# CHAPTER I
# INTRODUCTION

Hydrogel is a three-dimensional network of hydrophilic polymers in which a large amount of water is present. The most characteristic property of hydrogel is that it swells in the presence of water and shrink in the absence of water (Park and Park, 1996). Hydrogel covers both synthetic and natural hydrophilic polymers. For natural hydrophilic polymer, the hydrogel has attracted the increasing interest of polymer researchers from the viewpoints of its biocompatibility and biofunctionality as in the living body (Kaetsu, 1996). Hydrogels, which swell in aqueous environment, have been widely utilized in drug delivery systems. Charged polymeric networks have been recognized as useful matrices for delivering drugs because their volume changes in response to external pH variation. The main driving force responsible for such a volume change is the ionic repulsion between charged groups incorporated in the gel matrix by an external pH modulation. Such hydrogels have been applied to fabricate a glucose-sensitive insulin release device, an osmotic insulin pump, and site-specific drug delivery in the gastrointestinal tract (Park and Hoffman, 1992).

Chitin is an abundant biopolymer like cellulose and is distributed in the shell of crustacea, e.g. crab and shrimp, the cuticle of insects and also in the cell wall of some fungi and microorganisms. Chitin consists of 2-acetamido-2-deoxy-D-glucopyranose residues (*N*-acetyl-D-glucosamine units) which has intra- and inter-molecular hydrogen bonds and is water-insoluble due to its rigid crystalline structure. Chitosan ideally consists of 2-amino-2-deoxy-D-glucopyranose residues (D-glucosamine units) and has no or a small amount of *N*-acetyl-D-glucosamine units, and is water-soluble as the salt with various acids on the amino group of D-glucosamine unit. Recently chitin and chitosan have been considered as biomaterials in fields such as biomedicine,

pharmacology, and biotechnology due to their biocompatibility, biodegradibilty, and biological activities (Sugano *et al.,* 1978; Chandy *et al.,* 1990; Shigemasa *et al.,* 1995). There is problem in using chitin and chitosan that it is difficult to dissolve them in water at neutral pH range (Sugimoto *et al.*, 1998). So, various studies were conducted to obtain water-soluble derivatives of chitin and chitosan by chemical modification techniques. One of the chemical modification techniques is carboxymethylation of chitin under alkaline condition to give carboxymethyl-chitin (CM-chitin).

CM-chitin is a polyelectrolyte with properties resembling those of carboxymethyl-cellulose (CMC). CM-chitin has unique physical properties including the moisturization of human skin, protection against mechanical damage to hair, antielectrostatic function, antimicrobial function, and prevention of skin aging. These properties of CM-chitin are usable as a functional ingredient for cosmetics and as a functional material for textile fabrics. CM-chitin is thought much easier than chitin to load drugs either through chemical reaction or physical interactions due to its sophisticated properties. CM-chitin has been studied as a water-soluble drug carrier to prepare the pendant type of polymeric drug. High susceptibility of CM-chitin by lysozyme in the animal body permits its applications as a drug carrier for practical drug delivery systems (Ouchi *et al.*, 1992).

Poly(vinyl alcohol), PVA, is a nontoxic water-soluble synthetic polymer, which is widely used in biochemical and biomedical applications. Water-soluble PVA is rendered insoluble by the introduction of crosslinks into its specimen. PVA has good film-forming ability, highly hydrophilic properties and has been studied as a membrane in various ways. PVA gels can be used in the medical field because they possess good biosuitability (Nambu, 1983). According to Miya *et al.*, (1983) chitosan forms a clear homogenous blend with PVA, and the tensile strength of the blend is greater than the component value. Kim *et al.* (1992) studied a chitosan/PVA blend membrane

cross-linked with varying amounts of glutaraldehyde. The permeability coefficients of riboflavin and insulin through these membranes were found to be pH dependent (order of $10^{-6} - 10^{-7}$ $cm^2/s$). However, there has not been report of the blend between CM-chitin and PVA which may has possible application in biomedical field such as wound healing and drug delivery system.

In this study, CM-chitin/PVA blend films were prepared by varying blend compositions of CM-chitin and PVA. The effect of blend compositions on the physical properties, thermal properties, mechanical properties, water absorption, and oxygen permeability were studied. For water absorption of the blend films, the effect of pH and salt type on the degree of swelling of the blend films were investigated.

## Theoretical Background

### 1.1 Chitin

Chitin, poly-β-(1 → 4)-N-acetyl-D-glucosamine, a cellulose-like biopolymer, is the second most abundant renewable organic resource on earth next to cellulose. Chitin is often considered as a cellulose derivative although it does not occur in organisms producing cellulose. It is the most abundant organic skeletal component of invertebrates. In nature, chitin serves as a "glue" for chemical components making up the delicate wings of insects and the crunchy integuments of crustaceans such as crabs and shrimps. It is the characteristic polysaccharide of several important phyla, e.g., *Arthropoda, Annelida, Mollusca, and Coelenterata,* and many fungi, e.g., *Euasomycetes, Zygomycetes, Basidiomycetes, and Deuteromycetes.* Chitin is commercially manufactured from crustacean shell waste that provided $1.2x10^5$ matric tons annually accessible on a worldwide basic (Knorr, 1991). Shell of crabs, lobsters, shrimps, prawns, and krills are the best available sources of chitin. It

represents 20% to 50% of the dry weight of shrimp and crab processing waste (Muzzarelli, 1977). Moreover, chitin also represents 12% of fresh water crayfish meal, 13% of crab meal, and 8% of shrimp meal (Patton and Chandler, 1975). Since crab and shrimp are harvested in different seasons, raw materials for chitin production are always readily available. To obtain chitin from crustacean shell waste, it is usually ground and mixed with a dilute aqueous sodium hydroxide solution to dissolve the protein. The residual material is then treated with a dilute aqueous hydrochloric acid solution to dissolve the calcium carbonate as calcium chloride, leaving behind chitin as a white fiber.

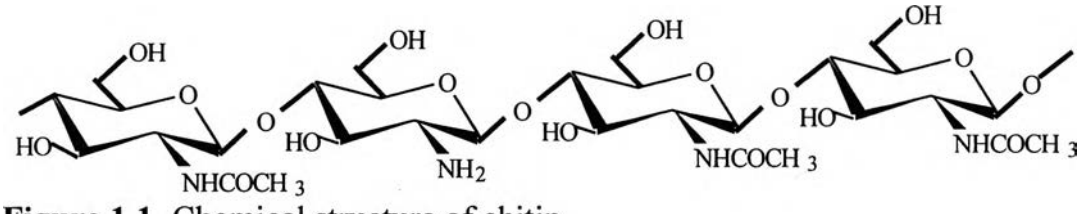


**Figure 1.1** Chemical structure of chitin.

Chitin is known as a potential useful biomedical material for wound healing, artificial skin, suture, and drug carrier (Lee *et al.*, 1996). The unique properties of chitin such as biocompatibility, non-toxic, non-allergic and antifungal properties make it be a promising polymer not only for the biomedical field but also for other industrial areas as summarized in Table 1.1.

**Table 1.1** Some applications of chitin-based materials.

| Area | Application |
|---|---|
| Biomedical | Absorbable surgical suture (Briachi *et al.*, 1997)<br>Drug carrier (Briachi *et al.*, 1997) |
| Cosmetics | Skin-care product (Elizabeth, 1993)<br>Hair stiffener (Elizabeth, 1993) |
| Environmental | Absorbent for waste-water treatment (Yang and Zall, 1984) |
| Biotechnology | Enzyme immobilaization (Muzzareli, 1977) |
| Food technology | Food additive (Elizabeth, 1993)<br>Edible film (Elizabeth,1993) |
| Paper and textile | Paper and fiber sizing (Muzzareli, 1977)<br>Polymeric dyeing (Muzzareli, 1997) |

## 1.2 Carboxymethylchitin (CM-chitin)

CM-chitin is a negatively charged ether derivative of chitin, with a chemical structure resembling to that of carboxymethylcellulose (CMC). In contrast to chitin and commercial chitosan, CM-chitin is soluble at neutral pH. The water solubility of CM-chitin becomes apparent when the fraction of substitution is more than 0.6 (Tokura *et al.*, 1983).

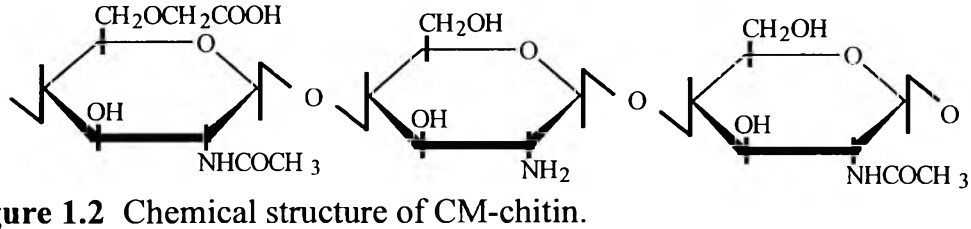


**Figure 1.2** Chemical structure of CM-chitin.

**Table 1.2** Current practical uses of CM-chitin.

| Applications | References |
|---|---|
| Drug delivery system | Nakano *et al.*, 1980 |
| Cosmetic ingredients for hair and skin cares | Imamura *et al.*, 1991 |
| Would healing | Muzzarelli, 1988 |
| Analytical reagents (e.g., colloid titration and enzyme substrates) | Nakano *et al.*, 1979 |
| Chelating agent | Uraki and Tokura *et al.*, 1991 |

CM-chitin has been considered to be one of advanced carriers for the polymeric drug, since CM-chitin was reported as highly biodegradable and non-toxic mucopolysaccharide in animal body (Nishimura *et al.*, 1984b). CM-chitin has been investigated to prepare adsorption or entrapping type of polymeric drug, because CM-chitin tends to adsorb phenyl group specifically in the presence of calcium ion and to precipitate gradually in the presence of trivalent iron ion following to gel formation. Two step biodegradations have been proposed by Ouchi and Inosaka (1992) by applying peptide spacer including phenylanaline residue to the preparation of pendant type drug, in which glycoside linkage will be hydrolyzed predominantly to produce the oligomeric drug (prodrug) by lysozyme and then peptide linkage between phenylanaline and drug were cleaved by α-chymotrypsin type enzymes. But the release of active drug from polymeric drug can be inhibited by the protection of cleavage site with CM-chitin-calcium complex when molecular weight of polymeric drug is high enough. However, the protection of drug can be unlocked remarkably when molecular weight become less than 4,000 (Tokura and Nishi, 1995). Some applications of CM-chitin are summarized in Table 1.2.

## 1.3 Poly(vinyl alcohol)

Poly(vinyl alcohol) is a water–soluble and high crystalline polymer even when atatic. PVA can be prepared by hydrolysis or alcoholysis of poly (vinyl esters). PVA cannot, of course, be made directly because vinyl alcohol is simply the unstable enol form of acetaldehyde. Dry, unplasticized PVA powders are white to cream colored, soften at about 200°C with decomposition.

The basic properties of PVA depend on its degree of polymerization, degree of hydrolysis, and distribution of the degree of hydrolysis. In general, fully hydrolysed grades of PVA are used mainly in paper coating, in textile warp sizing of hydrophilic fibers, such as cotton and rayon staple yarns, and in laminating film in safety glass. Partially hydrolysed grades are used mainly in protective colloids, emulsions, remoistenable adhesives, textile warp sizing for rayon filaments and polyester fibers, and printing plates. The most common grades in each area of application are fully and partially hydrolysed grades with a degree of polymerization of 1700.

PVA is used mainly in aqueous solution. Its solubility in water depends on its degree of polymerization and degree of hydrolysis; the effect of the latter is especially significant. The many hydroxyl groups cause it to have a high affinity to water, with strong hydrogen between intra- and intermolecular hydroxyl groups, greatly impeding its solubility in water.

On the other hand, the residual acetate groups in partially hydrolysed PVA are essentially hydrophobic, and weaken the intra- and intermolecular hydrogen bonding of adjoining hydroxyl groups. The presence of an adequate amount of these acetate groups increases the water solubility. Okaya (1992) showed that, with an increase in the number of acetate groups, the negative heat of dissolution (evolution of heat) increases, the critical temperature of the

phase separation is lower, and the solubility at high temperatures decreases gradually.

For plastics industries, especially in molding compounds, surface coatings, films resistant to gasoline, textile sizes and finishing compositions, PVA is applied to yield elastomers. Plasticized PVA can be used in manufacture artificial sponges, fuel hoses, etc., also in printing inks for plastics and glass, in pharmaceutical finishing, cosmetics, water-soluble film, and sheeting (Winholz *et al.*, 1976).