

论文

RP-HPLC法测定家兔血浆中甲苯喹派浓度和药代动力学参数

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摘要:

本文建立了以紫外230nm波长检测的反相高效液相色谱法(RP-HPLC)测定家兔血浆中甲苯喹派浓度。填料使用LiChrosorb RP-C18,流动相为甲醇-水-三乙胺-磷酸(63:37:1:0.8 v/v),血样(或尿样)经碱化后用乙醚提取,再以0.2 mol/L硫酸回提,进样。方法回收率为99.84±3.10(SD)%;天内、日间精密度平均CV为4.12%及3.95%(n=5);最低检测限3ng。经提取的标准线性浓度在25~2000 ng/ml范围内,Y=0.002865X-0.01346,r=0.9999,内源性物质及可能的合并用药不干扰色谱测定。文内用质谱法鉴定血样中甲苯喹派色谱峰纯度,并由尿样分析对其主要代谢物予以初步验证。本法可应用于药代动力学参数测定。家兔按8mg/kg静注后,药一时曲线符合二室模型T_{1/2}=4.8008±1.1522(SD)h。

关键词: 甲苯喹派 反相高效液相色谱法 药代动力学

RP-HPLC DETERMINATION OF 1-(P- METHYLPHENYL-2- (2-PIPERIDINOACETYL-1,2,3,4-TETRAHY-DROISOQUINOLINE HYDROCHLORIDE IN RABBIT PLASMA AND ITS PHARMACOKINETIC PARAMETERS

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Abstract:

A reversed phase high performance liquid chromatographic method (RP- HPLC)was developed for the determination of rabbit plasma levels of 1- (p- methylphenyl-2- (2-piperidinoacetyl) -1, 2, 3,4- tetrahydroisoquinoline hydrochloride(70026), a new antiarrhythmic agent with promising prospects. Its pharmacokinetic parameters were obtained from the rabbit plasma level-time curve meaSured. 70026 plasma sample was determined by extracting with ether and 0.2 mol/L sulfuric acid, chromatographing on LiChrosorb RP -C18 column, and detecting at 230 nm. The mobile phase selected was methanol- water- triethylamine- phosphoric acid (63 : 37 : 1 :0. 8 v/v). The average recovery of the entire procedure from plasma was 99.94±3.10 (SD)% ; the average CV of within-day and between-day were 4. 12% adn 3.95% respectively ; the minimum detection limit was 3 ng ; 70026 plasma concentration ranging from 25~ 2000 ng/ml yielded a good linear relationship with the peak area ratios,Y=0. 002865X-0. 01346, r=0. 9999. No endogeneous interference was found in chromatograms of plasma sample. The purity of chromatographic peak of 70026 was identified and proved by mass spectrometry. In urine sample, the hydrolysate of 70026 was found as the original and bound forms. The rabbit plasma level of 70026 after intravenous administration versus time curve was found to be in correspondence with two-compartment model, T_(1/2)=4. 80+1. 522 (h).

Keywords: RP-HPLC Pharmacokinetics 1-(p-methylphenyl-2- (2-piperidinoacetyl)-1 , 2, 3, 4 - tetrahydroisoquinoline hydrochloride

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