CHAPTER II
LITERATURE REVIEW

2.1 Wounds

Wounds can be defined as physical injuries to the body consisting of a laceration or breaking of the skin or mucous membrane, or an opening made in the skin or a membrane of the body incidental to a surgical operation or procedure.

2.1.1 Wound Classification

Wounds can be classified as opened or closed, whereas with open wounds there is a disruption of the skin or muscular membrane. With closed wounds the super facial layer is still intact and protects the wound against contamination. Further classification for wounds can be classified by focuses on three categories of fundamental characteristics which are type, age and depth of wound.

Wound Type

For the first category, two types of wounds are exist: surgical and non surgical wound. A surgical wound is caused by a surgical procedure. A non surgical wound can be caused by trauma or may be pressure ulcer, diabetic ulcer or vascular ulcer.

Wound Age

The second category is to determining wound age that the wound is acute or chronic. In chronic wound, healing has slowed or stopped and the wound is no longer getting smaller and shallower. Even if the wound bed appears healthy, red, and moist, if healing fails to progress, it is a chronic wound. Chronic wounds don't heal as easily as acute wounds. The drainage in chronic wound contains a greater amount of destructive enzymes, and fibroblasts (the cells that function as the architects in wound healing) seem to lose their oomph. They are less effective at producing collagen and divide less often. Examples of acute wounds include a cut, graze or burn. Examples of chronics wounds include leg ulcers, pressure ulcers pressure wounds and diabetic wounds.

Wound Depth

Wound is classified as partial-thickness or full-thickness (Fig. 2.1) according to its depth. Partial-thickness wounds involve only the epidermis or extend into the dermis but not through it. Full-thickness wounds extend through the dermis into tissue beneath and may expose adipose tissue, muscle or bone.

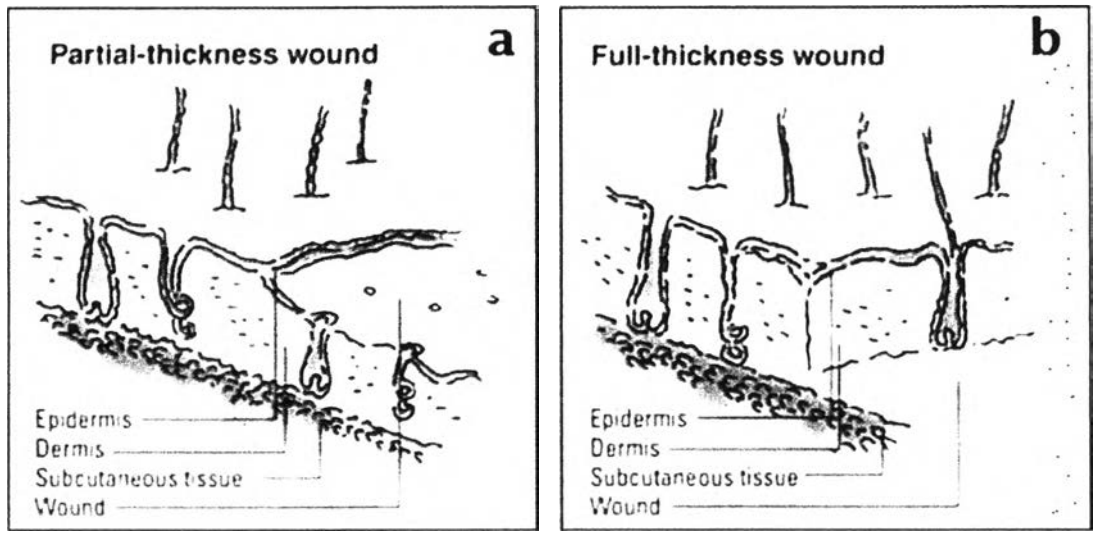

Figure 2.1 Wound depth classification, partial-thickness wound (a), full-thickness wound (b).

2.2 Wound Healing and Stage of Wound Healing

Wound healing is a prefered biological process. It is a combination of physical, chemical, and cellular events that restore wounded tissue or replace it with collagen. Wound healing begins immediately after injury or incision. Wound healing can be divided into four main phases which are the inflammatory, debridement, proliferation and maturation phases. Every wound will follow this path and can be in more than one phase at the same time.

2.2.1 Inflammatory Phase

After wounding the first thing that happens in the injured area is a short period of 5 to 10 minutes with a protective mechanism of the body to stop bleeding, together with blood clotting. This followed by the movement of fluid with cells like lymphocytes, growth factors to reach the injured area. The movement of fluid to the wound area not only delivery cells and growth factors to the wound bed, but also dilute toxin substances and provide nutrients.

The inflammatory phase is begins immediately after injury can be characterized by the classical signs which are redness, pain, heat, swelling and loss of function and lasts approximately 5 days. White blood cells leaking from blood vessels into wounds initiate the debridement phase.

2.2.2 Debridement Phase

Exudates composed of white blood cells, dead tissue, and wound fluid forms on wounds during debridement phase. Dead tissue impedes wound healing and thus the removal of it is an essential phase in wound healing. This dead tissue is a stimulus for inflammation and provides good circumstances for bacteria to proliferate. Neutrophils and monocytes appear in wounds (approximately 6 hours and 12 hours after injury, respectively) and initiate debridement. Monocytes become macrophages in wounds at 24 to 48 hours and haves an important function in removing the debris and cleaning the wound. This phase ends with the rejection of non-vital tissue.

2.2.3 Proliferation Phase

About 3 to 5 days after injury the signs of inflammation will become less, the wound will become cleaner because of the debridement and the repair of the wound can start. Granulation tissue is form and can be characterized by a red, irregular surface. It is very fragile tissue, but important for its function as a barrier to infection. Main factors for this part of proliferation phase are the supply of nutrients, removal of metabolites and presence of oxygen. An important nutrient is vitamin C, which is essential to the production of collagen. And wound contraction occurred, this wound contraction involved the process that pulls the borders of the skin

adjacent to the wound towards the centre of the wound. Wound contraction is very important part in the reduction of the wound area. Normally it is visible from 5 to 9 days after wounding and stops when the tension of the surrounding skin becomes too high or when the edges of the wound reach each other. Epithelialisation includes the proliferation of cells from adjacent skin border and their moving over and adhesion to the surface of wound. They fill in the rest of the area of the wound that is left ater wound contraction, upon the condition that the area is not too large.

2.2.4 Maturation Phase

After the proliferation phase it seems that wound healing has been completed, but one phase is still to be completed. In the maturation phase the strength of the wound increases by the remodelling of collagen. The newly-formed collagen arranges parallel to the tension lines of the skin. This can take several weeks up to 1 or 2 years. The newly formed skin will never get the same strength as the original, injured skin. Approximately about 80% of its strength will be regained. Scars also become less cellular, flatten, and soften during maturation.

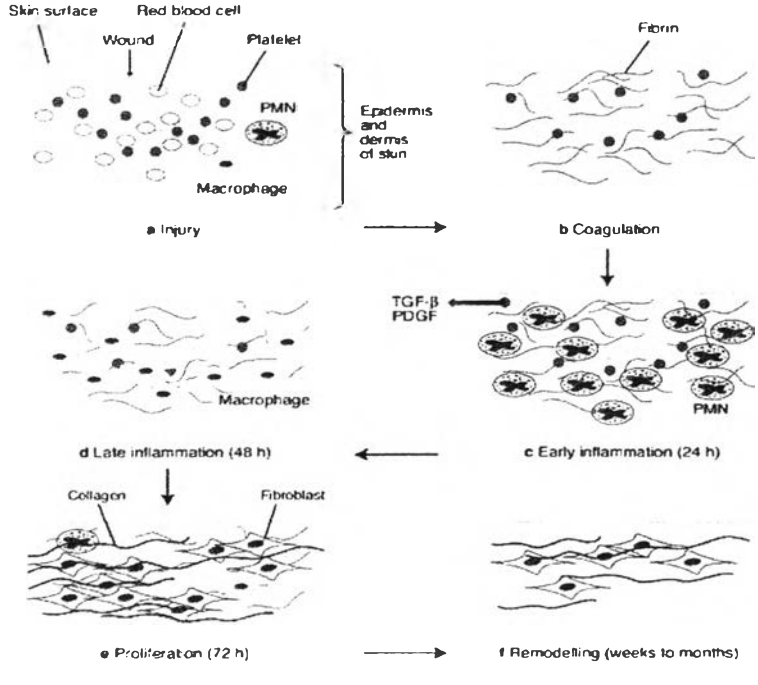

Figure 2.2 The phases of wound healing.

2.3 Wound Dressing

The dressings have many functions and play an important role on a wound. They are used to cover the wounds to accelerate wound healing and create better healing conditions without making any harmful to the wounds. Simply stated, dressings should allow wound to heal at the optimum rate under all clinical circumstances. Turner in 1979 outlined the performance parameters of an "ideal wound dressing" and they included the ability to: (1) absorb exudates and toxic components from the wound surface; (2) maintain high humidity at the wound/dressing interface; (3) allow gaseous exchange; (4) provide thermal insulation; (5) protect the wound from bacterial penetration; (6) be non toxic; and (7) be removed easily without trauma to the wound. And more criteria that were added later included that the material should have acceptable handling qualities (resistance to tear and disintegration when wet or dry), and be sterilizable.

Many of newer dressing are designed to create a moist wound healing environment which allows the wound fluids to remain in contact with the wound.

A moist wound free of infection provides an environment rich in enzymes, cytokines, white blood cells and growth factor which they are beneficial to the wound healing.

Knowledge and understanding of wounds, tissue and healing have grown rapidly over past 40 years, resulting in a major change in the method of wound management. There has been known that traditional wound care such as gauze and other absorbent materials (e.g. cotton and wool) were plugged and concealed the wound but did little to aid healing, and in many cases actually delay it. The clear disadvantages of traditional dressing are the scab, which is made up of the dehydrated exudates and dying dermis, is a physical barrier to healing because epidermal cells cannot move through the scab formed and this may lead to scarring. Another disadvantage of gauzes is that bacteria from the environment can migrate to the wound through the pores of the dressing.

Dr. George D. Winter (Nature, 1962) was able to demonstrate scientifically the difference between wounds of a similar nature when healing was open to the air, and when healing was under occlusive dressing. His work was to create artificial

wounds on pigs, with fifty percent of the wounds occluded and other fifty percent open to the air. The experiment showed that the wounds healing under moist conditions healed fifty percent faster that the wounds healing under dry condition (open to air).

The benefits of the moist wound healing include: (1) prevention of the scab's formation which can trap white blood cells that prevents them from participating in the wound healing functions, (2) prevention of bacterial strike through from outside to wound surface, and (3) more rapidly epithelialisation. Additional benefits to moist wound healing appear to be shortening of the inflammatory and proliferative phases of wound healing with more rapid progression into remodelling phase (Ted S. Stashak, 2004).

Wound dressing have been broadly classified as either adherent or nonadherent and absorbent or non absorbent. Adherent dressing are frequently made from gauze, cotton materials or wool. Gauze dressings are generally highly absorbent and are still used for heavily contaminated exudative wounds. So, the ability to absorb a large amount of extrudate from the wound is important and also resulted in minimization of removal of the dressing which is more cost-effective, these dressing are based polymeric hydrogel.

2.4 Hydrogel

Hydrogels are water-swollen, crosslinked macromolecular networks produced by reaction of monomer or by hydrogen bonding. Hydrogels having a high water content ranging between 30 to 90 percent. Hydrogels can be defined as two component systems where one of the components is hydrophilic polymer, insoluble in water because of three-dimensional network and the second one is water (Fig. 2.3). These tree-dimensional networks can retain a large amount of water or biological fluids in their structure. The extent of swelling and the content of fluids retained depend on hydrophilicity of the polymer chains and the crosslinking density (J.M. Rosiak *et al.*, 1995).

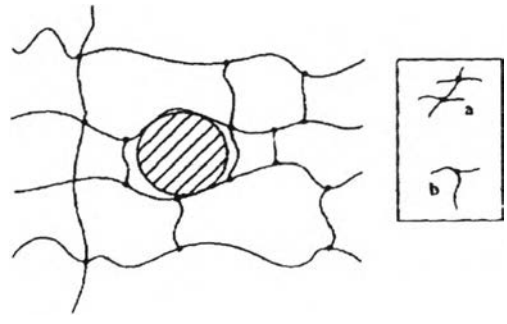

Figure 2.3 Scheme of hydrogel network. Circle donates available space for diffusion. In the insert functional (a) and trifunctional (b) points of chains junction are shown (Roisk & Ulanski, 1995).

2.4.1 Classification of Hydrogels

Polymeric hydrogels can be classified into two different ways as follows:

2.4.1.1 Based on Bonding Type of Cross-links

I. Chemical Hydrogels which are formed by chemical crosslinking through covalent bonding. They are also called permanent hydrogel because it cannot be dissolved in water or other solvents unless covalent crosslinking are cleavage. They are mainly prepared by using one of these approaches: (1) copolymerization of a monomer with crosslinker, (2) crosslinking of water-soluble polymer with crosslinker, and (3) crosslinking of water-soluble with irradiation.

II. Physical Hydrogels which are formed by physical cohesion forces that exist between the polymer segments such as hydrogen bonding, ionic bonding, strong Van Der Waals interactions, or forces that arise due to hydrophobic interaction.

2.4.1.2 Based on Sources of Polymers

III. Natural Hydrogel such as dextran, chitosan, and collagen which usually have high biocompatibility, produce low toxicity byproducts, have intrinsic cellular interactions, and they are biodegradable but there are also some disadvantages in their low mechanical strength and their batch variation.

IV. Synthetic Hydrogel such as poly (vinyl alcohol), poly(vinyl pyrrolidone), and poly (lactic acid) which they can be tailored to give a wide range of properties but they have low biodegradability and may include toxic substances.

V. Combination of Natural and Synthesis

2.4.2 Hydrogel Formation Method

Hydrogel formation processes are essentially due to monomer polymerization or crosslinking of preformed polymers. A great variety of methods to promote crosslinking has been used to prepare hydrogels including chemical and physical methods by using high energy radation method (e.g. gamma rays, electron beams) or radical polymerization (e.g. ultraviolet radiation, redox initiation)

2.4.2.1 Ultraviolet Radiation

Ultraviolet radiation technique, is an effective method to covalently crosslink polymer chains, can produce stable three-dimensional hydrogel networks of varying geometries as show in Figure 2.4 This process uses light to convert liquid macromer/polymer to solid gel (M.C.F.C. Felinto *et al.*, 2007).

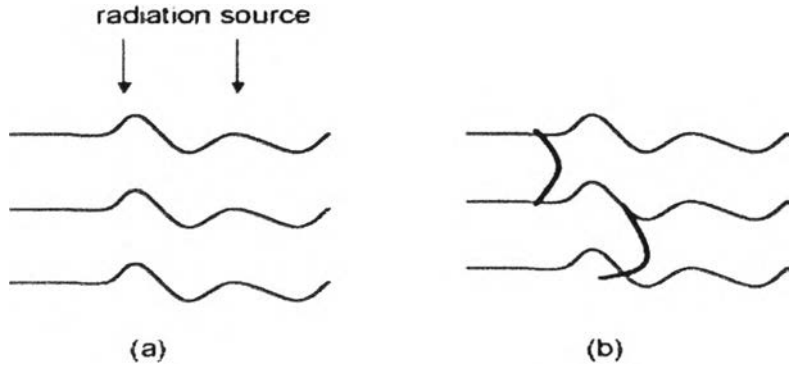

Figure 2.4 Interaction of ultraviolet radiation with linear polymer (a) to develop a crosslinked network structure (b) (SpecialChem website).

Ultraviolet radiation-curing equipment can emit light at specific frequencies matching the absorption bands of photosensitive groups in polymeric structure. The energy sources of UV light equipments are typically mercury lamps, electrodeless vapor lamps, pulsed xenon lamps, or lasers. These generally emit electromagnetic radiation in the region of 200-760 nm but the optimum curing occurs in the wavelength range of 250-400 nm with a radiant output of at least 150 mW/cm^2 (SpecialChem website).

The most common mechanism for UV curing is free-radical polymerization. There are three phases in free radical photopolymerization: photoinitiation (initiator radical formation and initiation), propagation, and termination. The reaction can be illustrated using a photoinitiator (I) and reactive monomers (R, R') as shown in Figure 2.5 Photoinitiators decompose on exposure to UV light to produce initiating free radicals and start the polymerization reaction (SpecialChem website).

Figure 2.5 Free radical ultraviolet curing mechanisms (SpecialChem website).

Ultraviolet radiation-curing reaction was widely used to synthesize polymers and hydrogels because of its distinct advantages, including a fast curing rate, low curing-temperature, low energy consumption, low heat production, and easy process control. However, several synthetic polymers can be toxic for humans, due to the residue of chemical crosslinker and unreacted toxic monomers that remained during polymerization might contain carcinogenic or toxic substances (Ren J,Ha HF. 2001).

2.4.2.2 Gamma Radiation

Gamma radiation technique is a useful tool to make hydrogels for biomedical applications. There are no initiators, which may be harmful and difficult to remove. The hydrogel formation and sterilization can be achieved in one step. Usually a dose of 25 kGy is applied in order to ensure sterility of the product (Ajji *et al.*, 2005)

The primary process involved in radiation synthesis of hydrogel is formation of hydroxy radical (•OH) reacts with polymer in aqueous solution to generate polymer radical that combines with each other, resulting in crosslinking of polymers (J.M. Rosiak, 1995). The net result of crosslinking is that the molecular weight of the polymer increases with increasing dose until a tree dimensional network is formed where each polymer chain is linked to one other chain on average. When scission predominates in an irradiation the molecular weight decreases as dose increases. The final product may be a low molecular weight liquid in some cases. The mechanism of radiation crosslinking in the presence of water can be described as follows (D.Darwis, 2009);

Radiolysis of water

$$H_2O \longrightarrow H^{\bullet}, OH^{\bullet}, e^-_{aq}$$

Hydrogen abstraction

$$RH + OH \longrightarrow R^{\bullet} + H_2O$$

Recombination of polymer radicals

$$R^{\bullet} + R^{\bullet} \longrightarrow R\text{-}R$$

2.4.3 2-Acrylamido-2-Methylpropane Sulfonic Acid (AMPS)

2-acrylamido-2-methylpropane sulfonic acid (AMPS) (Fig. 2.6) is a strongly acidic ionic vinyl monomer and easily dissolved in water (Kanarat Nalampang *et al.*, 2007), which can form polyelectrolyte gels after the flexible polymer chains are crosslinked and ionizable groups are attached. These ionizable

groups completely dissociate in solution, form strong electrolyte groups and produce an electrostatic repulsion force among them, thus influencing the expansion of the network (A. Pourjavadi *et al.*, 2007).

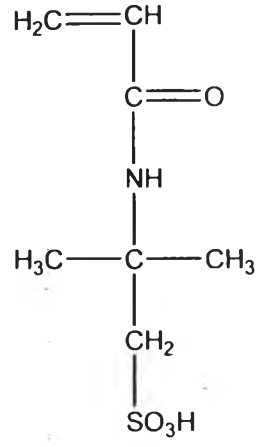

Figure 2.6 Chemical structures of the AMPS monomer.

Due to the excellent properties of 2-acrylamido-2-methylpropane sulfonic acid (AMPS) in hydrophilicity, high swelling capacity, thermal stability, stability over a broad pH range, resistance to hydrolysis, lack of toxicity, biocompatibility and , importantly, any residual unreacted monomer can be removed easily because the polymerization performed in an aqueous system (Kanarat Nalampang *et al.*, 2007), make these superabsorbent polymeric materials used in many biomedical applications and have been attracted interest as a wound dressing since it adheres to the healthy skin only but not to the wound bed, it is easily removable/replaceable without any harmful and also its gel transparency allows visual monitoring of the wound healing.

S. Durmaz and O. Okey., 2000 studied the relationship between the formation mechanism and the swelling behavior in water and in aqueous salt solution of acrylamide (AAm)/2-acrylamido-2-methylpropane sulfonic acid (AMPS)-based hydrogel. AAm-based hydrogels are usually prepared mainly by free radical crosslinkingcopolymerization with crosslinker such as *N,N'*-methylenebisacrylamide (MBA) and they selected AMPS as the ionic copolymer to increase the swelling

capacity. The equilibrium degree of swelling of the final hydrogels is increasing with AMPS content and reaching maximum value at 10 mol% AMPS.

In 2007, Kanarat Nalampang and coworkers synthesized hydrogels from 2-acrylamido-2-methylpropane sulfonic acid (AMPS-H^+) and its sodium salt (AMPS-Na^+) crosslinked with *N,N'*-methylenebisacrylamide (MBA) or ethyleneglycol dimethacrylate (EGDM) by redox-initiated free radical polymerization to complete conversion. They varying the percentages of crosslinker (0.5-1.5% mol/mol) and concentration of monomers (40-60% w/v) and found out that the balance between monomer concentration and crosslink density is importance in designing hydrogel as wound dressing materials; hydrogel sheets prepared from 60% w/v monomer concentration reach the equilibrium at a slightly higher rate and MBA crosslinker found to be more effective crosslinker than EDGM. Furthermore, their synthetic hydrogels can absorb large amount of water quickly within 10 minutes and these hydrogel can be refered as "high water-absorbing polymers".

P. Ninjiaranai *et al.*, 2008 synthesized hydrogels from 2-acrylamido-2-methylpropane sulfonic acid (AMPS-H^+) and its sodium salt (AMPS-Na^+) crosslinked with *N,N'*-methylenebisacrylamide (MBA) and use 4,4'-Azo-bis(4-cyanopentanoic acid) as a photoinitiator by UV radiation method. They studied their properties in swelling ratio, equilibrium water content, and water vapor transmission rate by varying the concentration of monomers (30-50% w/v) and percentages of crosslinker (0.1-2.5% mol/mol). The results showed that the hydrogel sheets prepared from the monomer contents of 40% and 50% w/v AMPS-Na^+ were uniform and coherent whereas those from the 30%w/v AMPS-Na^+ rather weak (low tear strength) and tacky. The % crosslinker plays an important role on the mechanical properties. It was found that the hydrated hydrogel sheets became weaker as an increasing of the % crosslinker in which the water absorption properties of these hydrogel sheets were studied at room temperature. Then the synthetic hydrogels can absorb large amount of water quickly and reach the equilibrium within 10-15 minutes. In addition, it was also found that the water content decreased with increasing AMPS and MBA content due to the increased crosslinking density of hydrogels. The less water absorption ability would be also attributed to the decreased molecular weight between chains (Mc), resulted in decreased of void to absorb

water. Finally, the hydrated hydrogel sheets showed the proper values of the water vapour transmission rate (WVTR) approximately in range of 83-121 g/hr.m^2. These results revealed that the hydrogel with a proper concentration of monomer and crosslinker could have potential to create and keep the moisture of the wound bed. Therefore, it is possible to develop these synthesized hydrogels to use as wound dressings.

L.P. Krul *et al.,* 2008 studied the process of radiation polymerization of AMPS in an aqueous solution and find the ways of forming the network structure of hydrogels on the basis of PAMPS obtained via the Gamma radiation-induced process. They determined the efficiency of radiation crosslinking of PAMPS in the absence of admixed crosslinker and in the presence of *N,N'*-methylenebisacrylamide (MBA). Irradiation of the aqueous additive-free AMPS solution, the conversion reach 100% even at a minimal radiation dose of 2 kGy and this polymer was completely dissolved in water but this water-soluble product was not observed in radiation doses more than an order of magnitude above 2 kGy (at a dose of 50 kGy). They concluded that irradiation of PAMPS primarily results in radiation degradation, rather than crosslinking processes. The crosslinking of macromolecules obtained via radiation polymerization dose not take place and it is impossible to obtain hydrogel unless special crosslinking agents are introduced. The gel fraction of hydrogel increases to 79% at radiation dose of 10 kGy and remains at this level up to a dose of 50 kGy and the maximal degree of crosslinking is reached at a dose of about 20 kGy.

2.4.4 Chitin

Chitin (Fig. 2.7a) is a polysaccharide formed by glucosamine and N-acetyl Glucosamine that is a component of the skeletal material of crustaceans and insects and also available as a component in cell walls of various fungi. A chemical structure of chitin is very close to cellulose except that the hydroxyl group in C(2) of cellulose (Fig 2.7b) is being replaced by an acetamido group ($NHCOCH_3$) in chitin (Roberts. G.A.F., 1992). Its structural unit is *chitobiase*, which is the bridge between the carbohydrate and the protein components of mammalian glycoprotein. It is made into various forms, including sponges, cotton, flakes and nonwoven fabric. Chitin has relevant biochemical significance, in particular it accelerates macrophage migration

and fibroblast proliferation, and promotes granulation and vascularisation. Chitin is non-toxic, odourless, biocompatibility with living tissues, and biodegradable (Ravi Kumar, 2000). The properties of chitin are hydrophilic, tough and inert solid, insoluble in water and most ordinary solvents.

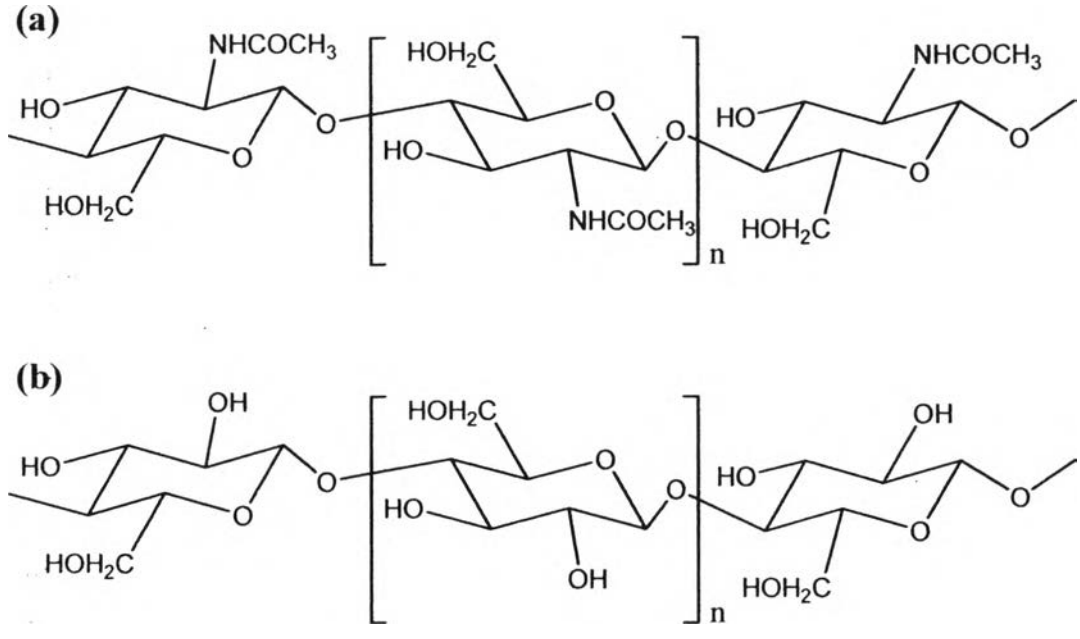

Figure 2.7 Chemical structure of chitin (a) and cellulose (b).

Chitin can be formed in three types of stereoisomers: alpha (α), beta (β), and gamma (γ). The molecules in orthorhombic α-chitin are arranged very tightly in an anti-parallel fashion. A-chitin is mainly present in shells of shrimps, crabs and lobsters. β-chitin takes the monoclinic form in which the chains are arranged in parallel fashion and its can be obtained from squid pens. For γ-chitin, the molecules are arranged in both parallel and anti- parallel manner. Therefore, alpha being the more stable form (Belamie E. *et al.*, 2004). The procedure of isolated chitin from the shells of crustaceans and exoskeletons of insects is showed in the following chart.

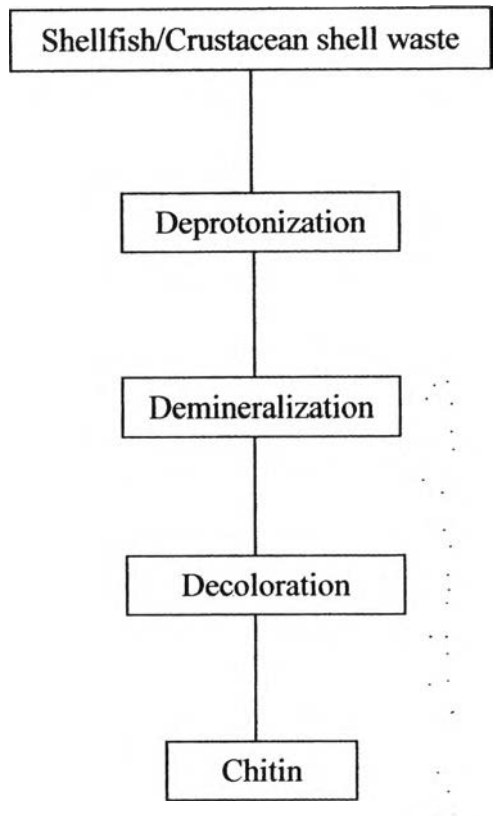

Figure 2.8 Schematic represent of isolation of chitin (Vasnev *et al.*, 2006).

The principles of chitin extraction are relatively simple. Proteins are removed by treatment in dilute solution of sodium hydroxide (1-10%) at high temperature (85-100 °C). Shells are then demineralised to remove calcium carbonate by treating in dilute solution of hydrochloric acid (1-10%) at room temperature. Shell also contains lipids and pigments. Therefore, a decolorizing step is sometimes needed to obtain a white chitin. This is done by soaking in organic solvents or in a very dilute solution of sodium hypochlorite.

2.4.4.1 Chitin Whiskers

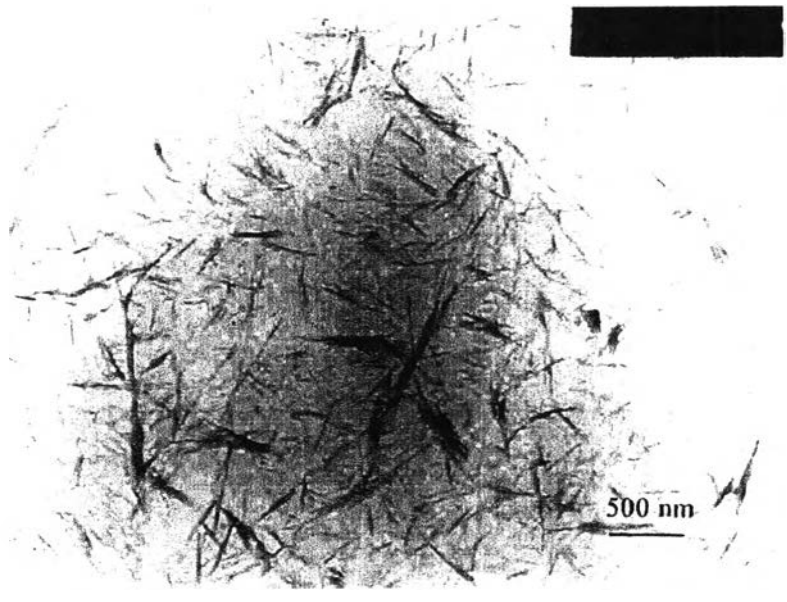

Figure 2.9 Transmission electron micrograph of dilute suspension of α-chitin whiskers from *Penaeus merguiensis* shrimp shells (J. Sriupayo *et al.*, 2005).

When chitin passes through the acid hydrolysis process, nanofibrous structure can be formed as called chitin whiskers (Fig. 2.9). Chitin whiskers of slender parallel piped rods have been successfully prepared from different chitin sources such as crab shells, shrimp shells, squid pens and tubeworms. Chitin whiskers were used as reinforcing fillers in both synthetic and natural polymeric matrices to achieve two main objectives: (1) to improve the properties such as tensile strength, tensile modulus or stiffness and (2) to accelerate the healing of wounds as a result of the presence of chitin oligomers that were released from the fibers due to enzymatic hydrolysis of the whiskers by lysozyme (Chung *et al.*, 1994). In case of biomaterials field, reinforced materials by chitin whiskers can found the delay of biodegradation. Thus, chitin whiskers can enhance biodegradability property due to chitin whiskers have some interaction with the matrix; hydrogen bonding is one of the example of interaction between chitosan and chitin whiskers that disperse in chitosan matrix (J. Sriupayo *et al.*, 2005). On the other hand, the limitation of materials which reinforced by chitin whiskers was showed lower elongation or

fragile when apply them into some application such as wound dressing that it need this property to resist the expansion and contraction.

J. Sriupayo *et al.,* (2005) prepared α-chitin whiskers by acid hydrolysis of α-chitin from shrimp shells to reinforced poly(vinyl alcohol) (PVA) films. The as-prepared whiskers exhibited the length in the range of 150-800 nm and the width in the range of 5-70 nm, with the average length and width being about 417 and 33 nm, respectively, with the average aspect ratio being about 17. Incorporation of α-chitin whiskers helped improve the thermal stability of the nanocomposite films. The tensile strength of the nanocomposite films initially increased with increasing whisker content and leveled off at 2.96 wt% of whisker content. Reduction in the affinity to water causes these nanocomposite films are more stable when being used in an aqueous environment.

In 2004, Tanodekaew *et al.* prepared β-chitin grafted with poly(acrylic acid) with the aim of obtaining a hydrogel characteristic for wound dressing application. Acrylic acid was first linked to chitin, via ester bonds between the chitin primary alcohol groups and the carboxyl groups of acrylic acid, the active grafted moiety that was further polymerized upon addition of an initiator to form a network. The chitin–polyacrylate films were synthesized at various acrylic acid contents: the degree of swelling of the chitin–polyacrylate films was in the range of 30 – 60 times of their original weights depending upon the monomer feed content. The chitin–polyacrylate film with 1:4 weight ratio of chitin: acrylate, possessed optimal physical properties. The cytocompatibility of the film was investigated with a cell line of L929 mouse fibroblasts. The morphology and behavior of the cells on the chitin–PAA film were determined after different time periods of culture up to 14 days. The L929 cells proliferated and attached well onto the film. These results suggested that the 1:4 chitin–PAA has a potential to be used as a wound dressing.

Watthanaphanit *et al.,* 2008 fabricated calcium alginate yarn and nanocomposite yarn based on chitin whisker-reinforced calcium alginate system. The chitin whiskers, consisting of slender rods with a broad distribution in both of their length and width (with the average length and width being 343 and 46 nm, resulting the aspect ratio of 7.5), were prepared by acid hydrolysis from decalcified and deproteinized shrimp shells, and the amount of the whiskers in the nanocomposite

fibers ranged between 0.05 and 2.00% w/w. Improvement in both the mechanical and thermal properties was observed when the amount of the whiskers in the nanocomposite fibers was low. The significant increase in these properties was postulated to be a result of specific interactions, i.e., hydrogen bonding and electrostatic interactions, between the alginate molecules and the homogeneously dispersed chitin whiskers. A remarkable wet spun alginate composite containing chitin nanofibrils was characterized in view of its use as awound dressing: the essential result is that the overall susceptibility to lysozyme is improved by the tiny amounts of chitin nanofibrils. Moreover, the release of chitin oligomers as a consequence of the enzymatic hydrolysis is a significant contribution to the efficacy of the Ca alginate dressings.

In 2007, Panya Wongpanit and coworkers improved the dimensional stability of silk fibroin sponge by incorporating chitin whiskers as nanofiller. Chitin whiskers exhibited the average length and width of 427 and 43 nm, respectively. The incorporating chitin whiskers into the silk fibroin matrix not only promoted the dimensional stability but also enhanced the mechanical properties of the silk fibroin sponges. Moreover, the nanocomposite sponges exhibited the absence of the cytotoxicity as well as promoting cell spreading. Thus, all of these results might indicate the potential utility of this nanocomposite system for further exploration as a scaffolding material.