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壳聚糖修饰的雷公藤多苷纳米粒的制备及其肾靶向性研究

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中文摘要:目的:制备壳聚糖修饰的雷公藤多苷聚乳酸纳米粒(LMWC-TG-PLA-NPs),并对其进行大鼠体内肾靶向性评价。方法:采用改良的自乳化溶剂蒸发法制备雷公藤多苷聚乳酸纳米粒(TG-PLA-NPs),并用50%脱乙酰度的低分子量壳聚糖(LMWC)对纳米粒进行表面修饰;透射电子显微镜观察其形态,粒度分析仪测定其粒径,离心法测定其包封率与载药量,透析袋法研究其体外释药特性。采用肾微透析与肾动脉插管给药联用的组合技术,将LMWC-TG-PLA-NPs分别经尾静脉和肾动脉2种途径给药,以TG-PLA-NPs为对照组,定时收集各组肾组织透析液,测定透析液中药物浓度,绘制药物浓度-时间曲线,计算2种途径给药后肾脏的AUC比值作为肾靶向参数(RTP),评价LMWC-TG-PLA-NPs的肾靶向性。结果:制备的LMWC-TG-PLA-NPs,形态圆整,平均粒径为(207.6±3.4) nm,多分散系数为(0.078±0.009),包封率为(61.83±2.43)%,载药量为(10.70±0.37)%,在含20%乙醇的pH 7.4的PBS缓冲液中体外释药有缓释特征,LMWC-TG-PLA-NPs的RTP为71.97%,是对照组TG-PLA-NPs的3.6倍。结论:制备的LMWC-TG-PLA-NPs包封率和载药量均较高,具明显的缓释特征和肾靶向性,壳聚糖修饰的聚乳酸纳米粒有望成为降低雷公藤多苷毒副作用的新型载体。同时,也建立了以静脉给药后与肾动脉给药后肾脏的AUC比值作为肾靶向参数来评价肾靶向性的新方法。

中文关键词:雷公藤多苷 壳聚糖 聚乳酸纳米粒 肾靶向性 肾动脉给药

Study on chitosan-modified tripterygium glycoside nanoparticles and its renal targeting property

Abstract:Objective: To prepare chitosan-modified tripterygium glycoside nanoparticles (LMWC-TG-PLA-NPs), and assess its renal targeting property in rats. **Method:** Chitosan-modified tripterygium glycoside nanoparticles (LMWC-TG-PLA-NPs) were prepared by modified spontaneous emulsification solvent evaporation method, and modified with 50% deacetylated low molecular weight chitosan (LMWC). The shape of nanoparticles was observed under a transmission electron microscope. The mean diameter of nanoparticles was measured by particle size analyzer. The drug encapsulation efficiency and drug loading were measured by centrifuge method. The *in vitro* release behavior was studied with dialysis bags. Renal microdialysis technique and renal artery administration technique were combined to study the renal targeting property of nanopartcles. LMWC-TG-PLA-NPs were administrated in rats by tail vein injection(TVI) and renal artery administration(RAA), respectively, with TG-PLA-NPs as the control group. Renal dialysis fluid was regularly collected to determine the drug concentration in the dialysis fluid, map drug concentration-time curves, and calculate AUC ratio in kidneys through the two injection approaches as the renal targeting parameter (RTP), in order to assess the renal targeting property of LMWC-TG-PLA-NPs.

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Result: The prepared LMWC-TG-PLA-NPs looked smooth and round. Their average diameter, polydispersity index, encapsulation efficiency and drug loading were (207.6±3.4) nm, (0.078±0.009)%, (61.83±2.43)%, and (10.70±0.37)%, respectively. The pH 7.4 PBS buffer solution containing 20% ethanol showed obvious sustained release behavior. LMWC-TG-PLA-NPs showed a RTP of 71.97%, which was 3.6 times of TG-PLA-NPs of the control group. **Conclusion:** The prepared LMWC-TG-PLA-NPs showed high drug encapsulation efficiency and drug loading, with obvious sustained release characteristics and renal targeting property. LMWC-TG-PLA-NPs are expected to become a new type vector for reducing toxic and side effects of tripterygium glycoside. Meanwhile, a new method is established for assessing renal targeting property with AUC ratio in kidneys after administrated through caudal veins and renal arteries as the renal targeting parameter.

keywords:tripterygium glycosides chitosan PLA nanoparticles renal targeting property renal artery administration

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