CHAPTER II
LITERATURE SURVEY

2.1 Chitosan Based Polymer Blend

Qurashi *et al.* (1992) studied on modification of chitosan by blending with poly(vinyl pyrrolidone) (PVP). It was found 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.

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

Yao *et al.* (1996) studied the swelling behavior of the complex film of chitosan and pectin. It was found that the swelling degree of the films increased sharply at pH less than 2 and larger than 7.

Lee *et al.* (1997) prepared polyelectrolyte complex of sodium alginate and chitosan for biomedical application in form of microcapsule. The drug release rate was also investigated. It was found that the release rate was controlled by the pH. The minimum release was occurred at pH = 4.8. The release rate varied with pH due to loop formation of backbone chains of polyelectrolyte. The long N-acyl groups introduced to the chitosan enhanced the release rate remarkably.

Wang *et al.* (1997) prepared crosslinked chitosan/poly(acrylic acid) complex forming semi interpenetrating polymer network (IPN). It was found that this semi-IPN showed not only pH-sensitivity but also salt sensitivity. In addition, it exhibited reversible response to valent variation of salts due to the ion-exchange ability of poly(acrylic acid).

Xiao *et al.* (2000) prepared the blend films from chitosan /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.

2.2 Silk Fibroin Based Blend Films

Yamaura *et al.* (1990) studied the properties of the blend film of silk fibroin and syndiotactic rich poly(vinyl alcohol). It was found that mechanical properties did not change. However, the presence of silk fibroin in the blend film promoted the permeation of neutral salts and ions.

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.

The blend films of silk and cellulose were prepared by Freddi *et al.* (1995). Both its strength and elongation at break were improved. The addition of cellulose to silk fibroin permited the preparation of membrane with excellent elastic behavior. Moreover hydrogen bonding was found between fibroin and cellulose by analyzing with Fourier Transform Infrared Spectroscopy (FTIR).

Lia *et al.* (1996) prepared the blend of silk fibroin and poly(vinyl alcohol) in order to obtain a good matrix for enzyme immobilization. It was found that the blend membrane retained the merit of silk fibroin and it posed better mechanical strength and higher water absorbance. The glucose biosensor could be prepared by immobilizing GOD (glucose peroxidase) in the blend membrane of silk fibroin and poly(vinyl alcohol) coupling the Clark oxygen electrode. The response time of biosensor was shortened by preparing porous blend membrane with poly(ethylene

glycol) as a removable component. The glucose sensor had the ability of resistance over a broad range of pH and temperature and had good stability.

2.3 Chitosan/Silk Fibroin Blend Films

Chen *et al.* (1997) prepared a semi-IPN crosslinked chitosan/silk fibroin. Both chitosan and silk fibroin had strong hydrogen bonding and formed an interpolymer complex. The semi-IPN showed good pH and ion sensitivity. The semi-IPN could shrink and swell with different concentrations of salt solutions and pHs.

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 tin 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 properties 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 properties.

Kweon *et al.* (2001) examined the 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 can 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 of 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.

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 coefficient 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 solutions was greater than that in neutral solutions due to the water content, amount of free water and freezing bound water of the membrane increased.

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 salicylic 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.

Shiraishi *et al.* (1993) prepared chitosan gel beads containing indomethacin, which used as model drugs, by a polyelectrolyte complexation of sodium tripolyphosphate and chitosan. It was found that the release of indomethacin depended upon the dispersion of indomethacin solid particles in the beads, as well as the porosity, tortuosity and surface area of the matrix.

Risbud *et al.* (2000) investigated a pH-sensitive freeze-dried and air-dried hydrogels of chitosan/poly(vinyl pyrrolidone) based controlled drug release 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 the model drug. The release rate of diclofenac sodium from the beads has been found to be slower in comparison 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.

Shu *et al.* (2001) prepared novel citrate crosslinked chitosan film for drug controlled release. Citrate/chitosan film possessed pH-sensitive swelling and drug controlled release properties. It was found that sodium citrate solution concentration and pH during crosslinking process affected film swelling and drug controlled release profiles, and using higher concentration an lower pH of sodium citrate resulting in less swelling and slower drug release.

Gupta *et al.* (2000) prepared spherical, semi-interpenetrating polymer network beads of chitosan and glycine crosslinked with different concentrations of glutaraldehyde. Chlorpheniramine maleate was used as the model drug. The release of chlorpheniramine maleate in solution of pH 2.0 and pH 7.4 at 37°C was studied. The results indicated that chitosan might be useful as a vehicle for controlled release of drugs.

2.5 Silk Fibroin Based Material for Controlled Release Studies

Chen *et al.* (1993) investigated the transport of pharmaceuticals through silk fibroin membranes prepared from Chinese cocoon. The permeability coefficient of 5 kinds of pharmaceuticals, i.e. 5 fluorouracil (5FU), L-(+)-ascorbic acid (Vc), resorcinal (res.), sodium phenolsulpahte (SPS), an benzyltrimethyammonium 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.

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 form 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 released of theophylline. Furthermore, it was found that the drug release from the fibroin tablets was diffusion-controlled through the matrix.