

论文
聚氧乙烯醚类表面活性剂对大鼠体内细胞色素P450 3A活性的影响

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摘要:

为研究药用辅料对大鼠体内细胞色素P450 3A(CYP3A)药酶活性的影响, 大鼠分别灌胃生理盐水、酮康唑(75 mg·kg⁻¹·d⁻¹), 曲拉通X-100(30 mg·kg⁻¹·d⁻¹)、聚氧乙烯蓖麻油(EL35, 150 mg·kg⁻¹·d⁻¹)、聚氧乙烯氢化蓖麻油(RH40, 150 mg·kg⁻¹·d⁻¹) 5 d后, 12 h禁食再经十二指肠给予上述试药, 20 min后给予咪哒唑仑作为探针。分别测定咪哒唑仑及其代谢物1'-羟基咪哒唑仑在大鼠体内的血药浓度并计算其药代动力学参数, 比较曲拉通X-100、EL35和RH40处理组与生理盐水组的药代动力学差异。结果显示, 阳性对照药酮康唑对CYP3A有明显的抑制作用; 而曲拉通X-100、EL35和RH40使1'-羟基咪哒唑仑与咪哒唑仑的AUC_{0-∞}比值分别从1.14降至0.90、1.03和0.64, 统计学分析表明曲拉通X-100和EL35对CYP3A没有明显的抑制作用, 而RH40对CYP3A有明显的抑制作用。因此, 在药物制剂研究及临床应用中, RH40有可能影响经细胞色素P450 3A转化的药物代谢及处置, 增加药物的生物利用度, 对药物的临床应用产生显著影响。

关键词: 细胞色素P450 3A 曲拉通X-100 聚氧乙烯蓖麻油 聚氧乙烯氢化蓖麻油 咪哒唑仑 高效液相色谱法 药代动力学

Effect of polyoxyl ether analogous surfactants on the activity of cytochromes P450 3A in rats *in vivo*

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Abstract:

To evaluate the effects of *p*-octyl polyethylene glycol phenyl ether (Triton X-100), polyoxyl 35 castor oil (EL35) and polyoxyl 40 hydrogenated castor oil (RH40) on the activity of Cytochrome P450 3A (CYP3As) *in vivo*. Rats were administered with saline, ketoconazole (75 mg·kg⁻¹·d⁻¹), Triton X-100 (30 mg·kg⁻¹·d⁻¹), EL35 (150 mg·kg⁻¹·d⁻¹) and RH40 (150 mg·kg⁻¹·d⁻¹) intragastrically for 5 consecutive days, and then given midazolam 10 mg·kg⁻¹ 20 min after the last treatment of ketoconazole or three surfactants with the same dose through duodenal administration. Pharmacokinetics parameters for midazolam and its metabolite 1'-hydroxymidazolam were estimated from the plasma concentration-time data by a noncompartmental approach. The results showed that multiple dose administration of Triton X-100, EL35 and RH40 decreased the ratios of 1'-hydroxymidazolam and midazolam AUC_{0-∞} from 1.14 to 0.90, 1.03 and 0.64, respectively. In contrast, multiple dose administration of ketoconazole caused the ratios of 1'-hydroxymidazolam and midazolam a significant decrease to 0.50. This study indicated that Triton X-100 and EL35 would have no inhibition on CYP3A, while RH40 had significant inhibition on CYP3A. Therefore, RH40 might be used to prepare drug formulations in pharmaceutical industry and would increase the bioavailability of some drugs transformed by CYP3As and further lead to significant clinical pharmacologic effects.

Keywords: *p*-octyl polyethylene glycol phenyl ether polyoxyl 35 castor oil polyoxyl 40 hydrogenated castor oil midazolam HPLC pharmacokinetics Cytochrome P450 3A

收稿日期 2007-10-18 修回日期 网络版发布日期

DOI:

基金项目:

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2. 王宇光;王升启;高月.PXR受体调控的CYP3A诱导及其在药物代谢中的重要意义[J]. 药学学报, 2006,41(1): 1-1

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