

论文

液相色谱-质谱联用法测定犬血浆中盐酸关附甲素的血药浓度及其药代动力学

吴民淑;王广基;蔡晓辉;孙建国;刘静涵

中国药科大学 1. 药代研究中心, 2. 植化教研室, 江苏 南京 210009

摘要:

目的建立用于测定盐酸关附甲素血药浓度的液相色谱-质谱联用分析方法,并探讨关附甲素在犬体内的药代动力学。方法犬6只iv盐酸关附甲素7.56 mg·kg⁻¹后采集一系列血样,利用LC-MS联用系统测定血浆药物浓度,并用3P87软件拟合求算药代动力学参数。结果盐酸关附甲素浓度0.42~21.2 μg·mL⁻¹线性关系良好(γ=0.9994)。绝对回收率高于80%,日内、日间RSD均小于15%,符合生物样品分析要求。6只犬iv盐酸关附甲素7.56 mg·kg⁻¹后的血药浓度-时间曲线符合开放三室模型,其快分布相、慢分布相和末端消除相的半衰期(t_{1/2}^β, t_{1/2}^α和t_{1/2}^γ)分别为0.07, 1.5和13.5 h。曲线下面积(AUC)、中央室分布容积(V_c)和血浆清除率(CL_s)分别为61.43 μg·h·mL⁻¹, 0.37 L·kg⁻¹和0.14 L·kg⁻¹·h⁻¹。结论建立的LC-MS联用方法专属性强,灵敏度高,可用于盐酸关附甲素的体内定量分析。

关键词: 关附甲素 液相色谱-质谱 药代动力学

DETERMINATION OF GUANFU BASE A HYDROCHLORIDE IN PLASMA BY LC-MS METHOD AND ITS PHARMACOKINETICS IN DOGS

WU Min-shu; WANG Guang-ji; CAI Xiao-hui; SUN Jian-guo; LIU Jing-han

Abstract:

AIMTo establish an analytical method for determination of guanfu base A (GFA) concentration in plasma and to study its pharmacokinetic profile in dogs. METHODSix dogs were given a 7.56 mg·kg⁻¹ dose intravenously. Blood samples were collected at various time-points after drug administration. Analytical method based on liquid chromatography-mass spectrometry (LC-MS) was established to determine the plasma concentration of GFA. Pharmacokinetic evaluation was carried out using the 3P87 program. RESULTThe calibration curves were linear over the concentration range from 0.42 μg·mL⁻¹ to 21.2 μg·mL⁻¹ (γ=0.9994). The intra-day and inter-day precisions were generally good (<15%) at low, medium and high concentrations. The overall recovery of the analytes was more than 80%. Six dogs were given an iv dose of 7.56 mg·kg⁻¹ of GFA hydrochloride, an open three compartment model best described the concentration-time profiles for GFA. The half-lives for the rapid and slow distribution phase and terminal elimination phase (t_{1/2}^β, t_{1/2}^α and t_{1/2}^γ) were 0.07 h, 1.5 h, and 13.5 h, respectively. The total area under the plasma concentration-time curve (AUC), the volume of the central compartment (V_c), and plasma clearance (CL_s) were 61.43 μg·h·mL⁻¹, 0.37 L·kg⁻¹ and 0.14 L·kg⁻¹·h⁻¹, respectively. CONCLUSIONThe analytical method was shown to be sensitive, specific, rapid and reproducible, and was suitable for pharmacokinetic studies of GFA.

Keywords: liquid chromatography-mass spectrometry pharmacokinetics guanfu base A

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作者简介:

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