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The synergistic effect of heterocycles as the amino group on gene transfection efficiency of polyethyleneimine

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Background and Aims: The present study was designed for improving PEI gene transfection efficiency while decreasing toxicity by modification of PEI by heterocycles as the amino group.
Methods: New vectors were synthesized with modification of PEI through the substitution of various percentages of its primary amines (10%, 30%, 50%) with Histidin, 3-Pyridyl acetate and Piperazin as the amination reaction. Modified polymers were complexed with plasmid and the particle size and zeta potential of the polyplexes was measured. Ethidium bromide dye exclusion was performed to confirm the DNA binding ability of the polymers. Buffering capacity of the polymers was evaluated. Transfection efficiency and cytotoxicity of polymers was measured in Neuro2A mammalian cells. In vivo experiment for determination of Polyplexe biodistribution was performed.
Results: Particle size of polyplexes was under 200 nm and these nanoparticles had the positive surface charge. 30 percentage substitutions of primary amines of PEI 25 by piperazine (c/p1) could increase transfection efficiency significantly up to 20 fold. Also 10 and 50 percentage substitution of primary amines of PEI 25 by piperazine and pyridyl respectively could increase transfection efficiency. According to MTT assay, cytotoxicity of these polyplexes was very low and cell viability was more than 95%. Luciferase activities in several tissues were determined 24 h after intravenous administration of the complexes in Balb/c mice. Polyplexes showed high gene expression in the lung in comparison with PEI 25 and mortality of these polyplexe was less than PEI25 in Balb/c mice.
Conclusions: These modifications of PEI 25 can improve significantly transfection efficiency. The alterations also reduced cytotoxicity. Polyplexes generated in 0.9% w/v Normal saline had the highest gene expression in the lungs, so can used for organ-targeted plasmid/DNA delivery.

Keywords: Gene delivery; Nonviral vector; Polyethylenimine; Primary amine grafting