# CHAPTER II
# LITERATURE REVIEW

## 2.1 Current Concepts in Wound Dressings

In 2011, Abdelrahman and coworkers defined that wound dressings have increased in efficacy and number as the scientific understanding of wound healing has improved. However current practice is governed by expert opinion as high-quality studies comparing the effectiveness of different dressings are lacking. An overview of optimal conditions for healing and the assessment of wounds is provided here. Dressings and their modes of action are discussed to provide guidance for their use in different wounds.

### 2.1.1 Wound Assessment

Wound assessment requires an accurate clinical history which includes the duration of the wound, any previous wounds, history of trauma, wound characteristics, medications and allergies. Wounds can be classified into four categories based on their appearance e.g. necrotic, sloughy, granulating, and epithelializing. Other important factors taken into consideration in dressing selection are the wound site, surrounding skin, and exudate level. If a wound is exuding a dressing needs to absorb and manage the levels of exudate, the extent of absorption varying with the dressing.

### 2.1.2 Wound Dressings

The appropriate selection of a wound dressing relies on informed knowledge of the wound characteristics and mode of action of the dressing itself. There are some types of dressing in present as following below (Rovee, 1991).

#### *2.1.2.1 Semi-permeable Film Dressings*

These consist of a thin, polyurethane-type film coated with an adhesive layer enabling the dressing to adhere to intact skin. They are semi-permeable, transmitting moisture vapor but do not absorb exudates. Film dressings

provide a protective environment, which is impermeable to bacteria and liquids and can stay in place for up to 7 days.

*2.1.2.2 Hydrocolloid Dressings*

Hydrocolloids are described as interactive as they use wound fluid to form a moist gel at the wound interface. They consist of carboxymethyl cellulose, gelatins and pectins which form the hydrocolloid base which is then secured onto a backing of polyurethane film or foam. These dressings are indicated for wounds with low to moderate exudates. They can promote wound debridement and angiogenesis, reduce pain through keeping the nerve endings moist and absorb excess exudate.

*2.1.2.3 Foam Dressings*

Foam dressings are made of polyurethane or silicone which enables them to handle large volumes of wound fluid. They are available in a range of thicknesses and in adhesive and non-adhesive formulations. The adhesive formulation needs to be used with caution on vulnerable skin. They are indicated for wounds with moderate to high levels of exudates and across a range of wound characteristics.

*2.1.2.4 Hydrogel Dressings*

The hydrogel dressings are composed of hydrophilic polymers which immobilize a large quantity of water to form a semisolid gel. These gel products are available as sheets which can be placed upon the wound bed as a primary dressing, or as amorphous gels which do not have a fixed dimension, but rather can be applied as a flowable gel to the wound where they can absorb additional wound fluid and hydrate the tissues.

*2.1.2.5 Alginate Dressings*

Alginate dressings contain calcium or sodium alginate derived from seaweed. When in contact with wound exudates a hydrophilic gel is formed which makes for easier dressing removal. They are indicated for moderate to heavily exuding wounds. The calcium component within the dressing acts as a haemostat and is therefore useful in bleeding wounds. Alginate ribbon and rope are available which are particularly useful in packing wound cavities.

2.1.3 Effects on Wound Healing

Prior to this time, the healing process was considered to be a passive process with respect to the physician. The work in the early 1960s, much has been learned about the cellular and biomechanical components of wound healing and the factors that affect them. It is now known that healing is not a passive process, but rather can be accelerated and enhanced by the use of specific wound care/dressing techniques and products (Hanna *et al.*, 1997).

Wound healing has commonly been simplified by dividing it into phases of hemostasis, inflammation, proliferation, and maturation. However, wound healing is actually a complex, precisely coordinated interaction between inflammatory cells and mediators, establishing significant overlap between the phases of wound healing. In Figure 2.1 showed the wound healing process in sequence four phases (Stojadinovic *et al.*, 2008).

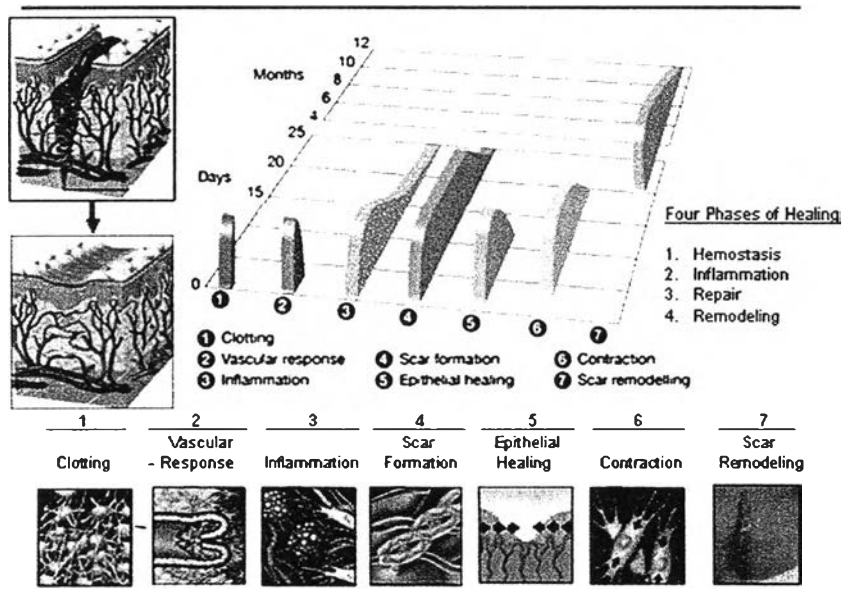


**Figure 2.1** Sequence of molecular and cellular events in skin wound healing (Hanna et al., 1997).

2.1.4 Antimicrobial Dressings

Recently, dressings that contain and release antimicrobial agents at the wound surface have entered the marketplace. These dressings usually provide a continuous or sustained release of the antiseptic agent at the wound surface to provide a long-lasting antimicrobial action in combination with maintenance of

physiologically moist environment for healing. Antimicrobial dressings refer to wound dressings which have an antiseptic agent incorporated and does not include products/dressings which incorporate antibiotics. As described above, traditionally the term antiseptic has been used to refer to solutions that damage healthy tissue. Such solutions have a broad action and can be highly effective in killing microorganisms but may compromise healthy tissue. Thus, their use in ongoing wound management has been questioned and limited to reducing the load of pathogens on intact skin (Ovington, 2007).

## 2.2 Polyurethane Film (PU Film)

### 2.2.1 The Basics and Advantage of Polyurethane Film

Polyurethane film is also commonly referred to as Urethane film, PU film, and TPU film.

Elongation: One of polyurethane film's most desirable qualities is its elongation capabilities. Many of our films are able to withstand 800% elongation before breaking. The material also has excellent memory, meaning that it will return to its original dimensions after being stretched to its limit.

Long-Term Durability: Polyurethane is manufactured without the use of plas ticizers, which means it will retain its original performance characteristics. Not having plasticizers also means it will not leach out hazardous compounds in the field. This is of particular importance in the medical industry.

Low Temperature Flexibility:- Polyurethane film has excellent low temperature flexibility. Most films retain their flexibility even when exposed to temperatures as low as -60°F, making it a perfect material for demanding environments.

Tensile Strength: Our films have tensile strengths that range from 4,000-9,500 psi. It is this strength that makes polyurethane film outperform a multitude of other materials. Because the material is so much stronger than other polymers, our customers are able to use less material while maintaining, or even improving, the strength of the product.

Biocompatibility/Anti-Microbial: Some grades of our films are inherently an timicrobial while others can have anti-microbial compounds added to them in process. Some grades of our film have been found to be highly biocompatible.

Environmental Impact: Polyurethane is an earth friendly material. With the proper equipment, it can be recycled easily and does not release hazardous compounds when being processed or recycled.

Application Flexibility: Polyurethane is a thermoplastic elastomer, meaning it can be melted and re-melted numerous times. This quality is of particular interest to companies doing work that involves altering the film's shape. Polyurethane film can be vacuum or thermoformed and still retain its flexibility and performance. The material can also be welded to form irregular shapes.

Abrasion Resistance: Polyurethane film handily outperforms many other common polymers when it comes to abrasion resistance. Abrasion resistance is measured by weighing the amount of material is lost when a material is subjected to a grinding wheel. Below is a table with comparative abrasion results. Lower numbers are better.

### 2.2.2 The Applying Polyurethane Film in Wound Dressing

In 1983 and 1984, Dellas and coworkers investigated in a high moisture vapor permeable film dressing with an adhesive backing and a release sheet are disclosed. The dressing has two opposed side edges which are free of adhesive and a perforation through the adhesive near the side edge to allow the dressing to be applied to the patient and the adhesive-free edges removed, which prevents the edges of the dressing from rolling off the patient and dislodging the dressing. Moreover, a film dressing with a high moisture vapor transmission rate is disclosed. The film dressing has a release sheet attached to the dressing. There is a central region of the film, defined by perforation lines, which is applied to the patient. There are cut lines in the release sheet which are parallel to but spaced outside the perforations in the dressing to allow the release sheet to be removed, the adhesive portion of the film to be applied to the patient and the exterior portion of both the release sheet and the film to be removed.

In 1988, Hoffmann *et al.* compared bioclusive transparent polyurethane (TP) dressing with a cotton gauze (CG) dressing for the incidence of phlebitis, catheter tip colonization, skin colonization, and catherer-related bacteremia and studied involving 598 ward patients. Culture of specimens from the skin and catheter tips of the majority of patients (91%) showed no growth. An association was

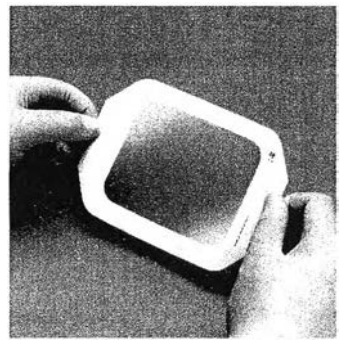

**Figure 2.2** PU film dressing.

found between those patients with >15 CFU isolated from catheter tips and those with phlebitis (p=0.022). In 1992 then , they studied in the toppic "Transparent Polyurethane Film as an Intravenous Catheter Dressing" by obtaining a quantitative estimate of the impact on infectious complications of using transparent dressings with intravenous catheters. The results pointed that a significantly increased risk of catheter-tip infection with the use of transparent compared with gauze dressings when used with either central or peripheral catheters. An increased risk of bacteremia and catheter sepsis associated with the use of transparent compared with gauze dressings for use on central venous catheters was suggested.

## 2.3 Ciprofloxacin

Ciprofloxacin in Figure 2.3 is a second-generation fluoroquinolone antibiotic (Nelson *et al.,* 2007). Its spectrum of activity includes most strains of bacterial patho-gens responsible for respiratory, urinary tract, gastrointestinal, and abdominal infec-tions, including Gram(-) (*Escherichia coli*, *Haemophilus influenzae*, *Klebsiella pneumoniae*, *Legionella pneumophila*, *Moraxella catarrhalis*, *Proteus mirabilis*, and *Pseudomonas aeruginosa*), and Gram(+) (methicillin-sensitive but not

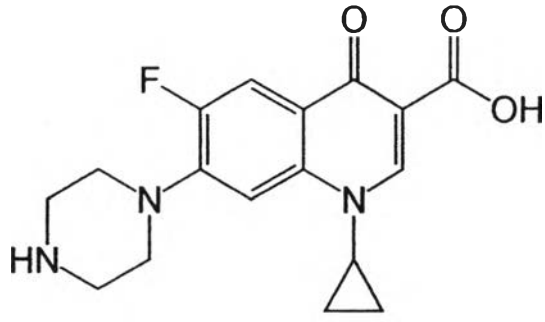


**Figure 2.3** The structure of Ciprofloxacin.

methicillin-resistant *Staphylococcus aureus*, *Streptococcus pneumoniae*, *Staphylococcus epidermidis*, *Enterococcus faecalis*, and *Streptococcus pyogenes*) bacterial pathogens. Ciprofloxacin and other fluoroquinolones are valued for this broad spectrum of activity, excellent tissue penetration, and for their availability in both oral and intravenous formulations (Laurence *et al.*, 2005).

Ciprofloxacin is used alone or in combination with other antibacterial drugs in the empiric treatment of infections for which the bacterial pathogen has not been identified, including urinary tract infections and abdominal infections among others (Solomkin *et al.*, 2010). It is also used for the treatment of infections caused by specific pathogens known to be sensitive. In 2010 over 20 million outpatient prescriptions were written for ciprofloxacin, making it the 35th most commonly prescribed drug, and the 5th most commonly prescribed antibacterial, in the US.

It is a second-generation fluoroquinolone antibacterial. It kills bacteria by interfering with the enzymes that cause DNA to rewind after being copied, which stops synthesis of DNA and of protein.

Ciprofloxacin was first patented in 1983 by Bayer A.G. and subsequently approved by the US Food and Drug Administration (FDA) in 1987. Ciprofloxacin has 12 FDA-approved human uses and other veterinary uses, but it is often used for unapproved uses (off-label).

There are many researches which were studied in applying ciprofloxacin in wound dressing or medical applications. In 2006, Öztürk *et al.* studied about preparation and characterization of alginate/chitosan sponges including a model antibiotic (i.e., ciprofloxacin) to use in wound and/or burn treatment. In the

**Figure 2.4** Ciprofloxacin in tablets.

antimicrobial tests, it was obtained that the antimicrobial activity is directly proportional with the release rates and water uptake.

Unnithan *et al.* (2012) investigated in an antibacterial electrospun scaffold prepared by electrospinning of a solution composed of dextran, polyurethane (PU) and ciprofloxacin HCl (CipHCl) drug. The obtained nanofiber mats have good morphology. The results indicated that the composite mat showed good bactericidal activity against both of Gram-positive and Gram-negative bacteria.

In addition, the synthesis of a novel functional biomaterial for wound healing treatment was carried out by adopting a free-radical grafting procedure in aqueous media. With this aim, ciprofloxacin (CPF) was covalently incorporated into collagen (TC1) chains. The observed antibacterial activity and stimulation of fibroblast growth support the applicability of CPF-T1C conjugate in wound treatment encouraging the healing process (Puoci *et al.*, 2012).

Moreover, Serinçay *et al.* (2013) designed and developed the new wound dressing materials based on PVA/PAA, ciprofloxacin HCl, and aloe vera so that the wound undergoes proper healing and scar formation is minimal by using the electrospinning method. The wound dressing materials are tested for microbial activity tests and drug release experiments. Controlled ciprofloxacin HCl release is observed.

## 2.4 Poly(Vinyl Acetate) or (PVAc)

### 2.4.1 Introduction to Poly(Vinyl Acetate)

Poly(Vinyl Acetate) (PVAc) is a thermoplastic polymer with a chemical formula of $(C_4H_6O_2)_n$. It is normally manufactured by the free radical polymerization of vinyl acetate. The procedure involves the reaction of monomer molecules of vinyl acetate by submerging them into water. This results in the formation of an emulsion that is milky white in color. The emulsion fluid can then instantly be processed as a polyvinyl acetate polymer in products comprising the PVAc as a constituent element.

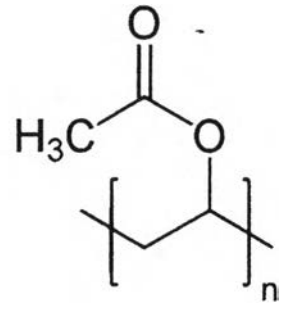


**Figure 2.5** Poly(vinyl acetate) structure.

PVAc is primarily a synthetic resin polymer, which, due its non-polar nature, is insoluble in water, oils, fats, or gasoline. On the other hand, it is soluble in alcohols, ketones, and esters. It has a molar mass of 86.09 grams per mole (g/mol). The ester groups in its structural lattice render it reactive with alkalis, and lead to the formation of polyvinyl alcohol (PVOH, PVA, or PVAL) and acetic acid ($CH_3COOH$). Since its discovery, it has been employed widely as a binding material, due to its adhesive properties for porous materials like wood and paper. Other than its use as glue, it is also used in paper and textile industry to produce coatings that lend a shiny touch to surfaces. PVAc is commonly used in the manufacture of latex paints, where it helps in forming a tough coating and a supportive film. It is also widely used for the production of adhesives, which are more commonly known as carpenter's or white glue.

Industrial applications of PVAc normally use it in the form of a liquefied emulsion. The polymer exhibits sound resistance to UV rays and oxidation.

This renders it an effective polymer with good aging characteristics, yet its water sensitivity can be a problem. This is typically taken care of by formulating it with plasticizers to increase its reliability and stability.

When PVAc is incorporated into emulsion coatings and adhesives, it is normally converted to polyvinyl alcohol first, which is a water-soluble polymer. This is done by means of partial hydrolysis. On a lesser level, it is also used as a protective coating for cheese to render it safe from humidity and fungi.

### 2.4.2 Poly(Vinyl Acetate) for an Adhesive

The most important poly(vinyl acetate) is an adhesive. It is used in solution, in aqueous dispersion, and by hot melt technique, in one form or another it is probably the most widely used thermoplastic adhesive.

Vinyl acetate is a flammable liquid made commercially from acetylene and acetic acid in the presence of a catalyst. As the molecular weight increases the polymer ranges from a soft to a hard solid, soluble mainly in polar organic solvents; adhesive solution are commonly made up in ketones, lower alcohols and esters. As the molecular weight reaches the order of 100,000 the polymer becomes soluble in toluene.

By the most important form in which the adhesive is used is the aqueous dispersion, made by the important industrial process known as emulsion polymerisation, a process in which the liquid monomer is first emulsified in water and then polymerised by heating in the presence of a catalyst. Although loosely referred to as an emulsion, the product is not a liquid/liquid system, but mainly an aqueous dispersion of swollen solid particles. The advantage of an aqueous dispersion is not only that it uses water as the conveying medium, but also that a higher solids/viscosity ratio is possible than with a solution. Poly(vinyl acetate) solutions increase in viscosity as the molecular weight material is desirable because of its film strength, a solution that is fluid enough to permit easy application must necessarily be of low concentration.

An interesting application is the use of a PVAc emulsion to increase the adhesion between old and new concrete. There are two ways in which this may

be done, either by coating to old concrete before applying the new cement mix, or mixing a proportion of the PVAc emulsion with the new mix.

These glues are non-toxic, clean and easy to use and rapidly assume a useful degree of strength especially with highly absorbent adherents. Their heat resistance is satisfactory up to 50° – 60°C. Gap filling is not usually good but the addition of thickening agents improves it. Tensile shear strength (at the normal rate of loading used in testing glued joints) has been shown with a variety of timbers to be comparable with urea and phenolic glues, while giving for reason that are not clear – consistently less wood failure.

### 2.4.3 Poly(Vinyl Acetate) in Previous Studies

In 1984, Motohashi *et al.* investigated the bond strengths of PVAc emulsion adhesives which were evaluated in the range from -130° to 140°C in both tensile shear and tensile cross-lap joints of wood. Both shear and tension bond strengths strongly depended on rheological properties and tensile strengths of adhesives. Higher shear bond strengths were observed in the lower temperature range, while the other bond strengths declined markedly. This phenomenon was explained by the possible occurrence of mechanical interlocking at wood surface and difference of its effectiveness with the direction of stress on the joint.

Kaboorani *et al.*, (2011) studied blending PVAc with MUF and MF which was evaluated as an approach to enhance the performance of PVAc towards water and elevated temperatures. Blends of PVA with MF and MUF were used as adhesives to bond wood joints. MF had more effectiveness in improving shear strength of wood joints than MUF in all conditions. Thermal stability of PVAc was increased by MF but the effect of MUF on thermal stability of PVAc was dependent on MUF proportions and temperatures. Considering costs, effectiveness and formaldehyde emission, adding 15% MF to PVAc seems the optimal proportion of MF in the PVAc blends.

## 2.5 Coconut Oil

### 2.5.1 Introduction to Coconut

Coconut, *Cocos nucifera L.,* is a tree that is cultivated for its multiple utilities, mainly for its nutritional and medicinal values. The various products of coconut include tender coconut water, copra, coconut oil, raw kernel, coconut cake, coconut toddy, coconut shell and wood based products, cōconut leaves, coir pith etc. It's all parts are used in some way or another in the daily life of the people in the traditional coconut growing areas. It is the unique source of various natural products for the development of medicines against various diseases and also for the development of industrial products (DebMandal *et al.*, 2011).

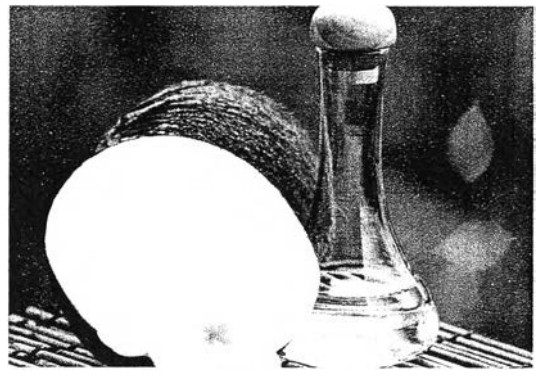

**Figure 2.6** Coconut oil and fruit.

### 2.5.2 Composition of Coconut Oil

Coconut oil consists of more than ninety percent of saturated fats with traces of few unsaturated fatty acids, such as monounsaturated fatty acids and polyunsaturated fatty acids. Virgin coconut oil is no different from this. Let us have a bit detailed study of this.

Saturated fatty acids: Most of them are medium chain triglycerides, which are supposed to assimilate well. Lauric acid is the chief contributor, with more than forty percent of the share, followed by capric acid, caprylic acid, myristic acid and palmitic.

Polyunsaturated fatty acids: 0.72 g/100gLinoleic acid.

Monounsaturated fatty acids: 5.22 g/100g Oleic acid.

Poly-phenols: Coconut contains gallic acid, which is phenolic acid. These poly- phenols are supposed to be responsible for the fragrance and the taste of coconut oil and Virgin Coconut Oil is rich in these poly-phenols.

Certain derivatives of fatty acid like betaines, ethanolamide, ethoxylates, fatty esters, fatty polysorbates, monoglycerides and polyol esters.

Fatty chlorides, fatty alcohol sulphate and fatty alcohol ether sulphate, all of which are derivatives of fatty alcohols.

Vitamin-E and vitamin K and minerals such as Iron.

### 2.5.3 Healing and Infections

When applied on infections, it forms a chemical layer which protects the infected body part from external dust, air, fungi, bacteria and virus. Coconut oil is most effective on bruises as it speeds up the healing process by repairing damaged tissues.

Infections: Coconut oil is very effective against a variety of infections due to its antifungal, antiviral, and antibacterial properties. According to the Coconut Research Center, coconut oil kills viruses that cause influenza, measles, hepatitis, herpes, SARS, etc. It also kills bacteria that cause ulcers, throat infections, urinary tract infections, pneumonia, and gonorrhea, etc. Coconut oil is also effective on fungi and yeast that cause candidiasis, ringworm, athlete's foot, thrush, diaper rash, etc.

### 2.5.4 Benefits of Coconuut Oil in Previous Studies

Aburjai *et al.* (2003) investigated the oil from the nuts which is valued as an emollient and used as an ingredient in remedies for skin infections. Coconut oil (or butter) is extracted from mature coconuts that have fallen to the ground. It is stable at high temperatures (up to 76.6 °C). Modified coconut oil containing polyunsaturated fatty acids in the form of mono-, di- and triglycerides, is useful as a constituent of a barrier lipid mixture in cosmetic and pharmaceutical formulations to protect and prevent drying of the skin. Coconut oil was formerly the main ingredient in marine soaps because coconut oil soap was, unlike other soaps, not readily

precipitated by salt solutions. However, because of its alkali laurate content some coconut oil soaps can irritate the skin.

In 2007, Ogbolu *et al.* studied to characterize Candida species in our environment and determine the effectiveness of virgin coconut oil as an antifungal agent on these species. Their susceptibilities to virgin coconut oil and fluconazole were studied by using the agar-well diffusion technique. It is noteworthy that coconut oil was active against species of Candida at 100% concentration compared to fluconazole. Coconut oil should be used in the treatment of fungal infections in view of emerging drug-resistant Candida species.

In 2010, Nevin *et al.* evaluated the effect of a topical application of virgin coconut oil (VCO) on excision wounds in young rats. After the experimental period, the healing property of VCO was evaluated by monitoring the time taken for complete epithelization as well as levels of various parameters of the wound's granulation tissue. The result showed that VCO-treated wounds healed much faster, as indicated by a decreased time of complete epithelization and higher levels of various skin components. Pepsin soluble collagen showed a significant increase in VCO treated wounds, indicating a higher collagen cross-linking. The beneficial effect of VCO can be attributed to the cumulative effect of various biologically active minor components present in it.

## 2.6 Electrospinning Process

In the past decade, (Huang *et al.*, 2003) electrospinning was recognized as an easy method for polymer nanofibers preparation in submicron range which is difficult to produce by using standard mechanical fiber techniques. The process allows fabrication of continuous polymer fibers from polymer melt or solution with fiber diameter from nano- to micro-size. Ability to apply electrospinning on natural and synthetic polymers, polymer blends, composite with metal or ceramic particles, nanocomposites, as well as obtaining higher surface area, provides wide range of material fabrication and its application (filtration membranes, catalytic nanofibers, fibrous sensors) (Rogina, 2014)

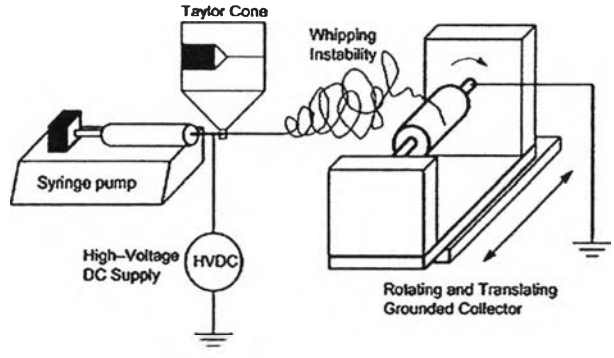


**Figure 2.7** Setup of electrospinning apparatus with rotating cylinder (Huang et al., 2003).

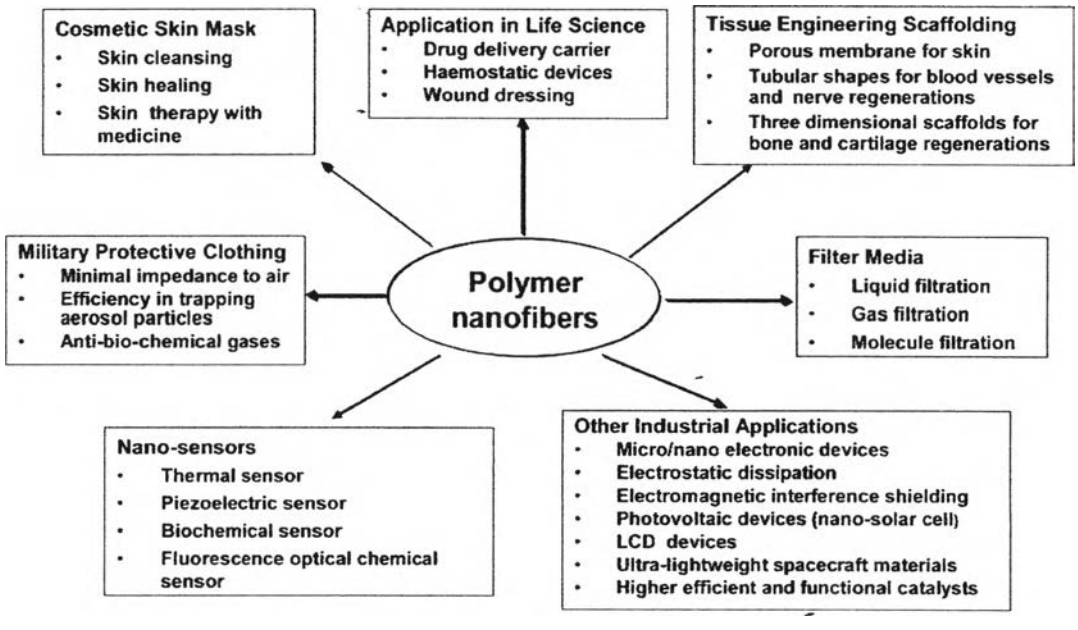


**Figure 2.8** Potential applications of electrospun polymer nanofibers (Rogina, 2014).

### 2.6.1 Electrospinning for Wound dressing

Polymer nanofibers can also be used for the treatment of wounds or burns of a human skin, as well as designed for haemostatic devices with some unique characteristics. With the aid of electric field, fine fibers of biodegradable polymers can be directly sprayed/spun onto the injured location of skin to form a fibrous mat dressing, which can let wounds heal by encouraging the formation of normal skin growth and eliminate the formation of scar tissue which would occur in a traditional treatment. High surface area of 5–100 $m^2/g$ is extremely efficient for fluid absorption and dermal delivery.

2.6.2 Electrospinning in Previous Studies

Unnithan *et al.* (2014) fabricated an antibacterial electrospun nanofibrous scaffolds with diameters around 400–700 nm. They were prepared by physically blending polyurethane (PU) with two biopolymers such as cellulose acetate (CA) and zein. PU was used as the foundation polymer, was blended with CA and zein to achieve desirable properties such as better hydrophilicity, excellent cell attachment, proliferation and blood clotting ability. To prevent common clinical infections, an antimicrobial agent, streptomycin sulfate was incorporated into the electrospun fibers and its antimicrobial ability against the gram negative and gram positive bacteria were examined.

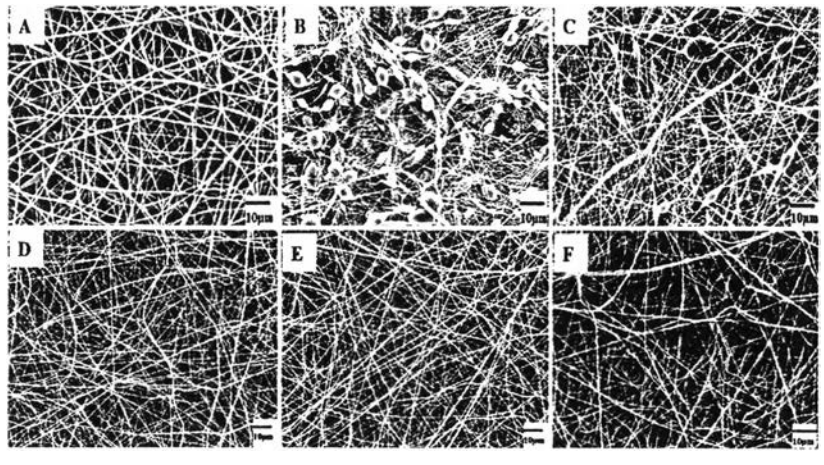


**Figure 2.9** SEM images of electrospun (A) PU, (B) PU–CA (1:1), (C) PU–CA (2:1), (D) PU–CA (3:1), (E) PU–CA–zein and (F) PU–CA–zein-drug nanofibrous mat (Unnithan *et al.*, 2012).

In 2011, Jannesari *et al.* studied to develop novel biomedicated nanofiber electrospun mats for controlled drug release, especially drug release directly to an injury site to accelerate wound healing. Nanofibers of poly(vinyl alcohol) (PVA), poly(vinyl acetate) (PVAc), and a 50:50 composite blend, loaded with ciprofloxacin HCl (CipHCl), were successfully prepared by an electrospinning technique for the first time. Blending PVA and PVAc exhibited a useful and convenient method for electrospinning in order to control the rate and period of drug release in wound healing applications. Also, the thickness of the blend nanofiber mats strongly influenced the initial release and rate of drug release.

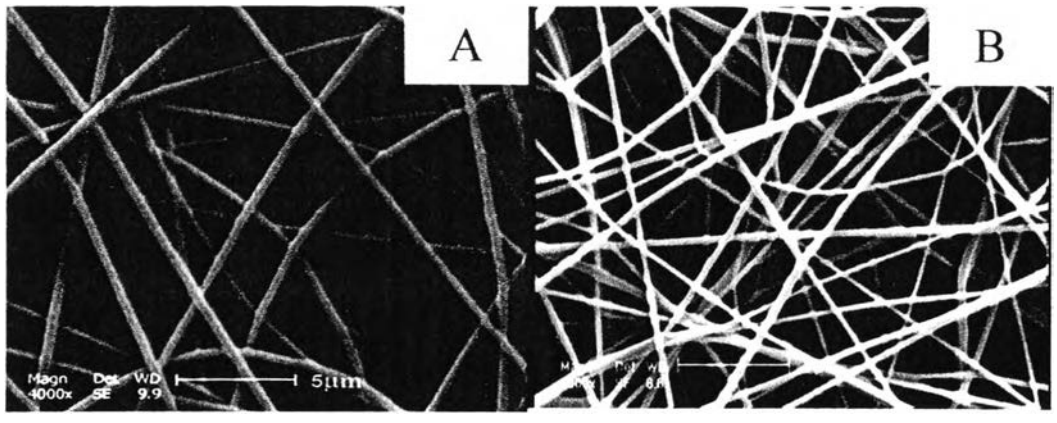


**Figure 2.10** SEM photographs of electrospun nanofibers without drug and with 10% w/w drug loaded: **A, B**) PVA (Jannesari *et al.*, 2011).