[3] Tang Y, Wang M, Le X, et al. Antioxidant and cardioprotective effects of Danshensu (3-(3, 4-dihydroxyphenyl)-2-hydroxy-propanoic acid from Salvia miltiorrhiza) on isoproterenol-induced myocardial hypertrophy in rats[J]. Phytomedicine,2011,18(12):1024-1030.

[4] Zheng lian xing. The effects and mechanism of Danshensu on vascular smooth muscle cells proliferation and apoptosis induced by oxidized low density lipoprotein[J]. Chinese Journal of Pathophysiology,2009, 25(10) : 2053.

[5] Zhang LJ, Chen L, Lu Y, et al. Danshensu has anti-tumor activityin B16F10 melanoma by inhibiting angiogenesis and tumor cell invasion [J] . Eur J Pharmacol, 2010, 643(2-3) : 195.

[6] Redman CW, Sargent IL. Latest advances in understanding pre-eclampsia [J] . Science, 2005, 308: 1592.

Author: QIAN Si yuan: email: XY223126@163.com HUANG Shu-ming email: huangshuminghljzyy@126.com Address: Heilongjiang University of Traditional Chinese Medicine, Harbin, Heilongjiang, Heping Road, No.24, 150040

STUDY ON METABOLISM OF THE MAIN ACTIVE COMPONENTS OF HUAQIZEREN TREATING TYPE 2 DIABETES WITH INSULIN RESISTANCE IN THE INTESTINAL FLORA

Qijing Huang1, Pengyang Yu1, Nannan Xing1, Pengling Ge1, *

1Department of Pharmacology, School of Basic Medical Sciences, Heilongjiang University of Chinese Medicine, Harbin 150040, China *Corresponding authors: Pengling Ge, Department of Pharmacology, School of Basic Medical Sciences,Heilongjiang University of Chinese Medicine, 24 Heping Road, Harbin 150040, China; E-mail: pengling-ge@126.com

Objective Huaqizeren is effective experience prescription for treating type 2 diabetes with insulin resistance. Through the metabolism study on main activeingredients of Huaqizeren in vitro and in vivo intestinal flora, we identified structure of metabolites, explored the relationship between the prototype components and metabolic products, and analysed the metabolism pathway about main active ingredients of Huaqizeren and their metabolites in intestinal flora in vivo, clarified the metabolism process in vivo and material basis of Huaqizeren treating type 2 diabetes with insulin resistance.

Materials and methods Intestinal bacteria metabolism experiment in vitro: To study the metabolism of the main active components of Huaqizeren in rat intestinal flora using culture methods in vitro, detect the content of main active components of Huaqizeren, identified structure of metabolite using UPLC-Q-TOF-MS analysis method, in order to investigate the its biological activity and safety.Intestinal bacteria metabolism experiment in vivo: After the mice were ig administered with Huaqizeren, we respectively collected 4 h and 12 h cumulative fecal, and quickly opened the abdominal cavity, removed the cecal contents after animal were sacrificed. Feces and the contents of the appendix were fully dissolved with 4 times MeOH, 12000 r·min-1 centrifuged for 15 min, the prototype compounds and their metabolites in supernatant were rapidly separated and determined by UPLC-Q-TOF-MS analysis to investigate intestinal bacterial metabolism of the main active ingredients of Huaqizeren.

Results The main active ingredients of Huaqizeren Ginsenoside-Rb1 (G-Rb1)、Alisol A 24-acetate and 9-hydroxy-octadecadienoic acid (9-HODE) could be metabolized by the intestinal flora, and the metabolism of G-Rb1 in the intestinal flora is faster, while Alisol A 24-acetate and 9-HODE metabolic rate is relatively slow. The study identified 4 metabolites of G-Rb1, such as Ginsenoside-Rd (G-Rd)、Ginsenoside-F2 (G-F2)、Compound K (C-K)、and 20(S)protopanaxadiol (Ppd), only one metabolite of Alisol A 24-acetate was Alisol A.

Conclusion Through intestinal bacteria metabolism experiments in vitro and in vivo, the study clarified that the metabolic regularity of main active components of Huaqizeren and its metabolites in intestinal flora, and identified structure of metabolites, it has vital significance to clarify pharmacodynamic material basis、metabolic process and rational administration after administration of the Huaqizeren.

Key words: Type 2 diabetes mellitus; Insulin resistance; Huaqizeren Intestinal flora; Metabolite

References:

[1]Panzer C, Lauer MS, Brieke A, et al. Association of fasting plasma glucose with heart rate recovery in healthy adults: a population-based study[J]. Diabetes, 2002, 51:803-807

[2]Himsworth. Diabetes Mellitus Its differentiation into insulin sensititive and insensititive type[J]. The Lancet, 1936, 18:127-130

[3]Yalow Rs, Berson SA. Immunoassay of endogenous plasma Insulin in man [J]. J Clin Invest, 1960, 39:1157-1751

[4]Xu Q F, Fang X L, Chen D F. Pharmacokinetics and bioavailability of ginsenoside Rb1 and Rg1 from Panaxnotoginseng in rats [J]. J Ethnopharmacol, 2003, 84(2) : 187.

[5]YANG Xiuwei, HAO Meirong, Hattori Masao. Metabolite analys is for chemical const ituents of traditional Chinese medicines[M]. Beijing: Chinese Medicinal and Pharm Science and Technology Press, 2003: 144-151.

[6]Li L, Jiang H, Wu H, et al. Stimultaneous determination of luteolin and apigenin in dog plasma by RP-HPLC[J]. J Pharm Biomed Anal, 2005, 37(3):615-620.