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Alkylcarboxylate grafting to polyethylenimine: A simple approach to producing a DNA nanocarrier with low toxicity

Oskuee, R.K.[ab], Dehshahri, A.[a], Shier, W.T.[c], Ramezani, M.[a]
[a] Pharmaceutical and Biotechnology Research Centers, School of Pharmacy, Mashhad University of Medical Sciences, PO Box ٩١٧٧٥-١٣٦٥, Mashhad, Iran
[b] Department of Modern Sciences and Technologies, School of Medicine, Mashhad University of Medical Sciences, Mashhad, Iran
[c] Department of Medicinal Chemistry, College of Pharmacy, University of Minnesota-Twin Cities, Minneapolis, MN, United States

View references (٤٤)

Abstract

Background: Various strategies have been examined to improve both transfection efficiency and cytotoxicity of polyethylenimine (PEI), a widely used polycationic nonviral gene vector. In the present study, we sought to improve PEI transfection efficiency by combining the osmotic burst mechanism for lysing endocytotic vesicles with the lipid depletion mechanism, which was accomplished by maintaining buffering capacity at the same time as adding a lipid-absorbing hydrophobic shell. Methods: PEI was altered via the substitution of various percentages of its primary amines with carboxylate-terminated short, moderate and long alkyl chains, by reaction with bromoacetic, ٦-bromohexanoic, ١٠-bromodecanoic and ١٦-bromohexadecanoic acids. Modified polymers were complexed with plasmid and the particle size and zeta potential of the polyplexes were determined. Ethidium bromide dye exclusion was used to show the DNA-binding ability of the polymers and their transfection activity and cytotoxicity was evaluated in Neuro٢A mammalian cells. Results: Decreased DNA-binding ability resulted from increases in either the degree of substitution or hydrocarbon chain length. Particle size and zeta potential measurements demonstrated that modified PEI polymers were able to form nanoparticles in the size range ٦٠-١٩٥ nm, and surface charge decreased with an increasing degree of substitution. Higher degrees of substitution resulted in decreased cytotoxicity of polymers. Alkylcarboxylate substitution of primary amines on PEI enhanced transfection efficiencies by up to approximately five-fold relative to underivatized PEI, with the greatest increases occurring with ٦-bromohexanoic acid derivatives at degrees of substitution below ١٠٪. Conclusions: The results obtained suggest that an appropriate balance between cationic and hydrophobic regions of alkylated PEI yields the optimal nonviral vector with high transfection efficiency and low toxicity. Copyright © ٢٠٠٩ John Wiley & Sons, Ltd.

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Indexed Keywords

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