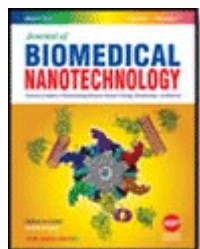


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Liquid Crystalline Nanodispersions Functionalized with Cell-Penetrating Peptides for Topical Delivery of Short-Interfering RNAs: A Proposal for Silencing a Pro-Inflammatory Cytokine in Cutaneous Diseases

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Abstract



References



Citations



Supplementary Data



Suggestions

Short-interfering RNAs (siRNAs) are a potential strategy for the treatment of cutaneous diseases. In this context, liquid crystalline nanoparticles functionalized with specific proteins and peptide-transduction domains (PTDs), which act as penetration enhancers, are a promising carrier for siRNA delivery through the skin. Herein, hexagonal phase liquid crystal nanoparticles based on monoolein (MO) and/or oleic acid (OA) containing (or lacking) the cationic polymer polyethylenimine (PEI) and the cationic lipid oleylamine (OAM) were functionalized with the membrane transduction peptides transcriptional activator (TAT) or penetratin (PNT). These nanoparticles were complexed with siRNA and characterized by particle size, polydispersity, zeta potential, complexation efficiency and siRNA release. The formulations containing cationic agents presented positive zeta potentials, sizes on the nanometer scale, and complexed siRNAs at concentrations of 10 μ M; these agents were successfully released in a heparin competition assay. Cell culture studies demonstrated that nanoparticles composed of MO:OA:PEI functionalized with TAT were the most efficient at transfecting L929 cells, and the uptake efficiency was enhanced by TAT peptide functionalization. Thereafter, the selected formulations were evaluated for *in vivo* skin irritation, penetration and *in vivo* efficacy using a chemically induced inflammatory animal model. These nanoparticles did not irritate the skin and provided higher siRNA penetration and delivery into the skin than control formulations.

Additionally, efficacy studies in the animal model showed that the association of TAT with the nanodispersion provided higher suppression of tumor necrosis factor (TNF)- α . Thus, the development of liquid crystalline nanodispersions containing TAT may lead to improved topical siRNA delivery for the treatment of inflammatory skin diseases.

Keywords: CELL-PENETRATING PEPTIDES; LIQUID CRYSTALLINE NANODISPERSIONS; PENETRATING; PSORIASIS; siRNA; TAT

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