CHAPTER II
LITERATURE SURVEY

2.1 Carboxymethylchitin (CM-chitin)

Nishimura *et al.* (1984a) reported that chitin was found to interact with bovine blood proteins and the affinities of these proteins for chitin tended to be decreased by the introduction of *O*-carboxymethyl (CM) groups onto the chitin surface. As the adsorption of blood proteins to the CM-chitin (d.s. 0.35) was assumed to follow an isothermal adsorption curve, the adsorption coefficients were estimated by applying the Langmuir equation. The binding site of bovine serum albumin (BSA) for CM-chitin was assumed to be regulated not only by the cationic groups of BSA but also by other factors such as the recognition capacity of BSA to bind to *N*-acetylglucasamine in CM-chitin.

Tokura *et al.* (1983b) presented carboxymethylation of chitin that was carried out effectively for preparing a cation exchange resin under basic conditions. The resulting CM-chitin was found to bind calcium ions specifically among alkali-earth metals even in the presence of monovalent cations such as sodium or potassium. The selectivity coefficient of CM-chitin for calcium ions over sodium ions was assumed to be 45.6 at neutral pH and 0.1-0.2 of ionic strength. The fibrous CM-chitin was prepared to investigate the effects of an increase in the number of surface ionic sites and degree of orientation on the binding capacity.

Tokura *et al.* (1990) reported that CM-chitin was employed as a sustained-release drug carrier for the subcutaneous injection. The induced specific antibody was applied to the titration of methamphetamine secreted into blood of rabbits. The methamphetamine concentration in blood serum was maintained for 120 h at fairly high levels. Methamphetamine was also

excreted into urine at high levels with a similar time course to that in blood serum.

Watanabe *et al.* (1992) studied 6-*O*-carboxymethylchitin that was gelled in the presence of 15 to 30 mM iron (III) chloride. At the time of gelation, a peptidic anticancer drug neocarzinostatin (NCS) was efficiently (> 50%) incorporated into the gel with 25 to 50 mM calcium chloride and iron (III) chloride. CM-chitin gel containing NCS was digested by lysozome *in vitro* and NCS was released from the gel in both a time- and dose- dependent manners. Antimetastatic effects of the CM-chitin gel containing NCS were studied in the spontaneous pulmonary metastasis model using B16-BL6 melanoma; these mean CM-chitin gel are useful as a sustained-release drug carrier.

Tokura *et al.* (1994) studied biopolymeric properties of a water-soluble and biodegradable chitin derivative, CM-chitin. These properties have been investigated to demonstrate the immunological function serving to induce a hapten-specific antibody and the chemotherapeutic function as a drug carrier of controlled release. When CM-chitin was linked by methamphetamine (MA) through a nonbiodegradable spacer, 1-amionobutane (MABA-CM-chitin), MA-specific antibody was produced by the subcutaneous injection, in rabbits, of MABA-CM-chitin in combination with Freund's complete adjuvent. When injected without intense immunoadjuvant, MABA-CM-chitin oligomer was secreted into blood for more than 120 h. Two-step hydrolysis of pendant-type of polymeric drug was also investigated in order to design a more sophisticated drug delivery system.

Khor *et al.* (1996) reported that reversible water-swellable chitin gel has been produced by the carboxymethylation of a dry chitin film. This material can take up water but is not soluble and retains a degree of rigidity even when wet. The degree of swelling depends on the reaction conditions and alkali (sodium or potassium hydroxide) used as a co-reactant during the

carboxymethylation. Upon drying, the gel returns to its dry film form. This water uptake and loss is cyclic, which is a desirable property in certain applications and is a tremendous advantage in the handling of this material.

Hjerde *et al.* (1997) studied that CM-chitin was degraded with hen egg white lysozyme. Initial degradation rates, *r*, were determined from plots of the viscosity decrease against time of degradation at pH 5.3 and ionic strength 0.1 M. The time course of degradation of CM-chitin with lysozyme was non-linear, suggesting different sequences in CM-chitin. All *r*-values of CM-chitins were higher than the highest rate determined for a partially *N*-acetylated chitosan with the fraction (F_A) of *N*-acetylated units of 0.6. The *r*-values were found to increase with increasing F_A of the CM-chitins, while *r*-values decreased with increasing fraction of carboxymethylation.

2.2 Poly(vinyl alcohol) Based Polymer Blend

Shibayama *et al.* (1991) studied the bulk characterization of cellulose/poly(vinyl alcohol) (CE/PVA) blend films. These films prepared from solutions in dimethylsulfoxide and tetraethylammonium chloride (DMSO-TEAC). The blend films were optically clear at any composition. Transmission FTIR measurements revealed that the indices of crystallinity of cellulose and PVA decrease with increasing concentration of PVA and cellulose, respectively, in the blends. These findings suggest strongly the miscibility of amorphous cellulose and PVA chains.

Chandy and Sharma (1992) suggested that PVA-blended chitosan membranes have superior permeability for small molecules as compared to standard cellulose membranes with adequate mechanical properties. It also appeared that membranes having biomolecules like heparin and PGE_1-immobilized on them via plasma treatments may have wider applications in the hemodialysis of patients by offering improved permeability and blood

compatibility. This may also be useful for patients who are at risk of internal hemorrhaging on heparinization since a reduction or elimination of the use of soluble heparin during dialysis may be possible. Finally, it is suggested that the above modification using plasma treatments would be useful toward improving the blood compatibility of existing membranes.

Kim *et al.* (1992a) studied the blend membrane consisting of PVA and chitosan prepared from the solvent-casting technique. IR analysis showed that intermolecular interaction between PVA and chitosan existed. The swelling study indicated that the cross-linking reduces the swelling capacity of the membrane mainly due to the cross-linking density and functional groups in the PVA and chitosan blend. This membrane showed a pH-sensitive swelling characteristic that would be applicable to a controlled-release system.

Kim *et al.* (1992b) reported the permeation of ribroflavin and insulin though PVA and chitosan blend membrane. The permeability coefficients of both solutes through the crosslinked PVA and chitosan blend membrane were in the order of 10^{-6}-10^{-7} cm^2/s and showed a pH dependence. The DSC thermograms of these indicated that the content of free water and the amount of freezing bound water increased with water content in the membrane. The higher permeation rate of solutes in acidic solution than that in neutral solution was due to an increase in both water content and the amount of free water and freezing bound water.

Lee *et al.* (1996) presented that mechanical properties of blend films of β-chitin and poly(vinyl alcohol) in dry and wet states were improved compared to those homopolymer. FTIR spectra of the blend showed the transition of hydroxyl and carbonyl stretching bands upon blending. Wide angle X-ray diffraction patterns of the blend also exhibited the loss of crystallinity of β-chitin and PVA upon blending. Transmission electron microscope (TEM) studies of blends using ruthenium tetraoxide as a staining agent were examined to reveal the micro-structure and miscibility of the

blends. The TEM micrograph of blend β-chitin 70: PVA30 shows some microseparations, but it is acceptable to be miscible in the blends.

2.3 Poly(vinyl alcohol) Based Hydrogel

Hirai *et al.* (1992) studied hydrogel was prepared by repetitive freezing and thawing of poly(vinyl alcohol) aqueous solution which was chemically crosslinked with glutaraldehyde. The chemically crosslinked hydrogel hardly changed its physical appearance, and maintained good elasticity and strength as original gel. However, after treating in boiling water, it swelled a little, depending on the condition of the chemical treatment. The melted gel obtained showed shape memorizing property, that is, it could firmly bold nearly 200% of strain, keeping its original high elasticity. The strain could be released very quickly (<1 s) in boiling water, and the gel was suggested to be applied to a new type of gel actuator.

Shiga *et al.* (1993) presented the deformation of poly(vinyl alcohol)-poly(sodium acrylate) composite hydrogel (PVA-PAA gel) under sinusoidally varying electric fields in electrolyte solutions. A cyclic bending straightening motion of the PVA-PAA gel rods of about 1 mm. in diameter have been observed in Na_2CO_3 aqueous solutions under the fields. The PVA-PAA gel had a response time of less than several hundreds milliseconds. The bending has also been observed in organic solvents containing an electrolyzed. It was found that the motion of the gel under electric fields of less than 1 Hz occurred mainly through swelling due to the change of the osmotic pressure based upon the difference of the ion concentration.

Gudeman *et al.* (1995) prepared the hydrogels from interpenetrating networks of poly(vinyl alcohol) and poly(acrylic acid) by varying cross-linking ratio and ionic content. It was observed that an increase in the average molecular weight between cross-links, M_c, yielded faster swelling and

deswelling rates, as the rates for membranes with M_c = 18,000 were about twice as fast as were the rates of membranes with M_c = 34,000. Oscillatory swelling behavior was investigated in response to changes in the pH and ionic strength of the swelling medium. A change in pH from 3 to 6 caused an ionization of the hydrogels and an increase in the weight swelling ratio, with a greater increase exhibited by inter penetrating polymer networks (IPNs) with a higher ionic content. Increase in pH also caused an increase in the average mesh size.

Vazquez-torres *et al.* (1993) studied miscibility of binary blends of poly(vinyl alcohol) (PVA) with poly(acrylic acid) (PAA). It was found that the PVA/PAA system was miscible in the full range of composition and their blends showed a hydrogel behavior. Water retention (absorbency) of these hydrogels was reduced by thermal treatment and their values depended upon both the heating time and the blend composition. The cross-linking degree was estimated for the PVA/PAA hydrogels by using their absorbency values in the Flory-Rehner equation. Based on this calculation, the higher of the cross-linking degree, the longer the heating time for a given blend composition. Cross-linking degree values were also increased by addition of glyoxal in these blends. This additive improved the thermal stability of PVA/PAA blends.