A COMPREHENSIVE REVIEW ON WOUND DRESSING USAGE IN CLINICAL SETTINGS

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ABSTRACT Wound repair is a complex dermal and epidermal tissue regeneration phenomenon consisting of several phases, including haemostasis, inflammation, migration, proliferation, and remodelling. The wound management procedures have evolved from ancient times that used honey, plant fibres, and animal fats to biopolymers. With the emergence of modern wound dressings, the wound healing process has been accelerated with extraordinary properties of dressing material. The dressing material contacts the wound and provides optimal conditions for healing, such as a moist environment, absorption of excessive exudates, permeability to gaseous exchange, etc. The main purpose of dressing is to stop the bleeding, prevention of exsanguination, protection from infection, and renew function. With the myriad of dressing types available in the clinical settings, such as hydrogels, hydrocolloids, alginates, anti-microbial-impregnated dressing, etc., the understanding behind the usage of a particular dressing for a specific wound type remains conjectural. In this comprehensive review, we first briefly discussed the wound repair process followed by wound dressing, the characteristics of ideal wound dressing, and its categorization. This review aims to provide a state-of-the-art overview of different aspects of wound dressing types contributing to the effective treatment of particular skin wounds.

KEYWORDS Wound; Wound healing; Dressing material.

Introduction

Wound dressing is any material that helps in the healing process and prevents further complications. In clinical settings, innumerable wound dressing materials are available. However, the aim and purpose of all wound dressing types remain the same: stopping bleeding by blood clotting, absorption of excessive exudates, protection against pathogens, etc. [1]. Each dressing has different characteristics and is used on a particular type of wound. Therefore, it is necessary to consider the underlying cause of tissue damage, perfusion, and pathogen or microbial load. The appropriate selection of wound dressing types can only be facilitated by proper knowledge and understanding of wound physiology, wound repair process, and properties of dressing material [1]. This review aims to simplify clinicians' decision-making process in selecting a wound dressing after a thorough assessment of a wound.

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Wound Definition

Skin is the largest and outermost organ of the human body. It acts as a protective barrier against external agents such as biological (pathogens), chemical (irritants and corrosives), mechanical (incisions and abrasions), and physical damage (temperature and radiation) [2]. It also plays a significant role in temperature sensation, excessive water loss prevention, shock absorption, and immunological surveillance [3].

Skin is considered the most exposed and challenged organ. Any kind of trauma or stress to the skin, organs or other tissues causing disruption of the normal anatomical structure and function is referred to as a wound [4]. In addition, internal factors such as illness or surgery and external factors including cuts, scrapes, burns, or abrasions may break the continuity and integrity of biological tissues.

Classification of wound

A wound can be classified in several ways depending on the type: (a) anatomical disruptions (an open or closed wound), (b) healing time (acute or chronic), (c) depth of injury (penetrating or blunt trauma), (d) cleanliness (clean, clean-contaminated, contaminated, and dirty-infected), and (e) wound thickness (superficial, partial-thickness or full-thickness) [5], which are as follow:

a) Open or Closed wounds:

An open wound is broken skin with exposed body tissue to the external environment. Thus, it is more prone to bacterial colonization. E.g., Cuts, surgical wounds, gunshot wounds, etc. Closed wound is damage to the internal tissue under intact skin. E.g.: Contusions, blisters, and hematoma, etc. [5].

b) Acute or chronic wounds:

Acute wounds heal in a predicted time without complications, whereas chronic wounds take a relatively long time of 12 weeks or more to heal and may have some complications. The Wound Healing Society classifies chronic wounds as pressure, venous, diabetic, and arterial insufficiency ulcers. Chronic wounds are also referred to as non-healing wounds.

c) Penetrating or blunt trauma wounds:

Penetrating is a type of open wound that breaks through the skin's full thickness. E.g., stab wounds, cuts, surgical wounds, etc. Blunt trauma wounds are non-penetrating wounds which occur due to friction with other surfaces. E.g., abrasions, lacerations, bruises, concussions, etc.

d) Class 1-4 wounds:

Clean, uninfected, no inflammation, and closed wounds are classified as Class 1 wounds, and these do not enter respiratory, alimentary, or urinary tracts. Class 2 wounds are clean-contaminated wounds that lack unusual contamination and may enter the bodily tracts under controlled conditions. Class 3 wounds occur due to insult from sterile techniques and are considered contaminated, fresh, acute inflammation, and open wounds. It occurs due to leakage from the gastrointestinal tract into the wound. Class 4 wounds result from improperly cared traumatic wounds and are dirty-infected, presence of pathogens and devitalized tissue [5].

e) Superficial, Partial-thickness or Full-thickness wounds:

Superficial wounds are defined as those in which only epidermis is affected whereas both epidermis and dermis are affected in partial-thickness wounds. Full-thickness wounds are those in which internal segments are also affected, along with the dermis and epidermis. Soon after the structure or function of a wounded organ gets compromised, the body proceeds to an orderly and timely reparative process. This cascade of events is known as wound repair or wound healing [6]

Process of wound healing

Wound healing is a natural physiological phenomenon for restoring anatomical integration and functionality, which involves crosstalk between numerous immunological cells, cytokines, matrix and the vascular system. The healing process involves a cascade of precisely synchronized and overlapping events in five crucial phases: haemostasis, inflammation, migration, proliferation, and remodelling (**Figure 1**). As the injury occurs, lymphatic fluid and blood firstly outpour from the damaged tissue, inducing haemostasis immediately. The healing process initiates with the formation of fibrin clots through vasoconstriction and platelet aggregation to stop bleeding and avoid pathogen contamination. This is followed by a complex inflammatory phase which involves the recruitment of inflammatory cells such as neutrophils, monocytes/macrophages and lymphocytes [7]. The inflammatory phase fosters fibroblast migration to the wound site, where fibroblast differentiates into myofibroblasts through platelet-derived growth factors to produce extracellular matrix components like fibronectin, collagen, and proteoglycan, which serve as scaffolding [8]. The proliferative phase is characterized by forming granulation tissue, angiogenesis, reepithelialisation, and neovascularization [9]. The last phase is maturation or remodelling, which involves the maturation and strengthening of the wound by degrading excessive collagen and ceasing all activated processes [8]. Hence, the wound is superficially sealed, forming a scar. These phases occur orderly and are well-connected depending upon the wound type [10].

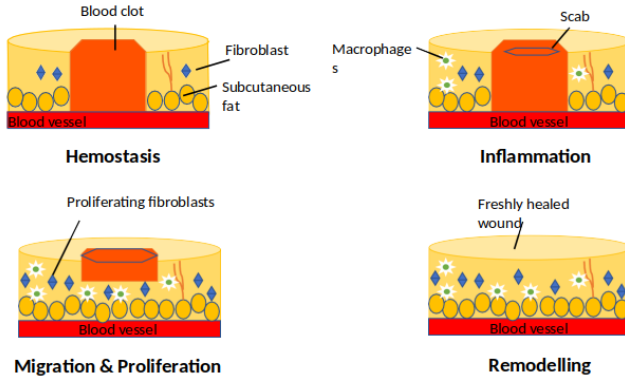

Figure 1 The wound healing process

Wound dressings

Definition

Wound dressing is a material designed to contact the wound for repair. To ensure the wound healing process, wound dressing provides optimum conditions for repair, protection against pathogens or further traumas, and maintains a moist environment. The choice of wound dressing highly depends on the type, depth, location, and extent of the wound. Thus, it is imperative to choose appropriate dressing material. For instance, serious wounds such as burns and ulcers produce excessive exudates, which can contribute to the invasion and colonization of pathogens. [11]. Such types of wounds can be treated best by moist wound therapy. The moist environment in the wound bed would help re-epithelialization by preventing cell death [11].

Historically, wet-to-dry dressings, oil-soaked strips cum plasters, honey or resin dressings, wool boiled in water and clay tablets, etc. have been extensively used as dressing materials for the treatment of wounds. In contrast, water, milk, wine, and vinegar were used to clean the wounds. This was followed by a breakthrough with medicated dressings to control infections.

Modern wound dressing emerged in the 20^{th} century. When a wound is properly covered with a dressing, the proteinases, chemotactic, and several growth factors help in wound healing by keeping the environment moist for faster re-epithelialization, neo-vascularization, and repair [12-13]. Plenty of wound dressing materials with unique properties are being recommended for different wound conditions in clinical settings. These are specific for a wound type. The wound healing process using a dressing material is shown in **Figure 2**.

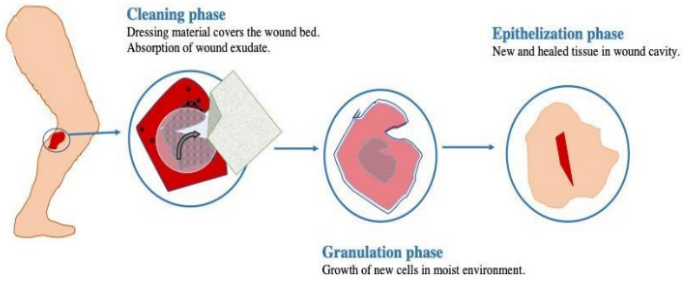

Figure 2 Wound healing process using a dressing.

Characteristics of an ideal wound dressing

Based on the contact with the wound, the dressing is categorized as a primary or secondary dressing. Primary dressings come in contact with the wound, whereas secondary dressings support the primary dressing. There is no "one" ideal dressing type. The ideal dressing choice depends on the wound type, depth, and level of injury. A suitable wound dressing should have the ability to:

i) ***Maintain a moist environment***: The concept of faster healing in moist wounds was documented in 1615 BC. In 1963, Hinman & Maibach used the moist dressing on human skin wounds and observed faster healing of wounds as compared to dry dressing [Dabiri et al., 2016]. The optimal level of moisture should be maintained to enhance the migration and proliferation of fibroblasts and keratinocytes across the wound surface. In addition, moisture may serve as a transporter for enzymes, growth factors, and cytokines. The moist environment also enhances natural autolytic processes. Further, skin renewal and eschars formation also occur in a moist environment. Hence, wet dressings are considered more suitable for wound dressing [14].

ii) ***Gas exchange between the wound and the environment***: Normal oxygen levels or hypoxic conditions are required at different phases of the wound healing process. The diffusion of gases between wounds and the environment maintains the migration and proliferation phases of the wound healing process. The permeability to fluids, gases, water vapour, and pathogens depends on the type of dressing [12].

iii) ***Thermal insulation***: Appropriate tissue temperature is necessary to improve blood flow and reduce pain. The dressing should have the ability to reduce the persistent pain at the injury site. The biological processes such as mitosis and enzymatic activity can be maintained at a constant temperature of 37°C.

iv) ***Promoting angiogenesis and re-epithelialization***: These are the crucial factors in wound healing that can result in proper scaffolding and remodelling.

v) ***Absorption of exudate***: Excess exudate may lead to pathogen contamination and colonization. The dressing should have the ability to regulate excessive exudate.

vi) ***Sterile***: Few materials shed into the wound and may cause irritation at the infection site. Thus, the wound dressing should be sterile and non-toxic to prevent the wound sites from further damage [15-16].

vii) ***Non-adherent/Adhesiveness***: The attachment of dressing to the wound surface is termed adherent, and to the surrounding skin of the wound is termed adhesiveness. The dressing material should be adhesive but non-adherent for the easy and atraumatic removal of the dressings after healing. In addition, it should not cause damage to the newly formed epithelium during wound healing.

viii) ***Protection against pathogens***: The invasion of pathogens can contaminate the wound and impair the healing process. It may prolong the duration of healing.

ix) ***Cost-effective***: The wound dressing should be cost-effective and available for all needed patients in the healthcare setting [12, 15].

x) ***Transparency***: A transparent dressing provides visual monitoring of the wound site, which lowers the risk of infection without being noticed. Frequent removal and changing of dressing can be avoided [17].

Classification of wound dressings

The wound dressings are classified based on traditional modalities (gauze, bandages, and tulle), advanced modalities(occlusive, hydrocolloid, hydrogels, 3D hydro cellular, scar, and antimicrobial), the origin of the material (animal, herbal, and synthetic origin), and physical form (film and foam) that are reviewed in the following sub-sections. The classification system of different types of wound dressings is shown in **Figure 3**; their characteristics and properties are summarized in **Table 1**.

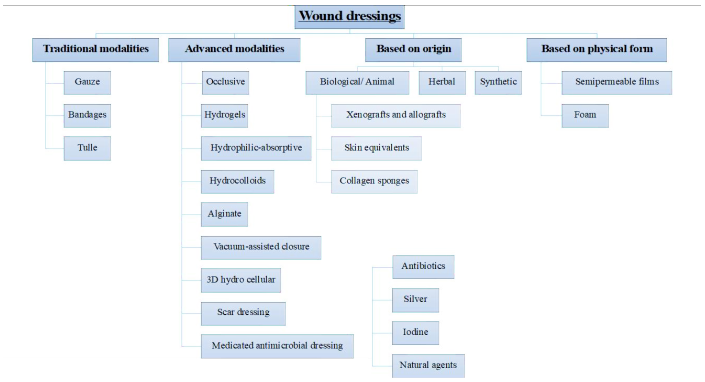

Figure 3 Classification of wound dressings.

Table 1 Characteristics and properties of wound dressings

Classification	Dressing type	Description	Advantages	Disadvantages
Traditional modalities	Gauze	• Fibres • Absorbent pads.	• Protection against infection	• Fail to maintain moisture. • Traumatic removal. • Frequent changes.
	Bandages	• Absorbent pads.	• Provides support	
	Tulle Gras Dressing	• Non-adherent • Impregnated with paraffin	• Moist environment	• Delayed healing • Cause allergies
Advanced modalities	Occlusive	• Air and watertight • Flat shape sheets	• Moist environment	• Risk of infection
	Hydrogels	• Insoluble • Cross-linked polymers • 70-90% water content	• Moist environment • Granulation tissue	• Bacterial proliferation.
	Hydrophilic	• Polysaccharides • Charcoal	• Absorb exudate. • Form gel-like mass after absorption.	-
	Hydrocolloid dressings	• Polyurethane film coated with adhesive mass	• Retains moisture • Painless removal. • Ideal for small abrasions.	• Formation of thick malodorous yellow gel (mistaken for infection)
	Calcium Alginate	• Natural polysaccharides from seaweed	• Moist environment. • Reduces pain. • Absorbs exudate • Promotes haemostasis	• Anaerobic infections
	Vacuum-assisted closure	• Negative pressure wound therapy	• Spontaneous healing	• Expensive
	3-D hydro cellular dressing	• DTAC technology (cationic surfactant)	• Antimicrobial action. • Gaseous exchange • Moist environment. • Non-adherent • Non-leaching	-
	Scar dressings	• Silicone gel sheets	• Antimicrobial action. • Moist environment. • Non-adherent	• Cause irritation
	Anti-microbial dressing	• Silver- impregnated dressing • Impregnated with povidone-iodine	• Bactericidal effects • Bacteriostatic effects	• Impaired healing
Based on origin	Biological/Animal	• Xenografts • Allografts	• Reduces healing time	• Chances of rejection
	Herbal	• Natural tissues	• Biocompatible • Biodegradable • Non-toxic	-
	Synthetic	• Polymers	• Good mechanical strength	-
Based on the physical form	Semipermeable dressing	• Thin • Adhesive • Transparent • Polyurethane film	• Moisture evaporation • Reduces pain • Prevent contamination	• Traumatic removal. • Regular inspection
	Foam dressing	• Polyurethane • Adhesive layer incorporated	• Moist environment. • Highly absorbent • Protective	• Fixed-size. • Traumatic removal.

A. Traditional dressing modalities

The traditional dressing materials, including gauze, plasters, bandages, and cotton wool, are used as primary or secondary dressings for clean and dry wounds or wounds with little exudates. These dressings help in the prevention and protection against pathogen invasion and contamination.

a) Gauge dressing

Gauze dressings are woven or non-woven cotton, rayon, and polyester fibres that protect against infection and further mechanical traumas. These are absorbent pads to remove excess exudate in an open wound. Gauze dressings fail to maintain a moist environment, a major drawback. The gauze becomes moistened with excessive fluid drainage from the wound resulting in dressing adherence to the wound. Removing dried gauze dressing is traumatizing and painful and may cause further tissue damage. In addition, the gauze dressings require frequent changing. These dressings may also lead to maceration of healthy tissues when failed to change frequently. However, these are cost-effective and can be impregnated with petroleum jelly or polyhexamethylene to become less adherent. Generally, these products are recommended for superficial, clean, and dry wounds following topical preparations [18].

b) Bandages

Based on the type of function, natural bandages are made up of natural or synthetic material. Natural bandages include cotton wool and cellulose, whereas synthetic bandages include polyamide materials. Cotton bandages are generally used as absorbent pads for cleaning excessive exudates or as a secondary dressing. On the other hand, synthetic bandages provide better compressions [18].

c) Tulle dressing

Lastly, tulle dressings are composed of open-weave cloth impregnated with soft paraffin, also known as low adherent dressings. It consists of greasy gauze, which is suitable for minimal to moderate exudates. These are designed to overcome the disadvantage of adherence at the wound site. Tulle dressings are cost-effective and are generally recommended in case of superficial clean wounds and/or patients with fragile skin. These maintain a moist environment by allowing exudates to pass through secondary dressings [18].

B. Advanced dressing modalities

Modern wound dressings have been developed due to the failure of traditional dressings to provide a moist environment for wound healing. These act as a protective barrier against invasion and penetration of pathogens at the wound site [19]. Currently, a substantial number of dressing materials based on differential needs of the wound type are commercially available in the market. However, there is a lacuna in the literature regarding the knowledge of dressing material for a specific wound type. The applications of dressing material for a particular wound type are summarized in **Table 2**. Modern wound dressings include the following modalities:

a) Occlusive dressings

Occlusive dressings are considered air and water-tight dressings that seal the wound due to the waxy coating on the dressing. These are available in the form of flat shape sheets. Occlusive dressings are designed to retain an optimum level of wound exudate resulting in increased cell proliferation and autolytic debridement of the wound. In addition, the moisture-retaining property of occlusive dressing augments the rate of epithelialization and promotes the inflammatory phase of the wound healing process. Therefore, they are particularly used to treat open wounds. The major concern with occlusive dressings is the increased risk of infection when failed to change regularly [20].

b) Hydrogels

Hydrogel consists of an insoluble hydrophilic matrix with a water content of 70-90%. The water content helps maintain the moist environment at the wound site and granulation tissues; therefore, these are recommended for dry wounds. These dressings provide a soothing and cooling effect as hydrogels can decrease the temperature of cutaneous wounds. The hydrogels are composed of synthetic crosslinked polymers such as poly (methacrylates) and polyvinyl pyrrolidine. Due to partially hydrated polymer material, they can absorb wound exudates. Hydrogels promote natural autolysis and wound debridement. These are available in sheets, amorphous gels, and impregnated gauzes. In a Cochrane Review, pooled data from three trials suggested hydrogel dressings are more effective for healing diabetic foot ulcers than other wound dressings [21]. Moreover, with their distinct physical and chemical properties, hydrogels can be used as a temperature and light-responsive material for drug delivery [22]. Hydrogels are non-irritant therefore, they are recommended for sloughy, necrotic, or burn wounds and avoided in case of excessive exudated wounds. Excessive exudation may cause maceration, infection, and a foul smell in wounds. Evidence in the literature reported the presence of gangrenous tissue when hydrogels were used for heavy drained wounds [23].

c) Absorptive dressings – Hydrophilic

Hydrophilic dressings are designed to absorb the wound exudate. Dextranomer hydrophilic granules are composed of hydrophilic polysaccharides with a diameter of 0.1-0.3 mm. They come in contact with the fluid and form a gel-like mass after absorbing exudate with subsequent swelling. They are efficient in reducing exudate and removing debris. These are also modified by adding iodine solution to provide an antiseptic effect.

The activated charcoal dressing is another example of an absorptive dressing bound to a semi-permeable membrane. These dressings protect against external infection and trauma by forming a moist environment optimal for wound healing. Activated charcoal dressings may be regarded as a form of mechanical debridement. Recently, silver-impregnated activated charcoal dressings have been developed, combining absorption and antimicrobial efficacy [16].

d) Hydrocolloid dressings

Hydrocolloid fibres are non-woven flat sheets composed of two layers, an inner colloidal layer and an outer water-impermeable layer (polyurethane). These dressings are bonded to a carrier of semipermeable film or a foam sheet to formulate flat sheet dressings. Hydrocolloids are also available in the form of powder and pastes. These dressings

are composed of gel-forming agents such as carboxymethylcellulose, gelatin, and pectin with elastomers adhesives [24]. Hydrocolloids are pathogen impermeable. When the hydrocolloid dressing contacts the wound site, it forms a gel coating to provide a moist environment and protection against pathogens. These dressings can rehydrate dry necrotic eschar, autolytic debridement, and absorption of wound exudates [18]. Hydrocolloid dressings induce the hypoxic environment to stimulate the proliferation of fibroblasts and angiogenesis.

Moreover, these may induce an acidic microenvironment to protect against the strains of Pseudomonas aeruginosa. In a systematic review, Chaby et al. (2007) suggested that hydrocolloid dressings are better than saline gauze or paraffin gauze for complete wound healing [25]. They are typically recommended for pressure sores, minor burns, traumatic wounds, and paediatric wound care management. They are best recommended for joint wounds as they provide mild cushioning. The removal of hydrocolloid dressing does not cause pain or damage. However, these dressings should be avoided in case of neuropathic ulcers or highly exudating wounds [24]. The major disadvantages include the opaque nature of dressing which restricts the frequent wound checks, and the formation of thick malodorous yellow gel, which can be mistaken for infection.

e) Alginate dressings

Alginates are naturally occurring polysaccharide fibre derived from seaweed belonging to the Phaeophyceae family. They occur in the form of calcium (100%) and sodium (calcium and sodium alginate in a ratio of 80:20) salts of alginic acid. Alginates comprise mannuronic and guluronic acid units. The level of these units influences the property of alginates to absorb wound exudates. Like hydrocolloids, they have a strong gel-forming ability, which is hydrophilic. In a study, Thomas et al. (2000) reported that alginate is involved in the activation of macrophages at the wound site that produces pro-cytokine such as TNF-α to initiate the inflammatory phase, thus, accelerating the wound healing process. In addition, the calcium ions on the alginate dressing are exchanged with sodium ions in the fluid at the wound site to form a protective film against pathogens [26]. In another study by Hasatsri et al. (2018), the morphological and physical properties of different absorbent wound dressings such as calcium alginate, calcium sodium alginate, hydrocolloids, and foam dressings were compared. The authors observed that the calcium sodium alginate had better absorption properties and the highest rate of dehydration and provided an optimal water vapour transmission rate than other dressing types [27].

Moreover, they are considered better than hydrocolloids in terms of stay due to a slower degradation rate. Alginate dressings are suitable for highly exuding or drainage wounds but are avoided for dry, third-degree burns and severe wounds [28]. Secondary dressing is required with alginate dressing to avoid wound dehydration and delayed healing. The major drawback of the alginate dressing is that it may dry or adhere to the wound if left unattended, causing painful removal [29].

f) Vacuum-assisted closure dressings

The negative pressure wound therapy using vacuum-assisted closure (VAC) is a new and promising therapy used for the management of "difficult to heal" wounds [30]. Historically, the technique was first proposed by Argenta and Morykwas in 1997. This technique is based on the exposure of the wound to sub-atmospheric pressure to promote debridement and healing. The wound bed is dressed with sterile foams firstly to apply even negative pressure, followed by fixation of a fenestrated evacuation tube connected to a vacuum pump. The wound is then sealed with an adhesive drape. The negative pressure ranges from 50 to 125 mmHg with continuous or intermittent mode. The sub-atmospheric pressure produces mechanical deformation of the tissue, further increasing cell proliferation due to the synthesis of protein and matrix molecules. It increases the blood flow and reduces localized oedema and bacterial growth [31]. VAC therapy yields good results and has effectively been used for spontaneous healing or to increase the rate of the wound healing process. It is used in various wound types such as soft tissue injuries, infected wounds, laparotomy wounds, and degloving injuries. It reduces the extent of reconstructive procedures during grafting or reconstructive surgeries. VAC therapy is a little expensive due to costlier VAC machines. However, the overall treatment is cost-effective [32].

g) 3D hydro cellular dressing

The 3-dimensional (3D) knitted fabric consists of polyethylene terephthalate and polyurethane with permanently bound Dimethyl tetradecyl [3-(trimethoxysilyl) propyl] ammonium chloride (DTAC) technology. Collectively, they form a 3D hydro cellular structure that acts as a physical barrier against contaminants. The 3D hydro cellular matrix helps gaseous exchange and maintains the moist environment through effective exudate management. DTAC is a cationic surfactant with antibacterial properties [33]. It is used at the concentration of 1% w/w. DTAC does not leach into the skin or the dressing, which is a major advantage. In addition, DTAC has the ability to inhibit the growth of bacteria, including S. aureus, L. *monocytogenes*, E. *faecalis*, E. *coli*, P. *aeruginosa*, and *K. pneumoniae*, yeast such as C. *Albicans*, and fungus, i.e., *A. niger*. *DTAC* is a unique technology that uses a physical kill mechanism resulting in 99.99% of bacterial protection in 1 hour; and fungal and yeast protection in 24 hours. These dressings are primarily used for exuding wounds, first and second-degree burns, and minor and surgical wounds.

h) Scar dressings

The scar is formed during the last phase, i.e., maturation or remodelling of the wound healing process. It usually occurs in full-thickness wounds, resulting in the restoration of dermal composition. Scars are of several types, such as cicatrix (normal scarring), hypertrophic (raised), keloid (extends beyond the margin of wounds), and contracture (in thickened tissues) [34]. Based on these scar types, the dressing material is recommended. For instance, anti-microbial dressings are used to prevent the area from bacterial contamination. Next, polyurethane dressings reduce the colour, hardness and size of raised scar. Lastly, silicone gel sheets (SGS) are also applied to prevent raising hypertrophic or keloid scars. SGS has clinically been used from past 30 years and favoured as a scar therapy. SGS functions in replicating

the occlusion properties of the stratum corneum, hydration of scar site, and sending inhibitory signals to fibroblasts to stop excessive collagen production. SGS possess the properties of biocompatibility, repositionable, preventing microbial contamination, and atraumatic removal [35].

i) Medicated–Antibacterial dressings

An infection can hinder the wound healing process. Primarily, the intact skin has its microflora, i.e., the presence of microbial population on the skin surface. When a pathogen or microbe gains access to the wound site, it develops and proliferates in a humid, warm, and nutrient-rich environment [36]. This results in an imbalance between the microbe burden at the wound site and the immune system. The good microflora may aggravate and cause infection. An open wound is recognized as a favourable place for pathogen invasion, and it can delay wound closing and healing due to the extended inflammatory stage. The infected wounds are generally polymicrobial. Initially, gram-positive organisms such as S. aureus and E. coli are predominant, whereas gram-negative Pseudomonas species are common at the later stages of infection, causing significant tissue damage. Other microbes, including Staphylococci and Streptococci species, can also be found.

Differential antimicrobial agents with unique properties are being used in medicated dressings, which are:

i) Antibiotics

Recently, therapeutic agents such as antibiotics, antimicrobials, and supplements (vitamins and minerals) have been incorporated in the dressings to prevent wound infections and dead tissues. The ideal antimicrobial dressing should cover a broad spectrum of microbes, should be non-toxic, can drain exudate, maintain a moist wound environment, and be cost-effective [37-38]. Using antibiotics as a therapeutic agent leads to the obstruction of functioning and metabolic pathways of bacteria by inhibiting bacterial walls, nucleic acids or protein synthesis (**Figure 4**). However, many pathogens, including S. *aureus* and P. *aeruginosa* strains, have become resistant to the most commonly used antibiotics. Thus, new healing substitutes such as nanoparticles and other materials are required against antibiotic-resistant pathogens.

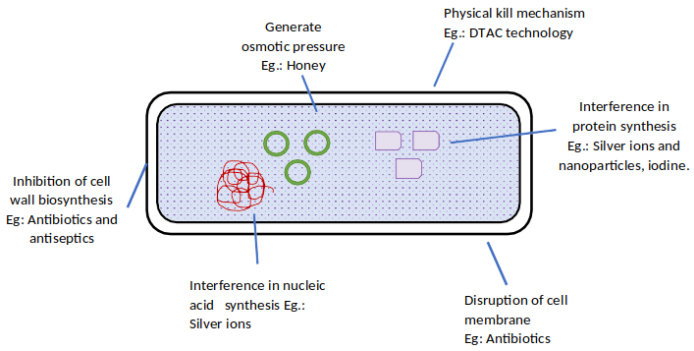

Figure 4 Mechanism of action of the antibacterial wound dressing.

ii) Silver

Other than antibiotics, silver ions or nanocrystals have been incorporated in dressings as antimicrobial agents, particularly for treating colonised or infected wounds. It exists in several forms, such as silver nitrate, silver salt, silver zeolite, silver sulfadiazine (SSD), and silver nanoparticles (AgNPs), cover a broad spectrum of microbes. Historically, silver nitrate was used on wounds by Ancient Romans. Silver is toxic to bacterial, fungal, and algal cells. It interacts with the thiol group of bacterial cells and stops respiration. In the case of E. coli and S. aureus, silver ions prevent phosphate uptake and undergo catalysation of disulphide bonds, thus, interfering in the protein structure of the microbe, which may lead to cell death [39]. Silver ions also penetrate through the cell membrane, inhibiting microbes' replication capabilities. Silver nanoparticles have shown the most effective and efficient antimicrobial property that inhibits all strains, including *E. coli, Vibrio cholerae*, *Salmonella typhi*, and *Pseudomonas aeruginosa* [39-40]. Silver particulates can be impregnated into alginates, hydrogels, and foams. To date, silver-based dressings have not shown any bacterial resistance.

iii) Iodine

Antiseptic iodine dressing is widely effective against the microbiological load. Iodine degrades the cell components and interferes in the functioning of proteins. Clinically, iodine is an old agent to be used as (a) povidone-iodine (polyvinylpyrrolidone-iodine complex) and (b) as cadexomer iodine with good absorptive properties. Povidone-iodine is impregnated into gauze. However, >0.004% and >0.05% concentrations of povidone-iodine are recognized toxic to keratinocytes and fibroblasts, respectively [41]. Compared to iodine solutions, these formulations are less toxic and cause lesser irritation [42]. Iodine covers a broad spectrum of microbes, including *S. aureus, E. coli, Pseudomonas, Candida, Enterobacter, Streptococcus, Salmonella, Klebsiella, Corynebacterium, Clostridium, and Mycobacterium* [43]. Due to the systematic absorbance of iodine, the iodine dressings are not recommended in patients with thyroid or iodine allergies or pregnant and lactating mothers.

iv) Natural antimicrobial agents

Essential oils, edible oils, chitosan, and honey are the naturally-occurring antimicrobial agents that retain regenerative properties. Since ancient times, honey has been used in wound care armamentariums. Several in *vitro* and in *vivo* studies suggest that honey can inhibit more than 60 species of bacteria, including *Citrobacter freundii*, *E. coli, Enterobacter aerogenes, Klebsiella pneumoniae, Mycobacterium phlei, Salmonella, Shigella sonnei, S. aureus, and Staphylococcus epidermidis* [44]. The antimicrobial properties of honey include low pH, peroxide-containing compounds, hygroscopic nature, generating high osmotic pressure to inhibit bacterial growth and proliferation. Honey can also promote autolytic debridement. In 2013, Sasikala et al. formulated and developed a honey-loaded chitosan-based dressing with ideal water absorption properties, tensile strength, and antibacterial activity against *E. coli and S. aureus* [45]. Lastly, antimicrobial polymers, including peptides, halogen-containing polymers and sulfur derivatives, are an important source of new antimicrobial dressings [46]. They are

biodegradable, biocompatible, and can handle wound exudates.

C. Based on the material of origin

Based on the origin of the material, the dressings are classified into three categories, which are:

a) Biological/Animal origin

Biological dressings include xenografts, allografts, and collagen sponges that protect the wound from physical trauma and bacterial contamination, reduce pain, and maintain temperature and moisture.

i) Xenografts and allografts:

Xenografts are the tissues obtained from different species such as dogs, cats, rats, pigs, and fish. Porcine xenografts are commonly used because they are inexpensive and readily available [47]. Conversely, an allograft is a freshly obtained tissue or cryopreserved tissue obtained from a cadaver that acts as a matrix for tissue growth during a wound healing process [48]. The allograft dressing is used for chronic wounds and to cover burn wounds. An allograft has the potential to adhere to the wound bed and thus, controls bacterial growth and pain, reduces the healing time, and stimulates neovascularization.

Moreover, it reduces the loss of water, electrolytes, proteins, and energy requirements from the wound and provides growth factors and cytokines on an excellent reepithelialisation rate. However, due to the risk of graft rejection, both the xenograft and allograft dressings must be inspected and changed regularly. Along with these, compression therapy is also applied to reduce oedema [49-50].

ii) Skin equivalents:

The 3D human skin equivalents (HSEs) are the bioengineered substitutes composed of skin cells and extracellular matrix. HSEs are bilayered, cultured, and allogenic products that mimic and recapitulate the important characteristics of native human skin. HSEs are a suitable substitute for xenografts and allografts as biological dressing. Similar to allografts, HSEs are also in direct contact with the wound bed; however, the chances of rejection are very rare with HSEs. Therefore, these are used for chronic wounds, such as venous ulcers and diabetic foot ulcers [51].

iii) Collagen sponges:

Lastly, collagen sponges are the type of wound dressing of animal origin. They have high porosity and high water absorption capacity. They are considered effective hemostats. E.g., the Tilapia collagen sponge as a wound dressing has greater thermal stability and swelling behaviour [51]. However, this dressing is not cost-effective, a significant drawback of collagen sponges. In a retrospective study by Singh et al. (2011), the authors compared collagen dressings with traditional dressings. They observed that healthy granulation tissue appeared earlier over collagen-dressed wounds compared to conventional dressings. Collagen dressings provide an additional advantage for patients' comfort [53]. They are preferred for partial and full-thickness wounds.

b) Herbal origin

Plants are crucial in providing the material used as a natural remedy for ailments, including skin diseases and wound infections. The herbal origin dressings are biocompatible, biodegradable, and non-toxic. These dressings are derived from natural tissues such as potato peel, collagen, chitosan, alginate, and elastin. These dressings are incorporated with growth factors to enhance the process of wound healing by promoting the formation of granulation tissue. The absorption ability depends on the hydrophilic property and porosity of the base material [54].

c) Synthetic origin

Due to the increased demand for cheaper dressings, synthetic dressings made of polymers such as polyurethane have been widely used. The polyurethane dressings are biocompatible, have good mechanical strength, and are super flexible. In addition, they allow gas exchange between the wound and the environment. Therefore, these dressings are highly recommended for scars [14].

D. Based on the physical form

a) Semipermeable films

Semipermeable films consist of polyurethane sheets with acrylic adhesive. They are transparent, therefore, are mainly used to cover the primary wound. These dressings are permeable to air and water vapour but impermeable to fluids and bacteria. Depending on the moisture transmission through semipermeable films, it maintains the moist environment at the wound site [55]. They are very flexible and can be used at awry anatomical sites or can conform to any complex-shaped or angled wounds. Films are suitable for superficial pressure wounds but are not recommended for drained wounds due to the development of maceration [55].

b) Foam dressings

Foam dressings comprise of outer hydrophobic layer and an inner hydrophilic layer of a polymeric material such as polyurethane. The hydrophobic layer is impermeable to fluids but allows gaseous exchange. Depending on the wound thickness, foam dressing can absorb exudates and provide thermal insulation to the wound bed. Secondary dressings are not required due to their properties of high absorbency and moisture vapour permeability [56]. They can provide comfort by cushioning around the wound. These are usually non-adherent. Foam dressings are recommended for ulcers and drainage wounds but not for dry wounds. E.g.: Silicone-based rubber foam (Silastic) [57].

Table 2 Application of wound dressings in various wound types

Wound Type	Requirements	Dressing type	Review times
Dry necrotic wound	Moisture retention	• Hydrocolloid • Semi-permeable • Hydrogels • 3-D hydro cellular dressing	3-4 days
Dry wound	Hydration	• Hydrogel	1-2 days
Maceration	Prevent moisture	• Protective films • Vacuum dressing	1-5 days
Slough - covered wounds	Moisture retention Fluid absorption	• Hydrocolloid • Alginate • 3-D hydro cellular dressing	3-4 days
Infected wound	Exudate absorption	• 3-D hydro cellular dressing • Hydrocolloid • Alginate • Anti-microbial dressing	1-2 days
Clean graze or abrasions	No antiseptic	• Film • Tulle • Fixation sheet • Gauze	2-3 days
Soiled graze or abrasions	Prevent infection	• Gauze • Tulle • Hydrocolloid • 3-D hydro cellular dressing	2-3 days
Puncture wounds or bites	Prevent infection	• Gauze	2 days
Laceration	Moist environment	• Gauze	3-7 days
Minor Burns	Protection against pathogens	• Film • Medicated tulle • Fixation sheet • 3-D hydro cellular dressing	4-5 days
Major burns	Protection against pathogens	• Medicated tulle	1-2 days
Chronic wounds (Ulcers)	Prevent infection	• 3-D hydro cellular dressing • Anti-microbial dressing • Hydrocolloid • Alginate • Foam • Hydrogel	3-5 days
Scars	Prevent infection Hydration	• Polyurethane • Silicone gel sheets • Anti-microbial dressing	3-5 days

Conclusion

In conclusion, the wound healing process is multifactorial and requires an appropriate environment and healing conditions at each stage. To address all the aspects of wound care, the field of wound dressings has experienced tremendous developments from traditional dressings to modern wound dressing with unique characteristics. Currently, more than 3000 types of dressings are commercially available. Moreover, the lacuna in the knowledge of the type of dressing specifically for wound type made it difficult for the clinicians to select a proper wound dressing. Therefore, this comprehensive review tried to elaborate and discuss the understanding of ideal dressings type incorporating antimicrobial agents and technologies. The ideal dressings' properties include maintaining a moist environment, allowing gas exchange, exudate management, improvement of blood flow, enhancing epidermal migration, protection against pathogens, non-adherent to wound bed, and adhesive to the surrounding skin, transparent, and cost-effective. Furthermore, the dressing material should be able to address all the interfering factors of the wound healing process with better safety and efficacy [58-59].

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Conflict of interest

There are no conflicts of interest to declare by any of the authors of this study.

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