ABSTRACT

Cationic polymeric systems are very promising for their potential in various important biological applications. Complexes of cationic polymers and biomacromolecules like DNA and proteins have immense potential for therapeutic applications such as non-viral gene delivery or drug delivery in near future. In the present dissertation work, we have aimed to study the interaction between different types of cationic polymers and negatively charged biomacromolecules like DNA and protein. From commercially available polyamidoamine (PAMAM) dendrimers to newly synthesized poly(ethylene glycol) based cationic block polymers (BCPs) with different architectures have been employed to investigate the complexation process. Besides equilibrium studies, kinetic aspects of the complexation process have been monitored.

To begin with, we have synthesized PEG based cationic block copolymers by RAFT polymerization technique. The cationic monomer used for copolymerization was [3-(methacryloylamino)propyl]trimethyl ammonium chloride (MAPTAC). Synthesized cationic polymers were well characterized by NMR and GPC techniques. Different instrumental techniques like steady-state fluorescence, DLS, CD, Gel electrophoresis, ITC and UV-visible spectroscopy employed to study the equilibrium binding process. Additionally, Stopped-flow fluorescence kinetic method and TCSPC technique were employed to study the kinetic behavior and dynamics of the complexation process respectively.

Iinteraction study between linear PEGylated BCPs and DNA showed that binding efficiency of the cationic polymers increases with increasing PEG proportion in the blocks. In another interaction study between DNA and cationic bottle-brush copolymers (BBCPs, where PEG units are present as brushes from polymeric backbone) showed similar findings. In both cases, hydrophobic interaction between alkyl chains of PEG units and DNA base pairs acts synergistically at close proximity of two macromolecules, in addition to the normal electrostatic binding force. Although, kinetics of the DNA polyplex formation processes showed some variations in results which presumably resulted from the difference in the architectures of the PEG units in the block copolymers.

Kinetics studies between DNA and PAMAM dendrimers of different generation revealed that the rate constants were vastly depended on dendrimer generation. With increase in the dendrimer generation the binding kinetics became significantly faster. Dynamic study of cationic polymers-DNA complexation by TCSPC method revealed the potential of higher PEGylated BCP as a candidate of better transfection efficiency.

Interaction between cationic block copolymers and HSA showed that binding efficiency gets weaken in presence of higher PEG content in the blocks. Here, hydrophobic interaction between hydrophobic alkyl chains of PEG and hydrophobic domains of protein weakens the electrostatic binding interaction. Determination of thermodynamic parameters elucidated more fundamental information about cationic polymer-protein binding.

Key words: Linear Block Copolymers; Bottle-Brush Block Copolymers; Dendrimers; Poly(ethylene glycol); RAFT polymerization; Human Serum Albumin; Stopped-Flow Kinetics; Time-Resolve Fluorescence; DNA-Polymer Binding; Gene Delivery; Polymer-Protein Interactions.