ABSTRACT

Gene therapy associates the transportation of DNA to specific cells by the use of vectors in order to reorganize the expression of a vital protein, in order to alleviate the symptoms of a disease. Again, gene delivery using non-viral vehicles holds some difficulties in between maximization of efficiency and minimization of risks because of the numerous biological barriers for a vector to deliver its genetic payload. Therefore, researchers should be fully aware of the actual relation between the bio-physical characteristics of the vectors and their transfection efficiencies. Our goal in this research was to not only characterize the polyplexes made by these vectors with DNA, but to design cationic polymers with different architechtures, by using reversible addition-fragmentation chain transfer polymerization (RAFT) technique and to provide general knowledge of polyplex formation and DNA release in response to external/internal stimuli, such as pH, temperature, and redox agent, ATP etc. as well as how it correlated to transfection efficiencies to develop a more sensible architecture of gene carriers in near future.

We have investigated the interaction behaviors of the synthesized thermosensitive block copolymer viz., PNIPA-b-PDMAEMA with *calf thymus* DNA in detail using various biophysical techniques for the evaluation of the potential of these polymers as gene carriers. The DNA condensation efficiencies of various compositions of these thermosensitive block copolymers were monitored before and after critical aggregation temperatures.

We also reported the formation of cationic micellar nanoparticles from a cationic fluorescent amphiphilic copolymer having cholate moiety linked through a redox-responsive disulfide bond. The encapsulation of hydrophobic anticancer drug (doxorubicin) and complexation with DNA as well as efficient release of drug and DNA from drug-loaded micelleplexes were thoroughly studied using various techniques.

The comparison between pH, redox and ATP responsive cationic cross-linked polymers and linear low molecular weight polymers towards the DNA condensation to form polyplexes has been highlighted. The polyplexes have the ability to selectively release complexed DNA under conditions similar to those prevalent in cancer cells such as acidic pH, ATP rich surroundings or presence of glutathione.

The condensation of DNA with *β*-cyclodextrin-scaffolded poly-histidylated polycations as well as redox responsive decondensation of CDplexes has been descripted by time-resolved fluorescence spectroscopy through the application of a DNA intercalating dye i.e. thiazole orange (TO), probably first implemented for this type of analysis.

Key words: Cationic polymer; RAFT polymerization; Self-assembly; Micelles; Stimuli-responsive polymers; Cross-linked polymer; Boronic ester; Host-guest interaction; DNA condensation; Polyplexes; Pyrene; Poly(ethylene glycol); *calf thymus* DNA; *plasmid* DNA; Doxorubicin; Co-Delivery; Time Resolved fluorescence.