ABSTRACT

Self-assembled polymer nanoparticles (micelles, vesicles, *etc.*) are known to be potent carriers of hydrophobic as well as hydrophilic molecules in aqueous solution with several other advantages like high drug loading capacity, prolonged circulation time in bloodstream, better bioavailability, lesser side effects, etc. Micellar nanoparticles from polymers containing stimuli-responsive functional groups can be used as stimuli regulated drug release systems. In the present dissertation work, I have aimed to design and synthesis of various new biocompatible stimuli-responsive (e.g. photo-, pH-, redox-, temperature-responsive) amphiphilic copolymers with controlled molecular weight and narrow dispersity (Đ) using reversible addition-fragmentation chain transfer (RAFT) polymerization technique, study their self-assembly behavior in physiologically relevant condition and their drug delivery potential.

I have synthesized a block copolymer poly(NVP-*co*-NVC)-*b*-poly(NVC-*co*-Boc PAPA). pH-Responsive free NH_2 groups were introduced in this polymer by the deprotection of Boc groups of phenylalanine derivative in poly(NVP-*co*-NVC)-*b*-Poly(NVC-*co*-Boc PAPA), whereas incorporation of N-vinylcaprolactam (NVC) in the block copolymer introduced thermo-responsiveness in the chain. The block copolymer nanoparticles were found to encapsulate anticancer drugs like DOX with high efficiency. The drug release from the nanoparticles was found to be higher at a higher temperature and at lower pH, suggesting to the present block copolymer as a potent drug delivery system in a cancerous environment.

In spite of having several advantages of micellar nanoparticles as mentioned above, there is always a possibility of premature drug release from the disrupted micellar nanoparticles in the bloodstream under dilution which causes a lower therapeutic effect and several unwanted side effects. To overcome this drawback, core cross-linked polymeric nanoparticles (CCNPs) were synthesized by employing a green method via formation of the isoxazoline ring through the 1,3 dipolar cycloaddition reaction of vinyl groups of the cross-linker N,N'-Bis(acryloyl)cystamine (BAC) with the *in situ* formed nitrile oxide groups of the copolymers in the reaction mixture. I have also synthesized glutathione catalyzed core cross-linked micelles from a new copolymer poly(NVP)-*b*-poly(LABPA) in buffer (pH 7.4) in the presence of the catalytic amount of glutathione. Their minimum drug release profile in the extracellular environment and rapid drug (DOX) release under the reductive intracellular environment of cancer cells definitely established them as potential drug carriers.

A polymer prodrug could be an alternative delivery technology. I have synthesized a photo-responsive polymeric prodrug poly(NIPA)-*b*-poly(HMNPPACbl)-*b*-poly(PEGMA-*stat*-BA) with biotin as receptors, and evaluate their potential as a photo-responsive system for delivery of dual or single drugs in cancer cells.

Key words: RAFT polymerization; Stimuli-responsive polymers; Block copolymer; Micelles; Cross-linked nanoparticles; Polymeric prodrugs; Green reactions; Chlorambucil; Doxorubicin; Cancer Drug delivery.