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论文

双环醇在大鼠和人肝微粒体的代谢

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摘要：

目的研究参与双环醇代谢的主要药物代谢酶及代谢动力学参数，分离鉴定双环醇代谢产物。方法双环醇与大鼠和人肝微粒体进行温孵，以高效液相色谱、质谱、核磁共振技术检测并分离鉴定双环醇及其代谢产物。结果双环醇在地塞米松诱导大鼠肝微粒体中的代谢速率显著高于正常大鼠肝微粒体，酮康唑可显著抑制双环醇的代谢。双环醇主要代谢产物为:4-羟基-4′-甲氧基-6-羟甲基-6′-甲氧羰基-2，3，2′，3′-双亚甲二氧基联苯和4-甲氧基-4′-羟基-6-羟甲基-6′-甲氧羰基-2，3，2′，3′-双亚甲二氧基联苯。结论双环醇在大鼠和人肝微粒体的主要代谢产物为4-羟基-4′-甲氧基-6-羟甲基-6′-甲氧羰基-2，3，2′，3′-双亚甲二氧基联苯和4-甲氧基-4′-羟基-6-羟甲基-6′-甲氧羰基-2，3，2′，3′-双亚甲二氧基联苯，细胞色素P450 3A主要参与双环醇代谢。

关键词： 双环醇 代谢产物 细胞色素P450 肝微粒体

Metabolism of bicyclol in rat and human liver microsomes *in vitro*

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Abstract:

AimTo study the drug metabolizing enzymes involved in the metabolism of bicyclol and identify the major metabolites of bicyclol in rat and human liver microsomes. MethodsBicyclol was incubated with rat and human liver microsomes. The metabolites of bicyclol were isolated by HPLC and identified by MS and ^{1}H NMR. ResultsThe metabolic rate of bicyclol in DEX-induced rat liver microsomes was obviously higher than that in untreated microsomes, while it was much lower in human liver microsomes. Ketoconazole was capable to exhibit strong inhibition (>90%) on bicyclol metabolism. Two metabolites of bicyclol were identified to be 4-hydroxy-4′-methoxy-6-hydroxy-methyl-6′-methoxycarbonyl-2,3,2′,3′-bis (methylene-dioxy) biphenyl and 4-methoxy-4′-hydroxy-6- hydroxymethyl-6′-methoxycarbonyl-2,3,2′,3′-bis(methylene-dioxy) biphenyl. ConclusionCYP3A was considered as the major catalyst involved in bicyclol metabolism *in vitro* and two metabolites of bicyclol in rats were identified as 4-hydroxy-4′-methoxy-6-hydroxy-methyl-6′-methoxycarbonyl-2,3,2′,3′-bis(methylene-dioxy) biphenyl and 4-methoxy-4′-hydroxy-6- hydroxymethyl-6′-methoxycarbonyl-2,3,2′,3′-bis(methylene-dioxy) biphenyl.

Keywords: metabolite cytochrome P450 liver microsomes bicyclol

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