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 desease 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 Saposhnicovia 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, Saposhnicovia divaricata group, Fuzi combined with Saposhnicovia 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 Saposhnicovia 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℃. 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 Saposhnicovia divaricata group and Paeoniae cinnamomi, Anemarrhenae decoction group could induce CYP1A2 and CYP3A4 activity slightly, but the effects was no statistically significant. Saposhnicovia divaricata group showed no effects on activity of CY-

P1A2 enzyme ; Radix Aconiti carmichaeli group has no effects on activity of CYP3A4 enzyme, Saposhnicovia divaricata group, Radix Aconiti carmichaeli compatibility of Saposhnicovia divaricata group and Paeoniae cinnamomi, Anemarrhenae decoction group could induce activity of CYP3A4 enzyme and the effects was statistically significant($P<0.05$).

Conclusions: It is based on the viewpoint of liver metabolic enzymes to verify Saposhnicovia divaricata cooperate with Radix Aconiti carmichaeli can induce the activity of CYP1A2 and CYP3A4, which was main reason of increase the metabolism of the toxicity ingredients of Radix Aconiti carmichaeli. Further confirmed scientific and rationality of the theory for traditional Chinese medicine compatibility, to provide direct basis in order to reveal the compatibility theory and reasonable combination of clinical drug use of traditional Chinese medicine.

Key words: Radix Aconiti carmichaeli; Saposhnicovia divaricata; attenuated mechanism

Reference

[1] Li jianbo, Zhang li, Zhang jie. Summary of drug compatibility theory and related research[J]. Journal of traditional Chinese Medicine, 2013, 54(15): 1335-1340.

[2] Ding tao. Modern pharmacological research and clinical application of Radix Aconiti Lateralis Preparata[J].Journal of traditional Chinese Medicine, 2012, 27(175): 1630-1631.

[3] Fu dailing. The sudy of compatibility law of Radix Aconiti Lateralis Preparata[D]. Beijing University of Chinese Medicine, 2013.

[4] Wang binhui, Feng jian, Zhao yanmin. The study on pharmacokinetics of Aconitum alkaloids in Radix Aconiti Lateralis Preparata in rats[J]. Chinese Pharmaceutical Journal, 2009, 44(18): 1412-1415.

[5] SOLYANIK G I, FEDORCHUK A G, PYASKOVSKAYA O N,et al. Anticancer activity of aconitine-containing herbal extract BC1[J].Exp Oncol, 2004, 26(4): 307-311.

[6] Wang rui. Study on quality evaluation of Radix Aconiti Lateralis Preparata and pharmacokinetics of Aconitine[D]. Beijing University of Chinese Medicine ,2007.

[7] Wang Y, Wang S, Liu Y, et al. Characterization of metabolites and cytochrome P450 isoforms involved in the microsomal metabolism of aconitine[J]. J Chromatogr B, 2006, 844(2) : 292.

[8] Pharmacopoeia of People's Republic of China [M]. Ed, 2005, (1): 102.

[9] Wang jianhua .The study on the chemical constituents of the essential oil from saposhnikovia divaricata[J]. Chin Pharm Bull, 1987, 22(6): 335-338.

STUDY ON THE QUANTITATIVE DETERMINATION FOR SCHISANDRIN A B IN DI SHUANG YIN ZI GRANULES

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Abstract: Objective To study the quantitative determination for Schisandrin A、B. Method Schisandrin A B were determined by HPLC. Results: Schisandrin A、B could be determined by HPLC. Conclusion: This method is simple ,accurate and responsible, which is suitable for thequantitative determination of Schisandrin A、B

Key words: HPLC; Schisandrin A、B ; quantitative determination

Dihuangyinzi granule is made from Rehmanniae, Cistanche, Dendrobium, Polygala Farms by the preparation of the compound preparation, with kidney sputum, spleen and dampness and other effects, can be used for dementia and other diseases. In order to better control the quality of the preparation, so the establishment of the content of Schisandrin A、B content determination method.

1.Laboratory Materials

DiShuangYinZi Granules(20141225,20141227,20141229);perchloric acid, ether, cyclohexane, Formic acid, etc; Methanol (DikmaPure, chromatographic alcohol).

2. Method

2.1 Preparation of the reference solution

Accurately weighed Schisandra reference substance 1 g, schisandrin 3 g, with the same 5 ml bottle, added methanol dissolved and constant volume to the scale.Then précised amount of 1 ml and set 5ml volumetric flask, added methanol dissolved and shaked, as the reference solution.

2.2 Preparation of Test Solution

Taked the sample particles about 12 g and set 25 ml volumetric flask, added methanol 20 ml and ultrasound 40 min, then added methanol constant volume to the scale, as the test solution.

2.3 Standard curve preparation

Precisely absorbed the Schisandrin A、B mixed reference solution 1,2,4,6,8,10,12 ul, that were injected into the liquid chromatograph. Obtained the standard curve A is: Y = 152526x-40734, B is: Y = 319207x-81694.

2.4 Precision experiment

Precisely absorbed the reference substance solution 8ul and injected, continuous determination of 5 times. The re-