CHAPTER I

INTRODUCTION

Rationale for the study

In recent years, magnetite nanoparticles (Fe_3O_4) have been markedly studied because of their potential applications in biomedical field such as target-drug delivery, hypothermia cancer treatment and magnetic resonance imaging (MRI) [1]. In particular, tailored surfaces with polymeric stabilizers play an important role in the development of magnetite nanoparticles for drug delivery application [2-7]. An external localized magnetic field gradient can be applied to a target organ to attract drug-loaded magnetic particles from blood circulation [8]. Entrapping magnetic nanoparticles into sustained-released polymeric drug delivery vehicles was limited due to only a few percentage of magnetite nanoparticles incorporated into the system [9]. Development of polymeric bilayer stabilizers for magnetite nanoparticles has recently reported [10]. It was hypothesized that hydrophobic drug can penetrate into hydrophobic inner layer, while hydrophilic outer layer extend from the particle surface and provide steric stabilization. Therefore, in the current work, we present a method for preparing a novel polymeric amphiphile comprising of hydrophobic polyester blocks and hydrophilic methoxy poly (ethylene glycol) (mPEG) blocks. Polyester blocks are hypothetically able to be adsorbed onto magnetite nanoparticles pre-coated with oleic acid primary surfactant and mPEG block can protrude outward from the particle surface to provide steric repulsion and also dispersibility in aqueous media.

The primary aim of this thesis was to prepare water dispersible magnetite nanoparticles containing hydrophobic inner shells for efficient entrapment of indomethacin model drug and hydrophilic outer layers for their good dispersibility in aqueous. Oleic acid in combination with amphiphilic block copolymers of poly (ethylene glycol) methyl ether (mPEG)-polyester were used as steric stabilizers for this purpose. Hydrophobic blocks can hypothetically be adsorbed onto the pre-synthesized magnetite nanoparticles coated with oleic acid primary surfactant, and hydrophilic mPEG blocks can protrude outward from the particle surface to provide

steric stabilization. The effects of mPEG and polyester block lengths of the amphiphilic copolymer on structural and magnetic properties as well as their drug entrapment efficiency of the copolymer-magnetite complex were investigated. $\overline{M_n}$'s of mPEG and polyester were systematically varied to obtain relatively short and long block lengths of each component reflecting different degrees of hydrophobicity and hydrophilicity in the copolymers. Therefore, the competency for controlling their dispersibility and stability in water together with drug releasing behavior may be gained. The influences of the copolymers composition on the particle size, stability in water, magnetic properties and drug releasing behavior were also discussed herein.

Purpose of the study

1. To synthesize water dispersible magnetite nanoparticles containing oleic acid and mPEG-polyester copolymer as bilayer surfactant

2. To study the effects of mPEG and polyester block lengths of the copolymers on the particle size, dispersibility and stability in water, magnetic properties and drug releasing behavior of the copolymer-magnetite complex

Significance of the study

This research is the first report, to our knowledge, in the synthesis of magnetite core-bilayer shell nanoparticles having mPEG-polyester copolymer dispersant to obtain hydrophobic inner shell and hydrophilic corona. This can provide a platform for efficient entrapment of hydrophobic therapeutic drugs in the inner layer of the particles, while the outer layer provided steric stabilization and dispersibility in water.

Scope of the study

1. To synthesize water dispersible magnetite nanoparticles containing bilayer polymeric surfaces

2. To study the effects of copolymer concentration on dispersibility, particle size, stability and magnetic properties of the copolymer-magnetite complex in water

3. To study of the copolymer-coated magnetite nanoparticles for entrapment of an indomethacin model drug