CHAPTER II
THEORETICAL BACKGROUND AND LITERATURE REVIEW

2.1 Wounds

Wound are the physical injuries that result in an opening or breaking of skin and appropriate method for healing of wound is essential for the restoration of disrupted anatomical continuity and disturbed functional status of the skin (Rawat *et al.*, 2012).

Wounds can divied into 4 catagories which are

2.1.1 Open Wounds

In this case blood escapes the body and bleeding is clearly visible. It is further classified as: Incise wound, Laceration or tear wound, Abrasion or superficial wounds, Puncture wound, Penetration wound and gunshot wound (Shao *et al.*, 2003).

2.1.2 Closed Wounds

In closed wounds blood escapes the circulatory system but remains in the body. It includes Contusion or bruises, hematomas or blood tumor, Crush injury etc.

2.1.3 Acute Wounds

Acute wounds is a tissues injury that normally precedes though an orderly and timely reparative process that result in sustained restoration of anatomic and functional integrity. Acute wounds are usually caused by cut or surgical incisions and complete the wound healing process within the expected time flame (Lazarus *et al.*, 1994).

2.1.4 Chronic Wounds

Chronic wounds are wounds that have failed progress though the normal stage of healing and therefore enter a state of pathologic inflammation chronic wounds either require a prolonged time to heal or recur frequently. Local infection, hypoxia, trauma, foreign bodies and systemic problems such as diabetes mellitus, malnutrition, immunodeficiency or medication are the most frequent causes of chronic wounds (Krishnan *et al.*, 2006).

2.2 Mechanism of Wounds healing

The response to injury, either surgically or traumatically induce, is immediate and damaged tissue or wound then passes through three phase in order to affect a final repair (Rawat *et al.*, 2012).

2.2.1 The Inflamatory Phase

The inflammatory phase starts immediately after the injury that usually last between 24 hrs 48 hrs and may persist for up to 2 weeks in some cases the inflammatory phase launches the haemostatic mechanism to immediately stop blood loss from the wound site. Clinically recognizable cardinal sign of inflammation, rubor, color, tumor, dolor and functional-laesa appear as the consequently vasodilatation and phagocytosis to produce inflammation at the wound site (Li, Jie *et al.*, 2007).

2.2.2 Proliferation Phase

The proliferation phase essentially involves the generation of the repair materials and majority of the skeletal muscle injuries (Guo *et al.*, 2010).

2.2.3 Remodelling Phase

The remodeling phase is an essential component of tissue repair and is often overlooked. The final outcome of these combine events is that the damaged tissue will be repaired with the scar (Guo *et al.*, 2010).

The most importance of wound healing is clean. For the example a 40 years old man was reffered by his medical officer to the emergency department with painful bilateral oedema of his lower legs and generalized abdominal pain. After investigation, the doctor found a growing of *A. baumannii* and MRSA (Ali *et al.*, 2014).

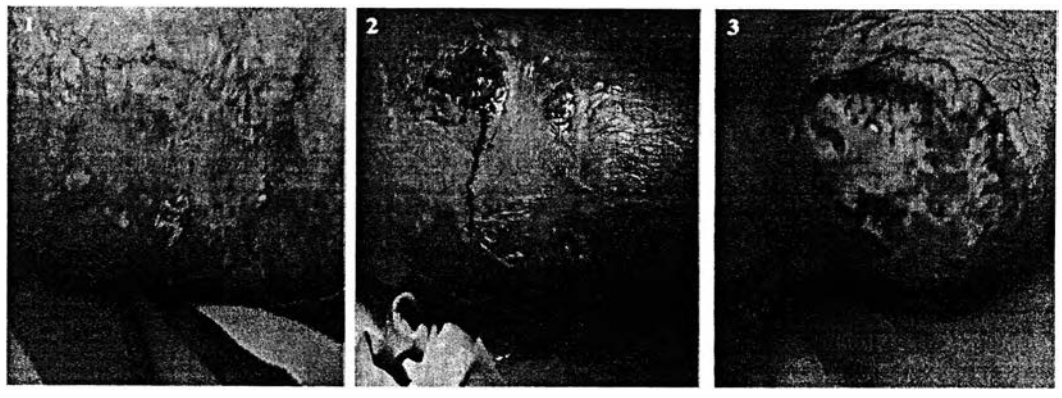

Figure 2.1 Cellulitis cause by *A. buamannii* on the left leg and forefoot.

2.3 Wound Dressing

Although wound management is an essential component of care, especially for surgical patients, it is a task that is frequently seen to be an area of nursing rather than medical practice and only when complications occur does the medical team become involved in direct treatment decisions. As a result many doctors are not specifically trained in wound care and have little or no knowledge of wound pathophysiology, dressing practice or the range and function of dressings available. This is somewhat surprising as the incidence of wound complications such as surgical site infection (SSI), pressure ulcer occurrence and amputation in diabetic foot ulceration are all seen as care quality indicators for surgical care provision (Vowden *et al.*, 2014).

2.3.1 Low or Non-adherent Contact Layer Dressings

These dressings are applied directly to the wound bed and do not adhere to the wound surface or cause significant trauma during or secondary dressing. These dressings are semipermeable, vary in size and thickness, and have an adhesive that holds the dressing on the skin. They conform easily to the patient's body. As films are transparent, the wound can be easily monitored. Film dressings generally require a border of dry, intact skin for the adhesive edge of the dressing; film dressings will not adhere to moist skin or moist wound beds because the moisture inactivates the adhesive. Therefore, the condition of the periwound skin

should be assessed before application to determine if a film dressing is appropriate. As film dressings are semi-occlusive and trap moisture, they allow autolytic debridement of necrotic wounds and create a moist healing environment for granulating wounds. Example products include Tegaderm and Opsite, which have similar MVTR characteristics. Some film dressings have a higher MVTR and are frequently used on IV or epidural sites. These dressings
when combined with an absorptive pad are suitable for use on minor injuries and as a post-surgery wound dressing. Barrier films (spray on or foam applicators) functions to
protect peri-wound skin from moisture damage and may help with dressing adhesion (Vowden *et al.*, 2014).

2.3.2 Hydrogel Dressings

Hydrogel dressings are water- or glycerin-based products. Because they are usually clear or transparent, the wound can be monitored without removing the dressing. Use hydrogels to maintain a moist wound environment on a clean, healthy, granulating wound and to facilitate autolytic debridement in wounds with necrotic tissue such as slough or eschar. Hydrogels can be used on pressure ulcers, skin tears, surgical wounds, and burns, including radiation oncology burns and are safe on neonatal skin. These dressings are suitable for wounds with minimal to moderate exudate. Hydrogel dressings are commonly available in three forms: amorphous gel, impregnated-gauze, and sheet hydrogel and can be useful when managing painful wounds. Hydrogel dressings that act as a release platform have also been developed containing hyaluronic acid, antimicrobials and antibiotics. Oxyzyme for example is a two component hydrogel dressing which releases both oxygen and iodine into the wound and is suitable for non-infected moderately exudating wounds (Vowden *et al.*, 2014).

2.3.3 Alginate Dressings

Alginate dressings are available in non-woven sheets and ropes and are a fibrous products derived from brown seaweed. The alginate forms a gel when it comes in contact with wound fluid. These dressings are capable of absorbing up to 20 times their weight in fluid, and can be used in infected and non-infected wounds. As alginates are highly absorbent, they should not be used with dry wounds or

wounds with minimal drainage. Alginates require a secondary dressing; foams or hydrocolloids will secure the alginate and keep it from drying out. If the wound is infected, the secondary dressing should be non-occlusive. The calcium component of the dressing acts as a haemostat and can be useful in managing wound bleeding (Vowden *et al.*, 2014).

2.3.4 Foam Dressings

Foam dressings are semipermeable and either hydrophilic or hydrophobic with a bacterial barrier. They are either polyurethane or silicone-based and are capable of handling moderate to high volumes of wound exudate. They provide thermal insulation to the wound, create a moist wound environment, are non-adherent, and allow atraumatic dressing removal. Foam dressings may also be used as the secondary dressing with hydrogel or alginate dressings and may be used in conjunction with a topical antimicrobial for infected wounds. Foam dressings may be manufactured with an adhesive border, which eliminates the need for a securing device or without an adhesive boarder. Shaped versions of these dressings are also available (Heel and Sacrum). Foam dressings are also available which release agents such as antimicrobials, moisturizers or anti-inflammatory analgesics into the wound (Vowden *et al.*, 2014).

2.4 Materials

2.4.1 Polyvinyl Acetate (PVAc)

Polyvinyl acetate (PVA or 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.

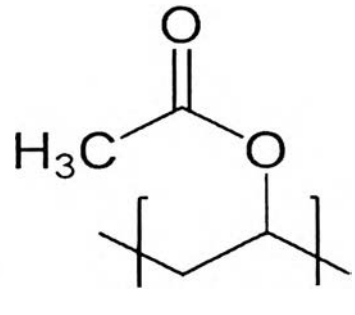

Figure 2.2 The structure of polyvinyl acetate.

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). Boron compounds like borax and boric acid also react with the polymer, under alkaline settings, leading to the formation of a complex borate-slime-precipitate.

Polyvinyl acetate was first discovered by a German scientist Dr. Fritz Klatte in 1912. 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 Mangosteen Extract

Mangosteen (Garcinia mangostana Linn.) (GML) is a tropical fruit. The mangosteen-fruit is dark purple or reddish, with white, soft and juicy edible pulp with slightly acid and sweet flavor. Mangosteen is know as "the queen of fruit" because it is one of the best tasting tropical fruits (Pedraza-Chaverri *et al.*, 2008). The pericarp of mangosteen-fruit has been used as a medicinal agent by Southeast Asians for centuries in treatment of skin infection and wounds (Ibrahim *et al.*).

The main biological and medical properties of GML following by

2.4.2.1 Antioxidant Properties

In the table 2.1 the antioxidant properties of mangosteen extract and xantones that have been studied and summarized.

In 2010, the antioxidant of the extract from peel, leaves, and bark of mangosteen (Garcinia mangostana L.) were investigated. The antioxidant activities (IC50) of peel, leaves, and bark extracted, which were evaluated by DPPH method, were 5.94, 9.44, and 6.46 μg/ml, respectively (Tjahjani et al., 2014).

2.4.2.2 Antitumoral Properties

In 2013, the researcher found that the ethanol extract of mangosteen (Garcinia mangostana L.) fruit rind had a strong inhibitory effect on mammalian DNA polymerase (pol) activity and isolated α-mangostin as a potent pol inhibitor from the extract. The inhibitory activities against mammalian pols by α-mangostin. This compound also inhibited human DNA topoisomerases (topos) I and II activities with IC50 values of 15.0 and 7.5 μM, respectively, but did not inhibit the activities of other DNA metabolic enzymes tested (Mizushina et al., 2013).

Several studies have been designed to examine the anticancer activities of xantones isolated from mangosteen pericarp (Table 2.2).

Table 2.1 Antioxidant properties of mangosteen extract

Articles	Ref.
Optimisation of ethanol modified supercritical carbon dioxide on the extract yield and antioxidant activity from Garcinia mangostana L.	(Zarena *et al.*, 2012)
Structural diversity and antioxidant activity of condensed tannins fractionated from mangosteen pericarp	(Zhou *et al.*, 2011)
Extraction of antioxidant pectic-polysaccharide from mangosteen (Garcinia mangostana) rind: Optimization using response surface methodology	(Gan *et al.*, 2011)
Effects of drying methods on assay and antioxidant activity of xanthones in mangosteen rind	(Suvarnakuta *et al.*, 2011)
Anti-skin cancer properties of phenolic-rich extract from the pericarp of mangosteen (Garcinia mangostana Linn.)	(Wang *et al.*, 2012)

Table 2.2 Antitumoral properties of mangosteen extract

Articles	Ref.
Inhibition of CHOP accentuates the apoptotic effect of α-mangostin from the mangosteen fruit (Garcinia mangostana) in 22Rv1 prostate cancer cells	(Li, Gongbo *et al.*, 2014)
Mangosteen xanthones, α-and γ-mangostins, inhibit allergic mediators in bone marrow-derived mast cell	(Chae *et al.*, 2012)
Investigation of fruit peel extracts as sources for compounds with antioxidant and antiproliferative activities against human cell lines	(Khonkarn *et al.*, 2010)
Development of a standardized and effect-optimized herbal extract of Wedelia chinensis for prostate cancer	(Tsai *et al.*, 2015)
Standardized rosemary (Rosmarinus officinalis) extract induces Nrf2/sestrin-2 pathway in colon cancer cells	(Yan *et al.*, 2015)

2.4.2.3 Anti-inflammatory and Antiallergy Properties

In 2009, The mitogen-activated protein kinases (MAPK) and nuclear factor κB (NF-κB) are involved in transduction cascades that play a key role in inflammatory response. the ability of preselected natural polyphenolic extracts (grape seed, cocoa, sugar cane, oak, mangosteen and pomegranate) to modulate intestinal inflammation using human intestinal Caco-2 cells treated for 4 h with these extracts and then stimulated by cytokines for 24 or 48 h. The researcher suggest that pomegranate extract could be particularly promising in dietary prevention of intestinal inflammation (Romier-Crouzet et al., 2009).

Table 2.3 shows studying of effectiveness of mangosteen extract on anti-inflammatory properties.

Table 2.3 Anti-imflammatory properties of mangosteen extract

Articles	Ref.
Anthelmintic, anti-inflammatory and antioxidant effects of Garcinia mangostana extract in hamster opisthorchiasis	(Aukkanimart *et al.*)
Anti-Inflammatory Properties of Botanical Extracts Contribute to Their Protective Effects in Brain Edema in Cerebral Ischemia	(Panickar *et al.*, 2015)
Effects of compounds from Garcinia mangostana on inflammatory mediators in RAW264.7 macrophage cells	(Tewtrakul *et al.*, 2009)
Anti-inflammatory activity of mangostins from Garcinia mangostana	(Chen *et al.*, 2008)
Anti-arthritis effect of mangostins from G. Mangostana	(Lee *et al.*, 2013)

2.4.2.4 Antimicrobial Properties

α-Mangostin, isolated from the stem bark of Garcinia mangostana L., was found to be active against vancomycin resistant Enterococci (VRE) and methicillin resistant Staphylococcus aureus (MRSA), with MIC values of 6.25 and 6.25 to 12.5 μg/ml, respectively (Sakagami et al., 2005).

Five natural xanthones were extracted and purified from the fruit hull of Garcinia mangostana and their antimicrobial properties were investigated. α-Mangostin was identified as the most potent among them against Gram-positive pathogens (MIC = 0.78–1.56 μg/mL) which included two MRSA isolates (Koh et al., 2013).

Moreover, the cytotoxic effect of three xanthone compounds (α-mangostin, γ-mangostin, and 8-deoxygartanin) from mangosteen pericarp was investigated using the human melanoma SK-MEL-28 cell line. Significant dose-dependent reduction in % cell viability was induced. γ-Mangostin and 8-deoxygartanine at 5 μg/ml increased the cell cycle arrest in G1 phase (90% and 92%) compared with untreated cells (78%). All compounds induced apoptosis, of the highest being α-mangostin at 7.5 μg/ml that induced 59.6% early apoptosis, compared to 1.7% in untreated cells (Wang et al., 2011).

Several studies have demostrated antibacterial, anti fungal and antivival properties of xantones and extracts obtained from GML (Table 2.4).

Table 2.4 Antibacterial properties of mangosteen extract

Articles	Ref.
Microbial metabolism of α-mangostin isolated from Garcinia mangostana L	(Arunrattiyakorn *et al.*, 2011)
Antibacterial tetraoxygenated xanthones from the immature fruits of Garcinia cowa	(Auranwiwat *et al.*, 2014)
Antibacterial Activity of Thai Medicinal Plants against Methicillin-resistant Staphylococcus aureus	(Chomnawang *et al.*, 2009)
α-Mangostin from Cratoxylum arborescens: An in vitro and in vivo toxicological evaluation	(Ibrahim *et al.*, 2015)
Laboratory evaluation of the antibacterial and cytotoxic effect of alpha-mangostin when used as a root canal irrigant	(Kaomongkolgit *et al.*, 2013)

However, the intestinal metabolism α-mangostin is comparable and still extensive in mice treated with α-mangostin and mangosteen extract. Intraperitorial LC50 of α-mangostin and mangosteen extract was 150 and 231 mg/kg, respectively (Choi *et al.*, 2014).

2.5 Spray Drying Application

Spray drying is a process that transforms feedstock from a fluid state to a dried particle form by spraying the feed into a hot drying medium. The benefits of the spray drying technique include the ability to produce powders of a specific particle size and moisture content, irrespective of the dryer capacity. It is a continuous and easy operation which is fully automatically controlled with a quick response time, and is also applicable to both heat sensitive and heat-resistant materials. Essentially, the spray drying process is a continuous drying operation which combines several stages in the process as presented in Figure 2.3.

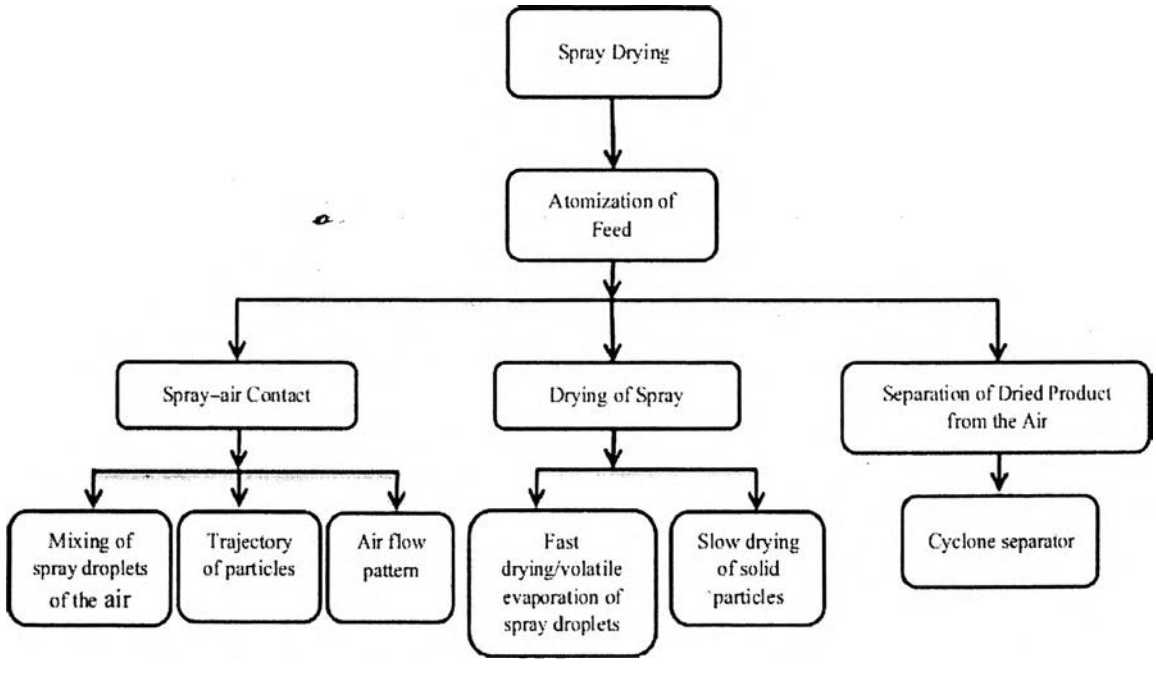

Figure 2.3 The diagram of spray drying process.

The spray drying process is mainly affected by several parameters as presented in Fig. 2.3 Since spray drying is usually the end-point of a process that also influences the quality of the final product, it has attracted more attention over the last two decades. A key processing problem in spray dryers is the wall deposition of particles that indirectly affects the quality of the product through the degradation of the deposited particles and the resulting pollution of the main product. Its understanding provides guidance in the selection of the operating conditions of the spray dryers that will minimize wall deposition and hence help to improve the quality of the product. Currently, the main challenges in the production of powders in spray dryers are the development of the desired powder properties and the costs. It is therefore important to identify the optimum operating criteria and processing conditions to ensure the preservation or enhancement of the quality of the dried products during the spray drying processes (Keshani *et al.*, 2015).

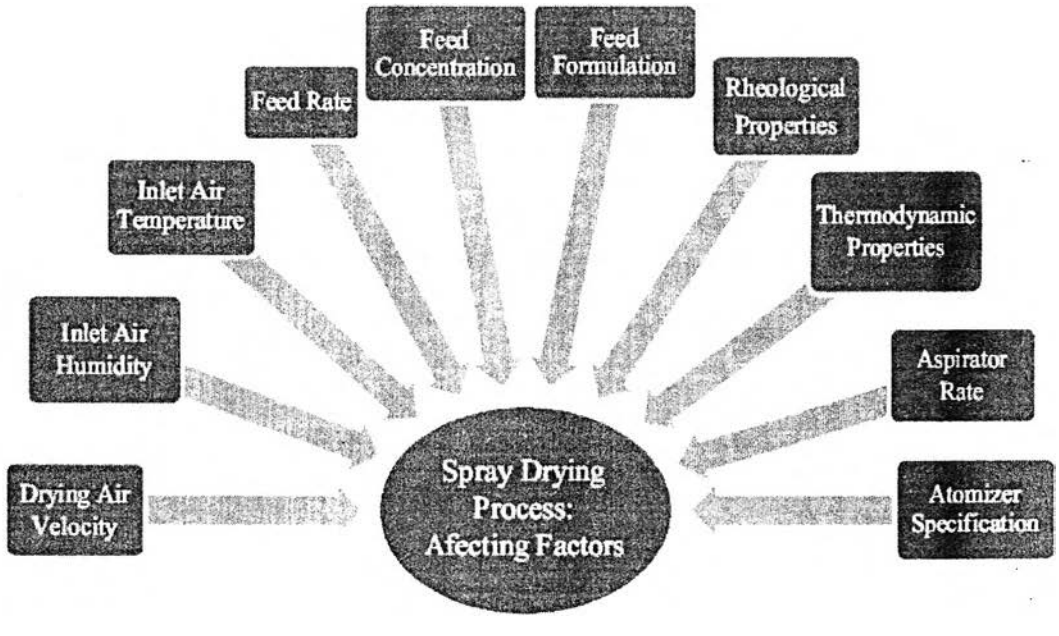

Figure 2.4 The diagram of affecting factor on spray drying process.