Abstract

The aim of the thesis is genesis and evaluation of a novel smart polymeric micelle (PM) for cancer cell targeted drug delivery. The work describes the preparation, characterization and application and future prospective of PM based nano-carriers for targeted and stimuli-responsive drug delivery. The contribution and future prospects of the present thesis is also presented at the end. PMs are prepared from the four armed, biodegradable, amphiphilic and stimuli responsive block copolymers. The pentaerythretol poly(ε-caprolactone) (PE-PCL) based block copolymers namely, PE-PCL-b-poly(ethylene carbonate) (PE-PCL-b-PEC), PE-PCL-b-poly(acrylic acid) (PE-PCL-b-PAA), PE-PCL-b-poly(N-isopropylacrylamide) (PE-PCL-b-PNIPAM) and PE-PCL-b-poly(N-vinylcaprolactam) (PE-PCL-b-PNVCL) are synthesized by ring opening polymerization and atom transfer radical polymerization techniques. The predicted structures of the polymers are confirmed by ^{1}H NMR, MALDI-TOP analysis and GPC.

In order to reduce the side effects, targeting moieties (folic acid/ magnetic nanoparticles) are attached/encapsulated into the PMs. The very low critical micelle concentration of the block copolymers suggests their potential applications in advanced drug delivery. The shape and hydrodynamic size of the prepared PMs are investigated from HRTEM and DLS, respectively. The PMs are spherical in shape and having an average size in between 15 to 180 nm, which are suitable for showing effective performance in drug delivery. The branched structure and hydrophobicity of PE-PCL support a very high degree of loading of DOX molecules compare to the literature reported PMs prepared from analogous linear block copolymers. The *in vitro* cancer cell targeted cell uptake and cytotoxicity are investigated against HeLa cell line. The administration of stimuli like, high frequency alternating magnetic field, pH and temperature assists the PMs to show the fruitful *in vitro* release of encapsulated drug (DOX) molecules. The *in vivo* administration of DOX loaded temperature responsive PMs into the sarcoma 180 mice tumor model imposed significant accumulation into the tumors. This significantly inhibits the growth of tumor volume (over 70 % more with respect to the control). These significant findings have opened the avenues for the future studies on next level of *in vivo* animal models and subsequently that may potentially direct to establishment of a novel nano-carrier for future cancer therapy.

Key words: Drug delivery; Polycaprolactone; Branched polymers; Block copolymers; Biocompatibility; Stimuli responsive moiety; Targeting moiety; Doxorubicin and Polymer micelle