CHAPTER II
LITERATURE REVIEW

2.1 Wound dressing

Wounds are generally classified as, wounds without tissue loss (e.g. in surgery), and wounds with tissue loss, such as burn wounds, wounds that are caused trauma, abrasions or as secondary events in chronic ailments eg: venous stasis, diabetic ulcers or pressure sores. When skin integrity is altered and a wound results, the healing process begins restoration of tissue continuity that is a natural phenomenon but during wound healing, infection, quality of healing, speed of healing, fluid loss and other complications enhance the healing time that cause to development of wound-care product. The recognition, in the 1960s, that gauze and other absorbent materials (eg, cotton and gamgee) were passive products that "plugged and concealed" the wound but did little to encourage wound healing resulted in the creation of a minimal set of criteria for an "ideal dressing"(Turner et al., 1979).

Ability of ideal dressing

An ideal wound dressing is included the ability to: (1) absorb exudates and toxic components from the wounds surface; (2) maintain a 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. Many of the newer dressings are designed to create a moist wound healing environment which allows the wound fluids to remain in contact with wound (Turner et al., 1979).

Moist wound healing environment

Proposed benefits to moist wound healing include: (1) prevention of the formation of a scab which can trap white blood cells preventing them from participating in their important wound healing functions, (2) the pH of the environment is reduced, thus adversely affecting bacteria, (3) prevention of bacterial strike through from outside the wound to the wound surface, (4) more rapid epithelialization, and (5) the moist environment favors colonization of bacteria without infection. Although a moist wound favors colonization of bacteria and increases bacterial numbers, despite this infection rates are not increased in most studies probably due to increase of white blood cell function.(Jones et al., 2001)

2.1 Silk fibroin

Silk fibroin produced by Bombyx mori silkworm has been used commercially as biomedical sutures for decades. Because it has impressive mechanical properties (Table 2.1) (Kaplan et al.,1998). In addition to silk has environmental stability and biocompatibility. Functional differences among silks of different species and within a species are a result of structural differences due to differences in primary amino acid sequence,processing and the impact of environmental factors (Vollrath et al., 2001). Silks represent a unique family of structural proteins that are biocompatible, degradable, mechanically superior, offer a wide range of properties, are amenable to aqueous or organic solvent processing and can be chemically modified to suit a wide range of biomedical applications. (Moy et al., 1991). Recently, Silks have been established as an invaluable material in the field of biomedical engineering ranging from skin,bone, and vascular grafts.

2.2.1. Structure of silk

The domesticated silkworm (B. mori) silk consist of two fibroin threads that is a light chain (26 kDa) and heavy chain (390 kDa) which are present in a 1:1 ratio and linked by a single disulfide bond.adhered together with a family of hydrophilic proteins called sericins gum (20–310 kDa) that is twenty-five to thirty percent of the silk cocoon mass and a 25 kDa glycoprotein, named P25, is non-covalently linked to these proteins (Tanaka et al., 1999)(Fig2.1).

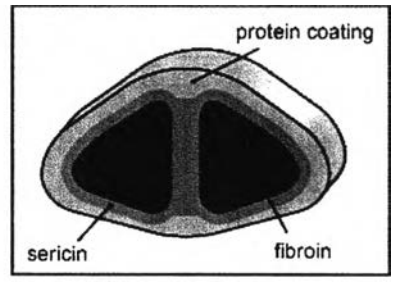


Figure 2.1 cross-section of silk fiber. (Tanaka et al., 1999)

Silk fibroin is purified from sericins by boiling silk cocoons in an alkaline solution, de-gumming process (Fig2.) because sericin affects antigenic.

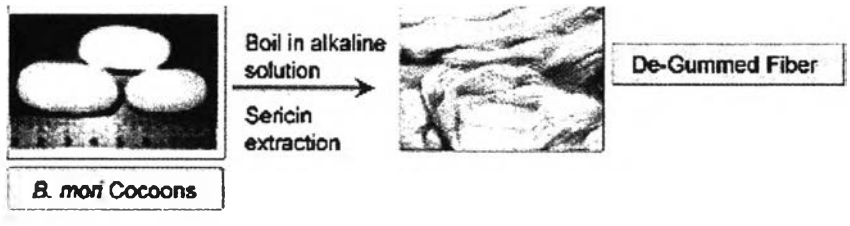
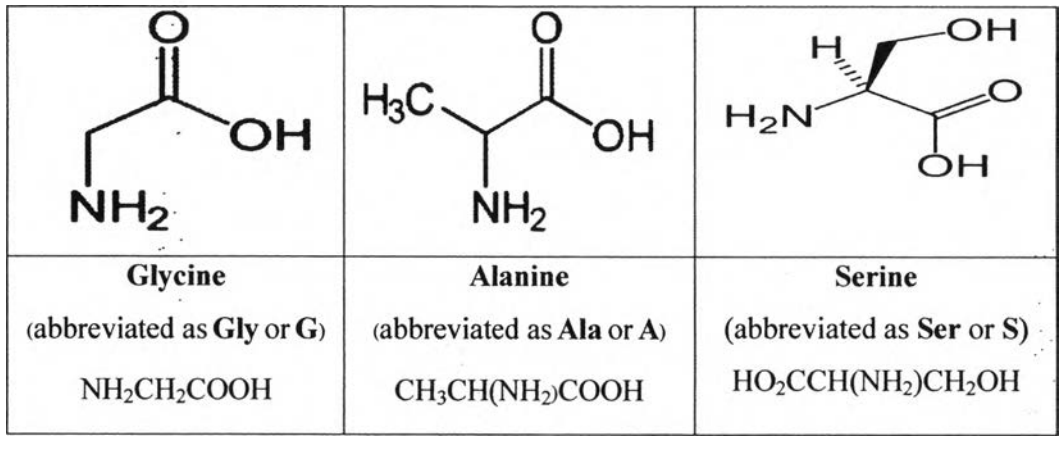


Figure 2.2 De-gumming process. (Vepari et al.,2007)

The purified B. mori silk fibroin (SF) consists primarily of glycine (Gly) (43%), alanine (Ala) (30%) and serine (Ser) (12%) (Kaplan et al., 1998),which is characterized as a natural block copolymer composed of hydrophobic blocks and hydrophilic block. The hydrophobic blocks are highly preserved repetitive

sequences, e.g., Gly-Ala-Gly-Ala-Gly-Ser. The hydrophilic blocks are more complex sequences that consist of larger side-chain amino acid residues as well as charged amino acid residues (Yao et al.,2004;Bini et al.,2004; Zhou et al., 2000). A number of silk polymorphs has been reported, including the glandular state prior to crystallization(silk I), the spun silk state which consists of the β -sheet secondary structure (silk II)(Fig 2.4), and an air/water assembled interfacial silk (silk III, with a helical structure) (Kaplan DL et al., 1998; Jin HJ et al., 2003; Motta A et al., 2002). The silk I structure is the water-soluble state and upon exposure to heat or physical spinning easily converts to a silk II structure. The silk I structure is observed in vitro in aqueous conditions and converts to a β-sheet structure when exposed to methanol or potassium chloride (Huemmerich et al., 2006).



Glycine	Alanine	Serine
(abbreviated as **Gly** or **G**)	(abbreviated as **Ala** or **A**)	(abbreviated as **Ser** or **S**)
NH_2CH_2COOH	$CH_3CH(NH_2)COOH$	$HO_2CCH(NH_2)CH_2OH$

Figure 2.3 Structure of primary amino acid in silk protein. (Kaplan et al., 1998)

The β -sheet structures are asymmetrical with one side occupied with hydrogen side chains from glycine and the other occupied with the methyl side chains from the alanines that populate the hydrophobic domains. So, the hydrophobic blocks can form crystals through the hydrogen bonding and hydrophobic interactions, resulting in the basis for the tensile strength of silk fibroin fibers. The less ordered hydrophilic blocks combined with the ordered hydrophobic blocks contribute to the elasticity, toughness and water absorbtion of silk fibroin fibers. In addition, it has good oxygen and water permeability, cell adhesion and growth

characteristics, relatively low thrombogenicity, low inflammatory response, protease susceptibility. So, it is attractive natural fibrous protein for biomedical applications. such as cell culture substrate (Gotoh et al., 1997)drug control release (Hofmann et al., 2006; Wang et al., 2007;Mandal et al., 2009) tissue engineering (Wang et al., 2006; Lawrence et al., 2009; Fang et al., 2009; Zhang et al., 2008; Cai et al., 2009) including wound dressing (Schneider, et al, 2009).

Figure 2.4 β -sheet secondary structure (silk II) (Eisenberg, 2003)

In 2006, Jeong et al. studied about structure changing of SF nanofibers from random coil(silk I) to more stable β-sheet(silk II) conformation by treatment with organic vapor such as methanol, ethanol, and propanol. Because direct immersing in these organic solvent often results brittle SF matrices due to the high content of crystalline structures. Especially methanol that is highly effective in inducing the transition structure. So, they were investigated in a time-resolved manner using IR spectroscopy to determine the area ratios of silk II and silk I structures (AII/AI) in the amide I region of the SF nanofibers during treatments with various solvent vapors at 35 ◦C (Fig. 2.5). It was found that the degree of transition from silk I to silk II (i.e., area ratio of silk II and silk I structures) was strongly dependent on the types of solvents used and treatment with water vapor was effective in inducing the conformational transition of SF nanofibers as compared to SF treated with alcohol vapor. This approach to controlling structures of regenerated SF nanofiber matrices without the use of organic solvents may have useful applications in biomedical engineering, including wound dressings and tissue regeneration

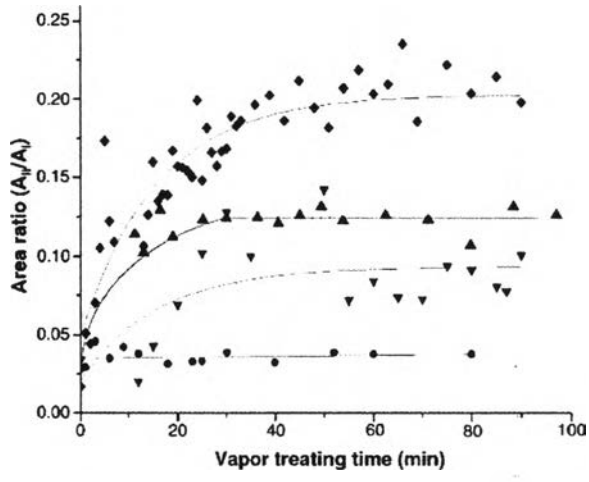


Figure 2.5 Changes in the area ratios of silk II and silk I structures (AII /AI) of the amide I region of SF nanofibers, as determined from IR spectra during solvent vapor treatments at 35 °C((▲) water; (♦) methanol; (▼) ethanol; (●) propanol). (Jeong et al., 2006)

In 2005, Taketani et al. prepared the silk fibroin thin films via colloid chemical routes (CC) and by pulsed laser deposition (PLD) and then characterized Surface morphology by field emission scanning electron microscope (FE-SEM) and atomic force microscope (AFM) and the secondary structure of the films on Si(1 0 0) and polyethylene (PE) substrates by fourier transform infrared (FT-IR) absorption spectra when post treatment with methanol. From FT-IR spectra of the films before treatment that are shown in fig 2.6(a), they found absorption bands amide I (C=O stretching) at around 1650 cm^{-1} amide II (N–H deformation) at 1530 cm^{-1}, and amide III (C–N stretching) at 1250 cm^{-1}. These peaks are good agreement with those of the random coil fibroin (Yamada et al.,2003). And after treatment by immersed in methanol for 2 min, FT-IR spectra of the films show all the amide peaks were shift; amide I by 20–1630 cm^{-1}, amide II by 10–1520 $cm^{-1}$and amide III by 20–1230 cm^{-1}. These new positions are attributable to the β-sheet structure that are shown in fig 2.6(b). The results are caused by diffussion of methanol into the films to induce swelling of the films, weakening the hydrogen bonds and easing their rearrangement

(Yamada et al., 2003; Nakayama et al., 2003; Magoshi et al., 1981; Magoshi et al., 1985).

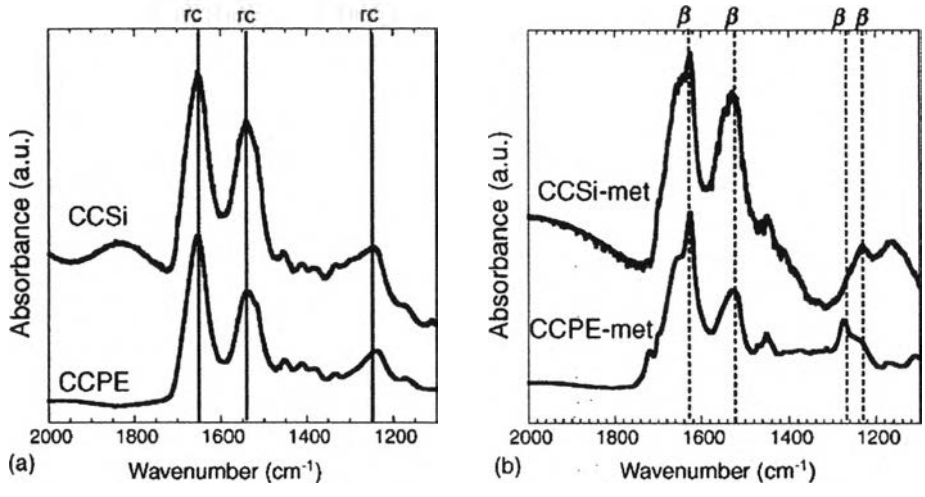


Figure 2.6 FT-IR spectra of SF films on Si (CCSi) and PE (CCPE) prepared via CC before (a) and after (b) the post treatment. The peak positions of random coil and β-sheet are marked by solid and broken lines.

2.2.2 Silk protein solubility

Before processing of silk to desirable morphology, the fibers must first be dissolved in solvent to give silk fibroin solution that is relative to solubility of silk protein. The solubility of a protein in water is affected by the presence of other solutes such as ions, organic solvents, polymers or surfactants. Ion effect relate to with salt concentration, low concentrations of salt tend to improve the solubility of proteins (known as 'salting in'), due to the formation of ion-rich hydration layers in the vicinity of charged and polar amino acid residues but high concentrations of salt tend to have the opposite effect, causing the protein to precipitate (known as 'salting out'). Organic solvents also affect the solubility of proteins in water, primarily because charged and ionic residues tend to be less well solvated by solvents with lower dielectric constants, and also due to the fact that they interfere with the non-covalent interactions that determine the protein's secondary structure. Alcohols are known to both promote and disrupt secondary structure elements, for example

trifluoroethanol generally stabilizes α-helices at the expense of β-sheets due to its interaction with carbonyl oxygen atoms and hydrophobic residues. In contrast, ethanol and methanol promote β-sheet formation at the expense of α-helices due to dehydration of the α-helices. In certain cases, it is possible to dissolve proteins in non-aqueous solvents, although the fact that the physical properties (dielectric constant, dipole moment, hydrophobicity, etc.) of such solvents are different from water. This may significantly affect the folding of the protein due to poor salvation of the charged and polar regions, favorable solvation of the hydrophobic regions of the protein and disruption of the hydrogen bonding patterns (Stevenson, 2000).Furthermore, temperature is another important factor governing the solubility of proteins.

2.2.3 Silk protein processing

Aqueous silk solution is used to prepare various morphologies (Fig2.7) to desirable applications.For wound dressing, silk morphology from aqueous silk fibroin solution is three-dimensional structure such as film and foam. Films are generally prepared by casting solutions of silk proteins onto a substrate and allowing the evaporation of the solvent. Once the solvent has evaporated, the films can be peeled off for further use, modified chemically (e.g. cross-linked), or modified structurally via treatment with another solvent. Foams can be prepared by a variety of techniques allowing fine control of their three-dimensional structure and mechanical properties, which ultimately dictates what they may be used for such as freeze-drying, gas foaming, salt leaching et al.

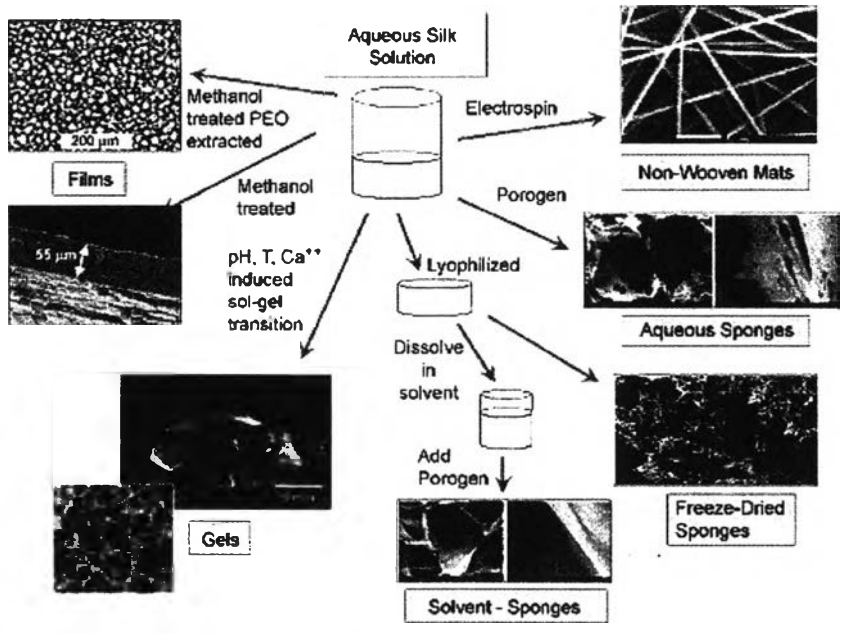


Figure 2.7 Processing of silk morphologies from aqueous silk fibroin solution into non-woven silk fibers (Li C. et al., 2006); aqueous- and solvent-based porous sponges (Nazarov et al., 2004; ; Kim et al., 2005); hydrogels (Rammensee et al., 2006) and films (Jin et al., 2004).

2.2.4 Mechanical properties of silk fibroin

Silk has impressive mechanical properties (Table 2.1) (Kaplan et al.,1998). The mechanical properties of silk relate to its structure. Silk has many structures including the glandular state prior to crystallization (silk I), the spun silk state which consists of the β-sheet secondary structure (silk II), and an air/water assembled interfacial silk (silk III, with a helical structure) (Kaplan DL et al., 1998; Jin HJ et al., 2003; Motta A et al., 2002).The desirable structure for biomedical application is the β-sheet secondary structure (silk II) because it is more stable and gives both high tensile strength and flexibility.

Table2.1 Mechanical properties of silk (Kaplan et al.,1998)

Source of biomaterial	Modulus (GPa)	UTS (MPa)	Strain (%)at break	References
B. mori silk (with sericin)	5–12	500	19	Perez-Rigueiro et al., 2000
B. mori silk (without sericin)	15–17	610–690	4–16	Perez-Rigueiro et al., 2000.
B. mori silk	10	740	20	Cunniff et al., 1994.
N. clavipes silk	11–13	875–972	17–18	Cunniff et al., 1994.

2.2.5 Biocompatibility of silk fibroin

In 2004, Min et al. prepared the electrospun silk fibroin (SF) nanofibers for cell culture of normal human keratinocytes (NHOK and NHEK)and normal human gingival fibroblasts (NHGF). Morphology and microstructure of as-spun and chemically treated SF nanofibers were investigated by scanning electron microscopy and mercury porosimetry. Moreover, they studied the cytocompatibility of electrospun SF nanofibers compared with ECM protein-coating SF nanofibers and another material (polystyrene) by studying cell adhesion and spreading in normal human keratinocytes and fibroblasts. The results show that rapidly proliferating NHOK, NHEK, and NHGF adherent to the electrospun SF nanofibers were microphotographed during the adhesion assay after washing, fixing, and staining the cells with hematoxylin and eosin. Relatively low cell adhesion was observed on polystyrene surfaces for NHOK, NHEK, and NHGF. Type I collagen promoted the adhesion of proliferating NHOK and NHEK but did not in NHGF (Fig 2.8). Tthe cell attachment and spreading of type I collagen was relatively good for both mucosal and epidermal keratinocytes and fibroblasts tested. In addition, the electrospun SF nanofiber nonwovens may provide a three-dimensional structure for cell attachment, growth, and migration. Therefore,cell morphology and the interaction between cells and SF nanofibers were studied in vitro for 7 days. SEM micrographs showed that NHOK cells adhered and spread on the surface of the SF nanofibers network and had

started to migrate through the pores and grow under layers of the fibers at day 3 (Fig. 2.9). Their results indicate that the SF nanofibers may be a good candidate for the biomedical applications, such as wound dressing and scaffolds for tissue engineering.

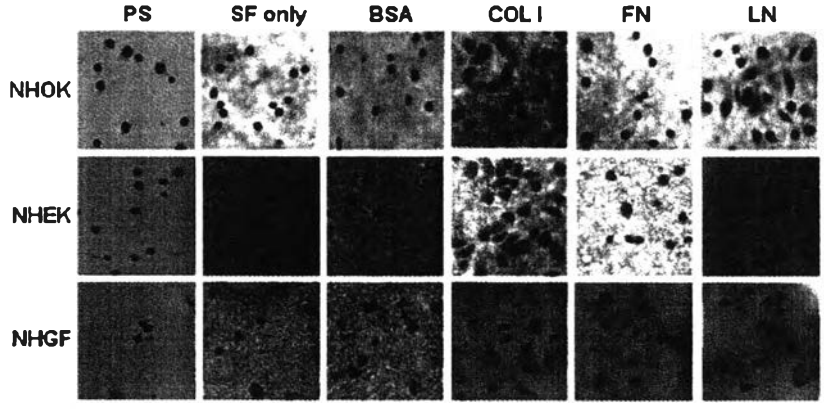


Figure 2.8 Examples of cell adhesion and spreading on polystyrene (PS) and silk fibroin (SF) with type I collagen, fibronectin, or laminin in NHOK, NHEK, and NHGF. (Min et al., 2004)

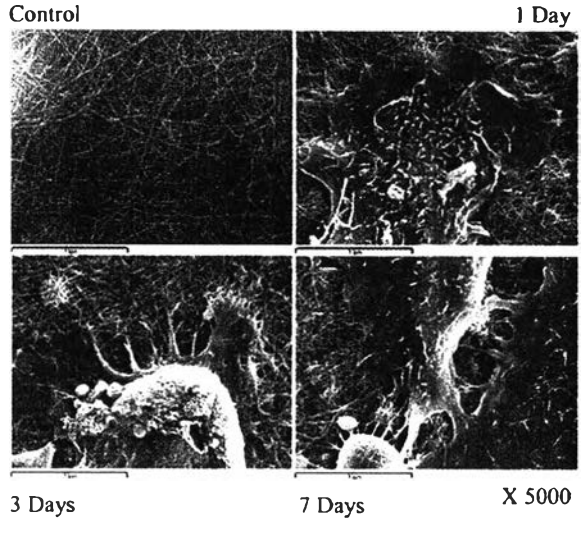


Figure 2.9 SEM micrographs of the interaction between NHOK cells and a methanol-treated SF nanofibrous structure after 0 (control), 1, 3, or 7 days of culture. Bar, 1 mm. (Min et al., 2004)

In 2005, Meinel et al. investigated the inflammatory potential of the silk fibroin in vitro and in vivo compared with collagen and polylactic acid (PLA) films on expression of the pro-inflammatory Interleukin1 beta (IL-1β) and infiammatory cyclooxygenase 2 (COX-2) in human mesenchymal stem cells(hMSCs).For in vitro studies demonstrated on transcript and on protein levels that IL-1β production by MSCs was equal or slightly less on silk than on collagen films.Essentially the same results were observed for the expression of the COX-2 gene and more PGE_2 was produced by human BMSCs grown on collagen than on silk films. Therefore, the inflammatory in vitro reaction on silk or silk-RGD films was similar to collagen films or slightly reduced. But in vivo studies, films seeded with rat MSCs suggested that the inflammatory response elicited by silk was equivalent to or less than that observed on collagen films and far less than to PLA films.

In 2008, Yoo et al. prepared extracellular matrix (ECM) mimic scaffolds of chitin/silk fibroin (SF) nanofibrous by electrospinning. The scaffolds have the same components but different bicomponent structures(blend scaffolds and hybrid scaffolds)because chitin and SF were immiscible in the as-spun nanofibrous structure. They investigated effect of chitin/silk fibroin nanofibrous bicomponent structures on interaction with human epidermal keratinocytes tissue engineering nanofibrous. The morphology and cellular response of the chitin/SF blend and hybrid nanofibers with water vapor after treatment were compared. It was found that SF in chitin/SF bicomponent nanofibers could be dimensionally stabilized by water vapor because it was induced crystallization. Furthermore, cytocompatibility was studied by using SEM for observing attachment and spreading of normal human epidermal keratinocytes (NHEK) onto the chitin/SF blend nanofibrous scaffold and hybrid scaffold. In their study, the normal human epidermal keratinocytes were isolated from the human foreskins of patients (1–3 years old) who were undergoing surgery. SEM micrograph show that NHEK interacted and integrated well with the surrounding chitin/SF blend and hybrid fibers and grew in the direction of fiber orientation, forming a three-dimensional network with the nanofibrous structure in vitro over 7 days. Though, pure chitin nanofibers had extremely low cell spreading for NHEK but cell spreading could be promoted on pure SF nanofibers.

In 2009, Jeong developed silk fibroin nanofibers by plasma-treated in the presence of oxygen or methane gas to modify their surface characteristics and investigated the cytocompatibility from effect of the modified silk fibroin surface on the cellular activities of normal human keratinocytes (NHEK)and normal human epidermal fibroblasts (NHEF) that are important cell for skin regeneration. Characterization of the silk fibroin nanofibers after plasma treatment by contact angle measurements and XPS analysis shown that the O_2 plasma treatment increase hydrophobicity on the nanofibers surface but the CH_4 plasma treatment decreased slightly after plasma treatment. Cell attachment and spreading of (NHEK) and (NHEF)on plasma-treated silk fibroin nanofibrous matrices were examined in vitro for 7 day. SEM showed that the NHEK and NHEF adhered and spread over the surface of the CH_4 plasma-treated and O_2 plasma-treated SF nanfibrous networks and began to grow onto the layers of the fibers on day 1 (Figs. 2.10 and 2.11).The cell attachment and spreading of NHEK cell on O_2 plasma treatment silk fibroin nanofibers were higher than on CH_4 plasma treatment silk fibroin nanofibers on day 7(Fig 2.10). The cell attachment and spreading of NHEF cell on O_2 plasma treatment silk fibroin nanofibers were higher than on CH_4 plasma treatment silk fibroin nanofibers that similar to pure silk fibroin nanofibers on day 1 and 3(Fig 2.11). This difference in cellular activity might be due to the hydrophilicity of the SF nanofibers surface. This approach to controlling the surface properties of nanofibrous structures might be useful in the design and tailoring of novel extracellular matrices for wound dressing and tissue engineering applications.

The previous literature about silk fibroin indicate that silk fibroin is interesting biomaterial for wound dressing and tissue engineering because it is biocompatibility and low inflammatory including good substrate for cell adhesion and growth. So, our research uses silk fibroin to preparing wound dressing incorporated with coconut oil for improve properties to accelerate wound healing.

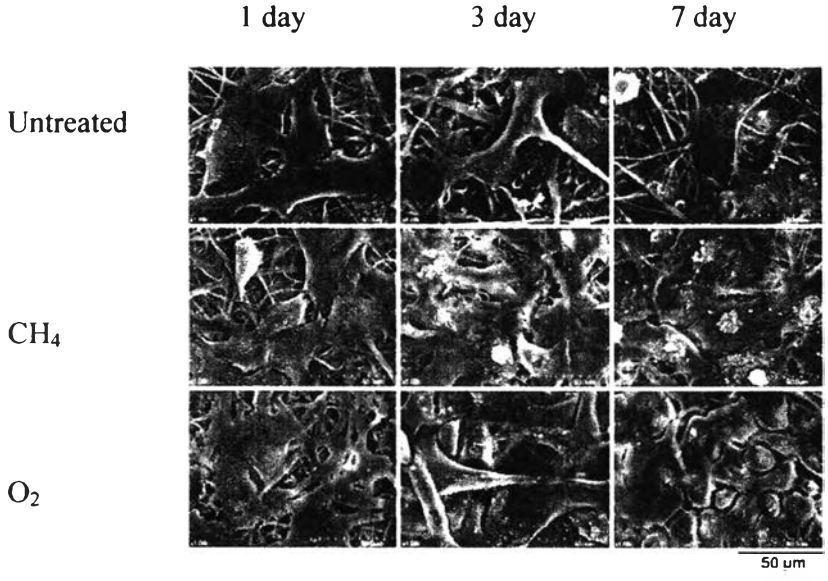


Figure 2.10 Cell attachment and spreading of normal human keratinocytes plated onto the SF nanofibers. SEM images showing the interaction between NHEK and SF nanofibers. Bar, 50 μm. [Jeong et al.,2009]

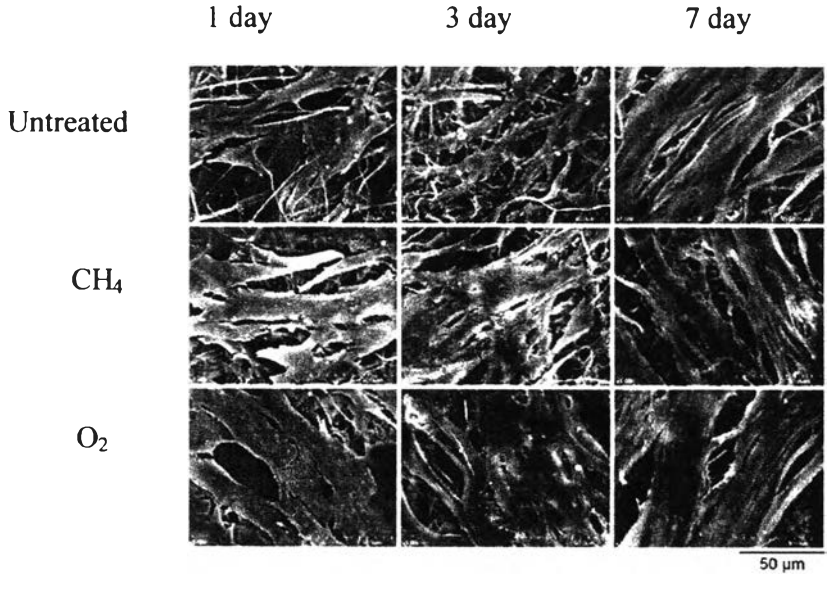


Figure 2.11 Cell attachment and spreading of normal human fibroblasts plated onto SF nanofibers. SEM images of the interaction between the NHEF and SF nanofibers. [Jeong et al.,2009]

2.2 Coconut oil

Coconut oil that is extracted from fresh coconut flesh is known as virgin coconut oil (VCO). The extraction involves a process that does not use thermal treatment or food preservatives. Coconut oil obtained from copra, dried coconut, has no taste or fragrance due to the refining process, whereas VCO has the fragrance and taste of coconut. The absence of heating and chemical during the extraction makes it tasty and healthy. The antioxidant activity of VCO is superior to that of regular coconut oil, which is extracted from copra, and also of groundnut oil (Nevin et al., 2005).

Table2.2 The composition of the coconut oil (Acharya et al.,2002)

Name of the acid	Formula	Nature of acid	Weight %
Caproic	$C_5H_{11}COOH$	Saturated	0.3
Caprylic	$C_7H_{15}COOH$	Saturated	9.2
Capric	$C_9H_{19}COOH$	Saturated	9.7
Lauric	$C_{11}H_{23}COOH$	Saturated	44.3
Myristic	$C_{13}H_{27}COOH$	Saturated	15.9
Palmitic	$C_{15}H_{31}COOH$	Saturated	9.6
Stearic	$C_{17}H_{35}COOH$	Saturated	3.2
Oleic	$C_{17}H_{33}COOH$	Unsaturated	6.3
Linoleic	$C_{17}H_{31}COOH$	Unsaturated	1.5

From table 2.2, it indicates that approximate 50% of the fatty acids in coconut fat are lauric acid. Lauric acid is a medium chain fatty acid, which has the additional beneficial function believed to have antimicrobial properties (Dawson et al., 2002). Moreover, coconut oil has antioxidant property because it has high saturated chain and it has high vitamin E because of the highest phenolic content (Marina et al., 2008). The phenolic compounds in VCO were tocopherol and tocotrienol. (Horvath et al., 2006).

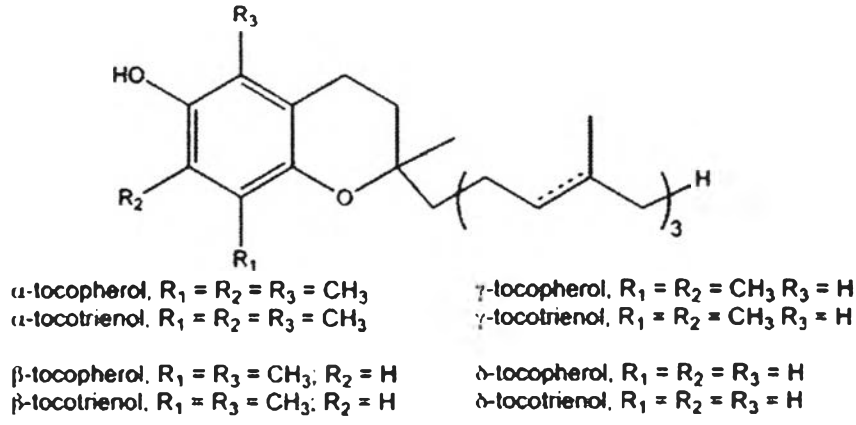


Figure 2.12 The structure of tocopherol and tocotrienol.(Horvath et al., 2006)

In 2008, Sado Kamdem et al. studied the effect of non-inhibitory concentrations of capric, lauric and α-linolenic acids (C10:0, C12:0 and C18:3 ,respectively) on the division time distribution of single cells of *Staphylococcus aureus*, being evaluated at pH 7 and pH 5 by using the methodology of Elfwing et al. (2004) complemented with the modelling approach of Pin and Baranyi (2006). From this work, they found that the division times were significantly longer in the presence of free fatty acids than in the control. Shorter division intervals were detected at pH 7 than at pH 5 in the control experiment and in the presence of C10:0 (capric acid). However, both C12:0 (lauric acid) and C18:3 (α-linolenic acid) slowed down the growth, regardless of the pH as shown in Figs. 2.13 and 2.14.

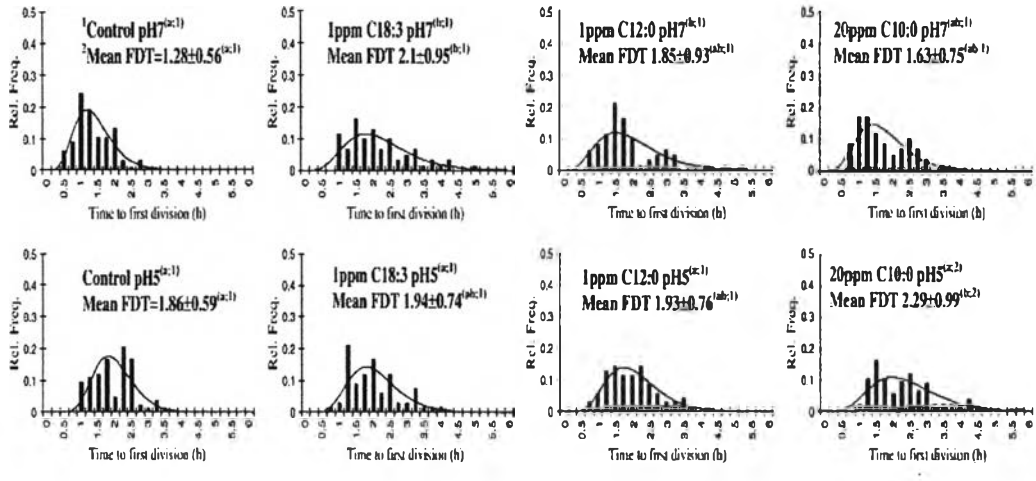


Figure 2.13 Distributions of the first division time (FDTs) of single cells of S. aureus in the presence of α-linolenic (C18:3), lauric (C12:0) and capric (C10:0) acids at pH 5 and 7. (Sado Kamdem et al., 2008)

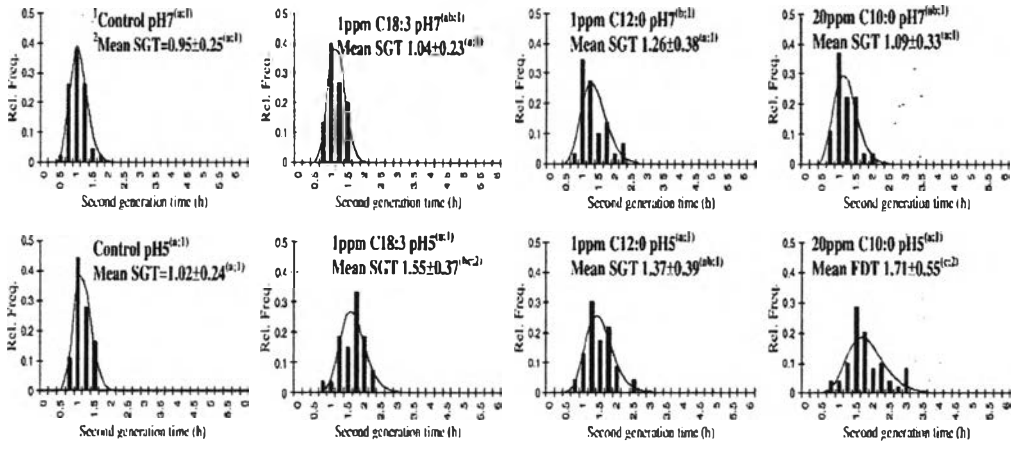


Figure 2.14 Distributions of the second generation time (SGTs) of single cells of S. aureus in the presence of α-linolenic (C18:3), lauric (C12:0) and capric (C10:0) acids at pH 5 and 7. (Sado Kamdem et al., 2008)

In this study, coconut oil is incorporated into silk fibroin but coconut oil and silk fibroin solution are immiscible liquid phase. Two immiscible, pure liquid cannot form an emulsion. So, it need the third component is called the emulsifying agent or surfactant to stabilize the system.

2.3 Emulsification

Emulsification is the formation of emulsions from two immiscible liquid phase that is stabilized by emulsifying agent or surfactant. An emulsion is a significantly stable suspension of particles of liquid of a certain size within a second, immisible liquid. The term significantly stable, relaties to the intended use and may range from a few minutes to few minutes to a few years. Emulsion is distinguished based on size of the dispersed particles: (1) macroemulsions, opaque emulsions with particles >400 nm, easily visible under a microscope; (2) microemulsions, transparent dispersions with particle <100 nm in size; (3) nanoemulsions (miniemulsions), a type that is blue-white, with particle sizes between those of first two types (100-400 nm). The most well-known type is macroemulsions. Macroemulsions are of two types, based on the nature of the dispersed phase: oil-in-water (O/W) and water-in-oil (W/O). The O/W type is a dispersion of a water immiscible liquid or solution, always called the oil (O), regardless of its nature, in an aqueous phase (W). The oil in this case is the "discontinuous" (inner) phase; the aqueous phase is the "continuous" (outer) phase. The W/O type is a dispersion of water or an aqueous solution (W) in a water-immiscible liquid (O). The type of emulsion formed by the water and the oil depends primarily on the nature of the emulsifying agent and, to some extend, on the process used in preparing the emulsion and the relative proportions of oil and water present. In general, O/W emulsions are produced by emulsifying agents that are more soluble in the water than the oil phase, whereas W/O emulsions are produced by emulsifying agents that are more soluble in the oil than the water phase. However, one type can be converted to the other by changing conditions. This is called inversion of the emulsion.

2.4 Surfactant

Surfactants are wetting agents that lower the surface tension of a liquid, allowing easier spreading, and lower the interfacial tension between two liquids. usually organic compounds that are amphaphilic, meaning they contain both hydrophobic groups (their "tails") and hydrophilic groups (their "heads").They also

reduce the interfacial tension between oil and water by adsorbing at the liquid-liquid interface. Many surfactants can also assemble in the bulk solution into aggregates. Examples of such aggregates are vesicles and micelles. The concentration at which surfactants begin to form micelles is known as the critical micelle concentration or CMC. When micelles form in water, their tails form a core that can encapsulate an oil droplet, and their (ionic/polar) heads form an outer shell that maintains favorable contact with water. When surfactants assemble in oil, the aggregate is referred to as a reverse micelle. In a reverse micelle, the heads are in the core and the tails maintain favorable contact with oil. Surfactants are also often classified into four primary groups; anionic, cationic, non-ionic, and zwitterionic (dual charge). Surfactants are used in many industries. Especially in food industry and drug industry that use non-ionic surfactant because it is non-toxic surfactant. (Kibbe, 2000)

In 1997, Dawn et al. selected Pluronic f68 that was non-ionic surfactant as the gel carrier for antimicrobial agents. Since Pluronic f68 was approved by the Food and Drug Administration for use in humans as a skin wound cleanser, it has been used extensively in patients without discernable toxic effects or allergic reactions. They found that it formed a water soluble gel that could serve as a carrier for antimicrobial agents when the concentration of this surfactant was increased to 46%. When they studied its antimicrobial activity compared with silver sulfadiazine that is currently the most widely used topical antimicrobial agent in silver sulfadiazine cream and polyethylene glycol carriers containing 0.2% nitrofurazone, the Furacin Soluble Dressing (FSD) that is an antimicrobial cream. They found that Pluronic f68 nitrofurazone gel suppresses the bacterial concentration of contaminated wounds to a greater degree than silver sulfadiazine. Its antimicrobial activity was comparable to that FSD but without the dangers of systemic toxicity from polyethylene glycol (Fig 2.15).

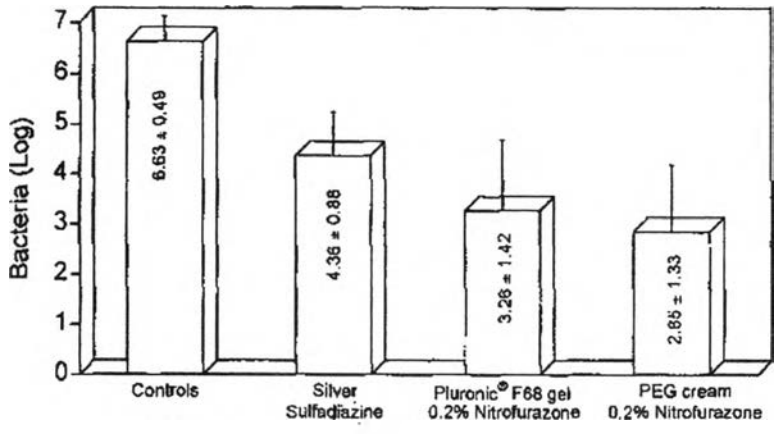


Figure 2.15 Nitrofurazone creams or gels significantly reduced the bacterial concentration of contaminated experimental wounds to a greater degree than did silver sulfadiazine. (Dawn et al., 1997)