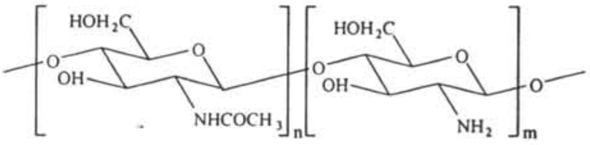
CHAPTER I
INTRODUCTION

Chitin, β-(1-4)-2-acetamido-2-deoxy-β-D-glucose, is the second most plentiful organic resource on the earth next to cellulose obtained from shells of crustaceans, cuticles of insects, cell-walls of fungi and yeasts. The acetyl group of chitin can be removed by a heterogeneous alkaline hydrolysis (Horton *et al.*, 1965) to obtain chitosan in the form of β-(1-4)-2-amino-2-deoxy-β-D-glucose. In nature, chitin extracted from those shells is in a random copolymer consisting of chitin and chitosan repeat units (Scheme 1.1). The term for chitosan is when the chitosan unit or the degree of deacetylation more than 70% (Sannan *et al.*, 1976).

Scheme 1.1



(chitin unit) (chitosan unit)

Based on the basic chemical structure, chitin-chitosan is a polysaccharide chain having two hydroxyl groups at C-3 and C-6 positions, and acetamide (for chitin) or amino (for chitosan) group at C-2 position. Chitosan is not only attractive in terms of biodegradability due to the glycoside linkage (Mark *et al.*, 1985), bioactivity (Dumitriu *et al.*, 1989), biocompatibility (Hirano *et al.*, 1988), and nontoxicity (Sugano *et al.*, 1978) as a result from pyranose ring but also the materialization either by physical modifications by preparing chitin-chitosan solution and casting in films (Xu *et al.*, 1996), spinning to fibers (Hirano *et al.*, 1999), crosslinking to gel (Zeng *et al.*, 1996), etc. or chemical modifications (Blair *et al.*, 1987). It is important to note that most modifications are proceeded in bulk or heterogeneous system due to its high molecular weight and strong inter- and intramolecular hydrogen bonding (Trujillo *et al.*, 1968). The homogeneous system such as water soluble, e.g. carboxymethylated chitin and carboxymethylated chitosan

(Muzzarelli *et al.*, 1988) and organo-soluble, e.g. *N*-phthaloylchitosan (Nishimura *et al.*, 1991) are developed.

In recent year, nanomaterials (size in the nanometer range) have received much attention due to its attractive characteristics, such as the effectiveness in functionalization close to molecular level, the large surface area, and the significant mechanical performances (Huang *et al.*, 2003). In general, there are two approaches to achieve nanomaterial, i.e. (i) the development at molecular level from the small molecules of angstrom size to the macromolecules of nanometer size, and (ii) the development at millimeter or micrometer level by reducing the size of particles via either the chemical or the physical process. In the case of development at molecular level, the molecular design and synthesis for macrocyclic compounds (Huszthy *et al.*, 2001), supramolecules (Knaapila *et al.*, 2001), molecular complexation (Sun *et al.*, 2003) including molecular assembly (Huang *et al.*, 2006) are good examples. In most cases, the nanomaterials obtained from this approach exhibit the specific properties that never achieved in the small molecules. For example, Tanaka *et al.* (2001) proposed monoazathiacrown ethers incorporated with lipophilic dodecyl and dodecanoel groups. The compounds show high binding selectivity for Ag^+ and Hg^{2+}. Majerski, *et al.* (2002) proposed *N*-adamantylaza-crown ethers which have high complexation with K^+ and Rb^+ as compared to the parent aza 18-crown-6 and *N*-benzylaza-18-crown-6. Demirel *et al.* (2003) prepared chiral diaza 18-crown-6 ethers from chiral amines for potassium and sodium salts of amino acids recognition. Considering the size reduction, the oligomerization or the depolymerization of polymers to obtain the chain in nano size by chemical treatment (acid or base hydrolysis), and irradiation is an effective and simple preparation method. The physical treatments such as grinding, dissolving in solution combining with lyophilization, are the basic approach proven to be practical for most water soluble and organo soluble cases. Miriam de Souza Lima *et al.* (2004) prepared nano-cellulose fiber, so-called cellulose whiskers, by treating the original cellulose in acid under specific condition. Balthasar *et al.* (2005) proposed gelatin nanoparticles by a two-step desolvation processes in the mixture of water and acetone. The nanoparticles obtained were stabilized by glutaraldehyde crosslinking agent. For chitin-chitosan, both approaches are considerable and in recent years many developments are reported. The introduction of supramolecules such as crown ether and lipo-hydrophilic units was demonstrated. Yang *et al.* (2000) prepared synthesized mesocyclic diamine-grafted chitosan-crown ether by using mesocyclic diamine crown ether as the grafting agent. The product has high selectivity for the adsorption of Cu^{2+} in the presence of Pb^{2+}, Cu^{2+}, and Cd^{2+}, and its adsorption selectivity is better than that of chitosan. Wan *et al.* (2002) investigated the adsorption capacity and selectivity of *N*-benzylidene chitosan (CTB), chitosan-dibenzo-18-crown-6 crown ether bearing Schiff-base group (CTBD) and chitosan-dibenzo-18-crown-6 crown ether (CTSD) for Ag^{+}, Cu^{2+}, Pb^{2+}, and Ni^{2+}. The results showed that CTBD has better adsorption properties and higher selectivity for metal ions than CTSD. Park *et al.* (2006) proposed self-assembled nanoparticles for drug carrier by chemical conjugation of fluorescein isothiocyanate or doxorubicin to the backbone of glycol chitosan. The chain scission to obtain whisker is an effective nanomaterialization demonstrated by Nair *et al.* (2003). Bhattarai *et al.* (2005) proposed chitosan-based nanofibers by electrospinning technique which might be applied as a matrix for tissue engineering.

The present work originally focuses on the specific development of chitosan based nanomaterial. The nanomaterialization of chitosan studied by two approaches, i.e. (i) the functionalization of low molecular weight chitosan with pseudocyclic polymer chains based on the supramolecular structured design, and (ii) The materialization of chitin flake to chitosan nanoscaffold via a simple reaction without organic solvents involved. The present work also focuses on the functionalization of chitosan nanoscaffold obtained with bioactive molecules, i.e. lactose and maltose, and the functionalization of chitin whiskers with poly(ethylene glycol) in water based system. The development in water system is concerned as it can be expected for the uses in bio-system without the safety problems.