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实验研究报道

HPLC法测定壳聚糖-聚天冬氨酸-5-Fu纳米粒子在小鼠肝脏中的浓度

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摘要

目的 建立测定小鼠肝脏药物浓度的HPLC法，比较凝胶化法制备的壳聚糖-聚天冬氨酸-5氟尿嘧啶(CTS-Pasp-5-Fu)纳米粒与5-氟尿嘧啶原药在小鼠肝脏中药物浓度。方法 雄性健康昆明小鼠（KW）分为2组，分别灌胃给予5-FU原药及其CTS-Pasp纳米粒，灌胃后0.25、1、2、4、6、8、12、16、24和48h10个时间点取小鼠肝脏，匀浆液用乙酸乙脂提取，氮气挥干，残渣用甲醇溶解后进样，HPLC法测定2组给药组肝脏内药物浓度。结果5-Fu原药组在肝脏中的药物峰浓度出现在灌胃后2h左右。此后肝脏药物浓度逐渐降低,CTS-Pasp-5Fu纳米粒组经小鼠灌胃后,肝脏药物浓度呈现出三峰型,在0.25h即达到一个药物峰浓度,此后峰浓度分别出现在4h和16h左右,16h时候达到最高峰,此后逐渐下降，CS-Pasp-5FU纳米粒的肝脏中药物峰浓度（Cmax）降低，肝脏中药物浓度时间曲线下面积（AUC）明显增加。结论 CS-Pasp-5FU纳米粒能延缓5-Fu在肝脏内的分布。

关键词 5-氟尿嘧啶；壳聚糖；聚天冬氨酸；高效液相色谱法,肝脏药物浓度

分类号

Determination of 5-fluorouracil level in mouse liver after intragastric administration of chitosan-polyaspartic acid-5-fluorouracil nanoparticles by means of HPLC

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Abstract

Objective To establish HPLC assay for the determination of chitosan-polyaspartic acid-5-fluorouracil （5-Fu）in mice liver, and to compare the drug concentration between 5-Fu and CTS-Pasp-5Fu in the liver. Methods One hundred and twenty Kunming mice were randomly divided into two groups. Each group was administrated with 5-Fu or its CTS-Pasp nanoparticles. The liver sample were taken after 0.25，1，2，4，6，8，12，16，24 and 48h .The liver sample was extracted with ethyl acetate and the solvent was evaporated to dryness with N2. The residue was dissolved with methanol.The separation was performed on a Dikma Inertsil ODS column (3.5μm ,250mm×4.6mm) with the mobile phase of acetonitrile- water (3：97)at a flow rate of 0.8mL/min.UV detection wavelength was set at 273nm.. The internal standard was 5-Bru. Results The Cmax of 5-Fu group occurred within 2h and decreased. The CTS-Pasp-5Fu nanoparticles group's concentration curve was triple-apex, the apexes occurred around 0.25h,4 and 16 hours after the administration, then the concentration decreased. The nanoparticles groups' Cmax of 5-Fu in liver was lower than the 5-Fu group, The half-life times(t1/2) was prolonged and the areas under curve (AUC) were higher. Conclusion Compared to 5-Fu, its chitosan nanoparticles can improve the disposition in liver of 5-Fu

Key words 5-fluorouracil polyaspartic acid chitosan high performance liquid chromatography liver concertration

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