药学学报 2007, 42(9) 973-977 DOI: ISSN: CN:

论文

HPLC-MS/MS法测定血浆中莪术醇浓度及Beagle犬体内的药代动力学研究

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摘要：

建立HPLC-MS/MS法测定血浆中莪术醇含量，研究其在Beagle犬体内药代动力学特征。Beagle犬9只，随机分为3组，分别静脉推注不同剂量(7.5，10.0和12.5 mg·kg^{-1})的莪术油脂肪乳剂，按设定时间股静脉取血，采用HPLC-MS/MS法测定莪术油脂肪乳剂主要有效成分莪术醇血浆浓度，计算莪术醇药代动力学参数。莪术醇血浓度线性范围为0.25～100 ng·mL^{-1}；相对回收率为91.33%～103.17%，绝对回收率为31.61%～37.20%，单次静脉注射不同剂量莪术油脂肪乳剂后，其主要有效成分莪术醇Beagle犬体内代谢过程基本符合三室模型，莪术醇主要药代动力学参数AUC呈明显剂量相关性。本法操作简便、快速、灵敏度高、专属性强，可用于莪术醇体内药代动力学的研究。

关键词： 莪术油脂肪乳剂 莪术醇 药代动力学 HPLC-MS/MS

Determination of curcumol in plasma by HPLC-MS/MS method and its pharmacokinetics in Beagle dogs

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Abstract:

To establish a high performance liquid chromatography (HPLC) coupled with tandem mass spectrometry quantitative detection method for the determination of curcumol, the main ingredient of zedoary turmeric oil fat emulsion, and investigate its pharmacokinetics in Beagle dogs, nine healthy Beagle dogs were divided into three groups, and blood samples were collected at scheduled time points after intravenous injection of 7.5, 10 and 12.5 mg·kg^{-1} zedoary turmeric oil fat emulsion. The concentrations of curcumol were determined and pharmacokinetics was calculated. A good linearity was obtained from 0.25 to 100 ng·mL^{-1} in plasma. The relative recoveries were from 91.33% to 103.17%, and the absolute recoveries were from 31.61% to 37.20%. The intra-day and inter-day variances (RSD) were <15%. The main pharmacokinetic parameters of curcumol after intravenous injection of 7.5, 10 and 12.5 mg·kg^{-1} zedoary turmeric oil fat emulsion were as follows, $T_{1/2}$: (2.0±0.4), (1.7±0.2) and (2.3±0.8) h, $AUC_{0-\infty}$: (15.1±2.7), (18.3±2.0) and (29.5±4.0) ng·mL^{-1}·h; MRT: (0.9±0.1), (0.8±0.2) and (0.8±0.1) h, CL: (21.9±4.0), (24.9±6.0) and (18.4±1.2) L·h^{-1}·kg; V_d: (65.4±26.5), (62.0±13.4) and (61.2±19.8) L·kg^{-1}, respectively. The developed method was rapid, highly sensitive and specific and could be used in curcumol pharmacokinetic studies *in vivo*. A three-compartment model was best fit to the plasma concentration-time curves obtained in Beagle dogs and the plasma AUC was increased proportionally with doses.

Keywords: curcumol pharmacokinetics HPLC-MS/MS zedoary turmeric oil fat emulsion

收稿日期 2007-01-05 修回日期 网络版发布日期

DOI:

基金项目:

通讯作者: 郭瑞臣

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