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Optimizing transfection of primary human umbilical vein endothelial cells using facial amphipathic deoxycholic acid conjugated polyethyleneimine

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Introduction: Currently, RNA interference (RNAi) based gene therapy has been investigated for treating various disease conditions. However, successful application of RNAi including siRNA or miRNA has been limited by several factors *in vitro* and *in vivo*. To overcome these challenges, various non-viral carriers have been developing for efficient RNAi-mediated gene silencing. However, it is necessary to improve the efficacy of these non-viral strategies to achieve desired therapeutic effect. In this study, we carried out synthesis, characterization, and optimization of a polymeric conjugate based on low molecular weight polyethylenimine which was modified by high membrane permeable deoxycholic acid conjugated polyethylenimine (DA PEI) for efficient delivery of RNAi-based therapeutics into primary human umbilical vein endothelial cells (HUVECs).

Methodology: Herein, DA-PEI conjugate was synthesized based on DCC/NHS chemistry at various DA to PEI molar ratios of 2 to 4 and used for delivery of a fluorescent labeled siRNA into HUVECs. Conjugates were characterized for chemical structure, size, and cell cytotoxicity. The effect of various parameters including DA/PEI molar ratio, polymer/siRNA weight ratio, and different buffer solutions was investigated on transfection efficacy of conjugates.

Results: DA was conjugated to the terminal amine groups of the PEI 1.8 via amide bonds. The polyplexes had smaller sizes (about 130~150 nm) than the parent PEI 1.8 at different weight ratios. MTS assay revealed that the conjugates were non-toxic at polymer concentrations used in transfection experiments. The higher intracellular uptake and transfection efficiency were achieved by the conjugates synthesized in DA/PEI molar ratio of 3 or 4, polymer/siRNA weight ratio of 5 when they were prepared in salty buffers.

Conclusions: These results suggest that the DA-PEI 1.8 conjugate can be applied as a promising candidate to enhance delivery of RNAi therapeutics into primary endothelial cells under the optimized transfection conditions.

Recent Publications

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5. Karimi M et al. (2013) Evaluation of chitosan-tripolyphosphate nanoparticles as a p-shRNA delivery vector: formulation, optimization and cellular uptake study. Journal of Nanopharmaceutics and Drug Delivery. 1(3):266-278.

Biography

Fatemeh Radmanesh pursued BSc Biotechnology and MSc Microbial Biotechnology from University of Isfahan, Iran. She is currently a PhD student of Medical Biotechnology at Shahid Beheshti University of Medical Sciences. She is a Member of Royan Cardiovascular and Cell Engineering Group. She is interested in nanoparticulate delivery strategies, especially for RNAi-based therapeutics delivery. She joined Royan Institute in 2015 and pursued PhD thesis on using polymeric nanoparticles to deliver RNAi therapeutics.

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