CHAPTER I
INTRODUCTION

Over the past few decades, prevalence of diseases involving immune system has been increasing significantly, such as allergic diseases which the sensitization to allergen is the major culprit causing inflammation in the end organs. The known allergens are dust-mite, pet dander, cockroach, molds and pollen. One effective treatment is allergen immunotherapy or 'allergy shot', which the immune system is gradually tolerated to the sensitized allergen by a series of increasing administration of allergen. The methods of administrations are injecting, sublingual or swallowing, etc. resulting in decrease allergic sensitization. However, allergen is administered with an adjuvant, of which the function is related to increase allergen activity in stimulating the immune response, for example alum, an effective adjuvant used in human system. For the fact that alum cannot be naturally metabolized by human organ system, and adverse reactions (e.g., granulomas) at injection sites were reported (Vogelbruch *et al.*, 2000), so the development of the biocompatible adjuvant has received much attention.

Natural polymer such as alginate, amino acid, starch and chitosan were proposed for adjuvants (Scholl *et al.*, 2005 and Shibata *et al.*, 2001). The basic properties of chitosan about the biodegradability, non-toxicity, non-irritation the immune response enhancement and the transport of drug across the epithelium make it to be an attractive material (Seferian *et al.*, 2001, Schipper *et al.*, 1997 and 1999).

Although chitosan is a potential material, it has poor solubility in water and most organic solvents except acid. It is well-dissolved in acetic acid, however, the acid might damage the cells when we consider the use of chitosan as an adjuvant and incorporation with allergen (Chew *et al.*, 2003). Considering the requirements of a material for adjuvant, chitosan needs (i) derivatization without contamination of organic solvents, (ii) effective allergen incorporation and (iii) hydrophilicity or water solubility for clinical treatment.

Choic acid is a bile acid which is in a family of steroid compounds. It has been used as a hydrophobic molecule in modifying the nanoparticle for drug delivery system (Yuan *et al.*, 2006 and Park *et al.*, 2004). It is important to point out that the

functionalization of chitosan with cholic acid may bring the synergistic effects in interacting with allergen. It is also important to consider the molecular design with a good balance of hydrophobicity and hydrophilicity to achieve the water solubility as well as the allergen incorporation which is one of the requirements for clinical use. Based on this viewpoint, methoxy end-capped polyethylene glycol (mPEG) is, then, considered for hydrophilic part to modify chitosan. The use of mPEG also cover the biocompatibility and non-toxicity which are suitable the requirement for medical application.