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论文

凝集素修饰乳酸-羟基乙酸共聚物纳米粒的制备及体外黏附性能评价

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摘要：

本文分别以麦胚凝集素、西红柿凝集素和天门冬豌豆凝集素为表面修饰材料，采用碳化二亚胺法制备了不同凝集素修饰的乳酸-羟基乙酸共聚物纳米粒。分别考察了活化剂的用量、活化时间、凝集素的用量、孵化时间对凝集素修饰纳米粒的影响，由此确定最佳制备条件。福林-酚法测定凝集素的修饰率为(18.97±2.9)%～(20.15±2.4)%，纳米粒表面的凝集素浓度为(9.46±1.45)～(10.05±1.19) μg·mg^{-1}。采用黏蛋白结合法对纳米粒的体外黏附性能进行评价，结果表明纳米粒与黏蛋白溶液在室温下孵化60 min后结合反应达到平衡，此时不同凝集素修饰纳米粒的黏蛋白结合量分别为15.5%，12.1%和11.8%，是普通纳米粒黏蛋白结合量的2.4～3.2倍。经Langmuir方程拟合计算得到各结合速率常数分别为2.373×10^{-3}，1.536×10^{-3}和1.714×10^{-3} (μg·min/mL)$^{-1}$。不同凝集素修饰纳米粒与黏蛋白的结合可被该凝集素的特异性单糖抑制。实验结果表明，与普通纳米粒相比，凝集素修饰纳米粒与黏蛋白的体外黏附能力显著增强，预计其口服后可与胃肠黏膜表面产生黏附作用，从而延长制剂在胃肠道内的滞留时间。

关键词： 凝集素 乳酸-羟基乙酸共聚物 纳米粒 黏蛋白 黏附性能

Preparation of lectin-conjugated PLGA nanoparticles and evaluation of their *in vitro* bioadhesive activity

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Abstract:

In this study, wheat germ agglutinin (WGA), tomato lectin (TL) and asparagus pea lectin (AL) were covalently coupled to conventional poly lactic-co-glycolic acid (PLGA) nanoparticles using a carbodiimide method to take the bioadhesive properties. The influences of the amounts of activating agents and lectins, as well as the activating time and incubating time on the effect of lectin conjugating were investigated to optimize the preparation conditions. The mean diameters of the performed nanoparticles with or without lectin conjugation ranged from (140.7±5.7) nm to (245.6±18.3) nm. The yields of lectin conjugating and the lectin surface concentrations on nanoparticles were determined by Lowry's methods, and were calculated to be (18.97±2.9)%-(20.15±2.4)% and (9.46±1.45)-(10.05±1.19) μg·mg^{-1}, respectively. The *in vitro* bioadhesive activities of nanoparticles were evaluated by pig gastric mucin (PM) binding experiments. After incubation at room temperature for 60 min, the equilibria of binding between nanoparticles and PM reached. The percentages of the bulk PM which had interacted with different lectin-conjugated PLGA nanoparticles were 15.5%, 12.1% and 11.8%, respectively. The conjugation of lectin enhanced the interaction about 2.4-3.2 fold compared with that of the non-conjugated one. A mathematical model was used based on the Langmuir equation, and the rate constants of interaction (k) were calculated to be 2.373×10^{-3}, 1.536×10^{-3} and 1.714×10^{-3} (μg·min/mL)$^{-1}$, respectively. These interactions could be competitively inhibited by their corresponding sugars of lectins. The results suggested that lectin-conjugated PLGA nanoparticles greatly promoted the interaction with PM *in vitro* compared with the conventional PLGA nanoparticles, thus would improve the bioadhesion on gastrointestinal mucosa after oral administration resulting in a prolonged residence time in the gastrointestinal tract.

Keywords: poly lactic-co-glycolic acid nanoparticle mucin bioadhesive activity lectin

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