

论文

手性和非手性联用色谱法研究尼卡地平对映异构体兔体内过程的差异性

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摘要:

目的研究尼卡地平(NCD)对映体在家兔体内药代动力学和组织分布的差异性。方法生物样品在碱性条件下,正己烷-醋酸乙酯(1:1)提取,用手性和非手性联用色谱法进行分离分析。结果尼卡地平及其对映体分别在反相色谱系统及手性色谱系统中分离良好,浓度为55-550ng·mL<sup>-1</sup>线性关系良好。对映体的平均日内、日间RSD分别为5.25%和8.97%,回收率分别为99.99%和97.10%;对映体间主要动力学参数T<sub>max</sub>, C<sub>max</sub>和AUC, S-NCD为(2.49±0.03)h, (134±2)ng·mL<sup>-1</sup>和(1082±32)ng·mL<sup>-1</sup>·h, R-NCD为(1.24±0.05)h, (109±2)ng·mL<sup>-1</sup>和(778±22)ng·mL<sup>-1</sup>·h;在主要脏器和细胞中S-NCD的浓度明显高于R-NCD。药代动力学和靶组织分布均有一定差异性。结论尼卡地平对映体兔体内过程包括代谢动力学和靶细胞浓度分布存在着立体差异性。

关键词: 尼卡地平; 对映体; 联用色谱; 手性拆分; 立体选择性

STUDIES ON *IN-VIVO* PROCESS OF THE ENANTIOMERS OF NICARDIPINE IN RABBIT BY COUPLED CHIRAL AND ACHIRAL HPLC

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Abstract:

AIM To study the differences of the pharmacokinetics and tissue distribution of two enantiomers of nicardipine in the rabbit. METHODS Biological samples were diluted by 1 mol·L<sup>-1</sup> NaOH solution and extracted with n-hexane - ethyl acetate (1:1). The concentrations of S-nicardipine and R-nicardipine in samples were determined by coupled achiral C<sub>18</sub> column (150 mm×4.6 mm, 5 μm) and chiral OJ column (250 mm×4.6 mm, 10 μm) chromatography. RESULTS The racemic nicardipine and the enantiomers in sample were separated well by the coupled system. The linear range was 55-550 ng·mL<sup>-1</sup> for both enantiomers. The within-day and between-days RSD (n=5) were 5.25% and 8.97%, and the relative recoveries were 99.99% and 97.10% for R- and S- enantiomer, respectively. The mean T<sub>max</sub>, C<sub>max</sub> and AUC values were (2.49±0.03) h, (134±2) ng·mL<sup>-1</sup> and (1082±32) ng·mL<sup>-1</sup>·h for S-nicardipine and (1.24±0.05) h, (109±2) ng·mL<sup>-1</sup> and (778±22) ng·mL<sup>-1</sup>·h for R-nicardipine. The concentration of S-nicardipine were generally higher than that of R-nicardipine in main target tissues and cells. CONCLUSION There were significant differences between the two enantiomers of nicardipine in rabbit in pharmacokinetics and tissue distribution.

Keywords: enantiomer coupled HPLC chiral separation seteroselectivity nicardipine

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