WWW.IJRPR.COM

International Journal of Research Publication and Reviews

Journal homepage: www.ijrpr.com ISSN 2582-7421

A COMPREHENSIVE REVIEW ON ADVANCED WOUND HEALING THERAPIES

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ABSTRACT :

Chronic and complex wounds, such as diabetic ulcers, venous leg ulcers, and pressure sores, have become a significant clinical challenge owing to the long-term healing process, a high threat of infections, and increased healthcare costs. Conventional wound care methods do not suffice in the case of such wounds; thus, an urgent need for advanced wound healing therapies. The present review pertains to current advances in the direction of wound healing and examines cutting-edge therapy methodologies such as stem cell therapies, growth factors, bioengineered skin substitutes, tissue-engineered scaffolds, and advanced wound dressings. The therapies address the underlying pathophysiological causes that inhibit the closure of wounds, thus promoting regenerative tissue therapy-enhancing cellular repair, and speeding up healing processes- poor circulation, infection, and chronic inflammation. Personalized treatment strategies and the application of new technologies in wound care are also discussed in the article. The review discusses current outcomes and future directions in the field, while stressing the need to continue research for optimization of treatment protocols and expansion in the availability of advanced features for wound healing. The ultimate dream is advanced wound healing therapy, bringing into value the most significant promise of transformation for the patient's outcomes and quality of life within modern wound management.

KEYWORDS: growth factors, hydrophilic polymers, silicone gels, skin substitutes, wound healing therapy.

INTRODUCTION

The body's natural process of mending damaged tissue is called wound healing, and it entails a complicated series of steps meant to restore the affected area's integrity and functionality. [1]

EPIDEMIOLOGY OF ADVANCES IN WOUND HEALING TECHNOLOGY

Innovative dressings, growth factor therapies, stem cell therapies, and bioengineered skin substitutes are examples of recent developments in wound healing technology that are driven by epidemiological patterns and aim to promote quicker, higher-quality healing with less scarring. [2] Among the significant developments in this area are:

1. Bioengineered Skin Substitutes:

Dermal Grafts: These artificial or biological grafts, like Integra or Apligraf, replicate the composition and functionality of the skin and aid in wound healing by fostering the creation of new tissue. By cultivating skin cells from a patient's own skin, cultured epithelial autografts (CEA) lower the risk of infection and rejection by covering extensive wound regions. [3]

2. Growth Factors and Cytokines:

Recombinant Growth Factors: By promoting collagen synthesis, angiogenesis (the development of new blood vessels), and cell proliferation, substances such as platelet-derived growth factor (PDGF) and epidermal growth factor (EGF) are used to speed up the healing process of wounds.
Stem Cell Therapy: Mesenchymal stem cells (MSCs) and other stem cells have demonstrated promise in reducing scarring and increasing tissue regeneration. These stem cells can help mend wounds and differentiate into different types of skin cells. [4]

3. 3D Bioprinting:

Skin Printing: The method of 3D skin bioprinting involves printing biomaterials and living cells one layer at a time to produce functioning skin tissue, which may help with skin regeneration and wound healing. This method makes it possible to create multi-layered, vascularized skin grafts by simulating the intricacy of real skin. It has potential for both individualized wound care and as a substitute for animal testing in pharmaceutical research. [5]

4. Nanotechnology:

Drug Delivery with Nanoparticles: By delivering medications, growth hormones, or antibacterial agents straight to the wound site, nanoparticles can speed up healing while reducing adverse effects. Nanofibrous scaffolds: They offer a physical matrix that promotes cell migration and development, enhancing skin regeneration in long-term wounds. [5,6]

5. Negative Pressure Wound Therapy (NPWT):

Vacuum-Assisted Closure (VAC): This technique increases the production of granulation tissue, decreases edema (swelling), and encourages blood flow by providing regulated negative pressure to a wound. It works very well on chronic sores like diabetic foot ulcers. [7]

6. Smart Bandages and Wearable Technology:

Sensors and Monitoring: Sensors that measure variables like pH, temperature, and moisture content are being incorporated into smart bandages to track the healing process. When help is required, these bandages can notify medical professionals. Drug-Releasing Bandages: Over time, certain bandages are made to gradually transport growth hormones or antibiotics to the wound site. [8]

7. Gene Therapy:

To address genetic abnormalities that hinder wound healing, especially in diseases like dystrophic epidermolysis bullosa (a rare skin ailment), researchers are investigating gene-editing technologies like CRISPR-Cas9. Gene therapy has the potential to provide focused and individualized care. [9]

8. Biological Dressings and Hydrocolloids:

Novel dressings derived from biological materials, including hydrocolloids, collagen, and alginates, are being utilized to keep the wound moist, which speeds up healing and lowers the risk of infection. These developments in wound healing technology are revolutionizing the treatment of severe, chronic, and complex wounds, resulting in quicker, more efficient healing with fewer problems and better patient outcomes. [10]

PHYSIOLOGY OF WOUND HEALING

The goal of the intricate, multi-phase physiology of wound healing is to restore tissue integrity following injury by means of a synchronized series of biological activities. Usually, it happens in four overlapping stages: remodeling, proliferation, inflammation, and hemostasis. [11] Below is a summary of every stage:

1. Hemostasis (Immediate Response)

Time frame: a few minutes to several hours.
Important Occurrences: Vasoconstriction: To lessen blood flow and stop excessive bleeding, blood vessels tighten. Platelet activation occurs when platelets clump together at the wound site to create a clot that halts the bleeding. Fibrin Formation: Fibrinogen is transformed into fibrin, which stabilizes the clot by forming a mesh.

2. Inflammation (Cleansing Phase)

Time frame: one to four days.
Important Occurrences: Vasodilation: To improve blood flow and deliver immune cells to the site of injury, blood vessels widen. Immune Cell Infiltration: The initial line of defense against infection is provided by neutrophils. Later, to aid in healing, macrophages take the position of neutrophils, remove debris, and release growth factors. The body enters the proliferative phase when cytokines and growth factors are released.

3. Proliferation (Tissue Formation Phase)

Time frame: a few days to a few weeks.

IImportant Occurrences: Angiogenesis: The development of new blood vessels to provide the developing tissue with nutrition and oxygen. Fibroblast Migration: Fibroblasts multiply and deposit collagen, which creates the structure for new tissue. Granulation Tissue Formation: At the location of the wound, a dense bed of fibroblasts and capillaries develops. Epithelialization: Keratinocytes, or skin cells, move over the wound to cover it.

4. Remodeling (Maturation Phase)

Time frame: months to years.

Important Occurrences: **Collagen Remodeling:** To strengthen the tissue, type I collagen replaces type III collagen. **Wound Contraction:** To lessen the size of the wound, myofibroblasts draw the margins together. **Scar Formation:** The tissue that forms from the wound is usually less elastic and functional than the initial tissue. Numerous cell types, signaling molecules, growth factors, and the extracellular matrix interact intricately during this series of events. Effective wound healing depends on each phase operating as intended. [11,12]

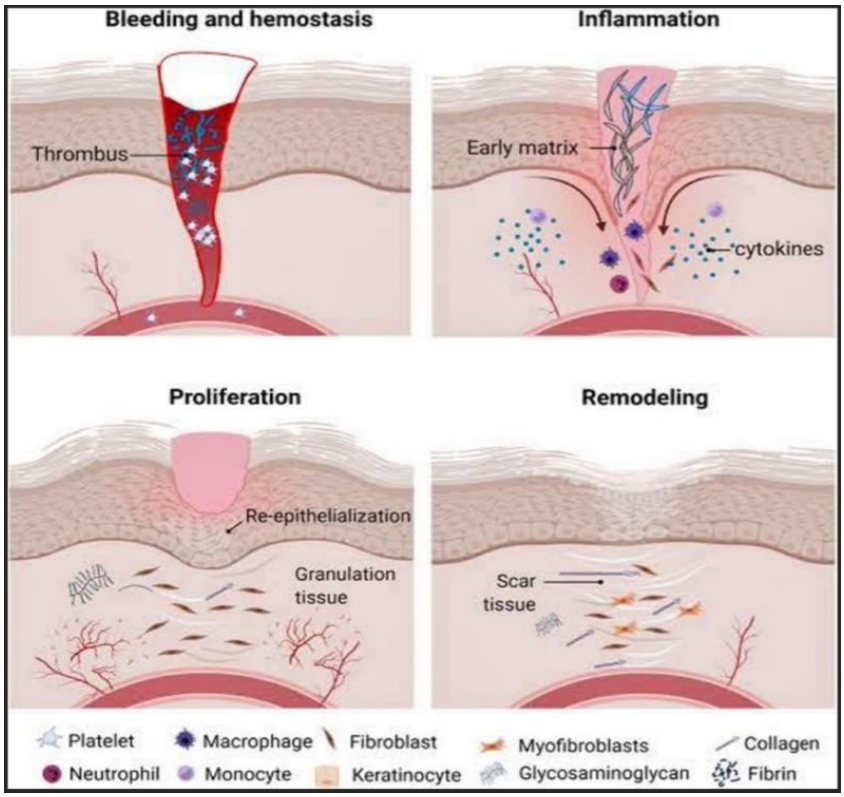

Figure 1. Physiology of wound healing

ADVANCED WOUND THERAPIES

1.HYDROGELS

MECHANISM OF ACTION

A moist wound environment is essential for the best healing results, and hydrogels, which are made of networks of hydrophilic polymers, are renowned for their capacity to hold onto enormous amounts of water. In addition to lowering pain and supporting epithelial cell migration over the wound bed, this moisture aids in autolytic debridement and promotes tissue regeneration. Hydrogels are especially helpful for wounds with low to moderate exudate because they can absorb extra fluid while keeping a gel-like consistency by reacting with the exudate. Hydrogels can also be used as delivery systems for medicinal substances like enzymes, growth hormones, or antibiotics, facilitating their long-term release and speeding up the healing process. There are numerous hydrogel formulations available to satisfy the unique requirements of various kinds of wounds. For example, amorphous hydrogels are gels that flow freely and can be They are perfect for cavities or wounds with odd shapes because they may be put directly to the lesion. Pre-formed hydrogel sheets are frequently used for superficial wounds with little exudate because they are easy to apply. In order to treat more complicated wounds, impregnated hydrogels—which are combined with materials like gauze or foam—offer further structural support and are frequently used in conjunction with other dressings. [13]

DRESSING

Advanced wound care devices called hydrogel dressings are composed of a gel-like material that is mostly composed of water. Burns, cuts, ulcers, and surgical sites are among the wounds they are used to heal. Hydrogel dressings operate by supplying moisture to the wound, which helps to foster a healing environment and keeping the tissue hydrated. Additionally, the high water content aids in wound cooling and pain relief. [14]

SAFETY

Healthcare providers should be informed of any possible issues even though hydrogels are generally regarded as safe. The biggest concern when employing hydrogels is the potential for maceration, which happens when the surrounding healthy tissue gets excessively wet from prolonged moisture contact. This may lead to skin degeneration and an increased risk of infection. To lessen this risk, it is essential to regularly assess the wound and adjust the frequency of dressing changes in response to the exudate levels. Another aspect of safety is the possibility of infection. [15]

2. ABSORBENT: GELATIN SPONGES

Since their creation in the early 1900s, absorbable gelatin sponges have been a vital component of surgical hemostasis. They were first created to offer a dependable way to stop bleeding, particularly in circumstances when mechanical techniques like cautery or sutures might not be enough or feasible. The primary innovation of gelatin sponges is their gradual absorption by the body, which lessens the need for follow-up procedures to remove homeostatic components.[16]

MECHANISM OF ACTION

Mechanical techniques are the main way that absorbable gelatin sponges control bleeding. The sponge collects blood when it is placed on a bleeding location, expands, and physically stops blood flow. By promoting platelet activation and fibrin clot formation, the sponge's porous structure amplifies the body's natural clotting cascade and intensifies the tamponade effect. As a result, the sponge fosters the development of clots and offers a surface on which fibroblasts and other cells necessary for wound healing can infiltrate. [17,18]

SAFETY

Although absorbable gelatin sponges are generally regarded as harmless, using them may come with some dangers. One significant worry is the possibility of infection as, if appropriate aseptic technique is not followed, the sponge's presence in a wound may foster the growth of germs. It is crucial to make sure the wound is completely debrided prior to applying a sponge in order to reduce this risk. The possibility of foreign body reactions, such as granuloma formation or fibrosis, is another concern, especially for individuals with autoimmune or hypersensitive conditions. [19,20]

3. OXIDIZED REGENERATED CELLULOSE (ORC)

An extensively used bioabsorbable hemostatic agent in advanced wound care and surgical settings is Oxidized Regenerated Cellulose (ORC). Cellulose, the most prevalent biopolymer in nature, is converted into ORC by oxidation, which improves its hemostatic qualities while preserving its bioabsorbability. ORC's adaptability and biocompatibility make it crucial for wound care, particularly in situations when traditional techniques are impractical or infection risk is high. [21]

MECHANISM OF ACTION

Because of its acidic composition, which speeds up the body's natural clotting cascade, ORC primarily serves as a hemostatic agent. ORC fibers stabilize a clot by encouraging platelet aggregation and improving fibrinogen conversion to fibrin when applied to a bleeding surface. Furthermore, ORC's physical characteristics aid in hemostasis by acting as a scaffold to support the growing clot and stop additional blood loss. Furthermore, because of its acidic environment, ORC has shown antibacterial qualities, especially against gram-positive bacteria. [22]

SAFETY

The safety profile of ORC is generally good, and side effects are rare. Even in patients who are immunocompromised or hypersensitive, long-term follow-ups in clinical trials have demonstrated that ORC is absorbed without causing notable inflammatory or foreign body reactions. To achieve the best results, however, proper use and placement are essential because improper or excessive administration may cause localized tissue responses or postpone recovery. In surgical and wound care contexts, oxidized regenerated cellulose is a flexible and useful tool. It has a good safety record and has hemostatic, antibacterial, and structural advantages. [23]

4. COLLAGEN WOUND DRESSINGS

MECHANISM OF ACTION

Advanced wound care solutions like collagen wound dressings are made to speed up the healing of chronic and non-healing wounds in particular. A naturally occurring protein called collagen is an essential part of the Extracellular Matrix (ECM), helping to promote tissue regeneration and provide structural support. Using the body's natural healing processes, collagen dressings control wound exudate, lower inflammation, and encourage the growth of new tissue. Pressure ulcers, diabetic foot ulcers, and venous leg ulcers are among the wounds they are especially helpful in treating since they interfere with the body's natural healing processes. Because they are available in a variety of forms, such as sheets, powders, and gels, collagen dressings can be used for both acute and chronic wound treatment. [24]

SAFETY

For the majority of patients, collagen dressings are typically regarded as safe. People who are known to be allergic to collagen originating from pig or cow sources, however, should use caution. Furthermore, collagen dressings might encourage the growth of bacteria in infected wounds even if they create a moist environment that aids in healing. Therefore, before using collagen dressings, infected wounds should be treated with antimicrobial medication. [25,26]

5. SILICONE GEL SHEET

MECHANISM OF ACTION

One of the most popular non-invasive methods for treating keloids and hypertrophic scars is silicone gel sheets. With multiple studies demonstrating their effectiveness in flattening, softening, and enhancing the aesthetic look of scars, they have emerged as the gold standard in scar care since their inception in the 1980s. Silicone gel sheets are incredibly adaptable since they provide a flexible, simple scar treatment alternative that may be placed to a range of scar forms and worn constantly. These sheets are designed to fit particular scar locations, including joints or huge surface regions, and are available in a variety of sizes and forms. Although the precise processes by which silicone gel sheets enhance scar results are not entirely understood, a number of theories have been put forth in light of scientific research as well as clinical experience. According to a popular notion, the sheets function by hydrating the stratum corneum, the skin's outermost layer. [27-29]

SAFETY

Several clinical research attest to silicone gel sheets' efficacy in enhancing scar results. When silicone gel sheets were applied within the first few weeks following wound closure, they dramatically decreased scar thickness, erythema, and pliability, according to a systematic review conducted by O'Brien and colleagues (2009). Because the sheets are hypoallergenic and can be used repeatedly for months without experiencing serious negative effects, they are usually regarded as safe for long-term use. However, because silicone sheets must be worn for 12 to 24 hours every day for several months to produce the desired effects, patient compliance is crucial to optimal results. [30]

6. SKIN SUBSTITUTES

Reverdin was the first to create skin substitutes as xenografts in 1871. These are bioengineered items that can take the place of skin in terms of both form and function. For burns and wounds that need extensive skin restoration, skin substitutes have long been employed. Because they can improve cytokine and growth factor production, minimize infection, decrease bodily fluid loss, and act as a covering to assist in shielding the healing wound, sophisticated skin substitutes are currently used globally for deep and chronic wounds. [31]

- ***Acellular skin substitutes***

To reduce the possibility of a foreign body reaction, acellular or synthetic skin substitutes are made of various matrices without any cells. The scaffold's composition can be altered to provide these replacements for particular uses. Numerous prospective randomised controlled studies (RCTs) have demonstrated that Biobrane, which is made of pig collagen type 1 on a silicone membrane6, reduces the pain, length of hospital stay, and wound healing time associated with partial thickness burns. Integra, a bilayer skin substitute, is made up of a collagen-based dermis10 and an epidermal substitute layer on top of chondroitin-6 sulphate. Integra encourages angiogenesis and the production of granulation tissue and helps macrophages migrate to the site. The human dermal matrix serves as a template for soft tissue regeneration and enhances burn patients' functional performance in AlloDerm, an allograft skin in which all epidermal and dermal cells are removed. Graftjacket, a micro-ionized human dermal collagen matrix, has been demonstrated to reduce ulcer size and healing time while increasing the number of cured ulcers in a treated DFU group. Omnigraft consists of a silicone layer on top of a matrix layer composed of collagen and the glycosaminoglycan chondroitin-6 sulphate. The Food and Drug Administration (FDA) recently gave its approval. [32,33]

- ***Cellular skin substitutes***

Living cells—mostly skin cells—encased in a matrix make up cellular or natural skin substitutes. They are more successful than acellular alternatives because they include cells in a matrix, but they are more costly, need certain storage conditions, and are more challenging to employ. Fibroblasts from newborn foreskins are used to create TransCyte, a temporary skin substitute that is seeded on a scaffold made of nylon mesh. TransCyte speeds up the pace of re-epithelialization and shortens the recovery period for partial and full-thickness burns, according to several clinical investigations.

Viable newborn foreskin fibroblasts are used to create dermagraft, which is a collagen mesh composed of polyglycolic acid. It has been demonstrated that administering Dermagraft to chronic DFU causes quicker wound closure, fewer ulcers, and less infection, indicating that this is a safe and efficient treatment. Allogenic keratinocytes on a type 1 bovine collagen gel are found in Apligraf, a bilayered skin counterpart that has been clinically investigated in chronic wounds. Complete wound healing was considerably more successful for patients with VLUs treated with Apligraf. The product OrCel is created by growing human dermal fibroblasts and allogeneic keratinocytes in two distinct layers on opposite sides of a type I collagen sponge.

About 90% of patients who had a substantial burn area (37% ± 17% TBSA) have been treated with Epicel, which is manufactured from human keratinocytes and murine fibroblasts that are applied to petroleum gauze. Cultured autologous keratinocytes on laser-perforated hyaluronic acid make up Vivoderm, also known as laser skin. The safety and efficacy of this bandage in treating deep leg ulcers have been validated by several trials. [34-36]

7. MONOCLONAL ANTIBODY THERAPY

Antibodies that can attach to target proteins and stop their activity are known as monoclonal antibodies. Targeting certain proteins with monoclonal antibodies may help promote better wound healing because it has been demonstrated that these proteins are higher in both acute and chronic wounds. [37]

Types of Monoclonal Antibodies

Depending on where they come from, there are four primary types of monoclonal antibodies (mAbs) that can be made using various techniques. The four categories of monoclonal antibodies and their names are as follows:

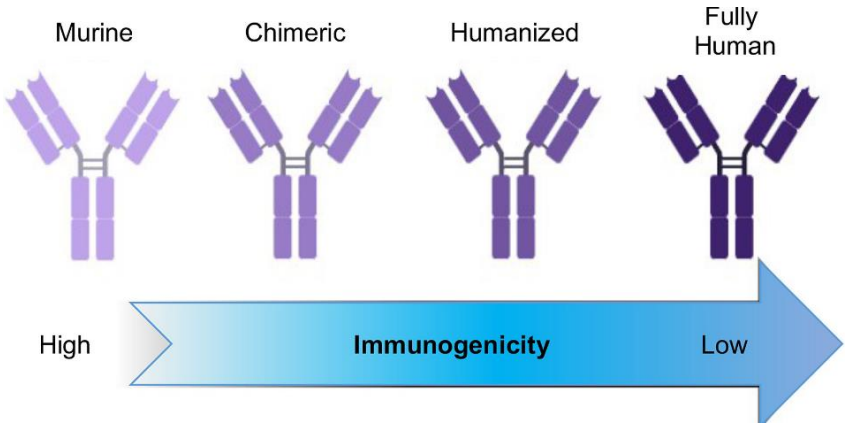

Figure 2. Types of Monoclonal Antibodies

1. Murine monoclonal antibodies

Mice are the complete source of these antibodies. Both the heavy and light chains' variable sections are derived from mice. The prefix "o-" or "-omab" is added to the general name to identify murine mAbs. For instance, "rituximab" is a chimeric antibody used to treat autoimmune disorders and some forms of lymphoma. It contains murine variable sequences.

2. Chimeric monoclonal antibodies

Human constant regions and mouse variable regions make up chimeric antibodies. While the variable regions offer antigen specificity, the consistent sections dictate the antibody's effector actions. Chimeric monoclonal antibodies are identified by appending the suffix "-ximab" to the generic name. A chimeric antibody called "infliximab," for instance, targets tumor necrosis factor-alpha (TNF-α) and is used to treat inflammatory conditions including rheumatoid arthritis.

3.Humanized monoclonal antibodies

Only a little amount of mouse sequence is included in the complementarity-determining regions (CDRs) of humanized antibodies, which primarily contain human sequence. Humanization lessens the immunogenicity of murine monoclonal antibodies. The suffix "-zumab" is added to the generic name to create humanized mAbs. For instance, a humanized antibody called "trastuzumab" is used to treat breast cancer that is HER2-positive.

4. Fully human monoclonal antibodies

Both the constant and variable portions of fully human antibodies are completely derived from human sequences. They are made to be as compatible as possible with the human immune system while minimizing immunogenicity. The suffix "-umab" is added to the generic name to identify fully human mAbs. For instance, "adalimumab," a completely human antibody that targets TNF-α, is used to treat a number of autoimmune conditions, including psoriasis and rheumatoid arthritis. [37]

MECHANISM OF ACTION

There are multiple ways that monoclonal antibodies treat illnesses:

1.Blocking or Neutralizing Antigens

Mechanism: Certain monoclonal antibodies (mAbs) function by attaching themselves to a particular antigen on the cell surface, like a protein or receptor, and blocking its interaction with other molecules or signaling pathways. For instance, bevacizumab inhibits the creation of blood vessels in tumors by binding to vascular endothelial growth factor (VEGF), which in turn limits the tumors' ability to grow.

2.Immune System Activation

Mechanism: The body's immune system is triggered by certain monoclonal antibodies to target and eliminate cells that express the specific antigen. For instance, rituximab targets B-cells' CD20 and triggers immune cells to destroy them, which is helpful in tumors like non-Hodgkin lymphoma.

3.Antibody-Dependent Cellular Cytotoxicity (ADCC)

The process involves the antibody attaching itself to the target cell, such as a cancerous cell, and enlisting immune cells, including natural killer (NK) cells, to assault and eliminate the target cell. For instance, Herceptin's trastuzumab targets HER2-positive breast cancer cells, triggering the ADCC mechanisms that destroy cancer cells.

4.Complement-Dependent Cytotoxicity (CDC)

Mechanism: Through a series of immunological responses, some monoclonal antibodies trigger the complement system, which destroys the target cells. Rituximab, for instance, causes the CDC to destroy B-cells in conditions like lymphoma.

5.Delivery of Cytotoxic Agents

Mechanism: To provide more accurate treatment and less harm to healthy tissue, monoclonal antibodies can be conjugated (attached) to medications, poisons, or radioactive particles and delivered directly to target cells (such as cancer cells). For instance, the antibody-drug combination trastuzumab emtansine (Kadcyla) targets HER2-positive cancer cells and delivers a chemotherapeutic medication straight to the tumor.

6.Inhibition of Immune Checkpoints

Mechanism: Immune checkpoint proteins that cancer cells use to evade immune detection are the target of certain monoclonal antibodies. These antibodies help the immune system identify and combat cancer cells more effectively by blocking these checkpoints. For instance, pembrolizumab and nivolumab improve the immune response against cancer cells by blocking PD-1, a checkpoint inhibitor on T-cells. [38]

8.PROTEASE INHIBITORS

MECHANISM OF ACTION

The balance between the formation and breakdown of extracellular matrix depends critically on the activity of proteases and their inhibitors. Protease overexpression in chronic wounds leads to aberrant extracellular matrix and protein breakdown, including growth hormones and cytokines. Protease inhibitors are implicated in these findings as a possible treatment strategy to enhance wound healing. Promogran is a dressing composed of oxidized

regenerated cellulose and collagen I. Proteases such matrix metalloproteinase and elastin are less active when this dressing is applied. Promogran dressing has been demonstrated to be successful in treating chronic wounds in a number of case studies.

A layer of polyester mesh, hydrocolloid polymers, and nano-oligosaccharide factor—a matrix metalloproteinase inhibitor factor—are all present in UrgoStart, a dressing. Based primarily on its protease inhibitor efficacy in a small pilot RCT, the antibiotic and matrix metalloproteinase inhibitor doxycycline has been demonstrated to enhance the healing of chronic diabetic ulcers. [38]

9.CONNEXIN INHIBITOR

MECHANISM OF ACTION

A protein found in gap junction channels called connexin 43 (Cx43) is involved in fibrotic and inflammatory processes. Although Cx43 expression rapidly declines upon wounding, it is increased in chronic wound fluids, indicating that this protein could be a viable target for wound healing treatments. The promotion of wound healing in superficial epidermal wounds in a mouse model was verified by an in vivo investigation examining the impact of Cx43 inhibition on a corneal wound.

SAFETY

Increases in skin cell migration, proliferation, and re-epithelialization were the outcomes of the treatment. Comparing the ulcer area after 12 weeks to conventional treatment, a notable decrease was noted, demonstrating the safety and effectiveness of ACT1 gel in the healing of skin lesions. [39]

10.OTHER MEDICATIONS

A variety of drugs have been used to treat wounds. Agents that target inflammatory or auto-immune mechanisms have been used successfully in cases where the wound aetiology includes these dimensions. These wounds include Necrobiosis lipoidica, pyoderma gangrenosum, and vasculitis ulcers.

- ***Immunosuppressive medications:*** It has been demonstrated that pyoderma gangrenosum can benefit from immunomodulatory medications such as cyclosporine, mycophenolate, tacrolimus, pimicrolimus, corticosteroids, and azathioprine. For certain wound disorders, other drugs, such as complementary and alternative medicines, have been used—mostly orally, but occasionally topically.

Among the examples are: Oxerutins, also known as rutosides, have been studied in relation to lymphoedema-related wounds. Patients with arm and leg ulcers experienced less discomfort and more flexibility of movement in two separate RCTs.

- ***Horse chestnut:*** This medication has been shown to be beneficial for lower limb edema from a variety of reasons as well as chronic venous insufficiency. However, there isn't much data to back up its application in wound healing. Topical phenytoin has been used to help cure chronic wounds such DFUs, leg ulcers, and pus. However, there is a dearth of recent data.

- ***Pentoxifylline:*** This medication has been effectively utilized to treat peripheral vascular disease symptoms and enhances oxygen delivery to ischemic regions. Additionally, it has been used for DFUs and arterials. In VLUs, a Cochrane study showed its effectiveness when used in conjunction with compression or in situations when compression is not an option.

- ***Thiosulphate of sodium:*** When given intravenously, this has been demonstrated to accelerate the healing of calciphylaxis-induced ulcers. The body's ability to manufacture arginine, an amino acid necessary for wound healing, is limited. In doses ranging from 3 to 9 grams per day, it has been shown in numerous trials to aid in the recovery of stage 2 and above-pressure injuries.

- ***Other nutrients:*** Although widely used, there is little evidence to support the involvement of zinc or vitamin C in promoting wound healing, even though these nutrients are crucial for the synthesis of collagen and wound healing. They should be given in replacement doses if a glaring deficiency is shown.

- ***Herbal:*** Although there is little to no evidence to support the benefits of several herbs, they have been touted as aiding in wound healing. [40]

FUTURE DIRECTION AND INNOVATIONS IN WOUND CARE

Emerging technologies that promise to improve patient outcomes and expand treatment options are driving significant advancements in advanced wound care. Wound care could be revolutionized in a number of important areas of innovation. One such field that is being actively investigated is nanotechnology. Nanomaterials are being developed to transport medications, growth hormones, and antibacterial agents straight to the wound site.

Examples of these materials include nanofibers, nanoparticles, and nanoscale hydrogels. By precisely focusing on dangerous bacteria, these nanoscale devices not only encourage quicker wound healing but also lower the chance of infection. Silver nanoparticles, for example, have demonstrated promise in decreasing bacterial colonization and speeding up healing, especially in chronic wounds. These advancements demonstrate the increasing interest in using nanotechnology to provide more advanced wound-healing treatments. Another cutting-edge instrument with revolutionary potential in wound treatment is 3D printing technology. Scaffolds and dressings are examples of customized wound care solutions that are made to perfectly match the size and particular requirements of a patient's wound. Better patient outcomes, less waste, and more effective treatment are all possible with this individualized strategy. Additionally, scientists are looking at the potential use of biocompatible materials in 3D-printed wound dressings, which could improve healing even more by offering structural support for tissue regeneration and cell growth. Advances in biomaterials are pushing the frontiers of wound treatment by generating products that closely mirror the body's natural healing processes. Bioactive dressings, smart materials that react to changes in the wound environment, and synthetic collagen analogs are all being developed. These intelligent dressings can adjust to the temperature, oxygenation, and moisture content of the wound, creating the ideal conditions for healing. Bioactive dressings are a major advancement in the treatment of chronic or non-healing wounds because they release therapeutic substances such as growth factors and antibacterial compounds. Another exciting future in wound treatment is provided by gene therapy and regenerative medicine. For example, gene therapy may introduce genes that support tissue regeneration and angiogenesis, giving patients with genetic diseases that hinder healing or persistent wounds preventions. Although this strategy is still in its infancy, it has the potential to address the molecular reasons of impaired wound healing. In the meantime, stem cell treatment is becoming a powerful wound-regeneration tool. Stem cells have the ability to accelerate healing and aid in the restoration of damaged tissues. Researchers are trying to build treatments that use stem cells to create bioengineered skin grafts for big or hard-to-heal wounds, or that apply stem cells directly to the wound site. Treatments are customized using personalized medication. Has the potential to significantly influence wound management based on each patient's particular traits. Clinicians can create individualized treatment programs that target individuals who are more likely to experience issues, such as poor wound healing or keloid formation, by using genomic data to identify these patients. Better outcomes and quicker recovery times can occur from customizing wound care regimens to each patient's skin type, wound kind, and general health. For instance, choosing particular dressings or therapeutic approaches may be part of individualized care if a patient has a genetic propensity to particular issues. With manufacturers and researchers working to create more environmentally friendly wound care solutions, sustainability is also becoming a top priority. [39,40]

CONCLUSIONS

These advanced therapies for wound healing have transformed the treatment of chronic and complicated wounds by offering the best possible solutions for wound healing. Stem cells, growth factors, bioengineered skin substitutes, and advanced dressings can enhance the chances for tissue regeneration, reduce the risk of infections, and speed recovery. Such therapies are to be directed toward correcting factors causing delayed wound healing- poor circulation, infection, or inflammation- to ensure a hastened recovery and an improved quality of life for patients with difficult-to-treat wounds. Research would continue to heighten the chances of finding future personalized medicine and biotechnology developments that can narrow and expand therapeutic ranges for wound care. In the long term, advanced therapies for wound healing may benefit health care systems by significantly reducing expenses for care, improving prognosis for many chronic wounds, especially in people with disorders such as diabetes, vascular diseases, and age.

CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

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