药学学报 2000, 35(11) 850-853 DOI: ISSN: CN:

论文

胰岛素聚酯微粒的制备及大鼠体内药效学研究

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摘要：

目的 探讨利用一种新型聚酯材料—ε-己内酯-*D*,*L*-丙交酯嵌段共聚物(PCLA)制备微粒型药物载体的可能性。方法 通过双乳化溶剂蒸发技术制备ε-己内酯-*D*,*L*-丙交酯嵌段共聚物微粒(PCLA-MP)，用扫描电镜观察其形态，粒径分析仪(particle analyser)测定粒径；以胰岛素(INS)为模型药物，制备胰岛素聚酯微粒(INS-PCLA-MP)；建立了测定INS包封率的HPLC方法；INS抗体捕捉实验考察PCLA-MP载药机理；以pH 7.4的磷酸盐缓冲液为介质，探讨INS-PCLA-MP体外释药特性；建立了药物致大鼠糖尿病模型，通过葡萄糖氧化酶法(GOD-PAP)测定血糖值来评价INS-PCLA-MP经皮下给药后的降血糖作用；以INS-SOL为对照，计算药理相对生物利用度。结果 制备的微粒大小均匀，表面光滑圆整，平均粒径1.9 μm；INS的包封率为76.46%；抗体捕捉实验证实，被包封的INS中只有小部分(18.25%)分布在MP的表面；INS-PCLA-MP的体外释放曲线包括突释相及随后的缓慢释放相；药效学研究表明，12 u.kg^{-1}的INS-PCLA-MP经糖尿病大鼠皮下给药后具有明显的降血糖作用，药理相对生物利用度为132.95%。结论 PCLA嵌段共聚物作为药物输送系统的载体材料有着良好的前景，PCLA-MP有可能成为一种新型的药物载体。

关键词： ε-己内酯-*D*,*L*-丙交酯嵌段共聚物 微粒 胰岛素 降血糖作用

STUDY ON PREPARATION AND PHARMACODYNAMICS OF INSULIN-LOADED POLYESTER MICROPARTICLES

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Abstract:

AIM To investigate the possibility of using poly (ε-caprolactone-block-*D*,L-lactide) (PLCA) as a kind of materials to prepare the microparticles drug carrier. METHODS PCLA-MP (microparticle, MP) was prepared by double-emulsification solvent evaporation method. Its morphology was examined by scanning electron microscope. Its size diameter was examined by particle analyser. Insulin (INS), as a model drug, was then encapsulated into PCLA-MP (INS-PCLA-MP). HPLC method was established for determining INS in INS-PCLA-MP. An “antibody-capture” procedure was devised for investigating encapsulation mechanism. The *in vitro* release behaviour of INS-PCLA-MP was determined in phosphatic buffer solution (pH 7.4). The diabetic rat model was established and blood glucose levels were measured using glucose oxidase (GOD-PAP) method to evaluate the hypoglycaemic effects after subcutaneous administration of INS-PCLA-MP. The pharmacological bioavailability (PBA) of INS-PCLA-MP was calculated from the area above the curve (AAC) in contrast with INS-solution. RESULTS The mean diameter of INS-PCLA-MP was 1.9 μm, while the encapsulation ratio of INS reached to 76.46%. Only 18.25% encapsulated INS was on the surface of the microparticles, it could be measured by “antibody-capture” experiment. The *in vitro* release curve of INS-PCLA-MP consists of initial rapid release stage followed by slower exponential stage. In pharmacodynamic studies, after subcutaneous administration of INS-PCLA-MP 12 u.kg^{-1}, the hypoglycaemic effect was significant. The PBA of INS-PCLA-MP was 123.08%. CONCLUSION PCLA might become a new drug carrier material in the future.

Keywords: microparticles insulin hypoglycaemic effect poly (ε-caprolactone-block-*D*,*L*-lactide)

收稿日期 2000-01-29 修回日期 网络版发布日期

DOI:

基金项目:

通讯作者: 张强

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