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论文

转铁蛋白修饰的载基因前阳离子脂质体制备及其表达研究

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摘要：

本文制备、优化转铁蛋白修饰的前阳离子脂质体，并研究其相关性质。通过薄膜分散膜挤压法制备空白前阳离子脂质体；以鱼精蛋白缩合质粒DNA与空白前阳离子脂质体作用形成载基因前阳离子脂质体(PLPD)；转铁蛋白(transferrin，Tf)再与PLPD作用形成转铁蛋白修饰的载基因前阳离子脂质体(Tf-PLPD)；中心组合设计优化制备工艺；以*lacZ*为报告基因转染人肝癌细胞株HepG2；测定形态、粒径、电位和转染效率。结果显示，PLPD形态近似于球体，平均粒径为(228.9±8.0) nm，多分散指数为0.122±0.020(*n*=3)；zeta电位为(-25.08±2.50) mV (*n*=3)，转染效率(12.18±3.80) mU·mg^{-1}(protein)。Tf-PLPD平均粒径为(240±12) nm，多分散指数为0.150±0.030(*n*=3)；zeta电位为(-24.10±2.50) mV(*n*=3)；转染效率(24.26±2.60) mU·mg^{-1}(protein)是裸质粒的20倍；实验结果也表明血清的存在不影响PLPD和Tf-PLPD的转染效率；PLPD和Tf-PLPD小于阳离子脂质体LPD对人肝癌细胞HepG2，SMMC7721和张氏正常肝细胞3种细胞株的毒性。由此可见，转铁蛋白修饰的前阳离子脂质体作为基因转运的非病毒载体具有良好的应用前景。

关键词： 转铁蛋白 前阳离子脂质体 制备 转染效率

Preparation and gene expression of transferrin modified gene loaded procationic liposomes

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Abstract:

A novel transferrin modified non-viral gene delivery system Tf-PLPD was developed and the related characteristics was investigated. Blank procationic liposomes were prepared by film dispersion-filteration method. PLPD was prepared as follows by first mixing the plasmid DNA and protamine together,then the resulted polyplexes were incubated for 10 min at room temperature, followed by addition of preformed blank procationic liposomes. Transferrin was adsorbed at the surface of PLPD via electrostatic interactions to form Tf-PLPD. Central composite design (CCD) was employed to optimize the formulation. The HepG2 cells were transfected using *lacZ* as reporter gene and characteristics such as the morphology, the mean particle size, the zeta potential and the transfection efficiency in HepG2 cells were further investigated by different methods. The resulting PLPD had a regular spherical surface with an average size of (228.9±8.0) nm (polydispersity index, PDI=0.122±0.02, *n*=3), a zeta potential of (-25.08±2.50) mV (*n*=3) and a transfection efficiency of (12.18±3.80) mU·mg^{-1}(protein). The Tf-PLPD had an average size of (240±12) nm (polydispersity index, PDI=0.150±0.03, *n*=3), a zeta potential of (-24.10±2.50) mV (*n*=3) and a transfection efficiency of (24.26±2.60) mU·mg^{-1}(protein), 20 times greater than that of the naked plasmid DNA. The presence of serum didn't affect the tansfection activity of PLPD or Tf-PLPD. Compared to one kind of cationic liposomes (liposome-protamine-DNA, LPD), the PLPD and Tf-PLPD had much less cytotoxicity to three hepatic cell lines (including HepG2, SMMC7721 and Chang's normal hepatocyte). The results indicated that the Tf-PLPD is a perspective non-viral vector for gene delivery systems.

Keywords: procationic liposome preparation transfection efficiency transferrin

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