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茶碱酰化改性壳聚糖骨架片体外释药影响因素考察

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摘要
目的 以茶碱为模型药物，研究酰化改性壳聚糖不溶性缓释骨架片的体外释药行为。方法 以酰化改性壳聚糖为辅料，采用直接压片法制备茶碱缓释骨架片。考察载药量、填充剂种类和用量、硬度、辅料粒径等因素对药物释放的影响。结果 药物的释放速率随载药量的增加而加快；乳糖作为填充剂可得到稳定的释药速率，调节乳糖与药物的比例可获得理想的释药行为；在所考察的硬度范围内，释药速率随硬度的增加而减慢；辅料粒径小于180 μm 时，释放以扩散为主，缓释良好；粒径为180~250 μm 和250~380 μm 时，片芯溶蚀剧烈，释药较快。结论 新型疏水改性壳聚糖具有良好的控制药物释放的性质，可作为茶碱口服缓释制剂的骨架材料使用。

关键词 药剂学 不溶性骨架材料 体外释药 酰化改性壳聚糖 茶碱

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Factors influencing in vitro release of theophylline from acylated modified chitosan matrix tablets

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Abstract
Objective To investigate the in vitro drug release kinetics from hydrophobic acylated modified chitosan matrix tablets using theophylline as a model drug. Methods Theophylline sustained-release tablets were prepared using 3-O-acetyl-6-O-steartyl-N-phthaloylchitosan(CTS18) as insoluble matrix material by direct compression. Factors influencing the drug release rate, including drug loading, species and amount of additives, hardness, particle size were studied. Results The release rate increased with increasing drug loading. Steady drug release rate could be obtained using lactose as the additive. Reasonable release profile could be acquired by adjusting the amount of lactose. The release rate decreased with the increase of hardness in the range investigated. When the particle diameter of CTS18 was less than 180 μm, the main release mechanism was diffusion and theophylline was released in a controlled manner. Tablets prepared with CTS18 of particle size 180-250 or 250-380 μm eroded seriously and drug release rate was fast. Conclusions Suitable controlled release profiles could be obtained with the new hydrophobic acylated chitosan derivative, which could be used as insoluble tablet matrix material for controlling theophylline release.

Key words pharmaceutics insoluble matrix material in vitro drug release acylated modified chitosan theophylline

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