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论文

五味子醇甲在大鼠肝微粒体内的代谢动力学和性别差异五味子醇甲在大鼠肝微粒体内的代谢动力学和性别差异

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摘要：

体外研究五味子醇甲(schizandrin，SZ)在大鼠肝微粒体内的代谢动力学和性别差异。制备正常雌、雄大鼠肝微粒体，与SZ共同温孵，以高效液相色谱法测定SZ及其代谢产物。SZ在雄鼠肝微粒体内代谢反应的最大速率V_{max}、米氏常数K_m和清除率Cl_{int}分别为(21.88±2.30) μmol·L^{-1}·min^{-1}·mg^{-1}(protein)，(389.00±46.26) μmol·L^{-1}和(0.056 3±0.000 7) min·mg^{-1}(protein)；在雌鼠肝微粒体内代谢反应的最大速率V_{max}、米氏常数K_m和清除率$Clint$分别为(0.61±0.07) μmol·L^{-1}·min^{-1}·mg^{-1}(protein)，(72.64±13.61) μmol·L^{-1}和(0.008 4±0.000 8) min·mg^{-1}(protein)，雌、雄鼠肝微粒体内SZ的主要代谢物不同，分别为7,8-顺二羟基五味子醇甲(M1)和7,8-顺二羟基-2-去甲基五味子醇甲(M2b)。酮康唑、奎尼丁和奥芬得林对SZ的在雌、雄大鼠肝微粒体内代谢均有不同程度的抑制作用，西咪替丁对其在雄鼠肝微粒体内的代谢也有一定的抑制作用。SZ在雌、雄大鼠肝微粒体中代谢动力学及代谢产物存在明显的性别差异，这种差异可能主要是由CYP3A和CYP2C11在大鼠肝微粒体内的性别差异引起的。

关键词： 五味子醇甲；代谢；性别差异；细胞色素P450；肝微粒体

Enzyme kinetics of schizandrin metabolism and sex differences in rat liver microsomes

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Abstract:

To study the enzyme kinetics of schizandrin metabolism in different gender in rat liver microsomes, liver microsomes were prepared from male or female rats. Schizandrin was incubated with rat liver microsomes. Schizandrin and its metabolites were isolated and identified by HPLC-UV method. V_{max}, K_m and Cl_{int} of schizandrin in male and female rat liver microsomes were (21.88±2.30) and (0.61±0.07) μmol·L^{-1}·min^{-1}·mg^{-1}(protein), (389.00±46.26) and (72.64±13.61) μmol·L^{-1}, (0.056 3±0.000 7) and (0.008 4±0.000 8) min·mg^{-1}(protein), respectively. The major metabolites of schizandrin in female and male rat liver microsomes were 7,8-dihydroxy-schizandrin (M1) and 7,8-dihydroxy-2-demethyl schizandrin (M2b), respectively. Ketoconazole, quinidine, and orphenadrine had different level effects on schizandrin metabolism in both male and female rat liver microsomes, and cimetidine still had some inhibitory effect in male liver microsomes. CYP3A and CYP2C11 may be the main P450 enzymes in schizandrin metabolism and their difference in rat liver microsomes may be the main reason for the sex difference of metabolic enzyme kinetics and metabolites of schizandrin in rats.

Keywords: metabolism sex difference cytochrome P450 liver microsome schizandrin

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