

the loss of memory. Dihuangyinzican improve the memory impairment of dementia rats and reduce the contents of MAO and AchE in the brain, thus proving that the decoction has the effect of delaying AD.

2 Antioxidant and reduce free radicals In the normal physiological conditions, the body's oxidation and antioxidant levels to maintain a dynamic balance, the body does not constitute harm, when the balance was broken by certain incentives, the emergence of balance disorders, free radicals were not cleared in time in the normal condition that causing the damage of body, The activity of antioxidant enzymes such as SOD, CAT and CSH-Px can be used as an indirect antioxidant to alleviate the toxicity of H₂O₂ and maintain the function of the cells, While reducing lipid peroxidation, improve the reduced antioxidant enzyme activity.

3 The effect of the neuronal apoptosis The studies have shown that pathological apoptosis is a pathogenesis of neurological diseases, Dihuangyinzicai decoction can inhibit apoptosis, It play a role in brain protection through the improvement of HPA axis disorders.

4 The effect on neurons Shi Rui suggested that Dihuang Yinzi may inhibit the expression of NOS through the experiment, reducing the formation of NO in the cerebral cortex and its toxic effects on nerve cells, which may be one of the mechanisms of protection of Dihuangyinzicai on vascular dementia.

5 Conclusion The studies have shown that Dihuang Yinzi has a significant role in prevention and treatment in the treatment of geriatric disease, The studies also showed that Dihuang Yinzi can reduce the activity of acetylcholinesterase in brain tissue, improve the ability of learning and memory, repair the cerebral ischemia-reperfusion injury, antioxidant and free radicals, reduce cell apoptosis, protect neurons. It could provides preparation on preventing the treatment of geriatric disease through the modern advanced scientific means and technology.

References

- [1] Song baohua, Peng xuejie, The effects of Dihuangyinzicai on Cognitive Ability and MAO and AchE Activity in Alzheimer's Disease Rats [J] The Traditional Chinese Medicine of Liaoning magazine, 2005, 32 (2) : 616-617
- [2] Zhou yanyan, Xie ning, Yao yinmin. The experimental study on the neuroprotective effect of Rehmannia glutinosa on senile dementia, [J] Journal of Traditional Chinese Medicine and Pharmacology, 2011, 39 (2) : 58-61
- [3] Ma tao, Yan yan. The effects of Bushen Filling on P13K / AKT Pathway Activation and Oxidative Stress in Alzheimer's Disease Mice [J] Beijing Traditional Chinese Medicine, 2014, 33 (7) : 492-495
- [4] Xie ning, Yu miao. The effects of Rhizoma Rheumatoid Recipe on Oxidative Stress in PC-12 Cells [J] SHIZHEN Chinese medicine medicine, 2012, 23 (8) : 1885-1886
- [5] Zhang geng, Wu jinjuan, Zhang miao, Research on Treating Alzheimer's Disease with Chinese Medicine exhibition [J] , Chinese Journal of Experimental Traditional Medical Formulas, 2014, 20 (6) : 217-222.
- [6] Li zijun, Liu chunna, Protective Mechanism of Rehmanniae Decoction on Hypoxia Injury in Hippocampal Neurons, [J] , Chinese medicine, 2012, 34 (8) : 1421-1424

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METABOLOMICS FOR LIVER DISEASES IN CLINIC

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Abstract Metabolomics has been instrumental for the identification of new biomarkers of liver disease which can be measured in plasma, serum and urine samples. New biomarkers are needed to help guide therapy by identifying patients with liver disease progression who might need aggressive treatment. It certifies that metabolomics had great potential on both discovering clinical biomarkers and elucidating previously unknown mechanisms of liver disease pathogenesis.

Key words: metabolomics, clinical use, liver diseases, biomarkers

Metabolomics is an emerging discipline that assesses the concentration of different metabolites in complex biological samples to understand the ongoing metabolism. Recently, metabolic-based liver disease studies have been used to screen plasma, and urine from control populations and patients [1, 2]. There are many reasons that can induce liver disease. Liver diseases are worldwide public health problems. Liver disease in accordance with the pathogenesis can be divided into viral liver disease and non-viral liver disease. Underlying pathophysiological mechanisms in progression of liver disease to cirrhosis are not yet understood.

Clinical Metabolomics A new opportunity to discover biomarkers in complex diseases has been provided by metabolomics, which may improve the clinical course and provide pathological understanding of the disease, beyond the traditional technology [3]. The potential of this approach for clinical diagnostics is enormous, since only minimal biological preparation is required. Recently altered metabolism has been identified as a key marker of liver disease and metabolism focused research has received renewed attention. Diagnostic liver disease biomarkers detected

by metabolomics have gained much attention in the field of clinical liver disease research, to further understand its complex heterogeneity, to indicate changes in metabolic biomarkers during therapeutic intervention and to explore pathways involving liver disease that can be used for new targets [4, 5]. These studies enable the construction of metabolic networks that link disease-associated metabolites from the studied biofluids with intervention outcomes in preclinical and clinical studies. These kinds of metabolic networks will provide a much better understanding of pathways leading to the development of disease and potentially provide insight into disease pathogenesis.

Metabolomics in liver diseases Routine detection of aminotransferase ALT and AST, initially identified as markers of liver injury, are increasingly considered to be an indicator of the “liver metabolic function”. However, metabolomic information have changed the classical conception of the meaning that serum concentrations of ALT and ALT are merely indicators of hepatocyte membrane disruption. In recent years, physicians have been exploring the potential for metabolite analysis to provide diagnostic and prognostic information for many diseases such as liver disease. For example, Rachakonda et al.[6] demonstrated that specific biomarkers can be used to determine the prognosis of patients with severe liver disease by metabolomics analysis. As a case study, Li et al. indicated that four potential biomarkers (i.e., serum glucose, lactate, glutamate/glutamine, and taurine) for diagnosis of NAFLD at various stages were selected[4].

Conclusion Despite its performance limitations, many novel liver disease biomarkers have been discovered during the past few decades, however, none have achieved broad acceptance in clinical practice as yet. Several biomarkers are currently under development to improve assay performance and to demonstrate proof of efficacy in clinical practice. Due to the heterogeneous nature of both liver diseases and humans, it is unlikely that a single ideal biomarker with excellent performance will be identified. Future studies should focus on efforts to combine biomarkers to achieve maximum diagnostic and predictive ability.

References:

- 1.Sharma R. K., Mishra K., Farooqui A., et al.1 H nuclear magnetic resonance (NMR)-based serum metabolomics of human gallbladder inflammation. // *Inflammation Research*, -2016: 1-9.
- 2.Osman D., Ali O., Obada M., et al.Chromatographic determination of some biomarkers of liver cirrhosis and hepatocellular carcinoma in Egyptian patients. // *Biomedical Chromatography*, -2016.
- 3.Zhang A., Sun H., Yan G., et al.Metabolomics for Biomarker Discovery: Moving to the Clinic. // *Biomed Research International*, -2014, -2015.
- 4.Yki-Järvinen HLuukkonen P. K..Heterogeneity of non-alcoholic fatty liver disease. // *Liver International Official Journal of the International Association for the Study of the Liver*, -2015, -35(12): 2498.
- 5.Eva J.H., Daniel M.K., Norberto Carlos C.T., et al.Biomarkers in Hepatocellular Carcinoma: An Overview. // *Expert Review of Gastroenterology & Hepatology*, -2017(1747-4124).
- 6.Rachakonda V., Gabbert C., Raina A., et al.Serum Metabolomic Profiling in Acute Alcoholic Hepatitis Identifies Multiple Dysregulated Pathways. // *PLoS one*, -2014, -9(12): e113860.

EFFECT OF ACONITE LATERLIS RADIX COMPATIBILITY OF SAPOSHNICOVIA DIVARICATA ON CYP1A2 AND CYP3A4

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Objective: Radix aconiti carmichaeli is crowfoot plants of aconite root processed products, aconitine-type alkaloids are the main component of Radix aconiti carmichaeli, aconitine-type alkaloids is diester-type alkaloids, that was metabolized mainly by CYP3A and CYP1A1/2 enzyme, and the metabolite is monoester-type alkaloid of low toxicity. From the perspective of drug-metabolizing enzymes, to discuss attenuated mechanism of Radix aconiti carmichaeli compatibility of Saposshnicovia divaricata, and clarify the rationality of use compatibility of Radix Aconiti carmichaeli, further to provide scientific basis for both the safety and efficacy of Radix Aconiti carmichaeli clinical application.

Methods: Male Wister rats (weighting 200±20 g) were divided into five groups: control group, Radix aconiti carmichaeli group, Saposshnicovia divaricata group, Fuzi combined with Saposshnicovia divaricata group, and Paeoniae cinnamomi, Anemarrhenae decoction group, respectively. Each group continuously gavage administered once a day for seven days. The control group receive physiological water. On the one hand, the eighth day intravenously administered. Then preparation and incubation of liver microsomes, using “Cocktail” probe drugs, which specific probe drugs include caffeine and midazolam, the RT-HPLC method was established to determine the concentration of the two probe substrates in the liver microsomal incubation system in order to evaluate the effect of Radix aconiti carmichaeli compatibility of Saposshnicovia divaricata on the activity of CYP1A2 and CYP3A4.

Results: (1) Simultaneous determination of caffeine and midazolam by HPLC. All samples (20 µL) were separated on a Diamonsil C18 reversed-phase column (150mm×4.6mm, 5 mm) by HPLC system. The mobile phase consisted of methyl alcohol and Diammonium phosphate buffer solution (51:49 V/V) at a flow rate was 0.8 mL/min. The separation was carried out at 35°C. UV detection wavelength was 254nm. Specificity, sensitivity, accuracy and stability of the method met the requirements of biological sample measurement.

(2) Compared with control group, Radix Aconiti carmichaeli group, Radix Aconiti compatibility of Saposshnicovia divaricata group and Paeoniae cinnamomi, Anemarrhenae decoction group could induce CYP1A2 and CYP3A4 activity slightly, but the effects was no statistically significant. Saposshnicovia divaricata group showed no effects on activity of CY-