质谱学报 2009 30 (增刊): 86-88 ISSN: 1004-2997 CN: 11-2979/TH

医学研究

LC-MS/MS法测定犬血浆中脂质纳米粒10-羟基喜树碱浓度

高瑞娜;钟大放;邓泮;陈笑艳

中国科学院上海药物研究所，上海 201203

收稿日期 修回日期 网络版发布日期:

摘要

关键词

分类号

Determination of Liposomal 10-Hydroxycamptothecin in Dog Plasma by LC-MS/MS

GAO Rui-na, ZHONG Da-fang, DENG Pan, CHEN Xiao-yan

Shanghai Institute of Materia Medica, Chinese Academy of Sciences, Shanghai 201203, China

Abstract 10-hydroxycamptothecin，camptothecin analogue，is an antitumor agent that targets the nuclear enzyme topoisomerase I. 10-hydroxycamptothecin is injected by sodium salt form in clinic, and myelosuppression is the major toxicity. To enhance water solubility and reduce the toxicity, lipid nanoparticle which is water-soluble was designed. The quantitative analyses of liposomal and total 10-hydroxycamptothecin in dog plasma were developed and validated by liquid chromatographic-tandem mass spectrometry(LC-MS/MS). Two preparation procedures were developed to separate liposomal 10-hydroxycamptothecin, one was solid phase extraction, the other was liquid-liquid extraction. The analyte and internal standand(camptothecin) were separated on a Zorbax SB-C_{18} column using the mobile phase consisting of *V*(acetonitrile):*V*(water):*V*(formic acid)＝70:30:0.2. Electropray ionization source of MS was applied and operated in positive ion mode. The peak area of the m/z 365→321 transition of 10-hydroxycamptothecin and that of m/z 349→305 transition of the IS were measured. The linear calibration curve for liposmal 10-hydroxycamptothecin is obtained in the concentration range of 1.00-1 000μg L^{-1}, and that for total 10-hydroxycamptothecin is obtained in the concentration range of 1.00-2 000μg L－1. The recoveries of solid phase extraction and liquid-liquid extraction methods are 48.1%-52.4% and 79.6%-83.0%, respectively. This validated LC-MS/MS assay is successfully applied to pharmacokinetic study of 10-hydroxycamptothecin loaded lipid nanoparticle in dogs after administration single dosages of 0.5, 1, 2 mg kg^{-1} and multiple dosage of 1.0 mg kg^{-1} d^{-1} 10-hydroxycamptothecin lipid nanoparticle.

Key words 10-hydroxycamptothecin _ liquid chromatographic-tandem mass spectrometry _ lipid nanoparticle _ non-clinical pharmacokinetics

DOI

通讯作者