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论文

环孢素A pH敏感性纳米粒的制备与大鼠口服药代动力学

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摘要：

目的研究环孢素A(CyA) pH敏感性纳米粒的制备工艺与口服药代动力学性质。方法采用改良的乳化-溶剂扩散技术(QESD)制备CyA pH敏感性纳米粒；经大鼠灌胃给药，HPLC法测定全血药物浓度，计算口服相对生物利用度。结果经3P87程序拟合，确定CyA在大鼠体内的药代动力学过程为二室模型；与Neoral微乳相比，CyA-E100，CyA-L100，CyA-L100-55和CyA-S100纳米粒的相对生物利用度分别为94.8%，115.2%，113.6%和132.5%。结论经统计分析，CyA-S100纳米粒可以显著改善CyA的生物利用度($P<0.05$)，而CyA-L100-55纳米粒，CyA-L100纳米粒和CyA-E100纳米粒与Neoral微乳相比无显著性差异。实验结果表明,pH敏感性纳米粒有望成为促进蛋白、多肽类药物及难溶性药物口服吸收的有效载体。

关键词： 环孢素A pH敏感性纳米粒 口服生物利用度 优特奇 新山地明

Preparation of cyclosporine A pH sensitive nanoparticles and oral pharmacokinetics in rats

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Abstract:

AimTo study the preparation conditions and its oral pharmacokinetic characteristics of cyclosporine A (CyA) pH sensitive nanoparticles. MethodsThe CyA pH sensitive nanoparticles were prepared by the quasi-emulsion solvent diffusion technique (QESD). Male Sprague-Dawley (SD) rats weighing (250±20) g were selected and randomly divided into five groups. The bioavailability of CyA from nanoparticles and Neoral microemulsion were assessed at a dose of 15 $mg\cdot kg^{-1}$ by gavage. The concentration of CyA in whole blood samples was detected by HPLC to evaluate the relative bioavailability of CyA pH sensitive nanoparticles. ResultsThe blood concentration profiles of CyA pH sensitive nanoparticles in rats fitted to two compartment models using 3P87 pharmacokinetic calculation program. Compared with the Neoral microemulsion, the relative bioavailability of CyA was 94.8%, 115.2%, 113.6% and 132.5% for CyA-E100, CyA-L100, CyA-L100-55 and CyA-S100 nanoparticles respectively. ConclusionCyA-S100 nanoparticles was shown to significantly improve the oral bioavailability of CyA compared with Neoral microemulsion ($P<0.05$). While there were no significant differences between Neoral microemulsion and other CyA pH sensitive nanoparticles. With these results, the potential of pH-sensitive nanoparticles for the oral delivery of CyA was confirmed. Furthermore, this formulation approach can be used to improve the oral bioavailability of other poorly soluble and poorly absorbable drugs.

Keywords: pH sensitive nanoparticles oral bioavailability Eudragit Sandimmune Neoral cyclosporine A

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