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生物药剂学与药物动力学

HPLC-MS法测定伪麻那敏渗透泵片犬体内马来酸氯苯那敏的药物动力学参数

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摘要

目的 建立动物血浆中马来酸氯苯那敏浓度的HPLC-MS分析方法，用以测定健康犬口服伪麻那敏渗透泵制剂后的血药浓度，估算受试制剂的药物动力学参数。方法 血浆中加入甲醇-水（体积比为50∶50）和金刚烷胺内标溶液，混匀后经氢氧化钠碱化，用正己烷-二氯甲烷-异丙醇（体积比为2.0∶1.0∶0.1）提取，提取液氮气流吹干，残留物用流动相复溶，供分析用。色谱系统：Diamonsil C18柱（5 μm，250 mm×4.6 mm）；甲醇-水-甲酸（体积比为40∶60∶1）为流动相；流速：1.0 mL?min-1；柱温：20 ℃。结果 血浆中内源性物质对样品测定无干扰。马来酸氯苯那敏的线性为0.7~28.0 μg?L-1，最低质量浓度为 0.7 μg?L-1，提取回收率为71.3%。日内、日间RSD均小于10.0%。测定6只比格犬口服受试制剂后的血药质量浓度经时过程，受试制剂及参比制剂的主要药物动力学参数分别为：t1/2=4.79 h；ρmax=5.95 μg?L-1；tmax=4.83 h；AUC0-t=37.69 μg?h?L-1。结论 统计学表明受试制剂马来酸氯苯那敏具有渗透泵的特征。

关键词 药剂学 伪麻那敏渗透泵片 HPLC-MS 马来酸氯苯那敏

分类号 R944

The determination of chlorpheniramine maleate in beagle dog plasma with HPLC-MS method after oral administration of pseudoephedrine hydrochloride and chlorpheniramine maleate osmotic pump tablets

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Abstract

Objective To develop a sensitive high performance liquid chromatography-mass spectrometry(HPLC-MS) method for the determination of the plasma concentration of chlorpheniramine maleate in healthy dogs after oral administration of pseudoephedrine hydrochloride and chlorpheniramine maleate osmotic pump tablets in order to investigate the pharmacokinetic parameters of the test preparation. Methods Methanol-water(the ratio of volume was 50:50) and adamantanamine solution as internal standard were added into plasma，which were mixed uniformly and adjusted with NaOH to alkaline solution. Then it was extracted with n-hexane: dichloromethane (DCM):isopropanol(the ratio of volume was 2.0:1.0:0.1) and the extract obtained was evaporated to dryness under nitrogen flow and the residue which was resolved with mobile phase was stored for analysis use. The chromatographic system consisted of Diamosil C18 column(5 μm，250 mm×4.6 mm I.D.) at a fixed column temperature of 20℃and methanol:water:formic acid(the ratio of volume was 40:60:1) as mobile phase with the flow rate of 1.0 mL?min-1. SIM was applied for the mass measuring.Chlorphenamine with a m/z of 275.1 and the internal standard with a m/z of 152.2 were used for the quantitative analysis. Results The endogenous substances in plasma had no interference on the measurement of the sample. Assay linearity was obtained in the range of 0.7~28.0 μg?L-1with the limit of quantitation (LOQ) of 0.7μg?L-1 and a extract recovery of 71.3%. The intra-day and inter-day relative standard deviations (RSD) were both lower than 10.0%. The main pharmacokinetic parameters of the test preparation were determined in eight beagle dogs which were administered orally with the test preparation， with t1/2=4.79 h，ρmax=5.95 μg?L-1， tmax=4.83 h，AUC0-t=37.69 μg?h?L-1 . Conclusions It is shown that method is sensitive and accurate ,and the chlorpheniramine maleate test preparation has the characteristics of osmotic pump.

Key words pharmaceutics chlorphenamine maleate osmotic pump tablet HPLC-MS chlorpheniramine maleate
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