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论文

尼卡地平在人肝微粒体代谢的酶动力学

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摘要:

目的 体外研究人肝微粒体中尼卡地平代谢的酶动力学及选择性的CYP酶抑制剂对其代谢的影响。方法 用人肝微粒体研究尼卡地平代谢的酶动力学,探讨CYP酶的选择性抑制剂对其代谢的影响及参与其脱氢代谢的CYP酶。结果 结果表明CYP3A的抑制剂酮康唑可以显著地抑制尼卡地平的脱氢代谢,使尼卡地平的代谢速率下降。CYP2E1的抑制剂DDC仅在高浓度时抑制尼卡地平二氢吡啶环脱氢代谢,而其他CYP特异性抑制剂对尼卡地平二氢吡啶环脱氢代谢没有明显的影响。结论 CYP3A参与了尼卡地平的代谢,CYP3A的抑制剂可能会与尼卡地平发生代谢相互作用,从而降低尼卡地平的代谢速率

关键词: 尼卡地平 微粒体 药代动力学

ENZYME KINETICS OF NICARDIPINE METABOLISM IN HUMAN LIVER MICROSOMES

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Abstract:

AIM To study the enzyme kinetics of nicardipine metabolism and the effects of selective CYP450 inhibitors on the metabolism of nicardipine in human liver microsomes. METHODS Human liver microsomes were used to perform enzyme kinetic studies. Various selective CYP inhibitors were used to investigate their inhibitory effects on the metabolism of nicardipine and the principal CYP isoform involved in dehydrogenation of nicardipine dihydropyridine ring. RESULTS The dehydrogenation of nicardipine was significantly inhibited by Ketoconazole. High level diethyldithiocarbamate was also shown to inhibit the above metabolism. While phenacetin, quinidine, sulfaphenazole and tranylcypromine showed little inhibitory effect on the dehydrogenation of nicardipine. CONCLUSION CYP3A was shown to be involved in nicardipine metabolism. CYP3A inhibitors and nicardipine may interact metabolicly, thereby reducing the rate of nicardipine metabolism.

Keywords: microsome pharmacokinetics nicardipine

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