ABSTRACT

This thesis aims to investigate the synthesis, characterization and the drug delivery applications of poly(ethylene glycol)-poly(ε-caprolactone) (PEG-PCL) block copolymers. Triblock and diblock copolymer of PEG and PCL were prepared by ring opening coordination polymerization. Prepared block copolymers were characterized using FTIR, NMR, GPC, TGA and DSC. PEG-PCL-PEG formed aqueous solution at room temperature and transformed into injectable hydrogel at 37 °C. Properties of PEG-PCL-PEG hydrogel was studied and compared with Pluronic, a well-studied non-biodegradable injectable hydrogel. Release behavior of insulin from PEG-PCL-PEG hydrogels followed Fickian diffusion. Insulin retained its secondary structure after release as confirmed by CD spectrum. A three-fold increase in Fickian diffusion coefficient was evidenced when temperature was increased from 34 °C to 40 °C due to crystalline melting of PCL part of PEG-PCL-PEG.

Labile drug molecules and proteins undergo degradation and denaturation while preparation of nanoparticles at organic solvent-water interface and at high temperature. In order to resolve this, a new organic solvent-free low temperature method of preparation of amphiphilic block copolymer based micellar nanoparticles is developed. This was achieved by disrupting crystallinity of the block copolymer by heating in distilled water at 60 °C followed by sudden chilling in an ice-water bath. Micellar nanoparticles (<120 nm) were prepared using amphiphilic diblock and triblock copolymers of PEG and PCL. Effects of molecular architecture on morphology, and stability of micellar nanoparticles were investigated. Celecoxib and insulin were used as model drug and protein,

respectively for encapsulation and release studies. Celecoxib release from micellar nanoparticles was controlled and drug release kinetics was satisfactory for more than 10 days. Micellar nanoparticles prepared using high molecular weight block copolymers exhibited higher insulin encapsulation efficiency and controlled insulin release characteristics. Insulin retained its secondary structure after encapsulation in nanoparticles as confirmed by CD spectroscopic studies. Furthermore, *in vitro* cytotoxicity assay using L 939 cell lines suggested that the prepared micellar nanoparticles are biocompatible. In summary, heat-chill method of micellar nanoparticles preparation is well suited for development of drug delivery vehicle containing labile proteins and other drug molecules.

Keywords: Block copolymers; Amphiphilic nanoparticles; Drug delivery; Injectable hydrogels, Protein delivery; Biodegradable; Polycaprolactone; Polyethylene glycol; Celecoxib; Insulin; Heat-chill, Degradation of proteins; PEG-PCL; Polymer micelle; Micellar nanoparticle.