CHAPTER I
INTRODUCTION

Magnetic nanoparticles (MNPs) have been used in various biological and biomedical applications such as biomagnetic separation, hyperthermia treatment, and drug targeting (Kluchova *et al.*, 2009). They act as magnetic resonance imaging (MRI) contrast agent, which already received some clinical acceptance. Development of molecular and cellular imaging aims for visualizing the disease-specific biomarker at the molecular and cellular levels, which led to prevalent recognition the magnetic nanoparticle as MRI contrasts (Gao *et al.*, 2009). Superparamagnetic iron oxide nanoparticles (SPIONs) have ability as an important material to enhance magnetic resonance contrast. For example, maghemite iron (II) nanoparticles attached to bentonite clay surface will result in a highly efficient negative oral contrast agent for MRI diagnostics of the adjacent abdominal areas and small bowel including pancreas and choledoch (Kluchova *et al.*, 2009). Although not yet capable of reaching levels of safety and efficacy for regulatory approval, pre-clinical studies indicated that some of the short coming of magnetic drug targeting, such as their toxicity (Seung-Jun Lee *et al.*, 2004), poor penetration depth, and diffusion of the released drug from the disease site (Sun *et al.*, 2008), can be overcomed by improvement in magnetic targeted carriers design. Furthermore, encapsulate MNPs as a drugs carrier that mean of real-time monitoring of drug delivery is an area of intense interest.

The use of external magnetic field with SPIONs as effectively direct to specifics tissue in the body, encapsulated magnetic nanoparticle with a layer of biodegradable polymer or evenly distributed in the matrix of polymer have also been reported and widely research to attain controlled release with respect to both time and location (Wessel *et al.*, 2007). The coated SPIONs with biocompatible polymer aim to form stable non-toxic aqueous dispersion of magnetic nanoparticle. The covered polymers have resulted in reduce aggregation problem of the uncoated MNPs and lower its toxicity (Gaihre *et al.*, 2009). These biodegradable and biocompatible include hydrophobic polyester such as poly(D,L-lactide-co-glycolide) (PLGA), Poly(D,L-lactide) (PLA), and poly(glycolide) (PGA) (Hans *et al.*, 2002).

Poly(D,L-lactide-co-glycolide) (PLGA) are significant for tissue engineering applications and delivery system because they are biodegradable, biocompatible, non-toxic (Cheng *et al.*, 2008), high regarding for safety biodegradability in the body and approval by the U.S. Food and drug Administration (FDA) (Arnold *et al.*, 2007). When microspheres formulated, drug depot was formed as advantage by direct injection in a tissue from which the slowly released of drug occurred. PLGA microparticles encapsulating a decoy oligodeoxynncleotide (ODN) against nuclear facto-κB (NF-κB) able to release decoy ODN at a constant rate for about 40 days (Stefano *et al.*, 2009). PLGA encapsulation of SPIONs was used to study the distribution of nanoparticle in chinchilla cochleae, the nanoparticle were distributed in the chinchilla round window membrane (Ge *et al.*, 2007). However, microsphere size has a significant effect on the efficient of drug loading and drug release rate and can potentially be varied to design a drug delivery system controlled with desired release profile. Mathematical modeling provide the effect of mean diameter of PLGA microsphere on drug release, Piroxicam-loaded PLGA microsphere having mean size from 13.5-76 μm, result in drug initial release rate decreased with an increase in microsphere size increase (Owen *et al.*, 2008).

Several methods have been developed to prepare magnetic polymeric nanoparticles including water-in-oil (w/o) single emulsion, water-in-oil-in-water (w/o/w) double emulsion, coaservation (Jain, 2000), inverse microemulsion polymerization, and miniemulsion polymerization (L.N. Okassa *et al.*, 2007). The main requirement is that the all the magnetite nanoparticles are transfered evenly into the resulting polymeric nanoparticles. The most interesting one is w/o/w double emulsion that best suited to encapsulated water-soluble drug like vaccines, proteins, and peptides (Jain, 2000).

In this work we encapsulated SPIONs with PLGA microparticles by using an emulsification diffusion technique. This technique forms a water-in-oil emulsion at the first which the SPIONs and the polymer are in the oil phase and dissolving the hydrophobic bioactive agent in the water phase (Wessel *et al.*, 2007). Also in the study, characterization of the resulting effect of amount encapsulates nanosphere on encapsulation efficiency were carried out.