CHAPTER I
INTRODUCTION

There are several possible routes of introducing controlled release medication into the body such as oral, injection, topical administration, and etc. However, the conventional oral and injection routes of drug administration may provide initially the maximum tolerable dose and the dose decreases dramatically in a short period which requires subsequent administrations (Gil *et al.*, 1996).

One recent effort at eliminating some of the problems of the conventional dosage form is the development of Transdermal Drug Delivery [TDD] without the adverse effects associated with the frequent oral administration (Kim *et al.*, 2006). Advantages of this system are to avoid first-pass metabolism, increase compliance, controlled plasma levels, and reduce overall dose (Xie *et al.*, 2005). However, its application has been limited to low amount of drug because of the extremely low amount of released drug from the matrix, and the low permeability of drug through the skin. Furthermore, a precise control over the release of drug from devices such as quantity, timing, is highly desirable in order to optimize drug therapy. This can be achieved if the drug carrier responds in a reproducible and predictable fashion to an internal or external stimulus such electric field (Murdan, 2003), pH (Gudeman *et al.*, 1995), and temperature (Xu *et al.*, 2006).

The use of an electric field as an external stimulus is one such method that has been successfully employed to enhance the amount of released drug along with the precise control through the magnitude of current. There were many literatures on the use of electric current in vivo, in the form of iontophoresis and electroporation, in the fields of the dermal and transdermal drug delivery (Bose *et al.*, 2001). Hofmann *et al.* studied the release of buprenorphine across human skin via iontophoresis using current density of $0.5 mA/cm^2$. They concluded that the drug concentration was significantly enhanced by the applied electric current.

Hydrogel are hydrophilic natural three-dimensional networks, held together by chemical or physical bonds. If interstitial space exists within the network, water molecules can become trapped and immobilized, filling the available free volume (Elvira *et al.*, 2002). It can be applied as an artificial skin (Young *et al.*, 1998),

contact lenses (Brinkman *et al.*, 1991), an interface between bone and implant (Netti *et al.*, 1993), and drug delivery systems. 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. PVA is interesting here because of its biocompatibility, non-toxicity, good water permeability, and ease of manipulation under swelling condition; these characteristics make it ideal for biomedical use especially drug delivery system (Morita *et al.*, 2000).

In the present contribution, the drug-loaded poly(vinyl alcohol) hydrogels were prepared by solution casting and these hydrogels were used as matrix/carrier of drug for TDD. The sulfosalicylic acid was used as an anionic model drug. The thermal properties, morphology, swelling behavior of the drug-loaded poly(vinyl alcohol) hydrogels, and polymer-drug interaction through the ionic nature of the drug were investigated. For the release characteristics of drug from their hydrogels, we were interested in the effects of matrix crosslinking ratio, electric field strength and electrode polarity.