$). When analyzing the effect of cytoflavin on the activity of the components of the antioxidant system, it was found that the content of ceruloplasmin and catalase in the blood of animals was significantly higher than the same indicator in the control group rats by 11-23% and 10-22%, respectively ($p < 0.05$). Thus, the combined drug cytoflavin prevents the accumulation of lipoperoxidation products in conditions of increased activity of the antioxidant system of a warm-blooded organism.

Keywords: cytoflavin, low frequency alternating magnetic field, lipid peroxidation, lipid hydroperoxides, diene conjugates, malondialdehyde, ceruloplasmin, catalase, experiment.

The results of scientific research in recent years confirm the presence of a wide range of effects in a low-frequency alternating magnetic field, including the ability to induce the formation of free radicals in a warm-blooded organism with prolonged exposure [1, 2, 4, 9]. Scientists associate an increase in the risk of neoplasia and non-oncological diseases with an increase in the endogenous production of free radicals during magnetic field induction [6, 10]. Considering that our previous studies have shown the antioxidant activity of the succinate-containing drug cytoflavin in various model systems (cold and thermal exposure, ultraviolet irradiation), an attempt to correct the processes of lipid peroxidation induced by exposure to a low-frequency alternating magnetic field is, in our opinion, justified [5, 7]. In this regard, it is of interest to study the possibility of correcting oxidative stress induced by exposure to a low-frequency alternating magnetic field using cytoflavin.

Materials and methods

The experiment was carried out on white mongrel male rats weighing 200-220 g for 21 days. The animals were divided into 3 groups, each with 30 rats: 1 – intact group, the animals were in standard vivarium conditions; 2 – control group, the animals were exposed to a low-frequency alternating magnetic field (induction of a magnetic field of 0.4 MT using Helmholtz rings powered from an alternating current source with a frequency of 50 Hz) for 3 hours daily for 21 days; 3 – experimental group, animals were injected daily intraperitoneally with cytoflavin at a dose of 100 mg/ kg succinate before exposure to a low-frequency alternating magnetic field. The slaughter of animals

was carried out by decapitation on 7, 14, 21 days of the experiment. The intensity of lipid peroxidation processes was assessed by examining the content of lipid hydroperoxides, diene conjugates, malondialdehyde in blood plasma by color reaction with thiobarbituric acid, and the main components of the antioxidant system – ceruloplasmin according to the V.G. Kolb method, catalase according to the N.D. Korolyuk method[3, 8]. Statistical processing of the results was carried out using the Student's criterion (t) using the Statistica v.6.0 program. The results were considered reliable at $p < 0.05$.

Results and discussion

The effect of a low-frequency alternating magnetic field on rats is accompanied by the accumulation of peroxidation products in the blood of control animals relative to the intact group: the content of lipid hydroperoxides increased by 14% by the end of the first week of the experiment, by 20% by the end of the second and third weeks; diene conjugates – by 14-17%; malondialdehyde – by 45-46% ($p < 0.05$). The introduction of cytoflavin under magnetic induction conditions was accompanied by a decrease in the concentration of lipid peroxidation products in comparison with the indicators in the control group: the level of lipid hydroperoxides decreased by 9% (day 7 of the experiment), by 18% (day 14) and by 15% (day 21); diene conjugates – by 12% (day 14) and 10% (21 days); malondialdehyde – by 26%, 22% and 32%, respectively ($p < 0.05$). The study of the activity of the antioxidant system showed that under the influence of a low-frequency alternating magnetic field, the content of ceruloplasmin in the blood of control rats decreased by 17% (day 7), 15% (day 14) and 16% (day 21 of the experiment) in comparison with intact animals; catalase activity – by 20%, 15% and 14%, respectively ($p < 0.05$). The use of a succinate-containing pharmacocorrector led to an increase in the activity of the antioxidant system in the blood of experimental animals compared with similar indicators in the control: the content of ceruloplasmin increased by 23%, 11% and 18%, respectively, catalase - by 22%, 10% and 16% ($p < 0.05$).

Thus, the prooxidant effect of a low-frequency alternating magnetic field has been experimentally confirmed. Under conditions of oxidative stress induced by the influence of a low-frequency alternating magnetic field on laboratory animals, intraperitoneal administration of cytoflavin leads to a decrease in the intensity of lipid peroxidation processes, preventing the accumulation of lipoperoxidation products against the background of increased activity of the main components of the antioxidant system.

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Effect of chronic manganese administration on working memory and morphology of basal nuclei, substantianigra, cerebellum, cerebral cortex and hippocampus of rats

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Abstract

Accumulation of manganese in the brain can have neurotoxic effects and cause extrapyramidal syndrome. To study the manifestation of chronic manganese encephalopathy in the form of changes in working memory and morphology of the central nervous system, in rats. Thirty-two female Wistar model rats, equally divided into intact, control and two experimental groups: to which nothing was administered, 0.9% NaCl solution, MnCl₂ 4-water 25 mg/kg rat and MnSO₄ 5-water 30.4 mg/kg rat were injected respectively. The working memory of the rats was assessed in the Barnes maze. Basal nuclei, substantianigra, cerebellum, cerebral cortex, and hippocampus are considered for morphometry. At this point, the study is incomplete. Hypotheses are highlighted: chronic manganese administration proved insufficient, to change organ structure and working memory; chronic manganese administration proved sufficient, to change organ structure, but did not affect working memory; chronic manganese administration proved sufficient, to change organ structure and working memory.

Keywords: rats, Barnes maze, manganese, neurotoxic effects, working memory, basal nuclei, substantianigra, cerebellum, cerebral cortex, hippocampus.

Chronic manganese encephalopathy is associated with actors working in small movie studios, manganese and manganese compound mining, steel and battery production industries, and the use of homemade drugs not purified of manganese compounds. Accumulation of manganese in the brain can have neurotoxic effects and cause extrapyramidal syndrome. To study the manifestation of chronic manganese encephalopathy in the form of changes in working memory and morphology of the central nervous system in rats.

Materials and methods

Equipment: Barnes maze, histological equipment, scales. Reagents: wiring reagents, hematoxylin, eosin, toluidineblue. Thirty-two (of which 29 survived to the end of the experiment) female Wistar model rats, equally divided into 4 groups: intact, control and two experimental; to which nothing was administered, 1 ml of 0.9% NaCl solution, MnCl₂ 4-water 25 mg/kg rat and MnSO₄ 5-water 30.4 mg/kg rat were injected respectively. All solutions were administered orally through a urinary catheter for small children. For dose calculations, animals were weighed every 15 days. During the administration of the solutions, two rats from the group whose rats were administered manganese chloride solution and one from the group whose rats were administered manganese sulfate died. Barnes maze testing. The labyrinth is a circular platform 1.22 meters in diameter, with 18 holes arranged radially one meter from the center of the platform. One of the 18 holes leads to a tunnel in which the rat can hide from negative stimuli (the main ones being light and white noise turned on speakers). The other holes outwardly mimic a hole with a tunnel, but you cannot hide in them. The rat is placed on the center of the platform in the box. After a while, the box is raised and a white

noise is activated, and runs until the rat hides in the tunnel. The time in which the rat first encounters the tunnel, the number of holes traveled to the tunnel hole, and the distance traveled are measured. These three measures correlate with working memory.

Results

Histological morphometry of the brain. Basal nuclei, substantia nigra, cerebellum, cerebral cortex, and hippocampus are considered for morphometry. Slices are 7 μm thick, 2 slides are prepared from each organ part for one way of staining one organ part, slices are stained by Nissl. Thyroid, nuclear envelope and nuclei blue or purple, cytoplasm of ganglion and glial cells pale blue, fibrous nerve substance not stained. Cerebellar morphometry assesses: total cerebellar volume; total volume for each major subdivision of the deep cerebellar nuclei; total number of neurons in each subdivision of the deep cerebellar nuclei; Purkinje cell density in each of the three cerebellar cortical regions; density of Purkinje cells containing vacuoles and other abnormal cytoplasmic inclusions; granular cell density for the corresponding regions of the cerebellar cortex in which Purkinje cell density was determined; thickness of the molecular layer, pear cell layer, and granular layer; area and volume of neurons in all three layers; and nuclear-cytoplasmic coefficient. In cortical and hippocampal morphometry, the cortex and hippocampus are evaluated: thickness of the cortex in the anterior parietal lobe (PTD); thickness of layer 1 of PTD; number of neurons in the field of view of PTD 2 and 5 layers; thickness of the cortex in the middle parietal lobe (CTD); thickness of layer 1 of CTD; number of neurons in the field of view of CTD 2, 5 layers and hippocampus; sectional area of neuron nuclei of layer 2, cytoplasm of neuron layer 2, neuron nuclei of layer 5, hippocampus neuron nuclei, cytoplasm of hippocampal neurons.

At this point, the study is incomplete. Hypotheses are highlighted: chronic manganese administration proved insufficient, to change organ structure and working memory; chronic manganese administration proved sufficient, to change organ structure, but did not affect working memory; chronic manganese administration proved sufficient, to change organ structure and working memory.

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Hematological indicators of intoxication and their prognostic significance in patients with community-acquired pneumonia associated with COVID-19

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Abstract

The aim of the study was to analyze the prognostic significance of hematological indicators of intoxication in routing patients with community-acquired pneumonia associated with the new coronavirus infection COVID-19 in the emergency department of an infectious hospital. The study presents an analysis of 146 case histories of patients with COVID-19-associated pneumonia. The evaluation of clinical blood analysis and hematological indicators of intoxication in this category of patients upon admission to the hospital was carried out. The high prognostic significance of individual hematological indicators of intoxication in terms of routing patients at the stage of the emergency department of an infectious hospital was revealed.

Keywords: pneumonia, COVID-19, hematological indicators, intoxication, acute respiratory distress syndrome, prognostic significance, emergency department, routing patients.

One of the important links of inflammation and the formation of acute respiratory distress syndrome (ARDS) in COVID-19 are neutrophils synthesizing proteases, prooxidants and other biologically active substances [1]. In addition, with intense inflammation, endogenous intoxication syndrome (EIS) is often formed - a dynamic process that accompanies the course of many critical conditions [2]. For EIS, hematological indicators of intoxication (HII) are described in the scientific literature, such as: neutrophil-to-monocyte ratio index (NMRI), neutrophil-to-lymphocyte ratio index (NLRI), lymphocyte-to-monocyte ratio index (LMRI), leukocyte Kalf-Kalifa intoxication index (LII) and its modification V.K. Ostrovsky (LIIm), integral index of intoxication (III) [3]. The literature describes changes in the parameters of clinical blood analysis and HII in community-acquired pneumonia associated with a new coronavirus infection, but there is no indication of the relationship of these indicators with the severity of the patients' condition [4,5]. Objective of our study – to evaluate the HII in patients with pneumonia associated with COVID-19 at the admission stage to the emergency department and to assess the prognostic significance of these indices in terms of routing.

Materials and methods

The analysis of clinical and laboratory features of the course of pneumonia associated with a new coronavirus infection in 146 patients hospitalized in the infectious diseases hospital of the city of Blagoveshchensk in the period from 2020-2021 was carried out. All patients were divided into 2 groups: group 1 – those who were treated in pulmonology departments (71 people); group 2 - patients who were admitted and treated in intensive care and intensive care units (ICU), the sample size was 75 people. During the initial assessment of the condition of patients in the emergency department, the indicators of a clinical blood test were examined, and based on the data obtained, the HII was calculated: III, LIIm, NMRI, NLRI, LMRI. The following methods of descriptive statistics were used in the study: calculation of the mean value (M), 95% confidence interval for the mean (95% CI), median (Me), interquartile latitude (IL). To compare the indicators, the calculation of the Mann-Whitney criterion was used; to determine the prognostic significance of the effect of HII on the routing of patients, a ROC analysis was performed with the determination of the area

under the curve (AUC). The optimal cut-off point was selected by determining the maximum sum of sensitivity (Se) and specificity (Sp) obtained as a result of ROC analysis. Significant results were considered at $p < 0.05$.

Results

Higher values of HII were registered in patients hospitalized in the ICU: The III was 38.6% higher ($p < 0.001$), the LII_m was 74.3% higher ($p < 0.001$), the NMRI was 28.7% higher ($p < 0.044$), the NLRI was 81.5% higher ($p < 0.020$). In group 1 patients, the LMRI was 44.9% higher ($p < 0.001$). As a result of the ROC analysis, a statistically significant prognostic value of HII in routing patients in the emergency department was revealed. (Table 1).

Table 1 Values of the area under the curve for hematological indicators of intoxication.

Indicator	AUC	95%CI	<i>p</i>
III	0,705±0,043	0,621 – 0,788	0,009*
LII _m	0,693 ± 0,047	0,608 – 0,778	0,014*
MNRI	0,597 ± 0,047	0,504 – 0,689	0,020*
LMRI	0,303 ± 0,044	0,218 – 0,389	0,362
NLRI	0,723 ± 0,043	0,642 – 0,805	0,008*

Note: *- the difference in indicators is statistically significant.

To determine the prognostic significance of the HII at the routing stage in the emergency department, the Se and Sp of each indicator of endogenous intoxication were calculated (Table 2).

Table 2 Sensitivity and specificity of hematological indicators of intoxication.

Indicator	Cut-off, ед.	Se%, (95%CI)	Sp%, (95%CI)
III	3,01	57,3% (от 45,4% до 68,7%)	51,2% (от 35,1% до 67,1%)
LII _m	5,1	73,3% (от 61,8% до 82,9%)	56,3% (от 44,1% до 68,1%)
MNRI	11,1	57,3% (от 45,4% до 68,7%)	59,1% (от 46,8% до 70,7%)
LMRI	2,84	68% (от 56,2% до 78,3%)	60% (от 47,6% до 71,5%)

Thus, statistically significant increases in HII indicators were revealed in patients referred for treatment in the ICU at the routing stage in the emergency department (III- 38.6%, LII_m- 74.3%, NMRI-28.7%, NLRI-81.5%); As a result of the study, a statistically reliable prognostic significance of HII in routing patients in the emergency department was revealed. The maximum sensitivity is determined for the III indicator at its value above 5.1 units.

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Peroxidation of liver lipids under the influence of magnetic field and the introduction of succinate containing drug

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Abstract

The influence of a low-frequency alternating magnetic field on the intensity of lipid peroxidation processes in the liver of laboratory animals has been studied. It was found that daily magnetic exposure for 3 hours a day for 14 days contributes to an increase in the content of lipid hydroperoxides in animal liver tissue by 33%, diene conjugates by 37%, malondialdehyde by 60% against the background of a decrease in the activity of the main components of the antioxidant system. The administration of cytoflavin to rats under the influence of a low-frequency alternating magnetic field made it possible to reduce the concentration of lipoperoxidation products in liver tissue by 18-33% against the background of an increase in catalase activity by 14% and ceruloplasmin by 35% relative to control group rats. Thus, the antioxidant activity of cytoflavin was confirmed under the influence of a low-frequency alternating magnetic field.

Keywords: alternating magnetic field, cytoflavin, liver lipid peroxidation, antioxidant system, rats.

The results of experiments on laboratory animals indicate changes in the cellular composition of blood during prolonged exposure to a low-frequency alternating magnetic field, a decrease in the functional state of neutrophils and the number of red blood cells [2, 4, 9, 10]. Considering that the study of the influence of the magnetic field on the intensity of lipid peroxidation processes has been disclosed in isolated works [3, 5, 7], and the study of the possibility of pharmacocorrection of changes in the antioxidant status under the influence of a low-frequency alternating magnetic field has not actually been engaged, the expediency of our experiment is fully justified. Objective – to study the intensity of lipoperoxidation processes in the liver under the influence of a low-frequency alternating magnetic field and the administration of a succinate containing drug.

Materials and methods

The experiment was carried out on white mongrel male rats weighing 200-250 g for 14 days. The animals were divided into 3 groups, each with 10 rats: 1 – intact group, the animals were in standard vivarium conditions; 2 – control group, the animals were exposed to a low frequency alternating magnetic field for 3 hours daily for 14 days; 3 – experimental group, animals before exposure to a low frequency alternating magnetic field daily intraperitoneally administered the drug cytoflavin at a dose of 100 mg / kg succinate. The rats were decapitated on the 14th day of the experiment. The content of lipid peroxidation products – lipid hydroperoxides, diene conjugates, malondialdehyde and the main components of the antioxidant system – ceruloplasmin, catalase - were determined in the liver homogenate [1, 6, 8]. Statistical processing of the results was carried out using the Student's criterion (t) using the Statistica v.6.0 program. The results were considered reliable at $p < 0.05$.

Results and discussion

Daily magnetic exposure for 3 hours a day for 14 days led to an increase in the content of lipid hydroperoxides in the liver tissue of relatively intact rats by 33%, diene conjugates by 37%, malondialdehyde by 60% against the background of a decrease in the activity of the main components of the antioxidant system ($p < 0.05$). The administration of cytoflavin to rats under conditions of an alternating magnetic field of low frequency allowed to reduce the concentration of lipid hydroperoxides in liver tissue by 23%, diene conjugates by 18%, and malondialdehyde by 33% compared with control group rats ($p < 0.05$). When analyzing the effect of the succinate-containing drug on the activity of the components of the antioxidant system, it was found that the content of ceruloplasmin in the liver of animals was significantly higher than the same indicator in rats of the control group by 35%, catalase - by 14% ($p < 0.05$).

Thus, the antioxidant activity of the succinate-containing drug was confirmed under the influence of a magnetic field on laboratory animals. The results of the experiment suggest the further use of a low-frequency alternating magnetic field as an experimental model for the formation of oxidative stress in a warm-blooded organism.

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Oxidative stress and inflammation during COVID-19 in ophthalmological patients

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Abstract

84 ophthalmic patients (50 with COVID-19, and 34 SARS-Cov2 negative) and 64 healthy people were involved in the study. In the blood and lacrimal fluid of ophthalmological patients the content of oxidized forms of lipids is significantly increased in relation to healthy people. In patients with COVID-19 significant additional increase in the content of oxidized forms of lipids and pro-inflammatory interleukins in the blood was observed.

Keywords: ophthalmic diseases, comorbidity, COVID-19, oxidative stress, inflammation, pro-inflammatory interleukins.

Complications from the organs of vision are often accompanied COVID-19 [1]. Inflammation and oxidative stress are considered important pathogenetic mechanisms for the development of COVID-19 [2]. Aim of the study – to find out the intensity of oxidative stress and inflammation in ophthalmic patients on the background of COVID-19.

Materials and methods

The study involved 84 ophthalmic patients with cataracts, glaucoma, diabetic retinopathy, epiretinal membrane, hemophthalmia and some other diseases. Of this number, 50 were diagnosed with COVID-19, and 34 were SARS-Cov2 negative (control group), 26 healthy people without clinical signs of acute and chronic diseases, comparable by age and gender, were examined for the content of oxidized forms of lipids, and 64 on the content of pro-inflammatory interleukins. The content of oxidatively modified lipids was determined in the blood. based on the registration of UV absorption spectra of lipid extracts, namely, diene conjugates (DC) by absorption at 233 nm, conjugated trienes and ketodienes by absorption at 278 nm. Relative indicators were calculated: the ratio of absorption of oxidized forms of lipids to unoxidized E_{233nm}/E_{204nm} and $278nm/E_{204nm}$ [3]. In addition to the above indicators, the content of lipid hydroperoxides (HL) was determined by the ability to oxidize Fe^{2+} ions [4]. The content of interleukins was determined by ELISA using diagnostic kits from Vector Best.

Results and discussion

The results of determination of the content of lipid oxidation products in blood plasma in the examined groups are shown in Table 1. The content of non-oxidized forms of lipids, which have an absorption maximum at 204 nm, did not differ between the examined groups. With the exception of lipid hydroperoxides, the content of which in the control group was significantly increased by more than 2 times in relation to healthy people, the content of other oxidized lipids did not differ between the control group and healthy people. In contrast, the content of all oxidized forms of lipids in patients with ophthalmic diseases and COVID-19 was 1.4-2.8 times higher compared to the group of healthy people and the control group. Lipid hydroperoxides were especially strongly increased (Table 1).

Table .1 Indices of blood plasma lipid oxidation in the examined groups

Groups	№	204nm	233nm	233/204	278nm	278/204	DC (nmol/ml)	HL (nmol/ml)
Healthypeople (n=26)	1	0,586± 0,046	0,037± 0,029	0,057± 0,007	0,013 ±0,002	0,021± 0,002	7,12± 0,85	27,5± 1,73
Ophtalmological patients SARSCov 2 negative (Control) (n=34)	2	0,505± 0,0230 P _{2,1} = 0,243	0,031± 0,0024 P _{2,1} = 0,905	0,063± 0,045 P _{2,1} = 0,792	0,011± 0,0013 P _{2,1} = 0,339	0,0215± 0,0035 P _{2,1} = 0,901	5,88± 0,455 P _{2,1} < 0,905	58,3± 1,18 P _{2,1} < 0,001
Ophtalmological patients COVID- 19 (n=50)	3	0,540± 0,018 P _{3,1} = 0,585 P _{3,2} = 0,216	0,051± 0,002 P _{3,1} < 0,001 P _{3,2} < 0,001	0,099± 0,0062 P _{3,1} < 0,001 P _{3,2} < 0,001	0,023± 0,001 P _{3,1} < 0,001 P _{3,2} < 0,001	0,0450± 0,0038 P _{3,1} < 0,001 P _{3,2} < 0,001	9,70± 0,467 P _{3,1} < 0,001 P _{3,1} < 0,001	78,1± 2,63 P _{3,1} < 0,001 P _{3,2} <0,001

Table 2. Indices of lipid oxidation in lacrimal fluid in the examined groups

Groups	№	204nm	233nm	233/204	278nm	278/204	DC (nmol/ml)
Healthypeople (n=26)	1	0,933± 0,335	0,087± 0,014	0,076± 0,010	0,0258± 0,0055	0,0213± 0,0039	2,24± 0,21
Ophtalmological patients SARSCov2 negative (Control) (n=29)	2	0,642± 0,089 P _{2,1} = 0,040	0,164± 0,051 P _{2,1} = 0,160	0,285± 0,0618 P _{2,1} = 0,007	0,0311± 0,0070 P _{2,1} = 0,535	0,0757± 0,0140 P _{2,1} = 0,081	4,52± 0,898 P _{2,1} = 0,142
Ophtalmological patients COVID-19 (n=10)	3	0,469± 0,10381 P _{3,1} = 0,004 P _{3,2} = 0,216	0,119± 0,018 P _{3,1} = 0,185 P _{3,2} = 0,481	0,286± 0,0271 P _{3,1} < 0,001 P _{3,2} = 0,986	0,0373± 0,0044 P _{3,1} = 0,113 P _{3,2} = 0,477	0,0921± 0,0094 P _{3,1} < 0,001 P _{3,2} = 0,339	6,57± 1,15 P _{3,1} = 0,014 P _{3,2} = 0,175

The UV spectroscopy method allows the analysis of lipid extracts from lacrimal fluid. The content of unoxidized lipids in the eye fluid of ophthalmic patients significantly decreased relative to healthy people by 1.45 times in SARS-Cov2 negative patients and by 2 times in patients with COVID-19. The only significant difference in the content of oxidized lipids in the lacrimal fluid of SARS-Cov2 negative patients was an increase in the index 233/204, which reflects the ratio of

diene conjugates to non-oxidized lipids. In contrast, in the group of patients with COVID-19, the relative indices 233/204 and 278/204, as well as the absolute content of diene conjugates in the lacrimal fluid, had significant differences with healthy people and were increased by 3-4.4 times. There were no significant differences in the determined parameters between the control group of patients and patients with COVID-19 (Table 2).

Table 3. The content of interleukins and CRP in blood plasma in the examined groups (pg/ml)

Groups	№	IL-6	IL-8	IL-10	IL-18
Healthypeople (n=64)	1	2,36±0,33	4,30±0,67	4,23±0,67	157±16
Ophtalmological patients SARS-Cov2 негативные (Control) (n=28)	2	5,73±0,66 P _{2,1} <0,001	6,97±1,02 P _{2,1} =0,271	3,92±0,71 P _{2,1} =0,702	266±23 P _{2,1} <0,001
Ophtalmological patients COVID-19 (n=51)	3	7,78±1,56 P _{3,1} =0,0013 P _{3,2} =0,232	26,2±3,28 P _{3,1} <0,001 P _{3,2} =<0,001	5.19±0,69 P _{3,1} =0,318 P _{3,2} =0,248	260±25 P _{3,1} <0,001 P _{3,2} =0,859

In the study of the content of interleukins in the blood, a significant increase in pro-inflammatory IL-6, IL-18 and a decrease in the control group in relation to healthy people by 2.4 and 1.7 times, respectively, were established. In the group of patients with COVID-19, the content of IL-6, IL-8 and IL-10 was significantly increased in relation to healthy people, and IL-8 to SARS-Cov2 negative patients. There were no significant changes in the content of anti-inflammatory IL-10 (Table 3).

Thus, in the blood and eye fluid of ophthalmic patients, the content of oxidized forms of lipids is significantly increased in relation to healthy people. The addition of COVID-19 is accompanied by a significant increase in the content of oxidized forms of lipids and pro-inflammatory interleukins in the blood.

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The effect of herbal medicines on the physical endurance of laboratory animals under the influence of an alternating magnetic field of low frequency

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Abstract

Modern environmental conditions have dramatically increased the level of radical-forming processes in the body. Under experimental conditions, the possibility of increasing the physical endurance of laboratory animals by oral administration of a phytopreparation containing a complex of natural antioxidants was investigated. The animals were divided into 3 groups, each with 10 rats: intact animals (1), which were kept in standard vivarium conditions; control group (2), where the rats were exposed to a low-frequency alternating magnetic field for 3 hours daily for 21 days; experimental group (3), where the animals were under the influence of a low frequency alternating magnetic field, eleutherococcus extract was administered orally daily for 21 days at a dose of 1 ml/kg. It was found that daily exposure to a low frequency alternating magnetic field contributes to a decrease in the resistance of the rat body to physical exertion. The introduction of phytoadaptogen to rats under the influence of a low-frequency alternating magnetic field increases the duration of swimming of animals by 22% by the end of the first week of the experiment, by 25% by the end of the second, by 36% by the end of the third relative to the control group rats. Thus, eleutherococcus extract has actoprotective activity under the influence of a low-frequency alternating magnetic field.

Keywords: herbal medicines, eleutherococcus extract, low frequency alternating magnetic field, physical endurance, rats.

Increasing the body's resistance to stress factors is an urgent task of modern medical science [1, 2, 4, 9, 10]. In solving this problem, the expansion of the evidence base for the effectiveness of adaptogenic herbal remedies is of great importance [5, 7]. For several decades, the Department of Pharmacology of the Amur Medical Academy has been studying the pharmacological effects of adaptogens, among which eleutherococcus is the most studied by Amur researchers [3, 6, 8]. The antioxidant, antihypoxant, and actoprotective activity of this adaptogen has been proven in various model systems (cold and thermal effects, ultraviolet irradiation). Currently, the department has conducted research on the pharmacological effects of Eleutherococcus extract under the influence of an alternating magnetic field of low frequency, some of the results of which we present to your attention. Objective – to study the effect of eleutherococcus extract on the physical endurance of laboratory animals under the influence of a low-frequency alternating magnetic field.

Materials and methods

Experiment was carried out on whitemongrel male rats weighing 200-220 g for 21 days. The animals were divided into 3 groups, each with 30 rats: 1 – intact group, the animals were in standard vivarium conditions; 2 – control group, the animals were exposed to a low-frequency alternating magnetic field (induction of a magnetic field of 0.4 MT using Helmholtz rings powered from an alternating current source with a frequency of 50 Hz) for 3 hours daily for 21 days; 3 – experimental group, animals were orally injected daily with eleutherococcus extract at a dose of 1 ml/kg

before exposure to a low-frequency alternating magnetic field. The actoprotective activity of the phytoadaptogen was assessed by the duration of swimming of rats in water for 7, 14, 21 days of the experiment. Statistical processing of the results was carried out using the Student's criterion (t) using the Statistica v.6.0 program. The results were considered reliable at $p < 0.05$.

Results and discussion

Daily exposure to a low-frequency alternating magnetic field on laboratory animals contributes to a decrease in the physical endurance of rats in comparison with intact animals by 24% (day 7), 18% (day 14) and 32% (21 days of experience) ($p < 0.05$). In turn, the duration of swimming of animals receiving eleutherococcus extract under magnetic induction was significantly higher by 22% by the end of the first week of the experiment, by 25% by the end of the second, by 36% by the end of the third ($p < 0.05$).

Thus, daily three-hour exposure to a low-frequency alternating magnetic field on laboratory animals leads to a decrease in the physical endurance of rats, more pronounced by the end of the third week of the experiment. Eleutherococcus extract has actoprotective activity under magnetic induction, confirming one of the positive effects included in the pharmacodynamic range of the adaptogen, and revealing the prospects for further preclinical studies of the phytopreparation under the influence of various stress factors.

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The course of pregnancy in women with progesterone deficiency who have undergone pregravidarpreparation with the use of acupuncture

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Abstract

Women with a low concentration of progesterone in the second phase of the cycle have a reduced ability of the endometrium to implant an egg. Low concentration of VEGF-R1, VEGF-A, PIGF, TGF-b1, IGF is a risk factor for early and late pregnancy complications. Pregravidar preparation is of great importance for the prevention of pregnancy complications. The aim of the study was to study the course of pregnancy, childbirth and perinatal outcomes in women with progesterone deficiency who received pregravidar training using didrogestosterone and acupuncture. The serum level of estriol, progesterone and growth factors (VEGF-R1, VEGF-A, PIGF, IGF, TGF-beta1) at 20-24 weeks of pregnancy was studied. Echographic examination of pregnant women at 11-14, 18-21, 30-33 weeks, Doppler examination in pregnant women at 30-34 and 36-40 weeks and cardiotocographic examination of the fetus after 33 weeks. In women who underwent pre-gravidar training, including acupuncture in the first and third trimester of pregnancy, the incidence of pregnancy complications was significantly lower than in women who received only didrogestosterone. The concentrations of growth factors VEGF-R1, VEGF-A in women who received acupuncture are significantly higher, this reduces the risk of late pregnancy complications.

Keywords: women, pregnancy, progesterone deficiency, pregravidar preparation, acupuncture, growth factors.

Women with a low concentration of progesterone in the second phase of the menstrual cycle have lower ability of the endometrium to implant a blastocyst. Progesterone deficiency leads to structural changes in the endometrium in the phase of proliferation and secretion. Deviations in the structure of the endometrium can lead to early pregnancy loss [1,2]. Insufficient thickness of the uterine mucosa during the "implantation window" is considered an important risk factor for pregnancy complications [3,4]. Incomplete implantation of the blastocyst into the endometrium leads to impaired angiogenesis in the villi vessels, their premature maturation, changes in hemodynamics in the functional mother-placenta-fetus system and the development of placental disorders [5]. Placental disorders and preeclampsia are detected more often in women who have a low concentration of vascular-endothelial growth factors, placental growth factor, transforming growth factor and insulin-like growth factor than in women with higher indicators [6, 7, 8]. Comprehensive pregravidar preparation is of great importance for the prevention of pregnancy complications. The aim of the study was to study the course of pregnancy, childbirth and perinatal outcomes in women with progesterone deficiency who received pregravidar training using didrogestosterone and acupuncture.

Materials and methods

The concentration of hormones in the blood serum (estriol, progesterone), as well as growth factors in the blood serum (VEGF-R1, VEGF-A, PIGF, TGF-b1, IGF) in 20-24 weeks of pregnancy was studied. Echographic examination of pregnant women at 11-14, 18-21, 30-33 weeks, Doppler

examination in pregnant women at 30-34 and 36-40 weeks and cardiocotographic examination of the fetus after 33 weeks were performed. Statistical data processing was carried out using the Microsoft Excel 2007 statistical software package.

Results

The object of the study was 50 pregnant women with progesterone deficiency. Group 1 included 25 women who received didrogestosterone from the 15th to the 25th day of the menstrual cycle at a daily dose of 10 mg for 3 months during the pregravidar preparation. In 2 groups of women (n=25), pregravidar preparation was carried out with the use of didrogestosterone from the 15th to the 25th day of the menstrual cycle at a daily dose of 10 mg for 3 months and acupuncture. The study included pregnant women with progesterone deficiency who gave their voluntary written consent. The study did not include patients with diseases of the endocrine system, sub- and decompensated extragenital diseases, congenital anomalies and chromosomal disorders, inflammatory diseases of the female pelvic organs (acute and chronic in the acute stage), non-inflammatory diseases of the female pelvic organs (endometriosis), neoplasms (uterine leiomyoma, ovarian neoplasms). The average age of the studied pregnant women in both groups did not differ from 26.8 ± 3.6 and 27.5 ± 3.9 years, respectively. The body mass index did not differ significantly and was 23.5 kg/m^2 . The patients included in the study groups were selected in such a way that they were in equal conditions at the time of the study.

When researching the study groups of the first trimester of pregnancy, threatening abortion was diagnosed in 8 (32%) pregnant women in group 1 and in 1 (4%) woman in group 2. The total number of pregnancy complications was significantly higher in group 1 ($p < 0.01$). In the second trimester of pregnancy, complications were revealed in women of both groups: pregnancy-induced hypertension, diabetes mellitus during pregnancy, anemia, placenta previa without bleeding, threatened abortion and premature birth without delivery. There were no significant differences between the study groups. When assessing the third trimester of pregnancy, the total number of complications is higher in group 1. Placental disorders in group 1 were detected four times more often: in group 1, placental disorders were detected in 8 (32%) pregnant women, in the second group in 2 (8%) women. Pregnancy-induced hypertension was diagnosed in women who received only didrogestosterone at the stage of pregravidar preparation - in 2 (8%). The level of progesterone and estriol had no statistically significant differences. In the study of growth factors, the concentration of VEGF-A in women of group 1 is statically significantly lower than in women of group 2: $217.2 \pm 11.2 \text{ pg/ml}$ and $283.3 \pm 11.1 \text{ pg/ml}$ ($p < 0.001$). The concentration of VEGF-R1 in group 1 is statistically lower than in women of group 2: 159.7 ± 3.9 and 194.9 ± 9.4 ($p < 0.05$). The concentration of PIGF, TGF- β 1 and IGF in the studied groups of women did not significantly differ. So, in women who received pregravidar complex training, including acupuncture, the frequency of pregnancy complications in the 1st and 3rd trimester was significantly lower. Acupuncture at the pregravidar stage enhances the effect of progestogens by improving microcirculation in the endometrium and ovaries. The concentration of growth factors in the blood (VEGF-A, VEGF-R1) in pregnant women who received acupuncture at the stage of pregravidar preparation is significantly higher than in women who received only didrogestosterone, which is important in predicting and reducing the risk of late pregnancy complications.

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OCT- diagnostics in assessing the progression of glaucoma opticopathy

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Abstract

Optical coherence tomography (OCT), OCT angiography (OCTA), static perimetry by comparing morphometric and functional parameters, to give comprehensive assessment of pathological changes in the optic nerve head, macular area, and also at the level of choriocapillaries. The objective of research – to study the patterns of changes in the parameters of the optic nerve head, peripapillary retina, macular area on OCT in patients with different stages of primary open-angle glaucoma. OCT was performed on an Optopol SOCT Copernicus tomograph. We examined 36 eyes of patients with the initial stage and 35 eyes of patients with the advanced stage of primary open-angle glaucoma, as well as 30 eyes of healthy individuals of the same age. The OCT method is highly sensitive in both diagnosis and monitoring of glaucoma. The morphometric parameters that are most informative in the early diagnosis of POAG based on OCT are the characteristics of the ganglion cell complex in the macular zone of the retina. In monitoring glaucoma opticopathy, the parameters of the macula and the peripapillary layer of retinal nerve fibers are the most informative, namely sectoral changes in their thickness.

Keywords: glaucoma, Optical coherence tomography, OCT angiography, monitoring, glaucoma opticopathy

The etiopathogenesis of primary glaucoma remains not fully understood, which makes early preclinical diagnosis difficult. In recent years, the improvement and implementation of high-tech diagnostic methods have opened up new opportunities for researchers and clinicians in solving this problem. Optical coherence tomography (OCT), OCT angiography (OCTA), coupled with static perimetry, allow, by comparing morphometric and functional parameters, to give a more complete, comprehensive assessment of pathological changes in the optic nerve head, macular area, and also at the level of choriocapillaries [1, 2, 3]. In this regard, the objective of our research – to study the patterns of changes in the parameters of the optic nerve head, peripapillary retina, macular area on OCT in patients with different stages of primary open-angle glaucoma.

Materials and methods

The study included both patients with glaucoma and healthy individuals. OCT was performed on an Optopol SOCT Copernicus tomograph. We examined 36 eyes of patients with the initial stage and 35 eyes of patients with the advanced stage of primary open-angle glaucoma, as well as 30 eyes of healthy individuals of the same age. The measurements were carried out in the area of the optic disc, peripapillary retina, in the macular region, including the fovea and parafovea.

Results

The most significant indicators that distinguish initial glaucoma from the norm were the parameters of the macular area: its thickness in the lower parafoveal sector, changes in the average thickness of the ganglionic complex, and the GCC Inferior thickness index.

In the study of the peripapillary retina, the characteristics of the parameters of the thickness of the peripapillary layer of nerve fibers in the lower temporal segment are the most informative at the initial stage of glaucoma. The indicators of the volume and area of the neuroretinal rim also have a significant value. The values of the volume and area of excavation of the optic disc were less significant.

In monitoring the progression of glaucoma, a sectoral decrease in the thickness of the peripapillary layer of nerve fibers (lower temporal and upper temporal segments) is more significant.

Thus, the prevention of blindness from glaucoma largely depends on the early diagnosis of morphometric changes based on the use of modern medical technologies. The OCT method is highly sensitive in both diagnosis and monitoring of glaucoma. The morphometric parameters that are most informative in the early diagnosis of POAG based on OCT are the characteristics of the ganglion cell complex in the macular zone of the retina. In monitoring glaucoma opticopathy, the parameters of the macula and the peripapillary layer of retinal nerve fibers are the most informative, namely sectoral changes in their thickness.

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The outcomes of childbirth and the condition of newborns in mothers who have suffered pneumonia caused by SARS-COV-2

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Abstract

Infection with SARS-COV-2 during pregnancy leads to numerous complications of infection and adverse outcomes of childbirth. In this regard the aim of the study is to study the outcomes of childbirth and the condition of newborns in women who underwent COVID-19 during pregnancy. The evaluation of the outcomes of childbirth and the condition of newborns in 152 pregnant women hospitalized in the infectious diseases hospital (Blagoveshchensk) with a diagnosis of viral pneumonia. The analysis of the history of childbirth, the history of the development of the newborn was carried out. The condition of newborns was assessed using the Apgar scale. The body mass index (BMI) was estimated until the ninth week of gestation. The presence of Atypical pneumonia-CoV-2 RNA was established by PCR. The results of the study showed that the average age of pregnant women who underwent COVID-19 was 30.7 ± 0.4 years, BMI – 25.3 ± 0.4 kg/m². 84.8% of women had delivery on time, 15.2% – prematurely. 56% of term deliveries were through the natural birth canal, 29% by cesarean section. 2.6% of women had antenatal fetal death. The average delivery period was 37.8 ± 0.2 weeks. Pre-induction of labor with #Mifepristone required 23.6% of pregnant women. The condition of newborns on the Apgar scale at the first minute was estimated at 8.07 ± 0.7 , at the fifth – 8.58 ± 0.5 points. Every tenth newborn had a body weight of less than 2500 g. or more than 4000 g. In the early neonatal period, cerebral ischemia (28.9%), motor disorders syndrome (22.3%) and hypertension syndrome (17.1%) were diagnosed with the highest frequency.

Keywords: SARS-COV-2, infection, outcomes of childbirth, condition of newborns, pneumonia.

According to the world literature, infection with SARS-COV-2 during pregnancy leads to numerous complications of infection and adverse outcomes of childbirth [1,2,3]. COVID-19 increases the risk of premature birth to 38.6%, birth of small children to 24.4%, cesarean section to 91.9%, maternal and perinatal mortality to 3% and 2% respectively [4,5,6]. "COVID-19". Objective – to study the outcomes of childbirth and the condition of newborns in women who underwent COVID-19 during pregnancy.

Materials and methods

The evaluation of the outcomes of childbirth and the condition of newborns in 152 pregnant women hospitalized in the infectious diseases hospital of the City Clinical Hospital with a diagnosis of other viral diseases complicating pregnancy, childbirth and the postpartum period (O98.5/U07.1), other viral pneumonia (J12 chronograph.8). The severity of the NCI was assessed according to the methodological recommendations "Organization of medical care for pregnant women, women in labor, maternity and newborns with a new coronavirus infection COVID-19", version No. 5 of 12/28/2021.

The analysis of the history of childbirth (registration form No. 096/1u-20), the history of the development of the newborn (registration form No. 097/y) was carried out. The condition of newborns was assessed at the first and fifth minutes of life using the Apgar scale (V. Apgar 1952), weight and height at birth were also taken into account.

All newborns were isolated from maternity hospitals with pneumonia caused by ATYPICAL pneumonia-COV-2 and transported to the state autonomous institution of the Amur Region "Amur Regional Children's Clinical Hospital". Transportation was carried out in the transport truck of the ITN-01 UOMZ.

The body mass index (BMI) was estimated according to the formula of G. Bray (1978) until the ninth week of gestation. The presence of Atypical pneumonia-CoV-2 RNA was established by polymerase chain reaction (PCR) by sampling material from the nasopharynx and oropharynx in pregnant women and newborns at intervals of 72 hours. All pregnant women underwent a computed tomogram of the chest organs on a Siemens tomograph Definition AS 128. Statistic 6.1 programs were used for statistical data analysis. For point estimation, continuous values were represented by standard deviations in the format $M \pm SD$, where M is the arithmetic mean, SD is the standard deviation.

Results

The average age of pregnant women was 30.7 ± 0.4 years, BMI – 25.3 ± 0.4 kg/m². Pneumonia caused by SARS-coronavirus-2 virus (ICD 10 - J12 c) was diagnosed in the I trimester in 14 (8.5%) pregnant women, in the second – in 36 (21.8%), in the third – in 115 (69.7%). The average gestation period at the time of the disease was 31.3 ± 0.7 weeks.

The outcomes of childbirth and the condition of newborns were assessed in 152 women, of whom 129 (84.8%) were delivered on time, 23 (15.2%) were delivered prematurely. The average delivery period was 37.8 ± 0.2 weeks. Of the 129 who were delivered on time, 85 (56%) were delivered through the natural birth canal, 44 (29%) by cesarean section. Of the 23 premature births, 5 (3.2%) were delivered through the natural birth canal, 18 (11.8%) by cesarean section. Extremely early premature birth (220-276 weeks) was in 6 (26.1%), early premature birth (280-316 weeks) – in 2 (8.7%), premature birth (320-336 weeks) – in 6 (26.1%) and late premature birth (340-366 weeks) – in 9 (39.1%). Antenatal fetal death occurred in 4 (2.6%) pregnant women. In women who delivered promptly on time, cesarean section was performed as planned in 22 (50%), emergency – in 20 (45.4%) and emergency – in 2 (4.6%). Indications for planned delivery were: scar on the uterus – in 15 (68.2%), pelvic presentation of the fetus – in 4 (18.3%), large fetus – in 2 (9%), placenta previa in one case (4.5%); for emergency cesarean section: premature discharge of amniotic fluid and lack of effect from induction to delivery – in 7 (35%), uncontrolled course of pneumonia – in 5 (25%), premature discharge of amniotic fluid and indications for planned delivery and non-correctable violation of uterine contractility occurred with the same frequency in 4 cases (20%); emergency: acute fetal hypoxia – in 2 (100%). Indications for premature caesarean section in an urgent order were: uncontrolled course of pneumonia – in 10 (62.5%), fetal distress accompanied by a questionable type of CTG – in 4 (25%), severe preeclampsia – in 2 (12.5%); in an emergency: acute fetal hypoxia due to premature detachment of a normally located placenta (100%).

Pre-induction of labor during full-term pregnancy with an immature or insufficiently mature cervix #Mifepristone orally once at a dose of 200 mg with repeated administration after 24 hours at the same dose was used in 39 (23.6%) women.

The condition of newborns on the Apgar scale at the first minute was estimated at 8.07 ± 0.7 , at the fifth – 8.58 ± 0.5 points, 5 (3.2%) newborns were born with moderate asphyxia. The average birth weight was 3461.2 ± 63.6 g, height 52.4 ± 0.3 cm. Normal birth weight (2500-4000 gr.) was in 119 (78.3%), body weight less than 2500 gr. – in 21 (13.8%), more than 4000 gr. – in 12 (7.9%). PCR for ATYPICAL pneumonia-COV-2 was negative in all newborns.

Brain ischemia was diagnosed in 44 (28.9%) newborns (P91.0), of which I and II degree – in 13 (8.5%), III – in 18 (11.8%), motor disorders syndrome – in 34 (22.3%), hypertension syndrome – in 26 (17.1%), vegetative-visceral syndrome – in 7 (4.6%). Every fifth newborn had posthypoxic cardiomyopathy (P29.8) and intraventricular hemorrhage (P52.0) – in 13.1% and 11.8%, respectively. Fetal growth retardation was diagnosed in 8 (5.2%). Signs of respiratory failure (P 28.5) were in 7 (4.6%) newborns, anemia (P 61.2) – in 5 (3.2%).

The results of the study showed that the average age of pregnant women who underwent COVID-19 was 30.7 ± 0.4 years, BMI – 25.3 ± 0.4 kg/m². 84.8% of women had delivery on time, 15.2% – prematurely. 56% of term deliveries were through the natural birth canal, 29% by cesarean section. 2.6% of women had antenatal fetal death. The average delivery period was 37.8 ± 0.2 weeks. Pre-induction of labor with #Mifepristone required 23.6% of pregnant women.

The condition of newborns on the Apgar scale at the first minute was estimated at 8.07 ± 0.7 , at the fifth – 8.58 ± 0.5 points. Every tenth newborn had a body weight of less than 2500 g. or more than 4000 g. In the early neonatal period, cerebral ischemia (28.9%), motor disorders syndrome (22.3%) and hypertension syndrome (17.1%) were diagnosed with the highest frequency.

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Development of a device for long-term 3D-cultivation of mammalian cells with the maintenance of physicochemical conditions close to a living organism

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Abstract

Cell cultures grow better in dynamic culture conditions, because nutrition and removal of metabolic products is better in conditions of dynamic movement of the nutrient medium. For dynamic cultivation, the researchers use a bioreactor. The purpose – to development of device for 3D-cultivation of mammalian cells with the maintenance of conditions close to a living organism. To test the work of a laboratory sample, we studied the adhesion and proliferation of fibroblasts during long-term cultivation in a device in biocompatible tissue engineering constructs (gelatin scaffolds) by viewing the scaffolds on a scanning electron microscope (SEM) and counting cells in a hemocytometer. Thus, the obtained results indicate the possibility of using the device for 3D-cultivation of mammalian cells on tissue-engineered constructs.

Keywords: dynamic cell cultures, 3D-cultivation, mammalian cells, bioreactor.

Innovation is the process of creating new approaches, technologies and ways of working.

In healthcare, innovations include the development of new unique methods for diagnosing and treating diseases, the development of new devices that facilitate the work of a doctor and a researcher.

Dynamic 3D cultivation is a way to recreate in vitro physicochemical conditions as in a living organism for cell growth and proliferation, which is provided due to the circulation of the nutrient medium in the sample area. According to numerous studies, cell cultures grow better in dynamic culture conditions, because nutrition and removal of metabolic products is better in conditions of dynamic movement of the nutrient medium.

For dynamic cultivation, the researchers use a bioreactor. The bioreactor has a peristaltic pump that ensures continuous circulation of the medium, which preserves the biologically active substances secreted by the cells.

Additional maintenance of temperature and gas concentrations as in vivo allows us to consider the continuous dynamic 3D cultivation of mammalian cells in a bioreactor as a basis for studying the response of cells to the effects of pathological conditions or drugs. So what's the problem? The fact is that not only large laboratories on an industrial scale are engaged in cell cultivation, but also small teams interested in conducting research, for example, testing drugs on 3D cultures. Of course, at the moment bioreactors are presented on the foreign market, but they have a high cost (from 200 thousand to 4 million rubles) and don't combine all the necessary functions or they are very large).

Moreover, all analogues are imported to Russia, which creates logistical difficulties in their purchase and consumables. In this regard, it was decided to create our own compact bioreactor that supports all the necessary functions to create physiological conditions for cultivation and, at the same time, is financially affordable.

The purpose of study – to development of a device for long-term 3D-cultivation of mammalian cells with the maintenance of physicochemical conditions close to a living organism. The device must be affordable, compact, easy to use and efficient.

Materials and methods

For the development of the device, materials were selected that are resistant to long-term continuous operation, and a laboratory sample of the device was created. To test the work of a laboratory sample, we studied the adhesion and proliferation of fibroblasts during long-term cultivation in a device in biocompatible tissue engineering constructs (gelatin scaffolds) by viewing the scaffolds on a scanning electron microscope (SEM) and counting cells in a hemocytometer.

Results

The laboratory sample consists of two parts: a control box and a culture chamber. Cultivation of dermal fibroblasts on gelatin scaffolds at a temperature of 37°C and a carbon dioxide concentration of 5% for 14 days with control points on the 3rd, 7th, and 14th days showed a fold increase in the number of fibroblasts and the volume of the scaffold filled with them.

Thus, the obtained results indicate the possibility of using the device for 3D-cultivation of mammalian cells on tissue-engineered constructs. Health care should be relatively cost-effective and efficient. We, young researchers, try to keep up with the times and promote the development of innovations in the field of studying the health of people.

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