ABSTRACT

The ability to regulate the formation of nanoparticles through self-assembly of amphiphilic copolymers is of immense significance in the field of biology and medicine. An amphiphilic smart block or random copolymer can form different types of nanoparticles in aqueous medium that are capable of undergoing structural transformation and self-immolation in response to small changes in their environment. In this dissertation work, we have aimed to design several nanoparticles from smart copolymers, which are potentially very stable at physiological conditions, have diseased cell targeting ability, and can act as stimuli triggered drug delivery vehicle. For this purpose, random, block copolymers with narrow dispersity (Đ) were synthesized by reversible addition-fragmentation chain transfer polymerization (RAFT) technique. We have introduced in situ Gold nano preparation, AIE effect, cross-linking to the stimuli-responsive nanoparticles to achieve superior drug delivery vehicle.

We have shown that cloud point (CP) of all random copolymers comprised of N-vinylpyrrolidone (NVP) and sub-NVP monomers in aqueous solution can be varied from 16 ºC to 64 ºC by changing the substituent groups in sub-NVP monomer and copolymer composition. The thermo-responsiveness of PVP based copolymers can also be tuned in binary mixture of solvents (water and water-miscible organic solvents).

pH and thermo-responsive prodrug-based drug delivery vehicle has been prepared by attaching anti-cancer drug doxorubicin covalently to polymer chain and manipulating the CP value of final prodrug to 41 ºC. The nanoparticles formed from the prodrug show potentiality for selective triggered drug release. The nanoparticles are also capable to reduce $HAuCl_4$ and stabilize resulting AuNPs which can be utilized to demonstrate imaging-guided dynamic release of drug molecules.

Dual responsive (pH and light) vesicles have been prepared from P(CM-*r*-HEMA) polymer by introducing light-responsive coumarin moiety and pH-responsive β-thiopropionate linker in the polymer chains. To enrich the stability of vesicles, bilayer of the vesicles has been cross-linked by light irradiation, which reduces premature drug leakage at physiological condition. These cross-linked vesicles are able to release physically encapsulated doxorubicin drug in a controlled manner under the influence of acidic pH.

Enzyme and pH-responsive AIE active nanoparticles prepared from PEG and glycine- based prodrug show selective triggered doxorubicin release in a controlled manner. Another AIE active nanoparticle achieved from linear PEG and lysine-based polymer show selective disassembly behavior in the influence of *E. coli* bacterial enzyme, which can be utilized in targeted antibiotics delivery.

Key words: RAFT polymerization; Smart polymers; N-vinylpyrrolidone; Poly(ethylene glycol); nanoparticles; Cross-linking; Doxorubicin; Polymeric prodrugs; Disassembly of nanoparticles; Drug release; Gold Nano; Aggregation induced emission.