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论文

壳聚糖和壳聚糖-EDTA接合物双层包覆胰岛素口服纳米脂质体的研究

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摘要：

目的研究壳聚糖和壳聚糖-EDTA接合物(CEC)双层包覆胰岛素脂质体的性质、降血糖作用和药代动力学。方法采用逆相蒸发法制备胰岛素脂质体；用胃蛋白酶、胰蛋白酶溶液和胃肠道内容物试验考察脂质体对胰岛素的保护作用；用酶-苯酚法测定小鼠血糖值；用放射免疫法测定血清胰岛素含量，并采用Pkanalyst程序进行拟合。结果在胃蛋白酶、胰蛋白酶和胃肠道内容物中，壳聚糖-CEC双层包覆胰岛素脂质体对胰岛素具有较好的保护作用；在正常大鼠葡萄糖耐药量试验中，与PBS对照组比较，壳聚糖及其CEC包覆胰岛素脂质体对负载葡萄糖大鼠的血糖升高均有一定的抑制作用，其中壳聚糖-CEC双层包覆胰岛素脂质体的抑制作用最佳；在大鼠降血糖试验中，壳聚糖及其CEC包覆胰岛素脂质体均具有一定降血糖作用，以壳聚糖-CEC双层包覆胰岛素脂质体的降血糖作用最佳，血糖在1 h降至最初血糖值的45.98%，作用时间延长；以皮下注射胰岛素(Ins)为对照，其相对生物利用度为17.02%；对血清Ins浓度-时间曲线进行拟合计算，均符合一室线性模型，以皮下注射Ins为对照，壳聚糖-CEC双层包覆胰岛素脂质体的相对生物利用度为8.91%。结论采用壳聚糖-CEC双层包覆的胰岛素脂质体更有利于胰岛素口服吸收。

关键词： 壳聚糖 壳聚糖-EDTA接合物 胰岛素 脂质体 降血糖作用

Studies on the insulin-liposomes double-coated by chitosan and chitosan-EDTA conjugates

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Abstract:

AimTo evaluate the characteristics, the hypoglycemic efficacy and the pharmacokinetics of the insulin-liposomes double-coated by chitosan (CH) and chitosan-EDTA conjugates (CEC). MethodsInsulin-liposomes were prepared by reversed-phase evaporation. The protection of insulin against peptic and tryptic digestion was studied with HPLC. The hypoglycemic effects of insulin-liposomes were investigated using the glucose oxidase method after oral administration to rats. Serum insulin concentration in rats were determined by radio-immunoassay, and were assessed by Pkanalyst computer program. ResultsThe insulin-liposomes double-coated by CH and CEC was shown to protect insulin against digestion of pepsin, trypsin and gastrointestinal contents. In glucose tolerance test in normal rats, as compared with phosphate buffer solution control group, the insulin-liposomes coated by CH and CEC could reduce the glucose-induced peak of hyperglycemia. The reduction of the insulin-liposomes double-coated by CH and CEC was superior to that of other insulin-liposomes. When administered intragastrically to normal rats, the insulin-liposomes coated by CH and CEC could reduce glycemia measured after an overnight fast. The hypoglycemic effect the insulin-liposomes double-coated by CH and CEC was superior to that of other insulin-liposomes, and the dosage of 50 $u \cdot kg^{-1}$ decreased by 45.98% of initial blood glucose level at 1 h. As compared with subcutaneous injection, the relative pharmacological bioavailability was 17.02% calculated by area under the curve of glucose level versus time profile after oral administration of the insulin-liposomes double-coated by CH and CEC to rats. The serum insulin concentration-time curves were found to best fit the one-compartment open model. As compared with subcutaneous injection, the relative bioavailability was 8.91% calculated by the area under the curve of serum insulin concentration versus time profile after oral administration of the insulin-liposomes double-coated by CH and CEC to rats. ConclusionThe stability and absorption of insulin-liposomes double-coated by CH and CEC was superior to that of the insulin-liposomes coated either by CH, or by CEC respectively.

Keywords: chitosan-EDTA conjugates insulin liposomes hypoglycemic effect chitosan

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