CHAPTER I
INTRODUCTION

In recent years, electrospinning process has attracted a great deal of attention due to its ability to produce ultrafine fibers with diameters in the range of nanometers to sub-micrometers and high surface area to volume or mass ratios (Lu, 2001; Doshi, 1995). The principle of electrospinning process is to use electrostatic force as the main driving force for fiber formation (Zhang, 2005; Shim, 2001; Theron, 2004). Morphology of the as-spun fibers depends on a number of parameters such as solution concentration, solution conductivity, applied electrostatic field strength, collection distance, and collection time (Shim, 2001; Ding, 2002). Among others, some potential uses of electrospun fibers in medicine are, for examples, immobilization of enzyme (Wu, 2005), tissue engineering scaffolds (Choi, 2004; Kim, 2004), and DNA (Luu, 2003) and drug delivery systems (Kenawy, 2002; Zong, 2002; Zeng, 2003; Verreck, 2003; Verreck, 2003). One of the obvious advantages of the electrospinning process over the conventional film-casting technique is the highly porous structures of electrospun fiber mats which exhibit much greater surface area that assumingly could allow drug molecules to diffuse out the matrix much more conveniently (Kenawy, 2002; Zong, 2002).

The as-spun fibers from a good number of polymers have been developed as the matrix for the delivery of drugs. Poly(lactic acid) (PLA) and poly(ethylene-co-vinyl acetate) (PEVA) were successfully as-spun in the presence of tetracycline hydrochloride (an antibiotic drug) as a model drug by Kenawy et al. (Kenawy, 2002). The total percentage of tetracycline released from the as-cast films was lower than that from the e-spun fiber mats due to the much lower surface area. For poorly water-soluble drugs, such as itraconazole (an anti-fungal drug) and ketanserin (a drug for ischemic acute renal failure), polyurethane, a non-biodegradable polymer, was used as the matrix (Verreck, 2003). They concluded that the release of poorly water-soluble drugs could be achieved using a water-insoluble polymer and the rate of release could be tailored by varying the drug to polymer ratio (Verreck, 2003).

Hydrogels are polymeric materials that do not dissolve in water at physiological temperature and pH, but are able to swell considerably in an aqueous

medium, and widely used as controlled release carriers of drugs and protein because of their good tissue compatibility, easy manipulation under swelling condition, and solute permeability (Kim, 1992; Kim, 2003). One of the most popular hydrogel polymers is poly(vinyl alcohol) (PVA). PVA is a hydrophilic, semi-crystalline polymer with good chemical and thermal stability (Koski, 2004). PVA is interesting here because of its biocompatibility, non-toxicity, good water permeability, and, particularly, excellent electro-spinnability. Over the past few years, many researchers have investigated various parameters affecting morphology of electrospun PVA fibers, e.g. solution concentration, solution flow rate, degree of hydrolysis, applied electrical potential, collection distance, ionic salt addition (Zhang, 2005), molecular weight of PVA (Koski, 2004), and pH (Son, 2005). It is therefore very interesting to explore the use of electrospun PVA fibers as carriers for transdermal drug delivery system (TDDS). TDDS exhibits great potentials in avoiding hepatic first pass metabolism, maintaining constant blood levels for a longer period of time, decreasing side effects, and improving compliance (Kshirsagar, 2000). Control over the release characteristics of the drugs can be done through partial cross-linking of the PVA fibrous matrix.

Cellulose acetate (CA) is the acetate ester of cellulose, the primary structural component of the cell wall of green plants and is one of the most common biopolymers on earth (Anonymous, 2006). CA has been fabricated as semi-permeable membranes for separation processes and fibers and films for biomedical applications. Electrospinning of 5 and 8 wt.% CA solutions in acetone produced short and beaded fibers with diameters being ~1 μm (Jaeger, 1998). An improvement in the electrospinning of CA was achieved when 2:1 v/v acetone/dimethylacetamide (DMAc) was used as the solvent system (Liu, 2002). This mixture allowed the resulting 12.5-20 wt.% CA solutions to be continuously spun into fibers with diameters ranging between ~100 nm and ~1 μm.

In this work, two types of polymeric materials were electrospun and used as the matrix for drug delivery system; PVA and CA. Four types of non-steroidal, anti-inflammatory drugs of varying water solubility property, i.e. sodium salicylate (SS) (freely soluble in water), diclofenac sodium (DS) (sparingly soluble in water), naproxen (NAP), and indomethacin (IND) (both insoluble in water), were

incorporated in the as-spun PVA mats. Moreover, in order to control the release characteristic of the drug, the as-spun fiber mats of PVA containing SS as the model drug were further cross-linked with the vapor from the aqueous solution of either glutaraldehyde or glyoxal. Beside hydrogel, it is of our interest to develop mats of electrospun CA nanofibers as carriers for delivery of either vitamin A acid or vitamin E to the skin. Morphology and thermal property of neat and drug-loaded or vitamin-loaded as-spun mats, chemical integrity of drugs within the drug-loaded or vitamin-loaded as-spun mats, swelling and weight loss behavior of neat and drug-loaded or vitamin-loaded as-spun mats in an aqueous medium, and release characteristics of drugs or vitamin from drug-loaded or vitamin-loaded as-spun mats were investigated.