

STUDY ON THE METABOLISM OF TRADITIONAL CHINESE MEDICINE COMPOUND PREPARATION HUAQIZEREN (HQZR) CORRELATION WITH CYP450 ENZYMES IN RATS

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Objective Type 2 diabetes is the most common type of diabetes[1]. Insulin resistance is one of the key mechanisms leading to the pathogenesis of type 2 diabetes[2]. Traditional Chinese medicine compound preparation Huaqizeren (HQZR) is the clinical experience of treating insulin resistance and related diseases. In this study, HQZR as the research object. On the one hand, through the study of the effect of CYP450 on the metabolism of the main active components of HQZR in rats, the metabolic rule of HQZR was recognized and predicted. On the other hand, through the study of the effect of HQZR on the activity of CYP450 enzyme, to understand HQZR on CYP450 enzyme induction or inhibition and to guide the rational application of clinical drugs.

Materials and methods

1. A study on effects of CYP450 on the metabolism of the main active components of HQZR in rats

The male Wistar rats were randomly divided into control group, phenobarbital sodium group and ketoconazole group. After 3 days of administration, the rats were perfused with HQZR decoction in situ perfusion method. The samples were collected by a series of time points. Each rat respectively take perfusion fluid samples by HPLC-MS/MS method for detecting the concentration of perfusate prototype drug comparison HQZR whether there are differences in the control group and the treatment group metabolism.

2. A study on effects of HQZR on the activity of CYP450 in rats

Male Wistar rats were randomly divided into blank control group, phenobarbital sodium group and ketoconazole group and HQZR group. Phenobarbital sodium group, ketoconazole group and HQZR group were induced for 5 days. The liver coefficients of each group were calculated and liver microsomes were prepared. The concentration of liver microsomal protein was determined by Lowry method, and the content of CYP450 was detected by CO reducing differential spectroscopy.

Results and discussion

1. A study on effects of CYP450 on the metabolism of the main active components of HQZR in rats

The result of researching methodology is that the linear relationship, recovery rate and stability of HQZR 3 kinds of components is good, reproducibility, precision and specificity conform to the requirements of the perfusate sample detection;

Study on the metabolism experiment of the main active components of HQZR in rat liver perfusion, we can clearly find the metabolic curve of the main active components of HQZR in rats after 60 minutes. And from the beginning of the perfusion 10 min compared with the control group, the rate of metabolism of phenobarbital sodium group was fast, but the rate of metabolism of ketoconazole group was slow. As time goes on, this trend is becoming more and more significant.

2. A study on effects of HQZR on the activity of CYP450 in rats

Compared with the control group, the weight of rats administered groups were not significantly different ($P>0.05$); The liver weight of phenobarbital sodium group was increased ($P<0.05$), other groups was no significant difference ($P>0.05$). The liver organ coefficient of the phenobarbital sodium group increased significantly ($P<0.01$), other groups was no significant difference ($P>0.05$); At the same time, in the determination of liver microsomal protein concentration test results, compared with the blank control group, the rats were not significantly changed ($P>0.05$); However, in the determination of rat CYP450 enzyme content of the experimental results, compared with the blank control group, the content of CYP450 in the phenobarbital sodium group was significantly increased ($P<0.001$), and the content of CYP450 in the ketoconazole group and HQZR group was significantly decreased ($P<0.05$).

Key words: Huaqizeren(HQZR), Metabolism, CYP450 enzymes

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