CHAPTER II
LITERATURE REVIEW

2.1 Wound dressing

Nowadays, there has been a wide variety of biomedical application in the area of biotechnology such as wound dressing, tissue engineering, cancer drug delivery, etc (Jayakumar *et al.*, 2010) because of its excellent properties in biocompatibility, biodegradability and non-toxicity. Among various types of biomedical devices, wound dressing is the one of an important tool in medical therapy which has been continuously developed to be further helpful in wound healing process.

A wound can be described as a defect or a break in the skin, resulting from physical or thermal damage or as a result of the presence of an underlying medical or physiological condition (Boateng *et al.*, 2007). Wound dressings are any of various materials used for covering and protecting a wound. Main functions of wound dressing include reducing or eliminating causative factors (shear, friction, etc.), providing systemic support for healing (blood, oxygen, fluid, etc.) and applying the appropriate topical therapy such as removing necrotic tissue, eliminating infection, exudate absorbing, maintenance moist environment, protect from trauma and bacterial invasion (Clark, 1996).

In recent years, the large number of new dressings has been developed to achieve improved wound healing. From the development of wound dressings, it can be divided into 2 types which are traditional wound dressings and modern wound dressings. Traditional dressings are dry and do not provide a moist wound environment. However, the essential characteristic of modern wound dressing is to retain and create a moist environment around the wound to facilitate wound healing (Boateng *et al.*, 2007). The modern wound dressing consists of 2 parts which are the matrix that can provide moisture and the incorporation of active ingredients to promote wound healing.

Generally, the active ingredients are released to the wound site with following mechanisms: diffusion, swelling and erosion. Hydrogel dressing is one of

the interested modern wound dressing which can response to the release of the active ingredients due to the hydration of the polymer by fluids and swelling capability.

2.1.1 Hydrogel Dressing

A hydrogel dressing is one of the most attractive types which fulfills with many advantages for wound treatment. Hydrogel is a three dimentional crosslinked hydrophilic polymeric network containing mainly of water which is excellent for helping to create moist environment that able to clean and remove necrotic tissue (Whyte, 2003). In addition, hydrogel dressing is not to stick to wounds, then, it can be easily taken out without damaging the wound and provide less pain for patients. As a result, hydrogel material is very suitable for development modern wound dressing containing active ingredients which facilitate in wound healing.

Hydrogels can be formed from both natural and synthetic polymers (Lin and Metters, 2006). Synthesic polymers include poly(hydroxyethyl methacrylate) or (PHEMA), poly(vinyl alcohol) or PVA, polyethylene Glycol or PEG, polyvinylpyrrolidone or PVP, etc. Bio-polymers include Calcium alginate, Gelatin, Chitosan, Bacterial cellulose, Carboxymethyl chitin, etc (Vlierberghe *et al.*, 2011). Hydrogels based on natural polymers can have insufficient mechanical properties, contain pathogens and evoke immune responses. On the other hand, they have numerous advantageous properties like inherent biocompatibility, biodegradability, bacteriostatic and wound-healing properties. Synthetic hydrogels do not have these inherent bioactive properties (Zarzycki *et al.*, 2010).

2.1.2 Mechanisms of Releasing from Hydrogels

Several unique properties that hydrogels possess make them useful in delivering biomolecules (Lin and Metters, 2006). Due to their hydrophilicity, hydrogels can imbibe large amounts of water (>90 wt.%). The mechanisms of release are divided following the drug delivery system. The development of controlled drug delivery technology is rapidly progressive in the area of medical health care. The molecule release mechanisms from hydrogels are very different from hydrophobic polymers. Both simple and sophisticated models have been previously developed to predict the release of an active agent from a hydrogel device as a function of time.

These models are based on the rate-limiting step for controlled release and are therefore categorized as follows (Lin and Metters, 2006):

2.1.2.1 Diffusion-Controlled Release

Diffusion-controlled is the most widely applicable mechanism for describing drug release from hydrogels (Ganji *et al.*, 2008) dividing into two major types: reservoir devices and matrix devices (Figure 2.1). Reservoir systems consist of a polymeric membrane surrounding a core containing the drug. In matrix devices, the drug is dispersed throughout the three-dimensional structure of the hydrogel. Drug release from each type of system occurs by diffusion through the macromolecular mesh or through the water filled pores. Fick's law of diffusion is commonly used in modelling diffusion-controlled release systems (Lin and Metters, 2006).

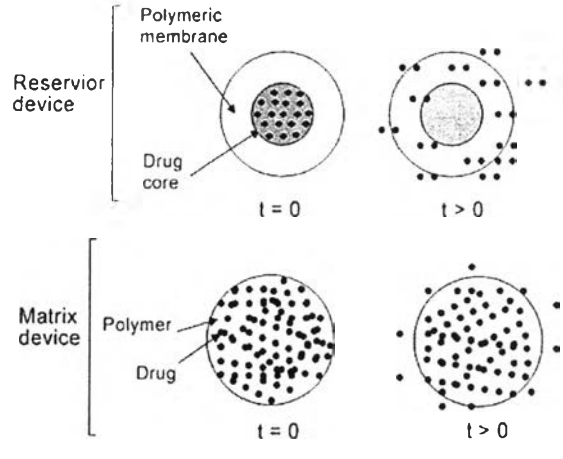

Figure 2.1 Schematic representation of diffusional controlled reservoir and matrix devices.

2.1.2.2 Swelling-Controlled Release

Swelling-controlled release occurs when diffusion of drug is faster than hydrogel swelling. The modelling of this mechanism usually involves moving boundary conditions where molecules are released at the interface of rubbery and glassy phases of swollen hydrogels. The rate of drug release is controlled by the velocity and position of the front dividing the glassy (dry) and rubbery (swelled)

portions of the polymer as shown in Figure 2.2 (Coviello *et al.*, 2005). This transition occurs when the characteristic glass-rubber polymer transition temperature is lower than temperature of fluid which surrounds the drug delivery matrix. In the glassy state, entrapped molecules remain immobile. In the rubbery state dissolved drug molecules rapidly diffuse to the fluid through the swollen layer of polymer. Released fluid molecules contact the external layer of hydrogel. This forms a moving front that divides hydrogel matrix into a glassy and swollen region. In these systems the rate of molecule release depends on the rate of gel swelling (Zarzycki *et al.*, 2010). In the swelling-controlled delivery system following phenomena take places (Siepmann *et al.*, 2008): 1) The length of drug diffusion way increases. This causes a decrease of drug concentration gradient (driving force of diffusion) and a decrease of drug release rates. And 2) The mobility of drug molecules increases. This causes an increase of drug release rates.

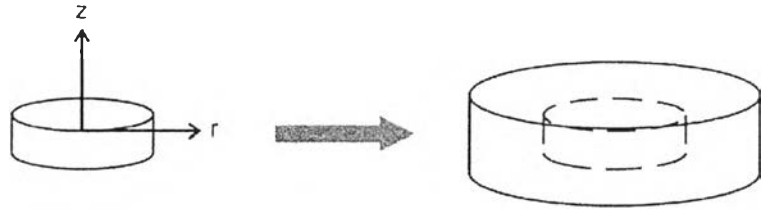

Figure 2.2 Schematic illustration of drug delivery device in glassy and rubbery state matrix.

2.1.2.3 Chemically-Controlled Release (Erosion-Controlled Release)

Chemically-controlled release is used to describe molecule release determined by reactions occurring within a delivery matrix. The most common reactions that occur within hydrogel delivery systems are cleavage of polymer chains via hydrolytic or enzymatic degradation or reversible or irreversible reactions occurring between the polymer network and releasable drug. Under certain conditions the surface or bulk erosion of hydrogels will control the rate of drug release (Ganji *et al.*, 2008).

In systems with surface erosion (heterogeneous erosion) drug release is caused by degradation of the polymer surface (Figure 2.3). Erosion occurs mostly in the external layers of the polymer matrix. The degradation takes place only on the surface (heterogeneous process). This system of drug release occurs only in enzymatic-degrading systems in which the rate of enzymatic degradation is much faster than the transport of enzyme into the hydrogel (Grassi *et al.*, 2005; Siepmann and Gopferich, 2001).

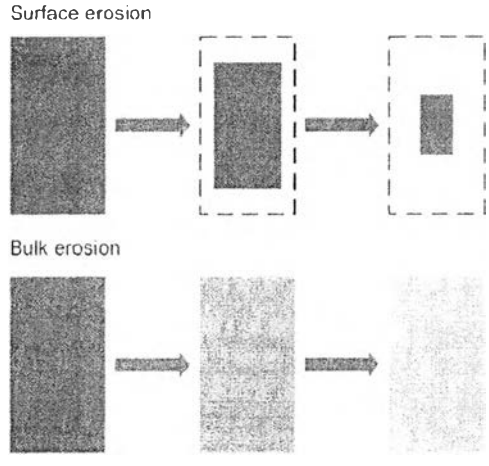

Figure 2.3 Schematic illustration of surface and bulk erosion.

In bulk degrading systems the drug release is governed by egradation of the network and molecule diffusion (Figure 2.3). Bulk eroding polymers degrade slowly and water infusion into the system is much faster than the degradation of polymer (Grassi *et al.*, 2005; Lin and Metters, 2006; Siepmann and Gopferich, 2001). Thus, the whole drug delivery device is rapidly hydrated and polymer chains break off throughout the system. Erosion takes place in the entire system (homogeneous process).

2.1.3 Hydrogel Dressings Containing Active Ingredients

Among the wound dressings, special attention has been paid to hydrogels because of their unique interesting properties which can meet the essential requirements of ideal wound dressings including: immediate pain control, easy replacement, transparency to allow healing follow up, absorb and prevent loss of

body fluids, barrier against bacteria, oxygen permeability, good handling, control of drug dosage and so on (Higa *et al.*, 1999). Therefore, hydrogels have being used as basic materials for manufacturing of wound dressings as invented in 1989 (Rosiak *et al.*) and also were futher studied to improve the efficiency of hydrogel wound dressings.

There are some reports which prepared hydrogels as the wound dressings and they found that the hydrogel dressings could accelerate the wound healing. For instance, in 1999, polyethylene oxide (PEO) hydrogel and PEO/poly(vinyl alcohol), PVA blend hydrogels were prepared and crosslinked with electron beam irradiation (Yoshii *et al.*, 1999). They studied the decresing of wound size area and they found that wound area covered by hydrogel decreases obviously with increasing healing period. In contrast, the wound covered by gauze dressing reduces by only half a percent even after 14 days (Figure 2.4). They concluded that the hydrogel gives a wet environment to wounds which caused faster healing compared with the gauze dressing with a dry environment and it can be peeled off easily from the wound when the dressing needs changing.

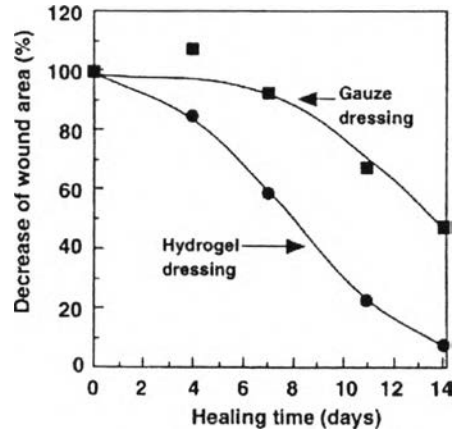

Figure 2.4 Healing of wound by gauze and hydrogel dressings.

For hydrogel dressings containing the active ingredients, the substances can be incorporated into hydrogel matrices by two ways (Lin and Metters, 2006): post-loading and in-situ loading. In the post-loading method a hydrogel

matrix is formed and then the active component is absorbed to this matrix. In the in-situ loading a polymer precursor solution is mixed with active component. Hydrogel network formulation and the encapsulation are accomplished simultaneously.

There are several reports that demonstrated the beneficial effect of hydrogel dressings with active ingredients. For example, Obara *et al.* (2003) prepared chitosan hydrogel films containing fibroblast growth factor-2 (FGF-2) stimulates wound healing in mice. It was found that wound treated with fibroblast growth factor-2 incorporated chitosan hydrogel showed the healing faster than without fibroblast growth factor-2 as represented in Figure 2.5. Moreover, in case of control, control wounds healed more slowly and about 80% wound closure was achieved only after over 20 days. In addition, chitosan hydrogel films also showed the ability of wound accelerator because they can promote faster healing rate than the control.

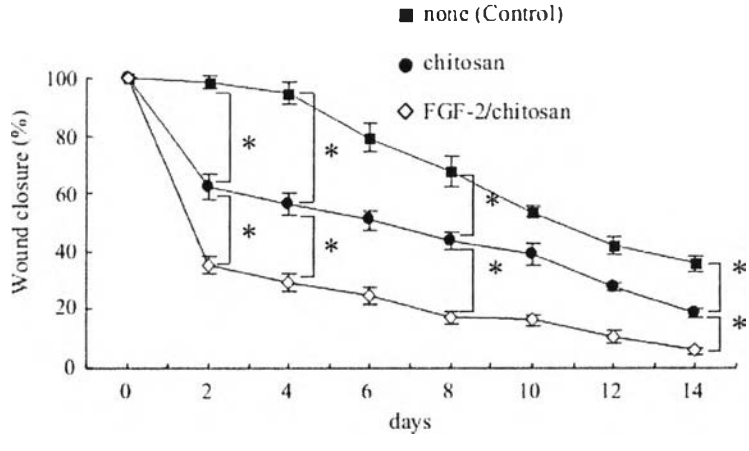

Figure 2.5 Wound closure of FGF-2-incorporated chitosan hydrogel-treated impaired diabetic mice.

2.2 Chitin

Chitin is the second most abundant natural polysaccharide in the world next to cellulose. The predominant sources exploited are in the shells of crustaceans such as crabs, shrimps and squid pens, the cuticles of insects, and the cell walls of fungi

(Jayakumar *et al.*, 2010). Chitin is a polysaccharide containing of 2-acetamido-2-deoxy-D-glucopyranose while chitosan is an *N*-deacetylated derivative of chitin as shown in Figure 2.6. Chitin may be observed as cellulose with hydroxyl at position C-2 replaced by an acetamido group.

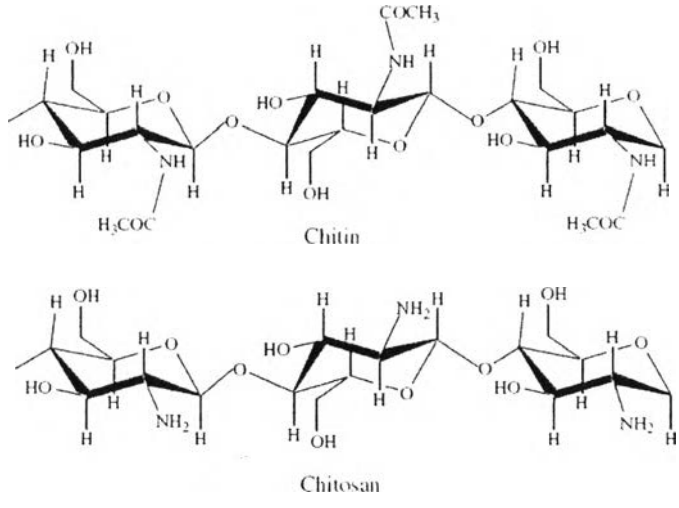

Figure 2.6 Structure of chitin and chitosan.

In the case of crabs or shrimp shells, the chitin production is associated with food industries such as shrimp canning. The typical proceture for the processing of chitin from the shells as follows: the shells of crab or shirmp were first cleaned and treated with diluted hydrochloric acid at room temperature to remove calcium carbonate. The decalcified shells were then cut into small flakes and heated in sodium hydroxide at 100 °C to decompose the proteins and pigments. This α-Chitin extracted from these shells was obtained as colorless to off-white powdery materials.

However, in cause of squid pens, due to ist loose in the molecular packing, β-chitin were easily received by by treating squid pens with hydrochloric acid and sodium hydroxide under mild conditions to give β-chitin (Jayakumar *et al.*, 2010).

Chitin possess great biological properties, such as antiviral activity, low-toxicity, low-allergy, high radiation resistance, biocompatibility, biodegradability, and etc (Jayakumar *et al.*, 2010) which made it attractive to use as biomaterial. However, the existence of hydroxyl and amino groups in the monomer unit of chitin

produce strong hydrogen bonds provided highly crystalline structure, then chitin presents a problem in solubility as shown in Figure 2.7 (Kameda *et al.*, 2005).

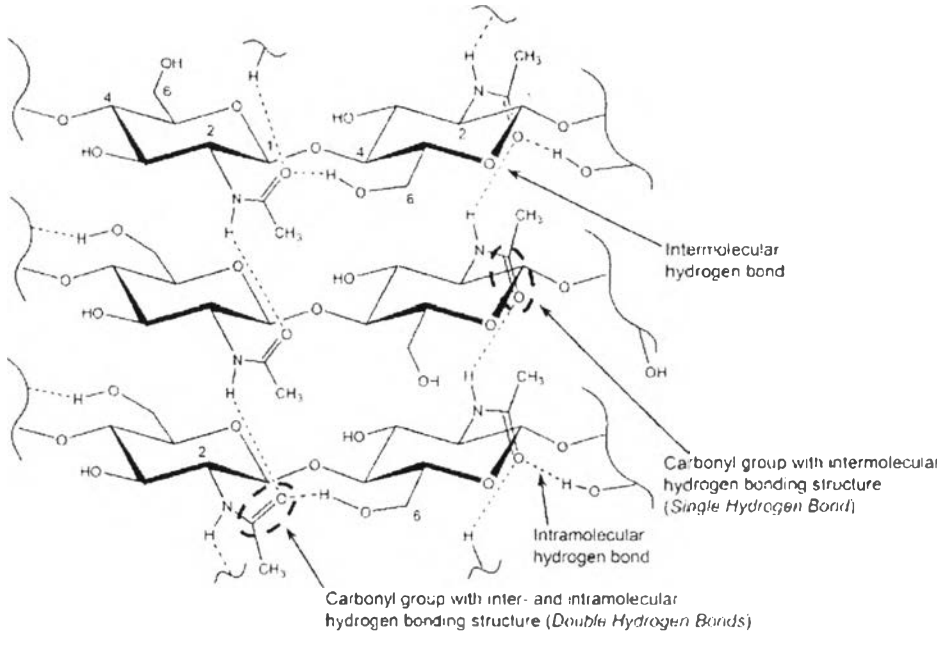

Figure 2.7 Diagram of the hydrogen bonding structure for α-chitin.

The solubility problem of chitin limits its applicatiion, therefore, chemical modification of chitin to enlarge its solubility in common solvents is necessary to extend its utilization.

2.2.1 Carboxymethyl Chitin (CM-Chitin)

Carboxymethyl derivative of chitin is one of water soluble derivatives of chitin which has been used as a biomaterals in many medical appications. The introduction of hydrophilic carboxymethyl (CM) groups into chitin structure is the interested approach to solve the solubility problem because these hydrophilic CM groups can effectively destroy the inter and intra hydrogen bonding between chitin structure, then drastically increase the solubility of chitin at neutral and alkaline pH values without affecting their characteristic (Jayakumar *et al.*, 2010). Since, CM chitin exhibit unique anionic derivatives as well as its low toxicity material (Tokura *et al.*, 1996), its would be useful in several applications such as pharmaceutical, veterinary medicine, biomedical and environmental fields (Jayakumar *et al.*, 2010).

2.2.1.1 Preparation of CM-Chitin

In 1983, Tokura *et al.* reported the praparation of CM-chitin by reacting chitin powder with monochloroacetic acid in isopropyl alcohol as a solvent under condensation reaction as shown in Figure 2.8. Before the reaction, chitin was pretreated with 60% sodium hydroxide solution at 20 °C for 12 hours. Then, the filtration on a sintered glass filter funnel under suction was performed to recover the alkali chitin. Subsequently, the substances were resuspended in a solution of monochloroacetic acid in isopropanol and followed by stirring at 20 °C. Afterward, distilled water was added into the mixture and then HCl solution was used to adjust pH to neutral. After 24 hours, the reaction mixtures was filtered and then precipitated with acetone. Finally, in order to purify the CM-chitin, the obtained product was reprecipitated, desalted by dialysis and later lyophilized. The degree of substitution was characterized by elemental analysis which was found to be 0.6.

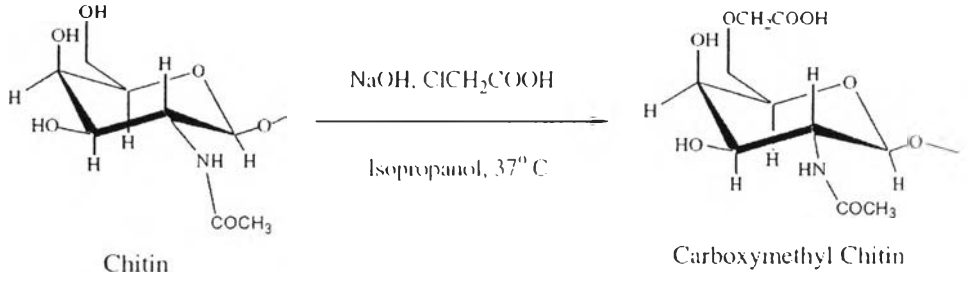

Figure 2.8 Synthesis of CM-chitin.

In another study, CM-chitin was prepared in alkaline chitin solution by suspending chitin powder in 42% NaOH solution (Wongpanit *et al.*, 2005). The suspension was settled in a desiccator for 30 min under reduced pressure. The obtained viscous alkaline chitin solution was mechanically stirred over a period of 30 min at 0-5 °C in an ice bath and then, a monochloroacetic acid solution (25% w/v in 14% v/v NaOH solution) was added dropwise into the alkaline chitin solution under stirring for 30 min. The mixture was settled overnight at room temperature, and neutralized with glacial acetic acid and dialyzed in running water for 2 days, followed by dialysis in distilled water for 1 day. The insoluble substances of the

dialysate were removed by centrifugation at the speed of 10000 rpm for 10 min. The supernatant was put in dropwise into acetone. The precipitate was settled overnight again and it was later collected and further washed with acetone. Finally, the CM-chitin-Na salt was resuspended in ethanol, collected and dried at room temperature. From elemental analysis, it was found that the degree of substitution is 0.4.

2.2.1.2 CM-Chitin and Biomedical Applications

Many forms of CM-chitin based materials for biomedical applications were reported such as water-soluble chitin hydrogel (Cho *et al.*, 1999), carboxymethyl modified surface of chitin beads (Yusof *et al.*, 2000) and CM-chitin films (Wongpanit *et al.*, 2005), etc.

In another case, Shalumon *et al.* (2009) prepared CM-chitin/PVA nanofibrous scaffold and studied the cell spreading result. From SEM images in Figure 2.9, it was indicated that the human stem cells can be attached and growth on the surface of the scaffolds. It can be concluded that the CM-chitin/PVA scaffolds can be used as a supported meterial for cell adhesion and proliferation which were useful for wound dressing.

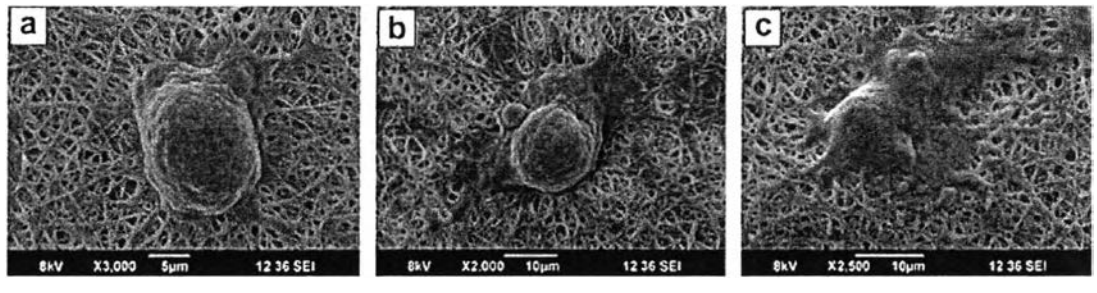

Figure 2.9 SEM images of human stem cells attached on the surfaces of CMC/PVA scaffolds after (a) 12 h (b) 24 h and (c) 48 h of incubation.

In case of CM-chitin film, the frabrictaed CM-chitin and CM-chitosan were crosslinked by microwave treatment (Wongpanit *et al.*, 2005). The cytotoxicity result of these materials showed that the number of living cells after cell seeding on neat chitin, neat chitosan, and microwave-treated CM-chitin films was

still greater than or equal to 90% in comparison with that of the control as shown in Figure 2.10.

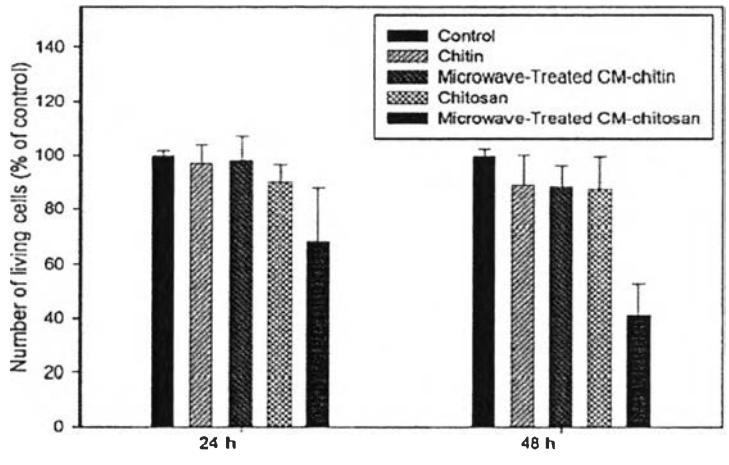

Figure 2.10 Number of living cells after chitin, microwave-treated CM-chitin, chitosan, and microwave-treated CM-chitosan films were deposited over NHGF cells confluence for a period of either 24 or 48 h.

Apart from the wound dressing, CM-chitin was also used as drug carrier in human body. For instance, Watanabe *et al.* (1990) prepared CM-chitin gel by addition of iron (III) chloride with CM-chitin for drug delivery studies. It was found that ferric (III) ion can support the forming gels. CM-chitin solution exhibited in anionic form which interacted with ferric cation (Fe^{3+}) as illustrated in Figure 2.11. In this study, the anticancer drug, doxorubicin (DOX), and bovine serum albumin (BSA) were loaded into CMC gels and the release of BSA or DOX from the gels was investigated. The amounts of bovine serum albumin (BSA) and the anticancer drug doxorubicin (DOX) incorporated into CM-chitin gels were more than 80% and 30%, respectively under the conditions described above. The release of BSA or DOX from the gels was observed to be increased by lysozyme digestion in a time-dependent manner as represented in Figure 2.12. The results indicated that CMC might prove useful as a carrier gel for the sustained release of drugs and cytokines, including vaccines.

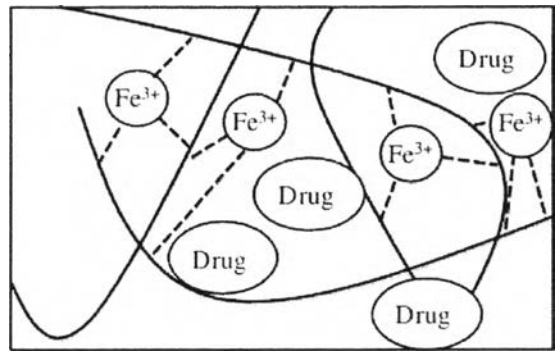

Figure 2.11 CMC gel formed by the addition of Fe^{3+}.

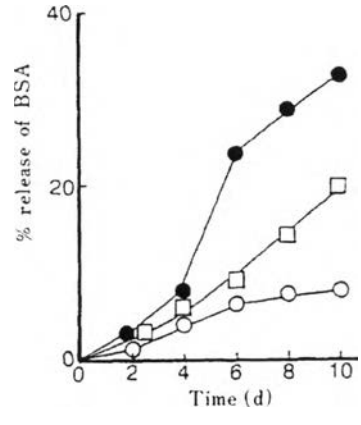

Figure 2.12 Release of BSA from CM-chitin gel by lysozyme digestion. CM-chitin gel containing BSA was incubated with medium (o), 500 U/ml (□) or 10000 U/ml (•) of lysozyme for the indicated days.

In addition, Watanabe *et al.* (1992) studied CM-chitin gel containing a peptidic anticancer drug neocarzinostatin (NCS). CM-chitin was gelled in the presence of 15 to 30 mM iron (III) chloride. 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. From Figure 2.13, they indicated that the releasing rate incresed with the presence of lysozyme. These results suggest that CM-chitin gels are useful as a sustained-release drug carrier.

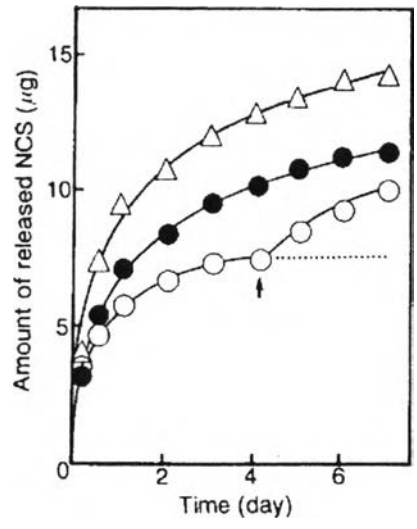

Figure 2.13 Release of NCS from CM-chitin gel by lysozyme digestion. CM-chitin gel containing NCS was incubated without (o) or with lysozyme, 500 U/ml (•) or 5000 U/ml (△) for the indicated days.

Furthermore, chemical crosslinking of materials for biomedical application has been reported as well. In 2011, Wang and Stegemann described the use of glyoxal to crosslink and therefore stabilize chitosan/collagen composite materials gelled with b-GP and seeded with hBMSC. The cytocompatibility of glyoxal and the crosslinked gels were evaluated in terms of hBMSC metabolic activity, viability, proliferation and osteogenic differentiation. These studies demonstrated that glyoxal was cytocompatible at concentrations below about 1 mM for periods of exposure up to 15 h, though the degree of cell spread-ing and proliferation were dependent on matrix composition. In general, glyoxal at low concentrations was not affected to the metabolic activity of hBMSC but there was a relatively clear cut-off point above which cellular activity decreased. The effect of glyoxal also was dependent on exposure time. The cytotoxicity studies were represented in Figure 2.14.

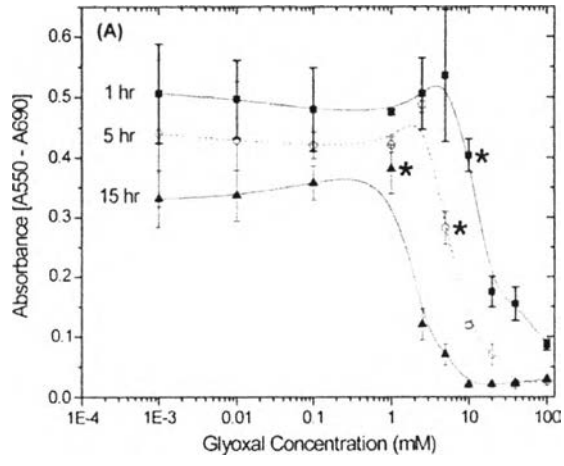

Figure 2.14 Cytotoxicity studies of glyoxal showed that the effect on hBMSC metabolic activity was both concentration- and time-dependent.

2.2.2 Chitin Whisker

Following its crystallographic patterns, chitin gives origin to polysaccharide chains, which are assembled one after another by hydrogen bonds, like the two edges of a zipper. Depending on how these chains are formed, three types of stereoisomers are produced: alpha, beta, and gamma, alpha being the more stable form (Belamie *et al.*, 2004). Figure 2.15 shows the hierarchical structure of chitin microfibrils in the cuticle of a lobster (Raabe *et al.*, 2005). The exocuticle (outer layer) is char-acterized by a very fine woven structure of the fibrous chitin–protein matrix ('twisted plywood' structure) and by a high stiffness (8.5–9.5GPa). The observation of a parallel array of microfibrils brings the hope that there is possibility of improving the mechanical properties of chitin fibers (Revol and Marchessault, 1993).

Whiskers are very hopeful reinforcing materials for composites, because of their high stiffness and strength (Tjong *et al.*, 1999). Owing to their small diameter, whiskers are nearly free of internal defects, thereby yielding strength near to the maximum theoretical value predicted by the theory of elasticity (Courtney, 1990). It was found that the enhancement of their reinforcement depends on such factors (Chazeau *et al.*, 2000) such as the nature of the matrix, the generation of a strong fiber-matrix interface through physicochemical bonding, the aspect ratio, and

dispersion of the whiskers in the matrix. Moreover, whiskers from renewable resources have many advantages such as renewability, low cost, easy availability, good biocompatibility, and easy modification chemically and mechanically, compared with inorganic whiskers (Zinai *et al.*,1996).

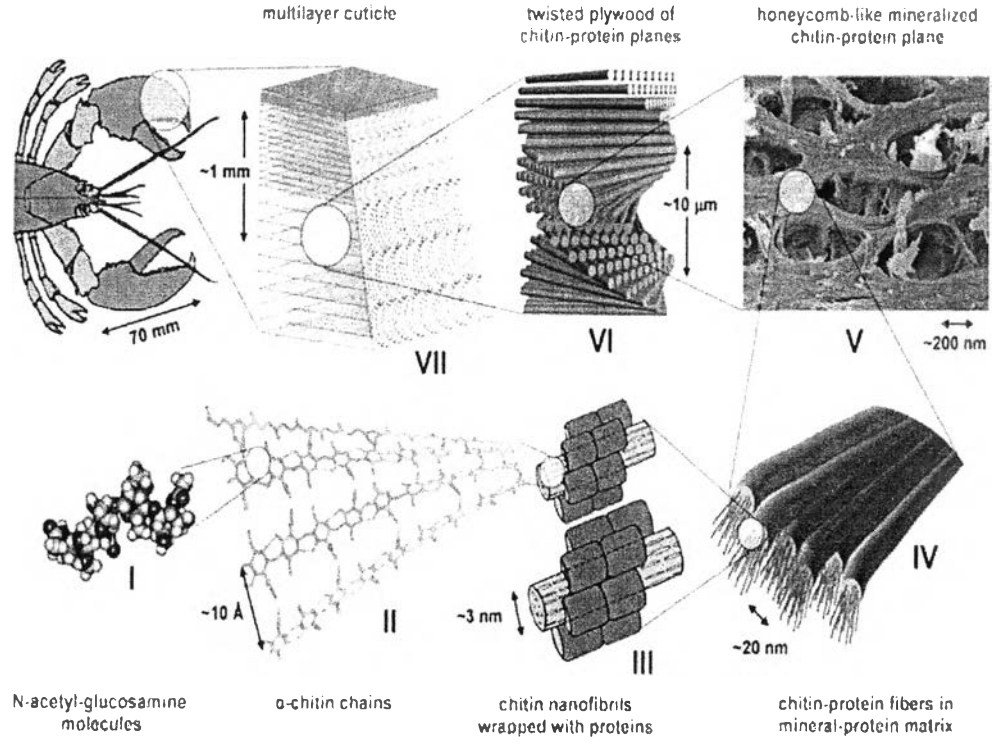

Figure 2.15 The Hierarchical structure of cuticles showing the ordered structure of chitin.

Chitin whisker is orderrd nanocrystallites embedded into low-ordered nano-domains, as shown in Figure 2.16a, which mostly found in the exoskeleton of crustacean. Chitin whisker is prepared by acid hydrolysis to remove low-ordered region, then high crystalline chitin is obtained as shown in Figure 2.16b. The vigorous mechanical shearing will generate individual chitin fibril or called chitin whisker as illustrate in Figure 2.16c (Nair and Dufresne, 2003a). The nanocrystallites of chitin are obtained which having aspect ratio ranges between 10-120, depending on the sources (Wongpanit *et al.*, 2007).

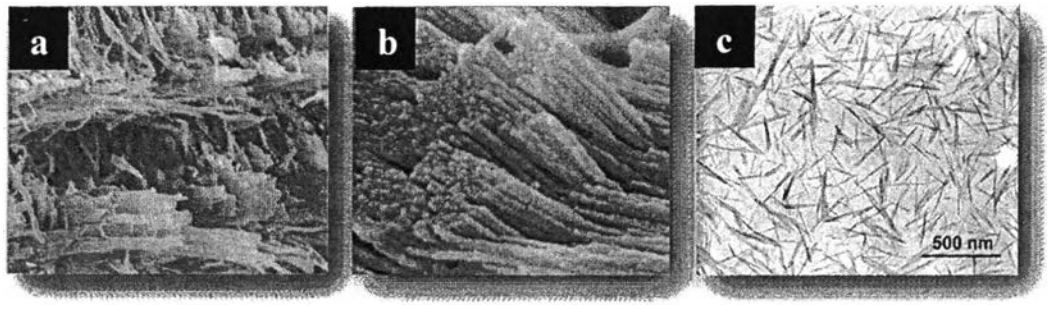

Figure 2.16 Illustration of (a) chitin, (b) crystallite chitin, and (c) chitin whisker.

Morin and Dufresne (2002) prepared nanocomposite materials from a colloidal suspension of high aspect ratio β-chitin whiskers as the reinforcing phase and poly(caprolactone) as the matrix. The chitin whiskers, prepared by acid hydrolysis of *Riftia* tubes (tubes secreted by a vestimentiferan worm called *Riftia.*), consisted of slender parallel rods with an aspect ratio close to 120. The chemical and mechanical treatments of *Riftia* tubes for the preparation of chitin whiskers can be seen in Figure 2.17.

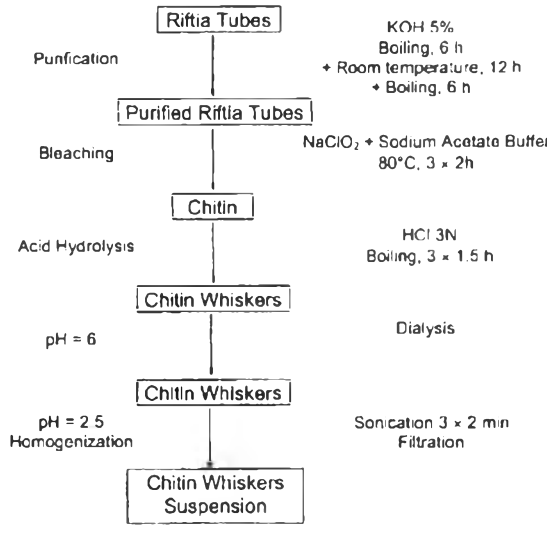

Figure 2.17 Chemical and mechanical treatments of Riftia tubes for the preparation of chitin whisker.

As Figure 2.18, transmission electron micrograph represents chitin whiskers which obtained from a dilute suspension. The suspension was constituted of

individual chitin fragments consisting of slender parallelepiped rods that had a broad distribution in size. These fragments had a length ranging from 500 nm up to 10 μm, and they were weakly distributed in width (around 18 nm). The dimensions of the whiskers were averaged on 240 representative items.

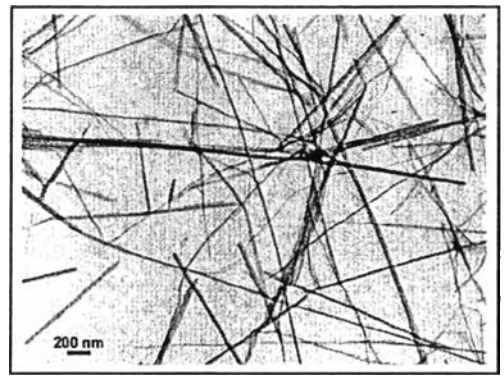

Figure 2.18 Transmission electron micrograph from a dilute suspension of chitin whiskers from Riftia tubes.

Because of their mechanical and biological properties, chitin whiskers has been extensively incoporated in various interesting biomaterials such as soy protein (Lu *et al.*, 2004), silk fibroin (Wongpanit *et al.*, 2007), and chitosan (Sriupayo *et al.*, 2005).

That all of these previously researches revealed chitin whisker in reinforcing field. However chitin is very useful in many applications such as water treatment, textile, paper, cosmetic, wound dressing and biotechnology (Goosen, 1997). Especially, chitin has an advantage in biocompatibility, which better than chitosan, because an acetyl amide group of chitin is similar to an amide group of protein in living body (Muzzareli, 1985). Moreover, chitin is very interesting in biomedical fields because when applied chitin to human wounds and surgical cloths, it accelerates the skin healing process (Usami *et al.*, 1998).

For instant, chitin could induce the collagen production (Minami *et al.*, 1996). Collagen deposition is important for the proliferation phase of wound healing process which can reduce scar tissue. Moreover, chitin was found that less

extensive inflammatory reaction compared with chitosan, which coated polyester nonwoven fabric (Kojima *et al.*, 1998).

Wongpanit *et al.*, (2007) mixed the chitin whiskers with silk fibroin to improving a dimensional stability of silk fibroin sponges by using freeze-drying method. The chitin whiskers were isolated from shrimp shells with the average aspect ratio around 10. The results revealed the chitin whiskers not only improved the dimensional stability, but also promoted a cell spreading. Moreover, the existence of chitin whiskers indicated that the sponges still cytocompatible, leading to suitable for tissue engineering applications.

Moreover, chitin whisker was incorporated in chitosan glycolate composites as wound medicaments (Muzzareli *et al.*, 2007). They reported that Chitin nanofibrils were expected to conform to the wound geometry, to have immediate contact with cells and slowly release N-acetylglucosamine. Furthermore, N-acetylglucosamine is able to regulate collagen synthesis at the level of fibroblasts, also facilitating the granulation and repair of altered skin tissues. (Morganti *et al.*,2008)

Then, the chitin whiskers reinforced alginate nanocomposite fibers were investigated in the objective of biodegradability (Wattanaphanit *et al.*, 2008). The chitin whiskers were prepared from shrimp shells which gave the average aspect ratio about 7.5. The mechanical and the thermal properties of the nanocomposite fibers significantly increased at the low content of chitin whiskers. The investigation of biodegradability using lysozyme/Tris-HCl solution found that the chitin whiskers in the nanocomposite fibers accelerate the biodegradation process in the presence of lysozyme.