中国药剂学杂志 2005 3 (4): 227-235 ISSN: 1476-8186 CN: 11-5350/TP

生物药剂学与药物动力学

去羟肌苷药质体的制备及其在大鼠体内行为的研究

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收稿日期 2005-4-11 修回日期 2005-6-11 网络版发布日期 2005-7-30 接受日期 2005-5-11

摘要

目的 制备去羟肌苷（ddI）药质体，考察其在大鼠体内的药物动力学和组织分布。 方法 用合成的去羟肌苷两亲性前药胆固醇基琥珀酰去羟肌苷（CS-ddI）通过四氢呋喃注入法制备药质体，透射电子显微镜和原子力显微镜观察其形态和粒径，HPLC法测定静注给药后大鼠血浆及组织中前药和原药的浓度，拟合药-时曲线并考察其组织分布规律。 结果 去羟肌苷药质体是一种管状粒子，粒径约200 nm；CS-ddI的大鼠血浆半衰期为7.64 min，静注后很快集中分布于肝脏中，脾和肺中也有分布；CS-ddI在靶组织内清除缓慢，肝脏中半衰期为10 d。结论 去羟肌苷药质体具有显著的肝靶向性和在靶组织内的缓释效应。

关键词 药剂学 药物动力学 四氢呋喃注入法 高效液相色谱法 组织分布 去羟肌苷药质体

分类号 R94

Preparation and in vivo behavior of didanosine pharmacosomes in rats

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Abstract

Objective To prepare didanosine (ddI) pharmacosomes and investigate the pharmacokinetics and tissues distribution behavior in rats. Methods ddI pharmacosomes were prepared from 5′-cholesterylsuccinyl-dideoxyinosine (CS-ddI), the lipophilic prodrug of ddI, using a THF injection method. Configuration and particle size were observed through TEM and AFM, and in vivo behavior of the pharmacosomes was investigated in rats by determination of CS-ddI and ddI in plasma and tissues with HPLC. Results ddI pharmacosomes were particles of tube-shape with a particle size of about 200 nm; t1/2 of CS-ddI in plasma of rat was 7.64 min, CS-ddI concentrated in liver quickly after iv administration, there were also some in lung and spleen; its elimination from target tissues was slow, t1/2 of CS-ddI in liver was 10 d. Conclusion ddI pharmacosomes show obvious liver targeting and sustained-release effect in the target tissues.

Key words: pharmaceutics; pharmacokinetics; THF injection method; HPLC; tissue distribution; didanosine pharmacosomes

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DOI:

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