## A COMPARATIVE STUDYON THE PHARMACOKINETICS OFALISMA ORIENTALIS AND ITS COMPATIBILITY

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Abstract Rhizoma Alismatis is the composition of the treatment of type Ⅱ diabetes experience of one of the three flavors of Citrus grandis,modern pharmacological indicate that it have fuction include diuretic, lowering blood pressure, lowering blood sugar, anti-atherosclerosis, immune regulation and so on.The results of the study on the pharmacokinetic process of the active ingredient in rat rats after administration of Citrobenzene and Alisma orientalis respectively showed that Alisma Ophiopogonjaponicuscouldincreaseitsactiveingredient,A-24-acetateabsorbsinthebodyandreducesitsplasmaclearance.

Key words Rhizoma Alismatis ; Alcohol A-24-Acetate ; Pharmacokinetics ; HPLC-MS/MS

Objective To study the pharmacokinetic differences of Alisma orientalis and Alisma orientalis in rats.

Materials and methods Twenty - four SD rats were randomly divided into two groups, namely, Huaqizeren group and Alisma group.According to 1mL / 100g body weight were given to the flower flag Ze, Alisma water decoction,take blood by the orbital venous plexus about 0.5mL before administration and after administration 0,0.25,0.5,0.75,1,2,3,4,6,8,12,24,48 h,determination of Alcohol A-24-Acetate by Liquid Chromatography / Quadruple-Flying Time Series Liquid Chromatography after processing。

Results and discussion Compared with Alisma group, the curve of Alcohol A-24-acetate was still bimodal。However, it was found that the first peak time (Tmax) of the A-24-acetate was prolonged and the peak concentration (Cmax) did not change significantly。The results showed that the effect of the combination of Citizen Zygren on the concentration of A-24-acetate in the evening was not obvious。However, AUC0-t increased significantly, the elimination rate CL decreased, and was statistically significant (P <0.05), indicating that the compatibility of Alisma alcohol A-24-acetate the first peak time to extend。At the same time, plasma clearance rate decreased, extending its role in the body time.It can be concluded that the degree of absorption of Alcohol A-24-acetate in the Citroblazuron group was higher than that in the Alisma orientalis group and the plasma clearance rate was decreased.

References:

[1]Peng G P, Lou F C.Isolation and indentificartion of diterpnoids from Alisma orientalis[J]. Acta pharmaceutica sinica. 2002, 37: 950-954.

[2] Zang Ping. Alisma research status and prospects [J]. Chinese Traditional Medicine Modern Distance Education, 2009,7 (6): 180-182.

[3] Wang Lixin, Wu Qidan, Zhang Qiao, etc. Alisma diarrhea in the study of active substances [J]. West China Pharmaceutical Journal, 2008, 23 (6): 670-672.

[4] Gu Shijian, Wu Juan, Liu Dongyue, Liu Ping, Fang Nianbo, Yu Shanggong. Alisma Decoction on mice blood pressure experimental study [J]. Shi Zhenguo medicine, 2010,02: 272-273.

[5] Yu Xiangyun, Zhong Jianhua, Zhang Xu. Alisma lipid-lowering pharmacological effects and material basis [J]. Chinese Journal of Traditional Chinese Medicine, 2010, 11: 250.

[6] YIN Chun-ping, WU Ji-zhou.Advances in immunoregulation of Alisma orientalis and its active components [J]. Chinese Traditional Medicine, 2001, 32 (12): 1132-1133.

[7] ZHANG Rui-fang, WAN Jian-xin, XU Yan-fang, YOU Dan-yu, CUI Jiong, PAN Yang-bin.Effects of Alisma alcohol B on C3a-mediated human renal tubular epithelial cell mesenchymal transdifferentiation [J]. Chinese Journal of Integrated Traditional Chinese and Western Medicine , 2012, 10: 1407-1412.

[8] Wang Zhenhai, An Xizhong, Ren Zengchao. Protective effect of Alisma orientalis on acute liver injury in rats [J]. Chinese Journal of Animal Quarantine, 2010,09: 56-57.

[9] Gao Hong, Hu Yinghe. New use of Alisma orientalis found by the method of screening with agonist M1 receptor agonist [P]. Chinese Patent: CN 1615981.

## THEPROSPECTS OF ANTI-PLATELETFUNCTION OF ASPIRIN

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Abstract Aspirin is integral to the secondary prevention of cardiovascular disease and acts to impair the development of platelet-mediated atherothromboembolic events by irreversible inhibition of platelet cyclooxygenase-1 (COX-1). Although aspirin is still effective, a large number of patients will still occur atherosclerotic thromboembolic events, Besides that about 10% of patients do not respond to aspirin, this phenomenon is called “aspirin resistance “. In this paper, we discuss the mechanism of aspirin resistance with these factors involved in aspirin resistance, and then analyze the potential mechanism of antiplatelet function, and provide a potential theoretical basis for promoting the formation of new antithrombotic drugs.

Key words: COX-1; platelet aggregation; aspirin resistance; antiplatelet;

Aspirin, one of theanti-platelet agents which most widely used in clinical has a significant effect on cardiovascular diseasein high-risk patients. Its main mechanism is irreversibly acetylates the enzyme cyclooxygenase(COX)-1 at serine 529 preventing conversion of arachidonic acid(AA) to thromboxane A2 in a dose-independent manner [1-2]. However, not all patients show an equal antiplatelet effect, some studies suggest that there're some multidrug resistence protein 4(MRP4) can overexpress in human platelet which can reducing aspirin action. Besides that other human tisuses can productthromboxane A2(TXA2),what's more, the residual platelet fuction is the most important reason which can result in aspirin resistance. This review aims to provide a brief mechanism summary on aspirin resistance,which including the pathway of TXA2 production and anion efflux pump.

1.Effect of TXA2 on antiplatelet effect Since the sensitivity of the platelets to antithrombotic effects of aspirin is largely determined by the inhibitory effect of the drug on COX-1, this inhibition is not completeso that it is a wide range of individual differences in the course of chronic treatment. It has been found thatsome patients can not inhibit platelet TXA2 formation in vitro or in vivo, requiring further addition of aspirin adjuvant therapy. In addition, studies have found that platelets are not the only source of TXA2 circulation [4]. Monocytes ,endothelial and vascular smooth muscle cells could synthesise TXA2 in response to stimuli[5], in a predominantly COX-1 mediated process which is poorly sensitive to the inhibitory effect of aspirin. What's more, COX-2, which is associated with thromboxane and prostaglandin synthase in platelets, is not susceptible to aspirin so that it could also form TXA2 by its own activation. These findings have shown that it is difficute in accutarely assigning in vivo measures of TXA2 synthesis to the action of aspirin specifically on platelet COX-1.

2. Anion efflux pump (the effect of MRP4 on antiplatelet effects) Multidrug resistance protein-4 (MRP4) is a member of the MRP / ABCC subfamily of ATP-binding cassette transporter. The expression of MRP4 has been found in many tissues,which can pumping a wide variety of endogenous and xenobiotic organic compounds out of the cells. Many studies have shown that aspirin is a target for MRP4 in human platelet and aslo determinate both aspirin and its metabolites ,salicylic acid are substrates of mouse ABCC4. In addition some studies have confirmed thatthe patients will synthesize a large number of multidrug resistance protein-4 (MRP4)increased with dosage of aspirin. However, theexpression is very littlein healthy patients.Mattiello etal found that the MRP4 over-expression is directly linked to anaspirin-reduced cell entrapment that leads to increased thromboxane B2（TXB2）production, as found in CABG patients, with residualplatelet activation despite aspirin treatment. Moreover, invitro inhibition of MRP4-mediated transport enhancesaspirin action in platelets. Above that aspirin can be mediated efflux by MRP4 transporter, thereby reducing its efficacy.

3. Discussion In summary, in vitro and vivo studieshave connected the antithrombotic effect of aspirin on the irreversible inhibition of platelet COX-1 with the formation of TXA2. Except as mentioned above, some other problems should be considered (1) although serum TXB2 can be used to determine the activity of platelet COX, whether TXB2 is a stable metabolite of TXA2 should be further exploration; (2)If platelets are able to obtain PGH2 by means of a mechanism that does not rely on COX, the effect of aspirin will fail. (3) Excepet COX-1, there are also isoforms COX-2 in human platelet. Somesurveys suggest that the production of TXA2 can be induced by COX-2 or other pathways. Despite this, our results paves the way to further studies of the possible direction about the aspirin resistance in anti-platelet.

References:

1. Michelson A D, Cattaneo M, Eikelboom J W, et al. Aspirin resistance: position paper of the Working Group on Aspirin Resistance[J]. Journal of Thrombosis & Haemostasis, 2005, 3(6):1309-1311.

2. Patrono C, Rocca B. Drug insight: aspirin resistance--fact or fashion?[J]. Nature Clinical Practice Cardiovascular Medicine, 2007, 4(3):E1; author reply E2.

3. Maree A O, Fitzgerald D J. Variable platelet response to aspirin and clopidogrel in atherothrombotic disease.[J]. Circulation, 2007, 115(16):2196-2207.

4. Catella F, Fitzgerald G A. Paired analysis of urinary thromboxane B2 metabolites in humans[J]. Thrombosis Research, 1987, 47(6):647-56.

5. Orlandi M, Bartolini G, Belletti B, et al. Thromboxane A2 synthase activity in platelet free human monocytes.[J]. Biochim Biophys Acta, 1994, 1215(3):285-290.

## EXPERIENCE OF ACUPUNCTURE IN THE TREATMENT OF OBSTRUCTIVE SLEEP APNEA HYPOPNEA SYNDROME

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Abstract Background Obstructive sleep apnea hypopnea syndrome (OSAHS) is a common and serious disease threatening people's health. Along with the changes of incidence increased year by year, the treatment of OSAHS is also developed, the continuous positive airway pressure (CPAP) and the surgical treatment is the preferred scheme at present, but because of poor compliance and acceptance. In the traditional medicine, Acupuncture has a significant effect on the treatment of the disease. This paper reviews the methods and thoughts of treatment, and draws the following conclusions.

Conclusion: In this paper, the main conclusions were

(1) Acupuncture has the exact curative effect on treating OSAHS, the clinical effect is prominent, the patient's compliance is good, the adverse reaction is few and so on.