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论文

LC-MS/MS法测定大鼠口服延胡索提取物后延胡索乙素和脱氢紫堇碱的药代动力学

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摘要：

建立检测大鼠血浆中延胡索乙素和脱氢紫堇碱分析方法，并应用有机溶剂沉淀法提取含药血浆中的生物碱类成分，色谱采用SB-C_{18}反相柱，流动相为乙腈-乙酸铵(0.1%乙酸)梯度洗脱，质谱采用多反应监测(MRM)方式进行正离子检测，用于定量分析的例子对分别为*m/z* 356.2→*m/z* 191.9(延胡索乙素)和*m/z* 366.2→*m/z* 350.2(脱氢紫堇碱)。测定血浆中这两种成分的线性范围均为1.0～1 000 ng·mL^{-1}，定量下限为1.0 ng·mL^{-1}，相关系数分别为0.994和0.992，延胡索乙素的回收率为71.71%～91.59%，脱氢紫堇碱的回收率为83.27%～103.15%，方法的精密度、准确度和稳定性均符合要求。结果显示，该法选择性强、灵敏度高、操作简便，适用于血浆延胡索乙素和脱氢紫堇碱的药代动力学研究。

关键词： 延胡索乙素 脱氢紫堇碱 药代动力学 液质联用

Pharmacokinetic studies of tetrahydropalmatine and dehydrocorydaline in rat after oral administration of Yanhusuo extraction by LC-MS/MS method

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Abstract:

A sensitive liquid chromatography-tandem mass spectrometric (LC-MS/MS) method was developed and validated for the quantification of tetrahydropalmatine (THP) and dehydrocorydaline (DHC) in rat plasma. The compounds were simply pretreated by protein precipitation using acetone. Chromatographic separation was achieved on a reversed-phase SB-C_{18} column with the mobile phase of acetonitrile-ammonium acetate (0.1% acetic acid) and step gradient elution resulted at a flow rate of 0.80 mL·min^{-1}. A tandem mass spectrometer equipped with electrospray ionization source was used as detector and operated in the positive ion mode. Quantification was performed using multiple reaction monitoring (MRM) of the transitions *m/z* 356.2→*m/z* 191.9 and *m/z* 366.2→*m/z* 350.2 for THP and DHC respectively. The method showed excellent linearity over the concentration range 1-1 000 ng·mL^{-1} of two components (r=0.994 for THP and r=0.992 for DHC). The low limits of quantification were both 1 ng·mL^{-1}. The extract recoveries of analytes were from 71.71% to 91.59% for THP and from 83.27% to 103.15% for DHC. The precisions, the accuracy and the stability of the analytes meet the requirements. The method was applied to a pharmacokinetic study of THP and DHC after oral administration of the total alkaloid extraction of Rhizoma Corydalis (Yanhusuo). The AUC were (1.90±0.04), (2.58±0.08) and (4.34±0.19) mg·L^{-1}h for low, medium and high doses of THP, respectively. While the DHC concentrations in plasma of low dose and medium dose were too lower to be detected, the AUC of high dose was (0.089 6±0.000 2) mg·L^{-1}h.

Keywords: tetrahydropalmatine pharmacokinetics LC-MS/MS dehydrocorydaline

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