CHAPTER I

INTRODUCTION

1.1 Statement of problem

A concept of loading water-soluble drugs in particles has been developed by researchers in pharmaceutical field continuously. The goal of this idea is to entrap drugs in polymeric matrices, in which the drugs can diffuse or be released out slowly from the carrier. If the drug is not contained in the carrier, it may be eliminated by physiological metabolism before it can be transported to a target site.

Currently, natural biopolymers, especially those that were proven to be biocompatible, biodegradable and low toxic, were widely used in drug delivery system. Chitosan and alginate are two biopolymers which have been used as carriers in controlled release systems. Chitosan is a cationic biopolymer which is widely used in agriculture and biomedical applications. Alginate is an anionic biopolymer, regularly used in food and pharmaceutics such as serving as thickening, gel forming and stabilizing agent. In the presence of calcium ions (Ca^{2+}), alginate can form loosely cross-linked networks that can entrap drugs making it one of the most widely used carriers for controlled release system. Because of their electrolytic character, cationic chitosan can form electrolyte complexes with anionic alginate to form small particles [1].

Glucosamine hydrochloride (GH), target drug in this work, was used to treat osteoarthritis, a degenerative joint disease, in human [2]. Glucosamine, the natural amino monosaccharide founded in the human body, plays an important role in the biochemical synthesis of glycosaminoglycans (GAGs). GAGs are mostly founded in articular cartilage. In the earlier work, the GH-loaded particles were prepared by ionic gelation that is a co-precipitate of two charged polymers, an anionic alginate (with Ca^{2+}) and a cationic chitosan. The particles were obtained with sizes ranging from 300-800 nm. Because GH is a water-soluble drug, its loading efficiency (LE) in the calcium alginate-chitosan ionic gelation system was rather low (0.7-1%) [3]. Therefore this work proposed the use of a hydrophobic chitosan derivative, *N*-butyl chitosan (NBC), together with calcium alginate to form small particles that can entrap a higher GH content in the particle, thus increasing the LE. The hydrophobic butyl group is possible to reduce water uptake by the particles and the subsequent diffusion of GH out of the particles. Also in this work, preparation of the GH-loaded calcium alginate-

N-butyl chitosan particles in carbopol (polyacrylic acid gel) was also evaluated for use as transdermal delivering gel.

1.2 Objectives

The purposes of this study were

1.2.1 To prepare the GH-loaded-calcium-alginate- N-butyl chitosan particles

1.2.2 To evaluate physical characteristics and loading efficiency of the obtained particles and study the release profiles of GH from the particles

1.2.3 To prepare the gel containing GH-loaded particles and study the permeation profiles of GH from gel

1.2.4 To evaluate stability in aqueous solution and gel forms of GH-loaded particles.