CHAPTER I
INTRODUCTION

1.1 Statement of problem

Intelligent polymers that exhibit unique property changes in response to external stimuli such as temperature, pH, light, and, ionic strength have been investigated for biomedical applications such as drug delivery, cell-surface adhesion control, bio-separation, and other stimuli devices. Poly(*N*-isopropylacrylamide) (PNIPAAm), the most investigated temperature-responsive polymer featuring a lower critical solution temperature (LCST) in water at 32°C, has gained considerable attention due to its temperature being close to human body temperature so that it is a promising material for biomedical applications. However, bioengineering applications of PNIPAAm are significantly limited because its structure does not contain active functional groups that are chemically bound with biomolecules. An effective way to integrate such functionalities to PNIPAAm is to copolymerize NIPAAm with monomers carrying reactive functionalities such as aldehyde, azide or acetylene/alkene, anhydride, and active ester. Among them, activated esters in the form of *N*-acryloxysuccinimide (NAS) and pentafluorophenyl acrylate (PFPA) are very attractive choices in that their resulting polymers are hydrolytically stable in air.

Recently, an irreversible light-responsive moiety of *ortho*-nitrobenzyl (ONB) based photolabile linkers has been introduced to the polymer structure as photocleavable units in the amphiphilic random and block copolymers, resulting in stable cross-linked micelles or fibrous mats which are commonly used as targeted drug delivery or scaffolds in tissue engineering, respectively. However, controlling the polymerization of ONB containing monomers is still difficult because the nitro aromatic compounds can act as inhibitors/retardants during the radical polymerization process.

Post-polymerization modification is a versatile method for the introduction of such chemical functionality that would otherwise interfere with the polymerization process. In addition, the post-polymerization modification of activated ester

polymers provides many synthetic advantages. In combination with controlled radical polymerization, for example, reversible addition-fragmentation chain transfer (RAFT) polymerization which is compatible with a wide range of functional monomers and does not involve the use of (transition metal) catalysts, one can achieve precisely defined reactive polymer structures. This procedure enables the synthesis of polymeric architectures, which cannot be realized by the classical way of radical copolymerization.

In this work, we report the synthesis and characterization of random and block copolymers consisting of activated esters (*N*-acryloxysuccinimide, NAS and pentafluorophenyl acrylate, PFPA) and *N*-isopropylacrylmide (NIPAAm). Optimized RAFT conditions can yield well-defined copolymers with controlled molecular weights and narrow polydispersities. Subsequent post-polymerization modification of the copolymers was performed to incorporate light responsive moieties of *o*-nitrobenzyl (ONB) into the activated ester parts of the copolymers. The ONB group is known to undergo irreversible transformation upon irradiation with UV-radiation. Finally, the ONB-containing copolymers were self-assembled into micelles or electrospun into fibers. Stable cross-linked micelles or fibers were then obtained after UV irradiation. It is anticipated that the unreacted of NAS or PFPA moieties in the copolymers should be available for further modification with bioactive species which should make this developed cross-linked micelles or fibrous mat of PNIPAAm copolymers more useful in biomedical fields.

1.2 Objectives

1. To synthesize and characterize random and block copolymers consisting of activated esters (NAS and PFPA) and NIPAAm by RAFT polymerization.
2. To explore the possibility of incorporating light responsive moieties of ONB into the activated ester parts via post polymerization modification.
3. To fabricate of the ONB containing copolymers as stable cross-linked micelles or fibers.
4. To study cytotoxicity of selected cross-linked electrospun copolymer fibers.

1.3 Scope of investigation

The stepwise investigation was carried out as follows:

1. Literature survey for related research work.
2. Synthesis and characterization of random and block copolymers consisting of activated esters (NAS and PFPA) and NIPAAm by RAFT polymerization.
3. Post polymerization modification of the ONB group into the activated ester parts of the copolymers.
4. Formation of cross-linked micelles and fibers.
5. Cytotoxicity test of selected cross-linked electrospun copolymer fibers.