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论文

SIRT1去乙酰化酶抑制剂引起人乳腺癌MCF-7耐药细胞凋亡的机制

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摘要：

本文建立一种高灵敏度的液质联用方法用于快速测定大鼠血浆中维胺酯的浓度。采用蛋白沉淀法制备样品； 色谱柱为Agilent TC C_{18}柱(150 mm×4.6 mm ID， 5 μm)， 流动相为甲醇-水-甲酸(93∶7∶0.1)， 辛伐他汀作为内标； 在三重四极杆串联质谱仪上， 采用大气压化学离子化(APCI)， 正离子方式选择性离子模式进行监测； 血浆浓度在0.05～50 ng·mL^{-1}线性关系良好， 定量限为10 pg·mL^{-1}， 日内、 日间精密度分别在95.97%～104.43%， RSD在4.63%～10.69%。本文利用该方法对大鼠进行药代动力学研究， 3个剂量 (2.5、 5和10 mg·kg^{-1})大鼠灌胃给药后的药代动力学参数分别为$T_{1/2}$: (11.28±7.23)、 (8.90±3.82)、 (8.01±5.65) h; $AUC_{0-\infty}$: (103.41±61.46)、 (190.23±74.99)、 (421.66±229.20) ng·h·mL^{-1}； MRT: (6.31±0.75)、 (5.98±0.71)、 (6.18±0.97) h； CL/*F*: (30.10±13.67)、 (29.58±10.59)、 (31.18±17.51) L·h^{-1}·kg^{-1}; V_d/*F*: (414.94±159.82)、 (356.16±139.85)、 (369.28±322.72) L·kg^{-1}。

关键词： 维胺酯 LC-APCI-MS/MS 药代动力学

Quantitative determination and pharmacokinetics of retinamido-ester in rat plasma by liquid chromatography-atmospheric pressure chemical ionization-tandem mass spectrometry

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Abstract:

A highly sensitive, rapid and selective liquid chromatography-tandem mass spectrometry (LC-MS/MS) method for the quantitative determination of retinamido-ester in rat plasma was developed and validated. A simplified protein precipitation with acetonitrile was employed for the sample preparation. The separation was carried out on an Agilent TC C_{18} column (150 mm×4.6 mm ID, 5 μm particle size) with the mobile phase consisted of methanol-water-formic acid (93∶7∶0.1). Simvastatin was used as internal standard. The detection was performed on a trap-quadrupole tandem mass spectrometer by selected reaction monitoring (SRM) scan mode *via* atmospheric pressure chemical ionization (APCI). The range of calibration curve was 0.05-50 ng·mL^{-1} and the limit of quantification was 10 pg·mL^{-1}. The intra- and inter-day precision values were between 95.97% and 104.43%, and RSD was between 4.63% and 10.69%, respectively. This method was applied to determine the pharmacokinetic parameters. The main pharmacokinetic parameters of retinamido-ester after oral administration *via* gastric gavage of 2.5, 5, 10 mg·kg^{-1} were as follows, $T_{1/2}$: (11.28±7.23), (8.90±3.82), (8.01±5.65) h; $AUC_{0-\infty}$: (103.41±61.46), (190.23±74.99), (421.66±229.20) ng·h·mL^{-1}; MRT: (6.31±0.75), (5.98±0.71), (6.18±0.97) h; CL/*F*: (30.10±13.67), (29.58±10.59), (31.18±17.51) L·h^{-1}·kg^{-1}; V_d/*F*: (414.94±159.82), (356.16±139.85), (369.28±322.72) L·kg^{-1}, respectively.

Keywords: LC-APCI-MS/MS pharmacokinetics retinamido-ester

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