CHAPTER II
LITERATURE SURVEY

2.1 Chitosan Based Polymer Blends

Ratto *et al.* (1996) reported that the phase behavior of chitosan/polyamide blends was influenced by the preparation conditions. Characterization of the blends by Differential Scanning Calorimeter (DSC) and Dynamic Mechanical Analyzer (DMA) revealed partial miscibility of chitosan with nylon 4. Blending of chitosan with nylon 4 could enhance mechanical properties of the blends.

Guan *et al.* (1998) presented paper describing the phase behavior of chitosan/viscose rayon blends. The phase behavior of the blend was influenced by its composition with or without carboxymethylated chitosan (CM-Cs). Characterization of the blend films by DSC and DMA revealed partial compatibility of chitosan with viscose rayon. Results of Transmission Electron Microscope (TEM) showed that the addition of CM-Cs into the blend could improve the compatibility of chitosan and viscose rayon.

Hasegawa *et al.* (1994) studied on preparation and characterization of cellulose-chitosan blend films. Blending of cellulose with chitosan led to desirable characteristics, including improved mehanical properties and increased solute permeability of chitosan. This is due to the interaction between cellulose, chitosan and water molecules in the films. The presence of chitosan molecules may lead to the decrease in the domain size of cellulose and increase in the interfacial region between cellulose and chitosan domain.

Qurashi *et al.* (1992) studied on modification of chitosan by blending with poly(vinyl pyrrolidone)(PVP). It was found that the modified films had water absorption capacities superior to those of pure chitosan films. But the other properties of chitosan such as elongation at break, relative crystallinities, and tensile strength were found to be decreased, when PVP in the blends was increased.

Xiao *et al.* (2000) prepared the blend films from chitosan and konjac glucomannan (KGM). The blend films gave high miscibility and thermal stability at the weight ratio of chitosan to KGM was 7:3. This is due to intermolecular hydrogen

bonding formation between hydroxyl groups, amino groups, and acetyl groups. The crystallinity of the blend films was inversely proportional to the amount of KGM. The water solubility of the blend film was improved by blending with KGM.

Sun *et al.* (2000) prepared chitosan and poly(ethylene glycol) composite fibres via solution spinning. The fibres were then crosslinked with epichlorohydrin and glutaraldehyde. They focused on the influence of crosslinking reagents on teh mechanical properties and mechano-electro-chemical (MEC) behaviors of chitosan/poly(ethylene glycol) fibres. Both epichlorohydrin and glutaraldegyde are effective crosslinking reagents for the chitosan-poly(ethylene glycol) fibre, as reflected in the XPS spectra, the swelling behavior, the mechanical strength and the bending behavior under a noncontacting electric field. Epichlorohydrin of a low concentration can improve the mechanical properties of the fibres for biomedical applications. The direction and the speed of bending can be modulated via pH, ionic strength, the applied electric field. As well as epichlorohydrin and glutaraldehyde concentration. From their point of view, the fixed charge density on the chitosan chains may play an active role in the MEC process.

2.2 Silk Fibroin Based Blend Films

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

Yoshimiza *et al.* (1990) presented the paper about the conformation transition from random coil to β-sheet occurred at the surface of silk fibroin membrane immersing in 80% aqueous methanol. The observation from high resolution 13C-NMR showed that the random coil conformation whose segmental motion was very fast remained in the inner part of the swollen membrane. The

fraction of this portion reduced with increasing methanol treatment time in the sample preparation.

Liang *et al.* (1992) improved physical properties of silk fibroin membrane by blending with sodium alginate, a natural polymer generally found in red algae. The addition of sodium alginate to fibroin showed that water absorbability, mechanical properties and thermal stability of fibroin membranes were improved. The water content of the membrane containing 50% by weight sodium alginate was 66% higher than that of pure fibroin. Because alginate is an ionic polymer, so the hydrophilicity is high. Furthermore, the tensile strength and thermal stability were also improved.

Sun *et al.* (1999) found that the poor mechanical properties of the blend fibres can be improved by adding a properly chosen copolymer, or, a compatilizer. Due to the incompatibility of these two polymers, the mechanical properties of the fibres would be deteriorated upon blending. In this article, the relationships between the mechanical behavior of the blend fibres and their composition, as well as the molecular weight and architecture of the compatilizers were studied with respect to morphological changes. If silk fibroin and acrylic polymer are too compatible, it will prevent the formation of the "sheath-core" structure of the blend fibres, which will thus deteriorate some desired properties of the blend fibres, such as handle, luster, etc. They believe that a suitable compatilizer should be enhance the adhesion between the two polymers, while the "sheath-core" structure can be maintained.

2.3 Chitosan/Silk Fibroin Blend Films

Chen *et al.* (1997b) studied a semi-interpenetrating polymer network (semi-IPN) composed of glutaraldehyde-chitosan and silk fibroin. The FTIR spectra of the semi-IPN manifested that the chitosan and silk fibroin had a strong hydrogen-bond interaction and formed an interpolymer complex. The semi-IPN showed good pH sensitivity and ion sensitivity and also act as an "artificial muscle" because its swelling-shrinking behavior exhibited a fine resersibility.

Park *et al.* (1999) prepared silk fibroin and chitosan blends. It was found that the tensile strength and initial tensile modulus of the blend films were greatly enhanced with increasing the chitosan content.

Suesat *et al.* (2000) prepared and characterized the blend films of chitosan/silk fibroin with and without glutaraldehyde, which used as crosslinking agent. It was found that the composition of chitosan/silk fibroin blend films had a large effect on the mechanical properties, physical properties, and swelling behavior of the blend films. Blending silk fibroin with chitosan resulted in an improvement in tensile strength and elongation at break, and an increase in crystallinity. On the other hand, silk fibroin enhanced the thermal stability of chitosan. The addition of crosslinking agent to blend films enhanced the mechanical properties. Furthermore, crosslinking was very important for the swelling behavior since it enabled retention of structural integrity of the films in the acidic pH buffer solution, even though it reduced the degree of swelling of the films. The swelling behavior of chitosan/silk fibroin blend films varied strongly with respect to changes in pH, salt type, and salt concentration. Therefore, these chitosan/silk fibroin blend films had pH and salt-responsive propeties.

Kweon *et al.* (2001) examined physical and mechanical properties of silk fibroin/chitosan blend films. It was found that the density, degree of swelling, and mechanical properties were strongly affected by the chitosan content in the blend films. The mechanical properties could be markedly improved by blending silk fibroin with 10-40% chitosan content. The coefficient of water vapor permeability of the blend films was comparable to that of commercial wound dressing. In particular, the blend film containing 40-50% chitosan content showed very high oxygen permeability. They concluded that these silk fibroin/chitosan blend films can be used as a wound dressing and artificial skin because of its good mechanical properties and good water vapor permeabilities.

Chen *et al.* (1997a) analyzed the conformation of silk fibroin/chitosan (SF/CS) blend membrane. The results demonstrated that the silk fibroin could show β-sheet conformation when the silk fibroin content in blend membranes was 10%(w/w) and 60-80%(w/w), while the pure silk fibroin membrane showed random coil conformation. A mechanism of the conformation transition was suggested that

the silk fibroin chain could use the rigid chitosan chain as a mold plate to stretch itself to form a β-sheet structure according to the strong hydrogen bond between chitosan and silk fibroin. "Polymer-Induced Conformation Transition" was proposed.

2.4 Chitosan Based Material for Drug Delivery Studies

Kim *et al.* (1992) studied the permeation of riboflavin and insulin through crosslinked poly(vinyl alcohol)/chitosan blend membrane. The permeability coeffecient of both solutes through the crosslinked poly(vinyl alcohol)/chitosan blend membrane exhibited a pH dependence and permeated through the free water region in the swollen blend membrane. The permeation rate of solutes in acidic solution was greater than that in neutral solution due to the water content, amount of free water and freezing bound water of the membrane increased.

Yao *et al.* (1994) studied the swelling kinetic and release characteristic of crosslinked chitosan/polyether polymer network (semi-IPN) hydrogels. These gydrogels exhibited the greater degree of swelling in an acidic pH range. The release of chlorhxidini acetas from the semi-IPN discs depended on pH of the solution. At the beginning of pH 1.0, the release rate was high, whereas no drug released at pH 7.8.

Puttipipatkhachorn *et al.* (2001) studied the drug-polymer interaction and drug release behavior from chitosan films. Four different grades of chitosan varying in molecular weight and degree of deacetylation were used. The model drugs used were salicylic acid and theophylline. The results of Fourier Transform Infrared spectrum and solid state ^{13}C NMR spectroscopy demonstrated the drug-polymer interaction between salicylic acid and chitosan, whereas no drug-polymer interaction was observed in theophylline-loaded chitosan films. Most chitosan film loaded with either salicylilc acid or theophylline exhibited a fast release pattern in distilled waters. The sustained release action of salicylic acid from the high viscosity chitosan films was due to the drug-polymer interaction.

Risbud *et al.* (2000) investigated a pH-sensitive freeze-dried and air-dried hydrogels of chitosan and poly(vinyl pyrrolidone) for antibiotic delivery. Amoxicillin was used as model drugs. It was found that freeze-dried hydrogels

exhibited superior pH-dependent swelling properties over non-porous air-dried hydrogels. Therefore, the amoxicillin release from freeze-dried hydrogels was higher than air-dried hydrogels, which may suggest that freeze-dried hydrogels could serve as potent candidates for antibiotic delivery in an acidic environment.

Gupta *et al.* (2000) studied drug release behavior of chitosan beads and microgranules by using diclofenac sodium as model drug. The release rate of diclofenac sodium from the beads has been found to be slower incomparison to the microgranule. The percent and the amount of diclofenac sodium release were much higher in acidic solution than in basic solution due to the swelling property of the matrix at acidic pH.

Lee *et al.* (1999) investigated interpenetrating polymer network (IPN) hydrogels composed of chitosan and poly(acrylic acid) (PAA) synthesized by UV irradiation method for their structures, crystallinity, swelling behavior, thermal properties, and mechanical properties. It exhibited relatively high equilibrium water content and also showed reasonable sensitivity to pH. It has formation of polyelectrolyte complex due to the reaction between amino groups in chitosan and carboxyl groups in PAA. Hydrogel have become excellent carriers for release of drugs either in their swollen equilibrium state or as dynamically swelling systems. Relatively low mechanical strength can be overcome either by cross-linking, by formation of interpenetrating network (IPN), or by crystallization that induces crystallite formation and drastic reinforcement of their structures. Chitosan has both reactive amino and hydroxyl groups. PAA has pH and electrical sensitive material due to ionic repulsion between anionic charged group, and thus forms polymer complexes with polybases. Chitosan is a weak base (pKa = 6.5). Thus, a swelling ratio of chitosan is high at low pH.

Mi *et al.* (1999) presented the results of application of chitosan-tripolyphosphate or chitosan-polyphosphoric acid beads as swelling-controlled or diffusional-controlled release of 6-MP (6-mercaptopurine, anticancer agent) in simulated gastric (pH 1.2) or intestinal fluids (pH 6.8) solution. The mechanism of chitosan gelled in pentasodium tripolyphosphate solution were deprotonation, accompanied with ionic cross-linking, whereas the mechanisms of chitosan gelled in polyphosphoric acid solution was the interpolymer complex. The releasing behavior

of the chitosan-tripolyphosphate or chitosan-polyphosphoric acid gel beads in pH 6.8 medium seem to be diffusion control, whereas in pH 11 medium the release behavior of the chitosan-tripolyphosphate exhibit chain relaxation swollen control. Another major factor controlling release rate in both media are considered to be the molecular weight of enzyme-hydrolyzed chitosan. It is indicated that the chitosan-polyphosphoric acid gel beads might prove useful as a polymer carrier for the sustained release of the anticancer drug, 6-mercaptopurine, in simulated intestinal and gastric juice medium.

Gupta and Kumar (2000) prepared spherical, semi-interpenetrating polymer network beads of chitosan and glycine, crosslinked with different concentrations of glutaraldehyde for controlled release of drugs. The mechanism of drug release is due to the diffusion through swollen beads in pH 2.0 solution, whereas swelling in pH 7.4 solution is less, resulting in less drug release. Chitosan for clinical applications, it is often important to distinguish clearly between biodegradable polymer and bioabsorbable polymer. Biodegradable polymers are those that decompose in the living body, but the degradation products remain in tissues for longer time. On the other hand, bioabsorbable polymers can be defined as the polymers that are eliminated form the body or metabolized therein. The results indicated that, chitosan might be useful as a vehicle for controlled release of drugs.

Ritsri and Taebounhoud (1986) investigated chitosan film for controlled release of drug. The permeability of chitosan blend with sodium alginate, with sodium carboxy methylcellulose, with sodium hydroxide,with chitosan acetated film was in the sequence from the highest permeability to the lowest permeability. The 1% concentration of sodium alginate gave suitable properties for permeability test of drugs. All of film could not be prepared if concentration of chitosan acetate was less than 1% because it was swelled and dissolved in polymer solution. If concentration was higher than 1%, the viscosity was so high that chitosan acetate and the other one are separated in two laminate. The other factors that effect on properties of film were concentration of polymer blend, soaking time in polymer solution.

Zhang *et al.* (2001) successfully prepared microcapsules of chitosan/sodium carboxymethyl cellulose (NaCMC) using a novel method of emulation phase separation. Bovine serum albumin (BSA) was encapsulated in the microcapsules to

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test their release behaviors. The microcapsules had a high encapsulation efficiency (75%) and had a suitable size of 20-50 μm. The BSA in the microcapsules was speedily released at pH 7.2. The BSA release was reduced with increase of chitosan content from 17 to 38% in the microcapsules. Acid-treated microcapsules had a compact structure, owing to a strong electrostatic interaction caused by $-NH_2$ groups of chitosan and –COOH groups of CMC, and the encapsulated BSA was hardly released at pH 1.0.

2.5 Silk Fibroin-Based Material for Controlled Release Studies

Chen and Minoura (1994) investigated the transport of pharmaceuticals through silk fibroin membranes. The silk fibroin membrane was an amphoteric ion-exchange membrane composed of both weak acid and weak basis groups. Membrane-potential measurements revealed that the isoelectric point of the membrane was about 4.5. The positively charged pharmaceutical, benzyltrimethylammonium chloride, was excluded from the membrane below the isoelectric point. The neutral molecule penetrated through the membrane independently of pH value over the measured pH range. The permeability of silk fibroin membrane to pharmaceuticals could be regulated by changing the pH value of the external solution. It is expected that silk fibroin membrane could be used as the matrix of a drug delivery system with pH-responsive functions.

Katayama *et al.* (2000) investigated the applicability of silk fibroin to controlled release type dosage tablets by using theophylline as model drug. The drug release from silk fibroin tablets was not affected by the pH of the release medium. The greater the fibroin content in the tablets, the lower the percentage release of theophylline. Furthermore, it was found that the drug release from the fibroin tablets was diffusion-controlled mechanism.