CHAPTER II
LITERATURE SURVEY

2.1 Carboxymethyl-chitin (CM-chitin)

Tokura *et al.* (1990) studied the sustain-release of methamphetamine-bound CM-chitin. After methamphetamine-bound CM-chitin (MAEA-CM-chitin) was injected subcutaneously in rabbits, it was found that the introduction of antibody production was significantly low. The MAEA oligosaccharide was released slowly after the biodegradation of MAEA-CM-chitin and maintained at a significant level in serum for more than 120 h, while the blood level of MAEA was out of the range of detection within 7 h after the injection, probably owing to rapid metabolism, CM-chitin was reveled to be a suitable drug carrier for controlled release.

Tokura *et al.* (1983b) reported that carboxymethylation of chitin was carried out effectively under basic conditions for preparing a cation exchange resin. 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 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.

Watanabe *et al.* (1992) studied the release of a peptidic anticancer drug, neocarzinostatin (NCS), which was incorporated into CM-chitin gel. The addition of iron (III) chloride into CM-chitin solution induced gel formation. CM-chitin gel containing NCS was digested by lysozyme *in vitro* and NCS was released from the gel in both a time- and dose- dependent manner. In-vivo studies in mice showed that free NCS was rapidly cleared from the circulation, but NCS released from the gel was detectable in plasma even 48 h after the subcutaneous injection of the gel. These results suggest that CM-chitin gels are useful as a sustained-release drug carrier.

Tokura *et al.* (1992) studied the two-step release of drug by a covalently drug-pendented CM-chitin in which the drug was couple through an enzyme-susceptible bond. In these conjugates, the drug will be released through several hydrolysis processes, since oligomerization of CM-chitin by lysozymic hydrolysis is the first step, and the release of parent active drug is followed by the cleavage of spacer-drug linkage with proteolytic hydrolysis as a second step. 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.

Hjerde *et al.* (1997) studied on degradation of CM-chitin 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 untits 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 Silk Fibroin

Park *et al.* (1999) prepared silk fibroin/chitosan blend films by solvent casting method. The conformation transition of silk fibroin from random coil form to β-sheet structure induced by blending with chitosan resulted in the increase of crystallinity and density of the blend films. The blend film containing 30 wt% chitosan exhibited a maximum increase in crystallinity and density. It was found that the tensile strength and initial tensile modulus of blend films were greatly enhanced with increasing the chitosan content and showed a maximum value at the composition of 30 wt%.

Freddi *et al.* (1995) studied the structure and physical properties of silk fibroin/cellulose blend films. The crystalline structures of regenerates fibroin and cellulose were β-form and cellulose II, respectively. The mechanical properties showed that both tensile strength and elongation at break of silk fiborin films were improved by blending with cellulose. IR spectra exhibited changes in the skeletal frequencies of silk fibroin, suggesting the occurrence of intermolecular interactions between fibroin and cellulose through hydrogen bond formation.

Tsukada *et al.* (1994) studied the structure and compatibility of Poly(vinyl alcohol)/silk fibroin blend films. The IR absorption spectra of the blends were identified as purely a composite of the absorption bands characteristic of both PVA and silk fibroin pure polymers. The thermal behavior of the blends was characterized by TMA. It would appear that the blends were intermediate to the pure components. It can be imply the possibility that there is incompatibility between silk fibroin and PVA, though the presence of some specific interactions cannot be completely excluded. Furthermore, the micrograph of SEM showed a dispersed phase formed by spherical particles of 3-7 μm diameter.

Agarwal *et al.* (1997) studied the effect of moisture absorption on the thermal properties of *Bombyx mori* silk fibroin films. Films of regenerated *Bombyx mori* silk are strongly affected by absorbed moisture. This phenomenon was studied by differential scanning calorimetry (DSC). Exposure of previously dried films to environments of controlled relative humidity produces test samples of well-defined equilibrium moisture content. The glass transition temperature, T_g, dropped by 40°C at moisture uptakes as low as 2%, and T_g depressions as large as 140°C were observed at higher relative humidity. The moisture-induced decrease of T_g was completely reversible, as a film remoistened and then redired possesses an unchanged T_g. Trends in T_g with water uptake correspond reasonably well to predictions of classical thermodynamic theory, indicating that the plasticization effect of moisture on the combined silk-water system can be satisfactorily explained

from macroscopic properties of the constituents without any reference to specific interactions.

Freddi *et al.* (1999) studied the structure and physical properties of silk fibroin/polyacrylamide blend films. It was found that the DSC curves of silk fibroin/polyacrylamide blend films showed overlapping of the main thermal transition characteristic of the individual polymers. The exothermic peak at 218°C, assigned to the β-sheet crystallization of silk fibroin, slightly shifted to a lower temperature by blending. The peak of dynamic loss modulus of silk fibroin at 193°C gradually shifted to lower temperature in the blend films, suggesting an enhancement of the molecular motion of the fibroin chains induced by the presence of polyacrylamide. IR spectra of silk fibroin changed in the NH stretching region, which attributed to disturbance of the hydrogen bond pattern of silk fibroin and formation of new hydrogen bonds with polyacrylamide. The values of strength and elongation at break of blend films slightly improved at 20-25% polyacrylamide content.

Chen *et al.* (1994) investigated the transport of pharmaceutical through silk fibroin membranes prepared from Chinese cocoon. The permeability coefficient of 5 kinds of pharmaceuticals, i.e. 5 fluorauracil (5FU), L-(+)-ascorbic acid (Vc), resorcinol (Res.), sodium phenolsulfonate (SPS) and benzyltrimethylammonium chloride (BTAC), could be regulated by changing the pH value of the external solution. The silk fibroin membrane was an amphoteric ion exchange membrane composed of both weak acidic and weak basic groups and it was expected to be used as the matrix of the drug delivery system with pH-responsive function.