Design and Development of Cationic Polyacrylamides for Precision Gene Delivery

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Gene therapy is a powerful tool in biomedical science for genetic modification and treating various genetic disorders and non-communicable diseases. These therapies use viral or non-viral vectors to transfect specific nucleotides. The carrier's structural and morphological properties are crucial for the safe and effective delivery of genetic material. Polymeric carriers are preferred over lipid-based ones due to their tunability, low immunogenicity, and ease of production. [1,2]

Cationic polymers are widely used in gene therapy because they condense with negatively charged DNA or RNA, enhancing cellular uptake and promoting endosomal escape. Polyethyleneimine (PEI) is highly efficient but has high cytotoxicity. [3] Amine-based polyacrylamides synthesized via RAFT polymerization offer a promising alternative, with high buffering capacity and improved gene transfection efficiency.

Amine-based polyacrylamides of pAEAM, pDMAEAM, and TMAEAM with varying architectures and chain lengths were synthesized via RAFT polymerization and characterized. These polymers showed high conversion rates and good dispersity. Their pKa values ranged from 7.8 to 8.5, indicating strong amine interactions with plasmid DNA (pDNA).

AEAM and TMAEAM copolymers efficiently complexed at N/P ratios between 2 and 4, while DMAEAM copolymers required different ratios. Statistical DMAEAM copolymers showed no agglutination and overall haemolytic effects of all polymers were lower than PEI. Polyplexes containing luciferase and GFP-expressing pDNA were formulated and incubated with CT26 colorectal cancer cells, showing good transfection efficiency and biocompatibility, outperforming PEI. [3]

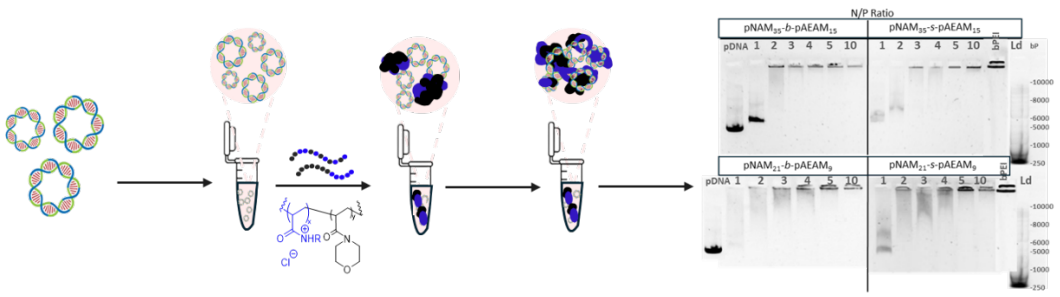

Figure 1: Polyplex formation and gel electrophoresis results showing complexation at N/P ratio ≤ 3

References:

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3. Sahiner, M., Suner, S. S., Demirci, S., Ayyala, R. S., & Sahiner, N. (2025). Toxicity Evaluation of Sulfobetainized Branched Polyethyleneimine via Antibacterial and Biocompatibility Assays. *Toxics*, *13*(2), 136.