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Novel formulation approaches for wound healing

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Abstract

A wound is damage to the typical anatomic structure. Wound healing is an immediate therapeutic response to injury. It is a creation of the combined response of some cell types towards injury. Wound healing takes place by a sequence of molecular events which cooperate to fix tissue integrity and cell work. In typical healthy individual under ordinary conditions, these physiological events take place smoothly. Though sometimes, these molecular events are arrested, this brings about in struggle to heal. There is an assortment of approaches for the way toward managing and controlling both acute injuries (acute wounds) and ceaseless non-mending wounds (chronic non-healing wounds). The principal objective of these two cases is to achieve better-wound healing. Ideal formulations of wound healing should not only enhance the healing process but also reduce pain, infection and loss of electrolytes, proteins and liquids from the injury. A broad scope of items typically introduced with target various parts of the wound healing process depends on numerous types of wounds and novel polymers utilised for the conveyance of medications to both acute and ceaseless injuries. These include alginate, hydrocolloids, hydrofibers, polyurethane, and hydrogels. This article gives particular importance to different novel approaches in the management of wound healing. This review draws out the data and hopes to provide understanding into traditional, current and imminent techniques and methods for wound management.

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INTRODUCTION

The skin is an intricate organ with primarily three particular histological layers. This includes the upper epidermis, middle dermis and lower hypodermis. A wound is damage of ordinary anatomic structure and cellular work (Lazarus *et al.*, 1994) while wound healing is an immediate restorative response to injury (Clark, 1985). Histological layers likewise have undifferentiated cells (stem cells) in basal layers of the epidermis, sebaceous organs, hair follicle, dermal papillae and dermis. The process of wound healing relies on unipotent and multipotent undifferentiated cells (stem cells). It also has fibroblast cells which help in wound healing by producing keratinocytes. It had noted by Greek physician Galen that wound heal ideally in wet condition. Though in the past, helpful endeavours had to keep the wound site dry with the help of absorptive gauzes serving as an anchor in management of the wound. They facilitate debridement, whenever utilised as a wet to dry dressing. Nowadays, the importance of dressings is diminished because of torment and harm that happens to neo-epithelium during the expulsion.

Table 1: Ideal characteristics of wound dressings

Sr. No.	Ideal characteristics of wound dressings
1	High moisture vapour permeability
2	Nonadherent
3	High capacity for absorption
4	Provide a barrier to external contaminants
5	Prevents capillary loops penetrating dressing material
6	Capable of being sterilised
7	Excellent adhesion to surrounding skin
8	Hypoallergenic
9	Comfortable to wear
10	Cost-effective

Table 2: Traditional wound dressing in the world market

Sr. No.	Dressing material	Brand name and manufacturer
1	Paraffin gauze containing 0.5% chlorhexidine acetate	Bactigras by Smith & Nephew
2	Paraffin gauze dressing	Jelonet by Smith & Nephew
3	Petrolatum gauze	Xeroform by Chesebrough-Pond's Inc
4	Petrolatum gauze containing 3% bismuth tribromophenate	Xeroform by Chesebrough-Pond's Inc
5	Scarlet Red dressing	Scarlet Red by Chesebrough-Pond's Inc
6	Sterile hydrogel dressing	2nd skin® by Spenco
7	Highly absorbent cotton wool pad	Gamgee® pad by 3M
8	Highly absorbent rayon/cellulose blend sandwiched with a layer of anti sheer high-density polyethene	Exu Dry Dressing by Smith & Nephew
9	Absorbent cotton pad	Telfa "Ouchless" Nonadherent Dressings by Kendall (Covidien)

Table 3: Classification of novel wound healing products

Sr. No.	Functional class	Examples
1	A product which enhances epithelialisation	Collagen dressings, Hydrogels, Hydro foams, hydrocolloid, growth factors
2	Products which prevent infection	Antimicrobials like silver-impregnated dressings, mupirocin, retapamulin
3	Desloughing and debriding agents	Maggots, Debridace, enzymatic agents (Collagenase, papaya extracts), Hydrocision
4	Products which enhance granulation tissue formation	Hydrocolloids, Hydrogels, Alginates, Collagen granules, VAC

The principle of wound healing by the wet environment was identified in 1962 by Winter and saw that occluded injuries required shorter time for epithelialisation contrasted with wounds stayed open to the air, later it was upheld in 1998 (Cho and Lo, 1998). the wounds persistently open to chemotactic, proteinases, supplement and development factors in the encompassing fluids by a closed dressing, which may be lost in case of an occurrence of wounds which stay open and dry (Moon and Crabtree, 2003). More current occlusive dressings accelerate re-epithelialisation, invigorate collagen combination, and make hypoxic surroundings at the injury bed to advance angiogenesis and reduction pH at the wound surface, making a situation unfriendly to bacterial growth, which diminishes the speed of wound infection (Varghese, 1986). It has a preferred position over gauze dressing concerning patient comfort and consistency just as better improving outcomes because of decreased scarring (Jones and Miguel, 2006).

The indication of evolving modern dressings is to control the injury condition in intentional manners. A large number of products accessible in the market today chooses the most suitable dressing for any wound twisted an extremely troublesome job.

Topical wound product

Dressings can be categorised as passive dressings and active or interactive dressings. Passive dressings simply assist a protective function and have no immediate/direct impact on the wound. At the same time, interactive dressing interacts with wound bed and promote the healing process by creating optimum moist wound condition at the interface of a wound dressing. The ideal wound dressing characteristics are given in [Table 1].

Technology has far ahead in development with the acknowledgement that wet condition is helpful in the healing of the wound. So it is currently conceivable to deliver dressing items which have attributes of a perfect dressing (Field and Kerstein, 1994). The moisture vapour transmission rate (MVTR) is a suitable apparatus for selection of dressing as per the type of wound, which calculates the moisture-retentive property of wound dressing and dressing is said to be moisture-retentive if its moisture vapour transmission rate (MVTR) is a smaller than 840g/m^2/24hrs (Field and Kerstein, 1994). The moisture vapour transmission rate (MVTR) of hydrocolloids is less than 300g/m^2/24hrs in contrast to gauze, which is having moisture vapour transmission rate of about 1200g/m^2/24hrs. Commercially many strategies and approaches are available for wound healing, but none is ideal for all types of wound. Various Formulation approaches are discussed below.

Approaches for wound healing

The wound healing formulations can be classified as traditional approaches and novel approaches.

Traditional approaches

The primary function of traditional approaches is to keep the injury dry by permitting vanishing of wound exudates and forestalling the passage of unsafe microbes. Traditional wound healing formulation includes gauze dressing, absorbent cotton pad, extremely absorbent cotton swab and extremely absorbent rayon-cellulose blend pack in with a layer of thick polyethene [Table 2].

Novel approaches

Novel wound healing formulation approaches concentrate on a natural healing process. Current dressings are produced using polymers which can fill in as a vehicle for the discharge and conveyance of medications at the site of the wound. The polymeric dressings utilised for controlling drug delivery at the site of wounds comprise hydrogels for examples poly (lactide-co-glycolide), poly (vinyl pyrrolidine), poly (vinyl alcohol), polyhydroxy alkyl methacrylate, polyurethane foam, alginate and hydrocolloid dressing. Other epic polymeric biomaterial detailed, for example, hyaluronic acid, chitosan and collagen. Manufactured polymers utilised as swellable dressings for controlled medication conveyance include lactic acid, silicone gel sheets. Novel wound healing products are classified as given in [Table 3].

Topical antimicrobials

Antimicrobial dressings can be extensively arranged into two groups as (1) antiseptic dressings and (2) antibiotic dressings. The antiseptic dressing has an expansive range of action which can forestall the growth of not only bacteria but also other microorganisms such as fungus, protozoa, viruses etc. It was determined through invitro considers numerous antiseptic agents have cytotoxic (Lineaweaver *et al.*, 1985) properties yet on the off chance that it is utilised in appropriate concentration they can be in effect in wound healing, povidone-iodine more prominent than 0.004 and 0.05% is poisonous to keratinocytes and fibroblasts, individually. Cadexomer iodine is accounted for to be nontoxic to fibroblasts in vitro at a concentration of up to 0.45% (Zhou *et al.*, 2002). Formulations of antiseptic utilise variety of mechanisms such as membrane disruption, protein coagulation or denaturation, oxidation of cellular components. It also acts at different rates and diligence intervals.

Table 4: Antimicrobial dressings

Sr. No.	Product name	Brand name	Description
1	Cadexomer Iodine Dressings	Iodoflex® by Smith and Nephew	Cadexomer Iodine is suggested for infected wounds. It contraindicated in children, pregnant or lactating women or patient with renal impairment or thyroid disorders or those who are getting treatment of lithium. A single dose should not be more than 50g and 150g weekly application. QIPP TIP– If the wound is not improving by treatment even after four weeks, the treatment refers to tissue viability service.
2	Honey Dressings	Activon Tulle® Algivon® Actilite® Activon® Tube by Advancis	Honey Dressings is beneficial in the treatment of chronic wounds, including the decrease of odour, anti-inflammatory activity and the encouragement of healing. It should be avoided to use on patients with allergy to honey bee stings/products or in patients sensitive to honey. QIPP TIP– Patients who have diabetes should be monitored with blood glucose.
3	PHMB Dressings	Suprasorb® X+PHMB Rope by Activa Healthcare	PHMB dressing is an antimicrobial hydro balance wound dressing. It is appropriate for use in several types of wounds such as leg ulcers, pressure ulcer etc. QIPP TIP–It is used to decrease the wound bioburden. If improvement is not observed even after four weeks, then refer to tissue viability service.
4	Silver Dressings	Acticoat® Acticoat® 7 Acticoat® Absorbent Acticoat® Flex 3 Acticoat® Flex 7 by Smith and Nephew	Silver Dressings should be reviewed frequently: Long term use should be avoided. The absorbent silver dressing should be used for Highly exuding wound. It is not compatible with saline. QIPP TIP-Not suggested for repetitive use in acute wounds, chronic venous leg ulcers, and uncomplicated ulcers. The dressing needs to be changed every 3-7 days. If the injury does not recover then refer to tissue viability service

QIPP: Quality, Innovation, Productivity and Prevention

It shows varying degrees of harmfulness and is pretty much prone to cause resistance. Present writing uncovers that antiseptics can be explicitly applied as the first line of treatment of basically colonised or tainted injuries, the annihilation of methicillin-resistant staphylococcus aureus (MRSA) from murky injuries, to invigorate already inert constant injuries and against biofilms. Commonly used antiseptics are iodine-based preparations, Hydrogen peroxide, Alcohols. Antibiotic dressings are nontoxic and affect target without damaging to the host cells. In contrast to disinfectant, antibiotic dressings are nontoxic and can work successfully on the target places without harming host tissues. Rundown of antimicrobial dressings are given in [Table 4].

Foam dressing

The foam contains a permeable light structure that is having the ability to retain liquids into air-occupied spaces by capillary activity. The most ordinarily utilised foam is polyurethane foam which is synthesised by the reaction between polyols with isocyanates. It forms open cells which are responsible for porosity which is caused by two reactions called gelling and blowing. CO_2 liberated in blowing reaction, which helps in the expansion of foam

and gelling reaction wound to produce the linkage, which increases foam strength.

This type of dressings is created with variable thickness and might be sticky or nonstick at the site of the wound. Foam dressing consists of a film-backing membrane, provides water and a bacterial impervious obstacle to the environment. Due to its porous structure, it absorbs exudate; permit gaseous exchange. It can keep up wetness at the injury bed. It is having a moisture vapour transmission rate of about 800-5000g/m^2/24hrs. It is easy to remove. It provides mechanical assurance, padding, and comply with body shape. Being a long shelf life, it is economical. According to some of the studies, it is found to be comparable in case of ulcer healing (Bradley *et al.*, 1999). The foam may produce excess smelly exudate, which requires dressing change (Rubin *et al.*, 1960). Commercially available foam dressings are given in [Table 5].

Alginate dressing

Alginate is comprised of delicate filaments containing sodium and potassium salts of alginic acid, which is derived from seaweeds. In the wake of putting the alginate dressing over a moist wound, exchange of happens between calcium in the alginate and sodium in the wound fluid delivering dissolvable calcium-sodium alginate gelatin which helps in keeping up soggy condition and encourage autocatalytic debridement (Kannon and Garrett, 1995). They adjust to the state of wound and ought to be cut as needs be in such a case that more they can cause peri-wound maceration as it is having propensity called lateral wicking to assimilate liquid across a whole surface (Agren, 1996). They are utilised as fillers for a tunnelled wound. They leave fibrous debris which is claimed to get biodegraded even it is reported that it causes long term body type reactions (Suzuki *et al.*, 1998). It is recommended that alginates act as an inhibitor for keratinocytes (Doyle *et al.*, 1996), while others have detailed that alginate quicken wound recovering when contrasted with others (Suzuki *et al.*, 1998). Alginate covering can absorb fluids 20 times greater than its weight, so it is useful in highly exudating wounds. It is available in sheet and rope form. Sheet form is used to place over the wound bed, and rope form is used as fillers for a tunnelled wound. It is also used for certain types of burns and diabetic foot ulcer. It is non-occlusive. Therefore, it requires a secondary dressing. Some commercial examples are given in [Table 6].

Hydrocolloid dressing

Hydrocolloids are made up of gelatin, pectin, carboxymethyl cellulose and serve as occlusive and semi-occlusive dressings. The dynamic surface of the dressing is covered with a cross-connected glue mass containing a scattering of gelatin, pectin, carboxymethyl cellulose along with different polymers and glues, framing an adaptable wafer. In the wake of interacting with wound exudate, it absorbs water, get swells and forms a gel due to polymer hydrophilicity They are impermeable to water, therefore, provides moist environment wound healing, It is likewise impervious to microorganisms and different contaminants however penetrable to water vapours. Its long wear time diminishes its cost problem and local injury during dressing changes.

They are disheartened for blood vessel/neuropathic ulcer, tainted and intensely exudating wounds as a result of danger of peri-wound maceration. It produces unpleasant smelly exudates which can be mistakenly from infection. Commercially available hydrocolloid dressings are given in [Table 7].

Hydrofiber dressing

Hydrofibre dressings are comprised of sterilised sodium carboxymethyl cellulose fibres. It is entirely hydrophilic and quickly absorbs liquid, keeps supporting it inside the assembly of fibres. On engrossing injury liquid, the fibres change into a clear, delicate gel and provide a moist environment for wound healing and facilitate autolytic debridement. Fibrin gets gathered between the dressing and wound surface and goes about as a glue, fixing the dressing set up and sticks to the injury. It used in a pressure ulcer, lower limb ulcers and surgical wounds. Commercially available Hydrofiber dressings are given in [Table 8].

Transparent film dressings

Transparent film dressing is a dainty sheet-like dressing prepared of translucent polyurethane (polymer) covered with glue. It provides a wet recuperating condition, energises autolytic debridement, shields the injury from mechanical injury and bacterial assault, and go about as rankle rooftop or second skin. This type of dressing can fit in with wounds present in the clumsy area because of their flexible nature. The clearness makes it simple to see the injury conditions such as healing progress and any drainage. These dressings are waterproof and impermeable to microscopic organisms and contaminants but permeable to moisture. It is used for little or no drainage wounds, pressure ulcer and grafts—[Table 9].

Hydrogel dressings

Hydrogels are hydrophilic polymer system and can absorb from 10% up to the vast extent of their dry load in water (Hoffman, 2012).

Table 5: Commercially available foam dressings

Sr. No.	Product name	Description
1	Allevyn® by Smith and Nephew	Foams dressing can be used as a primary or secondary dressing on various wounds such as leg ulcers, pressure ulcers, burns, surgical wounds, etc. Foams are best suited for highly exuding wounds, and these are not suggested for dry superficial wounds.
2	Biatain® by Coloplast	QIPP TIP-Consider the size of the injury when selecting the shape of dressings, if the wound is small, then it is superior to use a 10 cm X 10 cm dressing.

Table 6: Commercially available alginate dressings

Sr. No.	Product name	Descriptions
1	Kaltostat® by ConvaTec	Suitable for various types of wounds such as cavities, granulating and moderate-to-high exuding wound. Kaltostat is specifically useful for haemostasis in bleeding wounds. Caution is needed as blood clots can stick to the wound surface. QIPP TIP- Alginate dressing are required to cut to the size of the injury.
2	Kaltostat® Rope by ConvaTec	
3	Sorbalgon by Hartmann	
4	Cutimed® by BSN Medical	

Table 7: Commercially available hydrocolloid dressings

Sr. No.	Product name	Description
1	Comfeel Plus Ulcer	Comfeel is applied to debride necrotic tissue. Duoderm is used to protect delicate skin or as a secondary dressing. Can be applied to wounds such as leg ulcers, pressure ulcers, minor burns and surgical wounds. QIPP TIP-Bordered hydrocolloids should be avoided as these do not always stick to and may require regular changing due to increase exudate levels.
2	Sacral	
3	Contour	
4	By Coloplast DuoDERM® Extra-Thin by ConvaTec	

Table 8: Commercially available Hydrofiber dressings

Sr. No.	Product name	Description
1	Aquacel® Extra	It is appropriate for use in wound types such as leg ulcers and pressure ulcers with moderate to high levels of exudate. The dressing absorbs and retains exudate and decreases the likelihood of peri-lesion maceration or excoriation. QIPP TIP-Please make sure that you suggested Aquacel and not Aquacel AG as Aquacel AG contains silver and is not on the formulary.
2	Aquacel®	
3	Aquacel® Foam Adhesive	
4	Aquacel® Foam non-Adhesive by ConvoTec	

Table 9: Commercially available transparent film dressings

Sr. No.	Product name	Description
1	Tegaderm® by 3M Health Care	It is appropriate for shallow wounds; it protects epithelial lining injuries from trauma recently.
2	IV 3000 Adhesive IV Film dressing by Smith and Nephew	Besides, it can be used to protect the skin from friction.

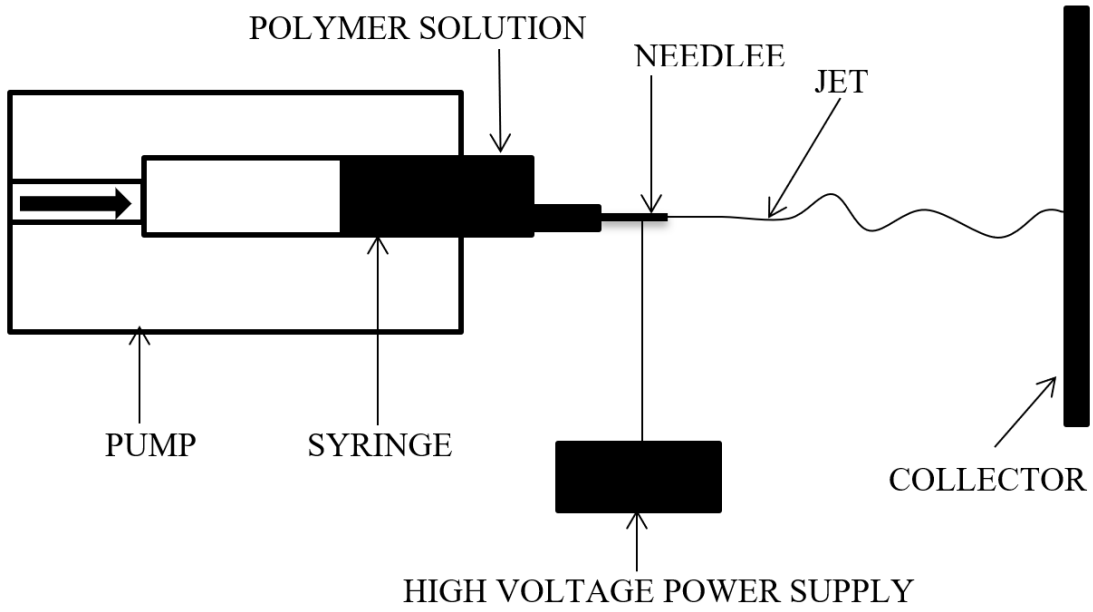

Figure 1: Electrospinning device

Table 10: Examples of natural and synthetic hydrogelpolymers

Sr. No.	Polymer type	Polymer	Properties related to wound management
1	Natural Polymer	Alginate	Wound dressing Ease of application Conformability Biodegradability
		Chitosan	Wound dressing In situ gelation, Biodegradability
		Gelatin	In situ gelation Conformability Biodegradability
		Collagen	Wound dressing In situ gelation Biodegradability
		Dextran	Skin substitute
		Cellulose	Moisture control
		Heparin	Hydrogel sheet Moisture control
		Glycosaminoglycans	Film dressing Ointment Moisture control
		Mixed extracellular matrix biopolymers	Sprayable elastic adhesive
2	Synthetic Polymer	Polyethene glycol	Moisture control
		Polyvinyl alcohol	Matrix support, Moisture control, Oxygen transport
		Polyvinyl pyrrolidone	Topical hydrogel-based formulation
		Acrylic polymers (Carbopol)	Oxygen transport Matrix support
		Polystyrene	Wound adhesive Moisture control

Table 11: Commercially available hydrogel dressings

Sr. No.	Product name	Description
1	Nu-Gel® by Systagenix Wound Management	These can be better utilised in hydrating.
2	Intrasite® by Smith and Nephew	Dry wounds as it provides a moist wound environment.
3	Intrasite® Conformable by Smith and Nephew	QIPP TIP- It should not be applied to highly exuding wounds.

Table 12: Naturally derived polymers for wound application through electrospun technology

Sr. No.	Polysaccharide based nanofibers	Sr No.	Protein-based nanofibers
1	Chitosan	1	Silk Fibroin
2	Cellulose Derivatives	2	Collagen
3	Alginates	3	Gelatin
4	Hyaluronic Acid		

Table 13: Types of conventional bioactive molecules incorporated in electrospun wound dressing mat

Sr. No.	Bioactive molecules
1	Growth factors
2	Antimicrobial peptide
3	Silver nanoparticles
4	Herbal Extract and Phytochemicals
5	Vitamins
6	Stem cells

Their high water content restricts them to ingest an enormous quantity of wound exudates. They rehydrate the necrotic tissue and gives effective desloughing action and debriding activity without damaging healthy tissue. This one reduces pain by cooling effect. They are non-adhesive so that it can be easily removed from the wound. Structure of hydrogel is shaped by crosslinking between polymer chains via various chemical bonds and physical associations, for example, hydrogen attachment and hydrophobic interaction. They closely resemble with a chemical structure of the extracellular matrix. They are of natural and Synthetic source. Examples of hydrogel polymers with its wound management related properties are given in [Table 10] (Francesko *et al.*, 2019).

Hydrogel encourages fibroblast expansion and keratinocyte relocation, which is fundamental for complete epithelialisation and mending of the wound. Furthermore, the tight mesh size of hydrogels structure guards wound from infection and avoids microorganism and bacteria to enter the wound area. There are mainly three types of hydrogel dressings, sheet hydrogel, impregnated hydrogel, and amorphous hydrogel dressing. In sheet type of hydrogel, a gel is present in the thin mesh which overlaps the skin. Impregnated hydrogel prepared by addition of gel compound into gauze strips, a gauze pad or a sponge rope. Amorphous hydrogel dressing is free-streaming. Even though it viscous (thick) nature, it can stream into the niches and corners of cut and other profound injuries. Commercially available hydrogel dressings are given in [Table 11].

Much of the research is going on hydrogel formulation for wound healing management. Several advanced hydrogel formulations are categorised as (1) pH-responsive hydrogel which display alluring chemical and physical properties at explicit pH ranges. The primary groups get protonated at low pH, and acidic groups get deprotonate at high pH (Chai *et al.*, 2017), (2) Temperature responsive hydrogel formulation in which a little temperature change can intrude equilibrium and actuate sol-gel conversion (Bajpai *et al.*, 2008). (3) A light-responsive hydrogel is hopeful functional material for possible application in the extents of microlenses (Dong and Jiang, 2007), drug/gene delivery and so forth because of the way that the initiation procedure through light can be remote and

noninvasive (Chai *et al.*, 2017).

Debridement

Debridement is a process of removal of dead or damaged infected tissue to enhance the healing of the wound. Methods of debridement are explained below.

Debridement by enzyme

In this process, enzymes are involved in the debridement process. Enzymes, for example, are papain and collagenase accessible as treatments. They help in digestion of dead tissue without influencing healthy tissue. The enzyme collagenase helps in proteolysis by involving in breaking of peptide bonds in collagen. It does not harm to viable tissue (Chai *et al.*, 2017), papain is an enzyme obtained from the papaya fruit. It helps in breaking of protein (cysteine residues) molecules into smaller fragments such as peptides and amino acids by hydrolysis. As it is nonselective in actions, it creates inflammation and pain due to breakdown of a viable portion of wound bed (Chai *et al.*, 2017). Papain is combined with urea to increase proteolytic activity. (Example: Debridace by Virchow Healthcare).

Debridement by medicated larvae (maggot therapy)

Maggot is a soft-bodied legless larva belongs to species of flies. Maggots of Calliphorid flies or green bottle flies, which belongs to species Phoenicia sericata nourish on dead and necrotic tissue. Their secretion contains proteolytic enzyme and compounds which are successful against methicillin-resistant staphylococcus and haemolytic streptococcus bactericidal; however, doesn't harm to living tissue (Bonn, 2000). They are selective in debridement activity which can be achieved in two days, but if the pain is occurring due to change in pH, then there is a need to change the larvae. Local discomfort, itching, cost of the treatment and short half-life are main drawbacks of this therapy, however, regardless of these, it is emerging to establish an identified role in wound management (Courtenay *et al.*, 2000).

High-pressure water irrigation

Hydrocision or pressurised irrigation is a method used in careful debridement and cleaning of the injury. Water, saline or antibiotic solution can be used in high or low-pressure thin razor stream. It is a better alternative method contrasted with all above. The high-pressure irrigation removes bacteria, necrotic debris and particulate matter issue from the injuries and therefore diminishes the contamination when compared with low-pressure irrigation (Doyle *et al.*, 1996). The main problem identified with it is that there is an opportunity of microorganisms to go into delicate tissue by the high pressure. It is for the most part utilised in the condition of pressure wounds (also known as bedsore), in tight spaces and joint spaces. It also used in dead tissue injury and deep burns as it does not harm the living dermal tissue and allows rapid wound healing.

Growth factors

Growth factors are protein substances which initially present in the body. During the normal tissue repair process, it plays a crucial role in controlling many key cellular activities. There are pieces of evidence that macromolecules existing in the injury bed that catch up growth factors into fibrin cuff in the nearby vessels or fix them to the extracellular fluid (Higley *et al.*, 1995), due to this, the inadequacy of growth factors at the site of injury due to which the cell cycle gets captured that affects the healing process. The growth factors can be achieved either autogenously or chemically or biochemically. Studies had recommended that the healing process got the benefit when these factors applied exogenously to the wound surface (Cha and Falanga, 2007).

Many examinations have indicated a gainful impact of factors like Epidermal growth factor (EGF), Fibroblast development factor, macrophage provoking factors and recombinant human platelet-derived growth factor (rhPDGF), accelerate healing in chronic wounds either alone or in combination (Greenhalgh, 1996). US FDA approved PDGF and EGF topical growth factor to treat the ceaseless injury (Margolis *et al.*, 2005). Platelet-derived growth factor advances chemotaxis and expansion of cells associated with wound mending. EGF likewise controls cell multiplication, chemotaxis and differentiation by binding to kinases receptor of target cells which leads to the development of blood vessels at the site of injury.

Negative pressure wound therapy

Vacuum-assisted closure (VAC) treatment which is also known negative pressure wound is a progression in wound mending. It increases the healing power of the wound at the cellular level by using negative pressure or sub-atmospheric pressure. The negative pressure is applied in the range of 100-125 mmHg continuously (Kajagar and Joshi, 2017).

The constant negative weight is applied at wound site through permeable dressing, which gives mechanical powers known as a macro strain which is a physical reaction and microstrain which is a biological reaction and later with the help of electrochemical pump the exudates are expelled out.

Future of wound healing approaches

The technology and engineering processes emerging day by day, it appears perfect to have composite dressings that consolidate the various attributes of current advancements. This will help in focusing on the numerous parts of the complex wound healing process, to safeguard effective, successful healing of a wound and smaller healing times for long-lasting injuries. Rather than all the previously mentioned strategies and approaches, numerous injuries are impervious to treatment and assortments of new procedures are being looked into. These comprise application of electrospinning technology for wound dressing and tissue engineering techniques.

Electron spin technology for wound healing

Electrospinning technology is used for the preparation of the nanofiber composite for wound healing formulation. This technology was patented in 1900 by Cooley. Electrospinning is a fibre creation technique which utilises electric power to draw charged threads/strings of polymer solution up to up to fibre diameter measurement in order of about few nanometers. In this procedure, a polymer solution is filled into a syringe and pumped at a consistent rate by a syringe pump to a needle tip. The syringe needle is supplied with a high voltage current. On particular voltage, the drops of polymer get stressed into a tapered shape at the end of the syringe, which is known as the Taylor cone. There is the formation of continuous jet occurs on increasing the electrical field, and a nonstop stream is extended and whipped consistently due to electrostatic revulsion, at the same time the stream becomes thinner and solvent vaporises due to which nanofibers collected continuously on the collector [Figure 1]. In this technology, both natural, as well as synthetic polymers, can be utilised. However, natural polymers are increasingly appropriate when contrasted with synthetic polymers because natural polymers arehaving higher biocompatibility and biodegradability as well as having the capacity to imitate the local extracellular lattice, which accelerates the wound to be closed and enhance the tissue rejuvenation (Fahimirad and Ajalloueian, 2019). Naturally, derived polymers are given in [Table 12]. Conventional bioactive molecules which are combined in electrospun for wound application are given in [Table 13]

Tissue engineering techniques

Gene therapy and stem cell therapy are tissue engineering techniques. Stem cells move towards a region of wound or inflammation and contribute to the rejuvenation of injured tissue and encourage production and differentiation of remained progenitor cells. It also plays a role in the release of growth factors, remodelling matrix, increases in angiogenesis and refining rigidity of the injury (Ko *et al.*, 2011).

CONCLUSIONS

Wound management is rapidly progressing from the last 30 to 35 years. Because of increment incomprehension of science of wound, development in wound management is continuous. This survey has secured numerous classes of wound dressings, ideal characteristics of new dressings together with an active topical ingredient, traditional dressings and modern dressings and novel technology such as electrospun technology for wound healing and tissue engineering techniques. It mainly focuses on innovative formulation approaches and technology (electrospun) for wound healing and their application and uses in different types of wounds. This review also covered some examples of marketed formulation of each kind of new dressings.

These more unique products and technologies are presently being utilised to substitute or enhance different substrates in the healing cycle of a wound and providing the optimum wound healing environment at the site of an injury. As wound healing is facing the view of an increased occurrence of pathogens that are resistant to antibiotics, reduced efficiency of existing therapies and increased demand more convenience to patients and fast wound healing. So it is now essential to give careful attention towards treatment options for wound healing. By the availability of products and technologies, the objective is to locate the most proper methodology or blend of modalities to increase the healing of a wound. This review stretches out the information and wants to give a vision into past, present and future treatment techniques and approaches, including novel formulation and technology for wound healing management.

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Conflict of Interest

The authors declare that they have no conflict of interest for this study.

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