ISSN: 2755-0184

Journal of Diabetes Research Reviews & Reports

SCIENTIFIC Research and Community

Review Article

Open Access

Diabetic Wound Healing: Navigating Physiology, Advancements and Research Frontiers

Prabhakar Kumar[1], Faizul Hasan[2], Vijender Kumar[2]*, Rakesh Chawla[3], Sandeep Kumar Goyal[3] and Gazanfar Ahmad[4]

[1]Department of Pharmacology, Delhi Pharmaceutical Sciences and Research University, New Delhi, India

[2]Department of Pharmacognosy & Phytochemistry, School of Pharmaceutical Sciences, Delhi Pharmaceutical Sciences and Research University, India

[3]University Institute of Pharmaceutical Sciences and Research, BFUHS, Faridkot, Punjab, India

[4]Prabha Harjilal College of Pharmacy and Paraclinical Sciences, Jammu, Jammu and Kashmir, India

ABSTRACT

Diabetes, a multifaceted metabolic disorder characterized by inadequate insulin production or resistance, intricately intertwines with the challenging landscape of wound healing, particularly in the context of diabetic wounds. This review embarks on a comprehensive exploration, commencing with an overview of diabetes physiology, setting the stage for understanding its intricate interplay with wound healing complexities. Navigating through the physiology of diabetic wounds, this review encapsulates their classification and the intricate molecular and cellular mechanisms orchestrating the healing process. However, amidst commendable advancements, a discernible research gap remains, urging a more nuanced comprehension of diabetic wound pathophysiology. Examining treatment approaches, this article critically assesses various methods for diabetic wound healing efficacy, rooted in recent studies. It explores advanced therapies and emerging technologies, envisioning possibilities such as 3D printing and smart dressing applications. Nonetheless, integrating these technologies into clinical practice awaits exploration, highlighting a research gap in standardizing these advancements. Infection control and antibiotics are pivotal in diabetic wound management. This review underscores their importance, stressing the need for refined research strategies to optimize antibiotic use and combat evolving bacterial resistance. Furthermore, advocating for patient-centered care and education, this review emphasizes holistic approaches, underscoring a persistent gap in seamlessly integrating patient education into routine wound management protocols.

This review offers comprehensive insights into diabetic wound physiology, treatment modalities, and emerging technologies while highlighting persistent research gaps demanding further exploration and refinement.

***Corresponding author**

Vijender Kumar, School of Pharmaceutical Sciences, Delhi Pharmaceutical Sciences and Research University, New Delhi, India.

Received: March 11, 2024; **Accepted:** March 19, 2024; **Published:** April 15, 2024

Keywords: Diabetes, Metabolic disorder, Myofibroblasts, Wound Healing, Hyperglycemia

Abbreviation

bFGF: Basic Fibroblast Growth Factor
ECM: Extracellular Matrix
IGF: Insulin-like Growth Factor
ILs: Interleukins
MMPs: Matrix Metallo-Proteinases
MSC: Mesenchymal Stem Cells
NPWT: Negative-Pressure Wound Therapy
PDGF: Platelet Derived Growth Factor
rh-PDGF: Recombinant Human Platelet-Derived Growth Factor
ROS: Reactive Oxygen Species
SMA: Smooth Muscle Actin
TENS: Transcutaneous Electrical Nerve Stimulation
TGF-β: Transforming Growth Factor-Beta
VEGF: Vascular Endothelial Growth Factor

Introduction

The elevated blood glucose is a defining feature of diabetes, a systemic illness brought on by inadequate or resistant insulin [1]. The International Diabetes Federation stated that 463 million persons between the ages of 20 and 79 received a diabetes diagnosis in 2019. By 2045, it is anticipated that this figure would rise to 700 million. Chronic diabetic wounds are a serious concern to public health everywhere, especially in the US. Compared to the general population, people with diabetes have a 10-20 times higher risk of needing an amputation because to persistent ulcers [2,3].

Diabetes patients have a complex wound-healing process that involves numerous biological and molecular processes. Diabetes has an impact on wound healing at every step of the process. Inflammation, proliferation, and tissue remodeling are the three stages that normal wound healing goes through. Because of the complexity of this process, several results for tissue repair may result from any malfunction. Myofibroblasts are a diverse subset of cells that are essential to the wound healing process during

both the proliferation and remodeling stages. After an injury, they maintain physical tissue integrity by producing and controlling collagen Extracellular Matrix (ECM) [4].

The production of Smooth Muscle Actin (SMA), which gives myofibroblasts their contractile capabilities, indicates the shift from fibroblasts to myofibroblasts [5]. Precursor cells that give rise to myofibroblasts include fibroblasts, smooth muscle cells in the skin and surrounding tissue layers, adipose tissue cells, and mesenchymal stem cells [6,7].

Diabetes can delay the process of wound healing by preventing myofibroblast development from precursor cells. This may lead to an increase in proteolytic activity, a decrease in wound contraction, insufficient cellular proliferation, and insufficient ECM deposition. We will go over myofibroblast biology, the effects of diabetes on wound healing, and pertinent signaling pathways in this review. We will also look at possible therapy approaches based on research on published clinical and experimental studies. This paper offers a foundation for comprehending how diabetes affects the wound healing process, specifically myofibroblast function [8].

Diabetic wound healing is significant and fraught with difficulties when it comes to managing diabetes mellitus. This procedure is essential since it directly affects the health of those who have diabetes. If left untreated, diabetic wounds especially foot ulcers represent a serious medical risk and can have life-threatening consequences.

Pathophysiology of Diabetic Wounds

Diabetes has multiple pathophysiological pathways that are closely linked to impaired wound healing in its patients.

- **Hyperglycemia and Glycation:** A person with diabetes typically has high blood glucose levels, which can raise the amount of glucose in the tissues. The extra glucose then attaches itself to proteins through a process known as glycation. The structure and function of the proteins are harmed by this. This can be particularly problematic for essential components of wound healing, such collagen, as glycation may prevent them from functioning properly [9].
- **Microvascular Complications:** Diabetes can cause microangiopathy, a disorder that narrows small blood vessels and decreases blood flow to wound sites. Consequently, the wound loses its supply of oxygen, nutrients, and immune cells all essential for a healthy healing process. For those who have diabetes, this illness can seriously obstruct the healing process and lead to complications [9].
- **Altered Inflammatory Response:** The long-term metabolic condition known as diabetes mellitus might impair the body's capacity to heal injuries naturally. Disrupting the typical inflammatory response, which is essential to the healing process, is one way this occurs. Because of this, inflammation may continue for an extended length of time, hindering the following stages of wound healing [10].
- **Oxidative Stress and Inflammation:** Hyperglycemia is a medical disorder characterized by elevated blood sugar levels that can initiate several harmful processes within the body. One such mechanism that results in oxidative stress is the overproduction of reactive oxygen species (ROS) and persistent inflammation. This impedes the healing process by further damaging cells and tissues [11].
- **Impaired Angiogenesis:** Diabetes is a disorder that interferes with the development of new blood vessels, that prevent blood from reaching wounds. The delivery of essential nutrients and oxygen to the wound area is hampered by this inadequate blood supply, which is detrimental to the successful healing process [9].
- **Deficient Growth Factors:** Diabetes patients have abnormalities in the synthesis and activity of growth factors that are essential for the healing of wounds. These growth factors Platelet Derived Growth Factor [PDGF] and Insulin-like Growth Factor [IGF] are essential for tissue regeneration and cell proliferation. Reduced amounts of these substances hinder the body's capacity to heal wounds, which causes healing to take longer and increases the risk of complications [9].

It is essential to understand and address the pathophysiological factors behind diabetes wound healing impairment through focused treatment strategies. Patients with diabetes may benefit from better wound healing outcomes if these processes are the focus of attention and strict glycemic control is maintained.

These all Elements Play a Crucial Role in Diabetic Wound Healing

- **Hyperglycemia:** Diabetes patients may experience difficulties healing from wounds because of high blood glucose levels. Nonetheless, the detrimental effects of hyperglycemia on wound healing can be mitigated by controlling blood sugar levels with the right medicine, food, and exercise regimen. It is critical to understand the dangers of diabetes and to take the appropriate action to encourage good healing [12].
- **Neuropathy:** Diabetes frequently results in diabetic neuropathy, a nervous system disorder that damages nerves and impairs feeling in the hands and feet. It could be more difficult to notice injuries due to loss of sensation, which might cause wounds to heal more slowly and prevent early intervention. For those suffering from diabetic neuropathy, proper management and observation are essential to avert future problems [13].
- **Vascular Changes:** Diabetes can cause a variety of vascular abnormalities in people that impact both tiny and big blood arteries. These alterations may result in compromised vasodilation, broken capillaries, and decreased blood flow, all of which may have a major effect on the healing process. Because of this, the wound site receives less vital nutrients, oxygen, and immune cells, which delays healing and increases the chance of infection [14].
- **Inflammation:** An essential part of the body's reaction to damage or infection is inflammation. Diabetes, on the other hand, causes it to become chronic and can hinder healing. The regular progression of wound healing can be interfered with by persistent and severe inflammation at the wound site, which can postpone the change from the inflammatory to the proliferative phases. Delays like this might leave open wounds that take a long time to heal, which can cause more issues. Thus, regulating inflammation in diabetes is essential for encouraging appropriate wound healing and lowering the possibility of developing new issues [15].

Appropriate treatment approaches, such as glycemic control, wound care, neuropathy management, vascular health maintenance, and inflammation control, are needed to improve wound healing results in diabetes patients. Mitigating poor wound healing requires comprehensive care that considers all these aspects.

Classification of Diabetic Wounds

Diabetic wounds are divided into several categories based on their underlying causes and characteristics

- **Neuropathic Ulcers:** Neuropathy is a disorder that affects

the nerves, particularly in the feet, and can be brought on by diabetes. Sensory neuropathy, which can result in loss of sensation, is the cause of neuropathic ulcers. Ulcers may form because patients are unable to perceive wounds or friction. These foot ulcers generally cause little discomfort and develop in high-pressure locations. The presence of callus tissue surrounding the incision and the depth of the ulcer are characteristics of neuropathic ulcers [16].

- **Ischemic Ulcers:** The lack of blood supply to the extremities that leads to ischemic ulcers is frequently exacerbated by vascular problems associated with diabetes. Reduced blood flow causes tissue damage and slow- or non-healing wounds. These ulcers might look deep, dry, and punched out, and they are usually painful. Ischemic ulcers typically occur on the lower limbs or toes, and they are frequently linked to delayed wound healing [16].
- **Infection-Related Wounds:** An infection can significantly worsen diabetic ulcers, particularly neuropathic and ischemic ulcers. Many consequences, such as cellulitis, the development of an abscess, and even infections of the bones (osteomyelitis), can result from the presence of bacterial infections. Infected wounds are easily recognized by their telltale signs of warmth, redness (erythema), swelling, and pus discharge. Fever and other systemic infection symptoms could also be present. It is crucial to treat infections promptly and effectively to stop these wounds from getting worse [17].
- **Additional Classifications:** A vital component of wound care is wound categorization, which aids in identifying the best course of action for the condition. The depth, size, and infection status of the wounds are only a few of the variables that determine the classification system. The University of Texas Diabetic Wound Classification is one of the most popular classification schemes. According to this approach, wounds can be categorized into several categories, from shallow cuts to serious cuts that penetrate the bone. Infection is taken into consideration by the classification system, which is important since it affects which treatment plan is best for diabetic wounds. Healthcare providers can use this technique to determine the extent of the wound and provide their patients with the best possible course of therapy [18].

To effectively manage wounds in people with diabetes, it is critical to comprehend their type and classification. Customized therapies are essential for enhancing results and averting complications. Examples include wound care, infection management, vascular interventions, and relieving pressure from afflicted areas.

Wound Healing Molecular and Cellular Mechanisms

Normal wound healing is a complicated and comprehensive system that involves several cellular and molecular events. These highly controlled events operate in concert to initiate a cascade of processes that aid in the restoration of damaged tissue and the promotion of healing. Normal wound healing entails a complex interplay of several cells and chemicals, each with distinct roles and activities.

- **Inflammation Phase:** When the body sustains tissue damage, it sets off a complicated chain of processes targeted at mending the damage. One of the first responses is the recruitment of immune cells, notably neutrophils and macrophages, to the wound site. These cells aid in the removal of waste and infections, as well as the preparation of the area for future healing processes.
- When immune cells arrive at the site of injury, they release inflammatory cytokines and chemokines, which act as chemical messengers, signaling for other immune cells to arrive. This recruiting process is critical for the proper repair of injured tissue, since immune cells collaborate to eliminate possible dangers and provide a conducive environment for healthy tissue regeneration [19].
- **Proliferation Phase:** Fibroblasts and endothelial cells collaborate to repair injured tissue during the tissue repair phase. Fibroblasts are specialized cells that form connective tissue. They also produce components of the ECM, such as collagen, which give the tissue stability and structure. In the meantime, angiogenesis the process by which the blood vessel lining endothelial cells creates new blood vessels helps supply oxygen and nutrients to the injured area. Growth factors, namely TGF-β and VEGF, play a pivotal role in regulating these activities and guaranteeing the efficient and effective healing process [20].
- **Remodeling Phase:** The ECM is rearranged by the body during this phase to strengthen the tissue. This stage is distinguished by a balance between the synthesis and breakdown of collagen, which aids in the formation of scar tissue. Matrix metalloproteinases (MMPs) are another enzyme involved in the ECM remodeling process that are essential in the breakdown and reconstruction of the ECM [19].
- **Cell Signaling:** The body's mechanisms for controlling cell division and repair depend on growth factors and cytokines. Among these, interleukins (ILs), platelet-derived growth factor (PDGF), and transforming growth factor-beta (TGF-β) are essential for regulating cell migration, proliferation, and ECM formation. The appropriate control of these signaling molecules is essential for preserving tissue homeostasis and averting disease since they can either promote or inhibit cellular activity depending on the situation [21].
- **Cellular Interaction:** The process of wound healing involves the intricate and well-coordinated interaction of multiple cell types, including immune cells, fibroblasts, endothelial cells, and keratinocytes. Together, these cells manage the healing process by corresponding through a process known as paracrine signaling. Through the process of paracrine signaling, these cells can release chemicals that instruct neighboring cells to carry out tasks required for the healing of wounds. The healing of injured tissue and the avoidance of infection depend on this procedure [22].
- **Angiogenesis:** Angiogenesis, the process of creating new blood vessels, is essential for providing the wound site with the nutrition and oxygen it needs to heal properly. To establish a network of functional blood arteries, this intricate process which is governed by growth hormones like VEGF needs the migration and proliferation of endothelial cells [23].
- **ECM Synthesis:** Fibroblasts are essential for healing because they produce different ECM components that enable tissue regeneration and offer structural integrity. Collagen, which is necessary for the formation of new tissue, is one of the most significant ECM components for fibroblasts. A complex interplay of growth factors and cytokines strictly regulates the creation of these ECM components, facilitating the smooth and effective healing process. Tissue healing and regeneration would be considerably more challenging and ineffective without meticulous synchronization of these cellular functions [22]. Proliferation, remodeling, and inflammation are all part of the wound healing process. It is essential for growth factors, cellular connections, and ECM formation.

Diabetic Wounds Exhibit Modifications in Cellular and

Molecular Mechanisms

Individuals with diabetes may experience notable disruptions to their wound-healing mechanisms. Changes in several biological systems brought on by diabetes may complicate the process of wound healing. Consequently, compared to people without diabetes, wound healing in diabetics may be less efficient and take longer. An examination of the systems and processes involved is essential to comprehending the impact diabetes has on wounds.

- **Inflammation Phase:** A slow and ineffective inflammatory response is a common feature of diabetic wounds, which can make the inflammation worse and last longer. A delay in the removal of pathogens and debris may ensue from this compromised immune cell recruitment. In addition to impeding the healing process, this persistent inflammation raises the possibility of infections as well as additional complications [24].
- **Proliferation Phase:** Diabetes patients frequently experience diabetic sores, which can be extremely painful and uncomfortable. The fact that these wounds frequently struggle with the process of angiogenesis the formation of new blood vessels is one of the primary problems with them. As a result, there may be less oxygen and nutrients getting to the wound site, which could hinder the growth of fibroblasts and the synthesis of collagen. Furthermore, hemoglobin can get glycated due to excessive blood sugar levels, which might make the problem worse. In general, managing diabetic wounds can be difficult and frustrating, therefore it is critical to collaborate closely with a healthcare professional to develop an efficient treatment strategy [25].
- **Remodeling Phase:** Diabetes can seriously compromise the healing of wounds, particularly when it comes to ECM remodeling. Diabetic wounds can cause an imbalance in the synthesis and breakdown of collagen due to disruptions in the ECM's (ECM) normal remodeling process. Poor wound closure may come from the scar tissue that forms being weaker than usual. Additionally, this weaker tissue may make it more likely for the incision to reopen, which would complicate healing [26].
- **Cell Signaling:** Growth factor and cytokine levels in diabetes wounds are significantly altered, which negatively impacts cell signaling pathways. Wound healing is delayed because of these alterations, which impede normal cell migration and proliferation [27].
- **Cellular Interaction:** Diabetes is a chronic illness that may negatively affect the well-coordinated interplay of several cell types involved in the intricate process of wound healing. This compromised cell-to-cell contact can seriously impede and postpone the healing process, increasing the risk of infections and other harmful consequences [28].
- **Angiogenesis:** Diabetes can make wound healing more difficult since it reduces angiogenesis. This disorder inhibits the growth of blood vessels, which reduces the flow of vital nutrients and oxygen to the area of the wound. This slows down the healing process and may result in more issues [25].
- **ECM Synthesis:** Diabetes causes a disruption in the ECM synthesis process, which modifies the wound site's composition significantly. The ECM's ability to offer structural support is impacted by this alteration, which jeopardizes the damaged tissue's ability to regenerate. This may result in further issues and delays in the healing of wounds [29].
- Diabetes impairs wound healing by interfering with several processes, which leads to chronic and delayed wounds. Targeted therapies targeting hyperglycemia, reduced blood flow, and thrown off cellular and molecular processes are necessary for effective management.

Treatment Approaches for Diabetic Wound Healing

Managing diabetic patients' wounds is a difficult process that necessitates a multidisciplinary approach. Specialized dressings and surgical procedures are frequently necessary to promote the healing process, in addition to wound care techniques such as cleaning and treating the affected area. There are numerous diabetic wound treatment strategies available today, and being aware of these options can assist healthcare providers in determining the best course of action for their patients.

Wound Care Techniques

Wound debridement is a medical technique that removes dead or infected tissue from a wound. This is usually accomplished through surgical or sharp techniques, and it is an important step in encouraging wound healing. By removing the damaged tissue, the wound bed is left clean and healthy, allowing for new tissue to develop and repair the wound. The procedure of debridement may be painful for the patient, but it is vital to avoid infection and promote recovery [30].

Maintaining a moist atmosphere surrounding the damaged area can aid in the healing process. This can be accomplished by putting saline or equivalent dressings daily, which will keep the wound moist and promote speedier healing. Keeping the wound moist also lowers the chances of infection and scarring [31].

Aspiring patients with non-plantar wounds must prioritize relieving pressure at the wound site. There are several ways to accomplish this, including heel relief and surgical sandals. Patients can slow down the healing process and avoid more injury by applying less pressure to the injured area. This is an important step that can greatly enhance patient outcomes when treating non-plantar wounds [32].

Specialized Dressings

The rh-PDGF dressing is a specifically designed dressing that includes growth factor generated from recombinant human platelets. This patch successfully promotes tissue regeneration and reduces inflammation, aiding in the healing of wounds in diabetic patients. It is frequently added to wound care treatments as an adjuvant to hasten healing and enhance overall patient results [33].

Advanced dressings are essential for the treatment of diabetic wounds because they provide several functions that promote healing. These dressings are specifically made to manage moisture, provide antibacterial qualities, and prepare the wound bed by debridement. Healthcare providers can guarantee that patients receive the finest treatment possible and that wounds are appropriately maintained by using sophisticated dressings [34].

Surgical Interventions

Surgical debridement is an essential surgical technique that helps a wound heal by removing dead or contaminated tissue and allowing fresh tissue to develop. Typically, a qualified surgeon will carry out this process in a sterile setting with specialized tools to carefully remove the damaged tissue. Surgical debridement creates a clean, healthy environment that promotes optimal healing and lowers the risk of infection by clearing the wound of dead or contaminated tissue [26].

For the care of diabetic wounds, negative-pressure wound therapy (NPWT) is a very successful treatment. It entails applying negative

pressure to the wound with a specific equipment to create a vacuum-like effect that aids in healing. By assisting in the removal of extra fluid, lowering swelling, and improving blood flow to the area, the therapy promotes tissue growth and quickens the healing process. Diabetes patients with chronic wounds can benefit greatly from NPWT, a painless, safe treatment that has been shown to be quite successful in this regard [35].

Adjunctive Therapies

For diabetics to heal their wounds effectively, blood sugar control is essential. Patients with diabetes who keep their blood sugar under control greatly lower their risk of problems, like infections, and help the body's natural healing mechanisms. Keeping blood sugar within normal ranges not only facilitates quicker recovery but also aids in averting the development of new issues. For this reason, it is essential that diabetes patients carefully check and control their blood sugar levels [36].

A non-invasive treatment called transcutaneous electrical nerve stimulation (TENS) uses low voltage electrical currents to activate nerves for therapeutic effects. By boosting the amount of oxygen and nutrients that reach the injured area, TENS therapy has been demonstrated to enhance blood flow and accelerate healing in diabetic wounds when used as an adjuvant treatment. This may aid in lowering swelling, easing discomfort, and quickening the healing process [37].

The treatment plan for diabetic wounds includes wound care practices, specialty dressings, debridement surgery, and adjuvant therapy. The patient's condition and the severity of the wound determine the course of treatment, which aims to improve the patient's quality of life, encourage healing, and avoid complications.

Based on Recent Studies, The Efficacy of Treatment Approaches for Diabetic Wound Healing

The current study offers insightful information about practical methods for diabetic wound healing. Diabetes-related foot sores are particularly challenging to cure and may need for specialist care. Silver dressings and polyherbal treatments are quite helpful at helping diabetic patients' wounds heal, according to recent studies. These therapies are a flexible choice for wound care because they have also been demonstrated to be successful in healing burn wounds. In general, the application of polyherbal remedies and silver dressings is a potential advancement in the management of burn and diabetic wounds (33).

Chronic diabetes wounds can be extremely difficult to heal, and typical treatment procedures are not always effective. A recent study, however, has looked at the use of Nanoparticle-Based Therapeutic Approaches, which entail the use of exogenous growth factors including VEGF and bFGF. These growth factors have demonstrated promising outcomes in wound healing and tissue regeneration. The effectiveness of these growth factors can be increased by delivering them directly to the wound site via nanoparticles, leading to improved wound treatment outcomes [38].

Polymeric biomaterials are becoming a popular alternative among clinicians for treating diabetic wounds. These materials have a variety of advantageous features that make them ideally suitable for wound care, such as biocompatibility, biodegradability, and the ability to maintain a moist environment, which is critical for effective wound healing. As a result, they are being actively researched for their usefulness in aiding healing in diabetes patients, who frequently face delayed wound healing and an increased risk of infection [39].

Functional hydrogels are a type of substance developed specifically for diabetic wound treatment. These hydrogels address the two main concerns encountered in diabetic wounds: prolonged inflammation and impaired healing mechanisms. By addressing these issues square on, functional hydrogels have the potential to make a major impact in diabetic patients' wound healing outcomes. These new materials are paving the path for more effective and efficient diabetic wound care through ongoing research and development [40].

Diabetes foot ulcers are a common consequence of diabetes that can have a substantial impact on a person's quality of life. However, there is promise for improved outcomes in the management of these ulcers with the development of innovative wound care medicines. These therapies have been well-researched and have shown promising results in terms of shortening recovery times. Continuous research is being undertaken to investigate and create even novel ways for diabetic wound management, which may improve the quality of life for persons suffering from this condition [41].

Diabetes frequently results in diabetic wounds, which can be challenging to treat. High-energy sound waves are used in shockwave therapy, a non-invasive treatment, to promote healing in the injured area. As a traditional approach to managing diabetic wounds, this therapy is becoming more and more popular. Its efficacy in enhancing healing outcomes and shortening healing durations is now being investigated. Shockwave Therapy is a potentially beneficial treatment for people with diabetic wounds because of its capacity to accelerate healing and lower the risk of complications [37].

Diabetic foot ulcers provide substantial issues in wound treatment because they are generally sluggish to heal and can progress to serious consequences. As a result, there is an urgent need for continuous research to find and develop effective therapies that can speed up recovery and lower the risk of additional problems. Despite the hurdles, there is reason to be optimistic, as novel approaches to wound care are continually being studied and perfected, with the possibility for improved results and enhanced quality of life for patients [42].

There has been progress in developing efficient methods for diabetic wound healing, according to recent studies. Treatments include hydrogels, polymeric biomaterials, silver dressings, nanoparticle-based therapies, and more recent approaches to wound care show promise in promoting better healing in diabetes patients. Effectiveness, however, may differ, and customized treatment regimens are crucial depending on the ailment and degree of the wound.

Advanced Therapies and Emerging Technologies

Advanced treatments for diabetic wounds, including tissue engineering, growth factors, stem cell therapy, and regenerative medicine, have a lot of potential.

- **Growth Factors:** The body naturally produces growth factors, which are proteins that are essential for several biological functions, including angiogenesis, cell division, and tissue repair. Among these, the ability of VEGF, bFGF, PDGF, and TGF-β to improve wound healing in diabetes patients has been thoroughly investigated. Studies show that growth factor-based treatments can improve wound healing and speed up the healing process for people with diabetic foot ulcers, a typical consequence of the disease.

Growth factors have shown considerable promise in the field of regenerative medicine by boosting the synthesis of new cells and supporting the formation of new blood vessels [38].

- **Stem Cell Therapy:** Therapies based on stem cells are quickly becoming recognized as a promising way to promote tissue regeneration in wounded or damaged tissues. Scientists are looking at using different kinds of stem cells to encourage tissue repair and healing. Mesenchymal stem cells (MSC) are one kind of stem cell that has attracted a lot of attention lately. Because of their special qualities, MSCs are especially well-suited for use in regenerative medicine. Two such qualities include their capacity to influence the immune system and encourage the development of new blood vessels. According to studies, MSC-based treatments may be beneficial for improving wound healing, particularly in those with diabetes who are known to have impaired natural healing abilities in their bodies. By boosting angiogenesis and lowering inflammation in diabetic wounds, MSC-based treatments hold considerable promise for improving outcomes and quality of life for diabetics [43].
- **Tissue Engineering:** Tissue engineering is an innovative field that creates tissue substitutes that operate similarly to genuine tissues by combining different components such as biomaterials, cells, and bioactive chemicals. Scaffold-based methods with biomaterials that can simulate the ECM appear to be very promising for diabetic wound healing. To promote cell proliferation and tissue regeneration in diabetic wounds, tissue-engineered skin replacements have been specially created. Using the most recent developments in tissue engineering, scientists hope to produce highly functional tissue replacements that will greatly enhance the quality of life for people with diabetes [44].
- **Regenerative Medicine:** The goal of the rapidly expanding field of regenerative medicine is to create novel treatments that can replace, regenerate, or repair diseased or damaged tissues. This calls for the application of several innovative approaches, including tissue engineering, molecular methods, and cell-based therapies. Using exosomes and microRNAs to alter the wound-healing process is one of the most exciting research directions. These microscopic molecules are perfect for treating diabetic wounds because they can affect cell behavior and stimulate the formation of new tissue. Scientists intend to create more potent remedies for a variety of illnesses by utilizing the potential of regenerative medicine [45].
- Novel approaches are being developed to improve the healing of wounds in people with diabetes. To verify their efficacy and safety, advanced medicines are being investigated and evaluated.

Future Technology Possibilities, Including 3D Printing and Smart Dressing

Emerging technologies like smart dressings and 3D printing show a lot of potential for improving diabetic wound healing. These breakthroughs have the potential to greatly enhance patient outcomes and shorten recovery timeframes.

Smart Dressings

Smart dressings are a new form of wound dressing that includes modern technology for wound treatment. These dressings are designed to give a real-time monitoring and control system, allowing the wound to heal faster and more efficiently. They are equipped with sensors that can measure parameters like as pH, temperature, bacterial presence, and moisture levels in the wound region. Based on these measurements, smart dressings can either release drugs to encourage healing or change the wound environment to enhance the healing process.

Smart dressings are especially effective for diabetics in controlling wounds that are prone to infection and delayed healing. Smart dressings can help to improve the healing process and reduce the risk of complications by providing an optimum wound environment and prompt intervention if necessary [46].

3D Printing

Diabetes wound healing is a challenging procedure that necessitates individualized care. 3D printing technology provides a viable answer by enabling the fabrication of biomaterials that may be adjusted to the unique needs of the wound. These biomaterials act as a scaffold or framework for cells to adhere, develop, and differentiate. Researchers can add growth factors and stem cells into biomaterials using 3D printing technology to improve tissue regeneration. Furthermore, advances in 3D printing have resulted in the development of skin substitutes and tissue-engineered constructions capable of replacing injured tissue more efficiently and precisely. This tailored approach to diabetic wound healing has the potential to improve patient outcomes and speed wound closure [47].

Role of Infection and Antibiotics

The Impact of Infections on Diabetic Wound Healing

Wound healing can be severely impacted by diabetes, and infections can make the problem worse. A diabetic's body may be less able to repair wounds, and healing may take longer if the wound is infected. To encourage the best possible wound healing, infections in diabetics must be managed.

Because diabetes causes infections, wounds can heal more slowly than other types of wounds. Patients with diabetes have elevated blood sugar levels, which allows these infections to flourish and impede the body's natural healing process, leading to improper wound healing. Because of this, diabetic individuals can need more medical care to control their wounds and stop subsequent problems, which could prolong their healing period [48].

A diabetic who has an infected wound runs a higher chance of developing catastrophic complications from it. The wound's surrounding tissues may sustain significant damage because of these complications, and in extreme situations, amputation may be necessary. To prevent these consequences, it is imperative that you get medical help as soon as possible if you have diabetes and an infection [49].

Infections can result in chronic inflammation, a persistent kind of inflammation that develops in people with diabetes who have wounds. Because it interferes with the body's natural processes for mending tissue, this kind of inflammation can significantly slow down the healing process [50].

Angiogenesis is the process by which the body forms new blood vessels in the injured area in response to a wound. Infections, on the other hand, have the potential to impede this process and lower blood flow to the wound site. This may seriously hinder tissue regeneration and lengthen the healing period, resulting in more issues [26,50].

Diabetic patients may have weakened immunological responses. They might therefore find it difficult to fend against illnesses. This may result in a concerning cycle in which the infection continues and obstructs the healing process of the wound, so making the

problem worse [48].

Diabetes-related wounds are more prone to infections, which can seriously impede the healing process. These infections frequently lead to additional problems, a slower rate of healing, and a higher likelihood of negative outcomes. Consequently, it is essential to take the right actions to treat and prevent infections in diabetic wounds.

The Use of Antibiotics and Antimicrobial Agents in Managing Infected Diabetic Wounds

Patients with diabetes are more likely to get bacterial infections, especially in their wounds. These infections have the potential to seriously injure the patient and swiftly worsen into a major consequence. Antibiotics must, therefore, be given as soon as possible to control these illnesses. The kind of bacteria in the wound and how susceptible they are to the medication are taken into consideration when prescribing antibiotics. This decision is crucial since it has an immediate impact on the treatment's efficacy. Physicians can stop the illness from spreading, speed up the healing process, and lower the chance of developing new problems by prescribing the appropriate antibiotics. Antibiotics are essential for diabetic patients' infection control [50].

Diabetes increases the likelihood of wounds taking longer to heal. These wounds have the potential to worsen and cause additional health problems. Antibiotic use is one method of avoiding these issues. Antibiotics aid in the prevention of infections that could aggravate wounds and spread to other parts of the body. This reduces the possibility that the infection may spread to nearby tissues or even the bloodstream, which in addition to hastening the healing process. Patients with diabetes may find it more difficult to heal from chronic wounds because of their heightened vulnerability to infections. To counter this, antimicrobial substances like silver, iodine, or honey have been added to wound dressings. By gradually releasing these substances into the wound site, they create a barrier that keeps dangerous bacteria and other microbes out. This constant release of antimicrobial agents contributes to the establishment of a sterile environment, which has the potential to hasten healing and encourage tissue regeneration. Antimicrobial dressings can generally help individuals with chronic wounds, particularly those who have diabetes, achieve better results [49,51].

The diabetes patients have a higher chance of getting infections from microbes that are resistant to drugs, which can be challenging to cure. Appropriate antibiotic treatment according to the resistance strains is essential to properly manage such infections and facilitate wound healing. This can necessitate the use of combination treatments or certain medicines that work well against the infection-causing bacteria [50].

It is essential to choose antibiotics and antimicrobial medicines carefully, considering the bacteria present in the lesion. Healthcare professionals can discover the best appropriate treatment plan that is successful against the identified microbes by performing a wound culture and identifying the pathogens. This individualized approach to care lowers the likelihood of antibiotic resistance while ensuring the best possible healing results [50].

Chronic wounds require continual, high-level care to promote healing and prevent recurrence infections. Antibiotic therapy, either prophylactic or long-term, is often necessary to facilitate the healing process. The sort and length of antibiotic treatment will depend on the nature and severity of the wound. It is critical to closely monitor the wound's progress and adjust the treatment approach as needed. With the correct care and attention, chronic wounds can eventually heal, allowing patients to return to their normal lives [50].

Infected diabetic wounds require the close supervision of antibiotics and antimicrobial medicines. They must be specifically designed for each patient to prevent infections, reduce problems, and speed healing. With patient history, comorbidities, and resistance as key considerations, healthcare practitioners must utilize clinical judgment to ensure safe and effective administration.

Patient-Centered Care and Education

Diabetes-Related Wound Prevention and Healing are made possible by Patient Education and Self-Management

The prevention of diabetic wounds and the acceleration of the healing process are largely dependent on patient education and self-management. Diabetes patients are more likely to get foot ulcers, which can be excruciating and challenging to cure. Preventative steps, however, can be done by teaching patients how to take care of their feet. The significance of routine checks to identify problems early, wearing suitable footwear to protect the feet, and maintaining excellent cleanliness to prevent infection are all emphasized in this instruction. Patients can maintain general foot health and dramatically lower their chance of developing diabetic foot ulcers by following these recommendations [52].

Controlling blood sugar levels is essential for general health, particularly in relation to the prevention and healing of wounds. It is crucial to teach patients the value of maintaining ideal blood sugar control through self-management. The chance of getting wounds is greatly decreased when blood sugar levels are kept within the advised range. Furthermore, appropriate blood sugar regulation speeds up wound healing and lowers the risk of complications [52].

Medication adherence is essential to the complicated work of managing diabetes. Patients' knowledge and comprehension of diabetes and available treatments can be greatly improved by education, which improves medication adherence. Thus, there is a decreased chance of complications and a faster rate of wound healing, both of which contribute to better diabetes management. Healthcare practitioners can assist patients in taking charge of their health and improving their quality of life by providing them with the appropriate information and skills [53].

Teaching high-risk patients about risk factors and self-care techniques can help prevent wounds in them, especially in diabetic patients. To prevent wounds, this entails developing a customized self-care strategy that includes foot care practices. People can take proactive measures to maintain their health and prevent ulcers by increasing awareness of risk factors and encouraging self-care planning [54].

A medical procedure called hyperbaric oxygen therapy includes breathing 100% oxygen in a pressured setting to boost the quantity of oxygen that reaches the body's tissues. Patients with diabetes may benefit most from this medication when it comes to the healing of chronic foot ulcers. Patients can be encouraged to pursue hyperbaric oxygen therapy and possibly experience accelerated ulcer healing by being informed about its advantages [36].

A key component of encouraging successful and long-lasting self-care activities is educating patients on the obstacles to and facilitators of self-management behaviors. Patients can make

decisions and take measures that result in better results and faster healing by knowing the elements that support or impede the implementation of self-management practices. This method of treating patients improves quality of life and lowers healthcare costs by empowering them to manage their own health and well-being actively [55].

The Responsibility of Medical Professionals to Instruct Patients about Wound Healing and Foot Care

Diabetes requires comprehensive care, including wound prevention and good foot hygiene, to be managed effectively. Healthcare professionals play a crucial role in providing patients with this education because they have the skills and knowledge required to guarantee that patients have the knowledge and resources, they need to avoid difficulties. Healthcare professionals are essential in teaching people the value of routinely checking their feet for indications of damage or infection, practicing appropriate foot cleanliness, and getting help right once if something is wrong. Healthcare professionals can guarantee that patients are empowered to take charge of their health and effectively manage their diabetes by giving them this crucial education.

A vital component of general health and wellness is education regarding foot care. When it comes to teaching patients the value of taking good care of their feet, healthcare providers are essential. This entails doing routine daily checks to spot any possible problems, maintaining clean, healthy feet through good hygiene habits, and wearing the proper footwear to avoid foot troubles like calluses, blisters, and infections. Healthcare providers can assist prevent major foot difficulties that can result in mobility issues and a lower quality of life by arming patients with the knowledge and resources they need to take care of their feet [56].

People can get professional guidance regarding how to take care of their feet in order to prevent problems. The guidelines emphasize variables that can negatively affect foot health in addition to providing appropriate self-care strategies that support and sustain foot health. This all-encompassing strategy seeks to assist people in identifying and reducing hazards, maintaining long-term foot health, and averting further issues [57].

Increasing patients' health literacy is a major responsibility of healthcare professionals. Healthcare practitioners can prevent foot ulcers and promote wound healing by teaching patients about the significance of maintaining normal blood sugar levels. Providing comprehensive guidance on controlling blood sugar levels through a balanced diet and consistent exercise is one way to do this. To empower people to take charge of their health and avoid major difficulties, healthcare providers should actively promote health literacy [58].

Preventing foot problems and complications requires routine foot exams. Patients can identify any early indications of soreness, edema, or discoloration by routinely inspecting their feet. This will enable them to seek medical attention as soon as possible, halting the progression of the problem. Patients can avoid long-term issues and make sure their feet remain pain-free and healthy by adopting a proactive approach to foot health [59].

To provide effective foot care, patients, their families, and other medical professionals must all be educated. A thorough awareness of foot care and prevention can be attained by involving family members and healthcare professionals in the educational process. This will improve health outcomes and general well-being [60].

Challenges and Future Directions

The Challenges and Limitations in Current Diabetic Wound Healing Strategies

Diabetes is a long-term condition that impairs the healing of wounds. The process of wound healing is difficult in diabetes individuals and poses several obstacles to successful therapy. Elevated blood sugar levels have the potential to harm nearby blood vessels, neurons, and cells. This damage can result in compromised immunological function, decreased sensitivity, and poor circulation all of which can impede the healing of wounds. Achieving the best results in the treatment of diabetic wounds may be challenging due to these constraints.

Patients with diabetes who experience chronic hyperglycemia run the risk of damaging their blood vessels and preventing the growth of new blood vessels, which are vital for the healing of wounds. Diabetes-related wounds therefore have a propensity to heal slowly and can result in consequences like infection and amputation. Diabetic patients' quality of life can be greatly diminished by this prolonged healing process, which emphasizes the significance of appropriate diabetes control and wound care [26].

Individuals suffering from diabetes mellitus are more susceptible to infections due to a compromised immune system. Because of their heightened vulnerability to infections, diabetes patients have an increased risk of serious consequences including sepsis and gangrene, which can exacerbate the already difficult process of wound healing [61].

Patients with diabetes are frequently reported to have hypo-immunity, a disorder that impairs the response of the immune system. Further delaying the healing process, this compromised reaction may make it more difficult for the body to fight infections that arise at the site of a wound [61].

Diabetes-related foot ulcers are an example of a chronic wound that can be difficult to maintain and heal. These wounds can be frustrating for both patients and healthcare professionals since they need ongoing care and may take a while to heal fully. Despite the difficulties, it is critical to keep administering efficient care to increase the likelihood of full recovery and stop more issues [62].

Diabetic foot ulcers are extremely prone to worsening due to their compromised healing capabilities, which can lead to serious complications for patients. The restricted regeneration potential of the wounds makes the healing process even more difficult. Therefore, to avoid any potential problems, diabetic foot ulcers need to be carefully and consistently monitored [63].

Treating diabetic wounds can be difficult, particularly when they are accompanied by long-term conditions like diabetes. This is because the interaction of multiple illness variables makes the healing process more difficult (64).

The lack of dependable animal models that can accurately mimic the pathophysiology of diabetic wounds is impeding the advancement of research on diabetic wound healing. Because of the inconsistent use of animal models, the problem is not well understood, which makes it difficult to create efficient treatments [65].

The Possible Paths for Future Study, Including Areas that

Could Use Innovation and Enhancement

To enhance the diabetic wound healing, researchers should investigate a range of cutting-edge and better wound care techniques. Advanced wound dressings, fresh approaches to tissue regeneration and debridement, cutting-edge drug delivery strategies, and individualized therapy regimens based on patient-specific variables are a few possible areas of concentration. Researchers can improve the care of diabetic wounds and ultimately improve patients' quality of life by looking into and enhancing these areas.

Wound healing and tissue regeneration could be transformed by two rapidly emerging research fields: advanced biomaterials and nanotechnology. Researchers want to create innovative solutions that help speed up the healing process, reduce infections, and improve patient outcomes overall. To this end, they apply state-of-the-art technology and materials. Cutting-edge wound dressings or medication delivery methods created specially to encourage tissue regeneration and lessen scarring might be examples of these treatments. Through further investigation and advancement, biomaterials and nanotechnology provide countless opportunities to enhance tissue regeneration and wound healing [26].

Diabetes Patients frequently experience compromised immune systems, which impairs the healing of wounds. Researchers are looking at immunomodulation techniques that can improve these people's immune responses to solve this problem. By employing such techniques, researchers hope to enhance the wound-healing process and, in turn, the quality of life for individuals with diabetes [61].

Personalized medicine and precision diagnostics have transformed wound care techniques by giving enhanced diagnostic tools that enable healthcare practitioners to build individualized treatment plans based on the patient's unique profile. Healthcare practitioners can give a customized strategy that helps to maximize the healing process and minimize the risk of complications by taking the patient's genetics, comorbidities, and other pertinent factors into account. This technique is a considerable divergence from the typical one-size-fits-all approach to wound treatment and has the potential to enhance patient outcomes significantly [66].

A deeper understanding of the intricate mechanisms governing diabetic wound healing can be attained through the fascinating field of bioinformatics and computational modeling. Researchers may examine enormous quantities of data and build complex models that can help forecast wound healing trajectories and design more successful treatment regimens by utilizing strong computational tools and methodologies. By using this method, we can gain a fresh understanding of the biology underlying diabetic wound healing and strive toward providing patients with more individualized and effective care [26].

The way patients receive care has been completely transformed by telemedicine and remote monitoring technology. Healthcare professionals can diagnose, treat, and monitor patients at a distance via telemedicine, and remote monitoring technologies allow for ongoing observation of wounds, vital signs, and other health indicators. Better patient outcomes have resulted from healthcare providers' ability to act quickly, when necessary, thanks to this technology. Furthermore, by giving patients immediate feedback and support, remote monitoring systems have improved patient compliance with treatment plans. In general, telemedicine and remote monitoring technologies have changed the healthcare environment, making it more patient-centered, comfortable, and accessible [63].

Wound healing procedures, patient involvement and education are essential. Patients can actively participate in their own recovery process and follow recommended treatment plans by receiving information and skills related to wound management, self-care, and prevention efforts. This method improves overall results and gives patients more power, which promotes faster wound healing and higher quality of life [63].

Conclusion

Research on diabetic wound healing is extremely important for improving patient outcomes. Efficient wound healing techniques can speed up the healing process, shortening the amount of time a patient must live with a chronic wound, relieving pain, and lowering the chance of complications like infections. Effective wound healing can dramatically save healthcare expenditures for people as well as the healthcare system by averting serious complications such as infections, gangrene, and amputations. It can maintain or enhance limb functionality and mobility, which is essential for diabetic patients' everyday activities and has a favorable impact on their independence and general well-being. Mental health may be impacted by emotional discomfort brought on by chronic wounds. Effective wound healing, however, can lessen the emotional toll that having a persistent wound and worrying about problems getting worse takes on patients. This helps patients feel less stressed, anxious, and depressed. Effective wound healing also helps to minimize systemic issues linked to chronic wounds and maintain long-term health. Diabetic people can potentially prolong their life expectancy and preserve improved overall health by swiftly and efficiently tending to wounds [67,68].

References

1. Chapple ILC, Genco R (2013) Diabetes and periodontal diseases: consensus report of the Joint EFP/AAP Workshop on Periodontitis and Systemic Diseases. J Clin Periodontol 84: 106-112.
2. Gan D, King H, Lefèbvre P, Mbanya JC, Silink M, et al. (2023) Diabetes Atlas Second Edition. www.idf.org.
3. Falanga V (2005) Wound healing and its impairment in the diabetic foot. The Lancet 366: 1736-1743.
4. Hinz B (2016) The role of myofibroblasts in wound healing. Curr Res Transl Med 64: 171-177.
5. Hinz B, Lagares D (2020) Evasion of apoptosis by myofibroblasts: a hallmark of fibrotic diseases. Nat Rev Rheumatol 16: 11-31.
6. Hinz B, Phan SH, Thannickal VJ, Prunotto M, Desmoulière A, et al. (2012) Recent Developments in Myofibroblast Biology. Am J Pathol 180: 1340-1355.
7. Hinz B, Phan SH, Thannickal VJ, Galli A, Bochaton-Piallat ML, et al. (2007) The Myofibroblast. Am J Pathol 170: 1807-1816.
8. Wan R, Weissman JP, Grundman K, Lang L, Grybowski DJ, et al. (2021) Diabetic wound healing: The impact of diabetes on myofibroblast activity and its potential therapeutic treatments. Wound Repair and Regeneration 29: 573-581.
9. Geetha BS, Nair MS, Latha PG, Remani P (2012) Sesquiterpene Lactones Isolated from Elephantopus scaber L. Inhibits Human Lymphocyte Proliferation and the Growth of Tumour Cell Lines and Induces Apoptosis In Vitro. J Biomed Biotechnol 2012: 1-8.
10. Meng H, Ren X, Tian Y, Feng X, Xu L, et al. (2000) Genetic study of families affected with aggressive periodontitis.

Periodontol 56: 87-101.

11. Nichols LS, Eagerton G, Bordelon C (2020) Promoting Sustainable Nursing Leadership: The Nightingale Legacy. Creat Nurs 26: 272-276.
12. Breki CM, Dimitrakopoulou-Strauss A, Hassel J, Theoharis T, Sachpekidis C, et al. (2016) Fractal and multifractal analysis of PET/CT images of metastatic melanoma before and after treatment with ipilimumab. EJNMMI Res 6: 61.
13. Bryant C, Fischer M, Linz S, Semple C (2017) On the quirks of maximum parsimony and likelihood on phylogenetic networks. J Theor Biol 417: 100-108.
14. Lin L, Li R, Cai M, Huang J, Huang W, et al. (2018) Andrographolide Ameliorates Liver Fibrosis in Mice: Involvement of TLR4/NF- κ B and TGF- β 1/Smad2 Signaling Pathways. Oxid Med Cell Longev 2018: 1-11.
15. Yang X, Wang Z, Guo L, Zhu Z, Zhang Y (2017) Proteome-Wide Analysis of N-Glycosylation Stoichiometry Using SWATH Technology. J Proteome Res 16: 3830-3840.
16. Leathers SJ, Falconnier L, Spielfogel JE (2010) Predicting family reunification, adoption, and subsidized guardianship among adolescents in foster care. American Journal of Orthopsychiatry 80: 422-431.
17. Johnson L, Bhutani VK (2011) The Clinical Syndrome of Bilirubin-Induced Neurologic Dysfunction. Semin Perinatol 35: 101-113.
18. Estrozi LF, Boehringer D, Shan S ou, Ban N, Schaffitzel C (2011) Cryo-EM structure of the E. coli translating ribosome in complex with SRP and its receptor. Nat Struct Mol Biol 18: 88-90.
19. Eming SA, Krieg T, Davidson JM (2007) Inflammation in Wound Repair: Molecular and Cellular Mechanisms. Journal of Investigative Dermatology 127: 514-525.
20. Gonzalez AC de O, Costa TF, Andrade Z de A, Medrado ARAP (2016) Wound healing - A literature review. An Bras Dermatol 91: 614-620.
21. Velnar T, Bailey T, Smrkolj V (2009) The Wound Healing Process: An Overview of the Cellular and Molecular Mechanisms. Journal of International Medical Research 37: 1528-1542.
22. Li H, Cheng F, Wu G, Tyavambiza C, Meyer M, et al. (2022) Cellular and Molecular Events of Wound Healing and the Potential of Silver Based Nanoformulations as Wound Healing Agents. Bioengineering 9: 712.
23. Wallace HA, Basehore BM, Zito PM (2023) Wound Healing Phases. StatPearls https://www.ncbi.nlm.nih.gov/books/NBK470443/.
24. Diabetes and wound healing: Causes, complications, and prevention https://www.medicalnewstoday.com/articles/320739.
25. Chakraborty R, Borah P, Dutta PP, Sen S (2022) Evolving spectrum of diabetic wound: Mechanistic insights and therapeutic targets. World J Diabetes 13: 696-716.
26. Burgess JL, Wyant WA, Abdo Abujamra B, Kirsner RS, Jozic I (2021) Diabetic Wound-Healing Science. Medicina (B Aires) 57: 1072.
27. Baltzis D, Eleftheriadou I, Veves A (2014) Pathogenesis and Treatment of Impaired Wound Healing in Diabetes Mellitus: New Insights. Adv Ther 31: 817-836.
28. Ji JY, Ren DY, Weng YZ (2022) Efficiency of Multifunctional Antibacterial Hydrogels for Chronic Wound Healing in Diabetes: A Comprehensive Review. Int J Nanomedicine 17: 3163-3176.
29. Goulding V (2015) The effects of diabetes on collagen within wound healing. The Diabetic Foot Journal 18: 75-80.
30. Everett E, Mathioudakis N (2018) Update on management of diabetic foot ulcers. Ann N Y Acad Sci 1411: 153-165.
31. Medscape Registration (2023) https://emedicine.medscape.com/article/460282-treatment?form=fpf.
32. Hingorani A, La Muraglia GM, Henke P, Meissner MH, Loretz L, et al. (2016) The management of diabetic foot: A clinical practice guideline by the Society for Vascular Surgery in collaboration with the American Podiatric Medical Association and the Society for Vascular Medicine. J Vasc Surg 63: 3-21.
33. Kavitha KV (2014) Choice of wound care in diabetic foot ulcer: A practical approach. World J Diabetes 5: 546-556.
34. Steed DL, Attinger C, Colaizzi T, Crossland M, Franz M, et al. (2006) Guidelines for the treatment of diabetic ulcers. Wound Repair and Regeneration 14: 680-692.
35. Yadav AK, Mishra S, Khanna V, Panchal S, Modi N, et al. (2023) Comparative study of various dressing techniques in diabetic foot ulcers in the Indian population: a single-center experience. Int J Diabetes Dev Ctries 43: 647-653.
36. Yazdanpanah L (2015) Literature review on the management of diabetic foot ulcer. World J Diabetes 6: 37-53.
37. Oyebode OA, Jere SW, Houreld NN (2023) Current Therapeutic Modalities for the Management of Chronic Diabetic Wounds of the Foot. J Diabetes Res 2023: 1-10.
38. Ezhilarasu H, Vishalli D, Dheen ST, Bay BH, Srinivasan DK (2020) Nanoparticle-Based Therapeutic Approach for Diabetic Wound Healing. Nanomaterials 10: 1234.
39. Sathyaraj WV, Prabakaran L, Bhoopathy J, Dharmalingam S, Karthikeyan R, et al. (2023) Therapeutic Efficacy of Polymeric Biomaterials in Treating Diabetic Wounds—An Upcoming Wound Healing Technology. Polymers (Basel) 15: 1205.
40. Ghosal K, Chakraborty D, Roychowdhury V, Ghosh S, Dutta S (2022) Recent Advancement of Functional Hydrogels toward Diabetic Wound Management. ACS Omega 7: 43364-43380.
41. Mulder G, Tenenhaus MD,Souza GF (2014) Reduction of Diabetic Foot Ulcer Healing Times Through Use of Advanced Treatment Modalities. Int J Low Extrem Wounds 13: 335-346.
42. Vas P, Rayman G, Dhatariya K, Driver V, Hartemann A, et al. (2020) Effectiveness of interventions to enhance healing of chronic foot ulcers in diabetes: a systematic review. Diabetes Metab Res Rev 1: 3284.
43. Buchert F, Hamon M, Gäbelein P, Scholz M, Hippler M, et al. (2018) The labile interactions of cyclic electron flow effector proteins. Journal of Biological Chemistry 293: 17559-17573.
44. Shi M, Kumar SR, Motajo O, Kretschmer F, Mu X, et al. (2013) Genetic Interactions between Brn3 Transcription Factors in Retinal Ganglion Cell Type Specification. PLoS One 8: 76347.
45. Khan SU, Ahemad N, Chuah LH, Naidu R, Htar TT (2022) G protein-coupled estrogen receptor-1: homology modeling approaches and application in screening new GPER-1 modulators. J Biomol Struct Dyn 40: 3325-3335.
46. Fu T, Stupnitskaia P, Matoori S (2022) Next-Generation Diagnostic Wound Dressings for Diabetic Wounds. ACS Measurement Science Au 2: 377-384.
47. De La Maza C, Davis A, Gonzalez C, Azevedo I (2019) Understanding Cumulative Risk Perception from Judgments and Choices: An Application to Flood Risks. Risk Analysis 39: 488-504.
48. Patel S, Srivastava S, Singh MR, Singh D (2019) Mechanistic insight into diabetic wounds: Pathogenesis, molecular targets and treatment strategies to pace wound healing. Biomedicine & Pharmacotherapy 112: 108615.

49. Jiang P, Li Q, Luo Y, Luo F, Che Q, et al. (2023) Current status and progress in research on dressing management for diabetic foot ulcer. Front Endocrinol (Lausanne) 14: 1221705
50. Chang M, Nguyen TT (2021) Strategy for Treatment of Infected Diabetic Foot Ulcers. Acc Chem Res 54: 1080-1093.
51. Zhang J, Liu H, Che T, Zheng Y, Nan X, et al. (2023) Nanomaterials for diabetic wound healing: Visualization and bibliometric analysis from 2011 to 2021. Front Endocrinol (Lausanne) 14: 1124027.
52. Understanding Diabetic Wounds: Causes Treatment and Prevention (2023) https://www.medanta.org/patient-education-blog/everything-you-need-to-know-about-diabetic-foot-wounds.
53. Lim JZM, Ng NSL, Thomas C (2017) Prevention and treatment of diabetic foot ulcers. J R Soc Med 110: 104-109.
54. Astasio-Picado Á, Cobos-Moreno P, Gómez-Martín B (2021) Self-Care Planning and Sanitary Education in the Prevention of the Diabetic Foot. Applied Sciences 11: 7281.
55. Zhu X, Lee ES, Lim PXH, Chen YC, Chan FHF, et al. (2023) Exploring barriers and enablers of self-management behaviours in patients with diabetic foot ulcers: A qualitative study from the perceptions of patients, caregivers, and healthcare professionals in primary care. Int Wound J 20: 2764-2779.
56. Aalaa M, Malazy OT, Sanjari M, Peimani M, Mohajeri-Tehrani M. (2012) Nurses' role in diabetic foot prevention and care; a review. J Diabetes Metab Disord 11: 24.
57. Green-Morris G The Aquila Digital Community an Evaluation of the Effectiveness of Providing Foot Care Education in a Rural Clinic Setting https://aquila.usm.edu/dnp_capstone.
58. Sonal Sekhar M, Unnikrishnan MK, Vijayanarayana K, Rodrigues GS (2019) Impact of patient-education on health related quality of life of diabetic foot ulcer patients: A randomized study. Clin Epidemiol Glob Health 7: 382-388.
59. Dorresteijn JA, Kriegsman DM, Assendelft WJ, Valk GD (2014) Patient education for preventing diabetic foot ulceration. Cochrane Database of Systematic Reviews 2014: CD001488.
60. Miranda C (2018) Therapeutic education patient in prevention of diabetic foot: a neglected opportunity. J Diabetes Metab Disord Control 5: 127-130.
61. Yang L, Rong GC, Wu QN (2022) Diabetic foot ulcer: Challenges and future. World J Diabetes 13: 1014-1034.
62. Frykberg RG, Banks J (2015) Challenges in the Treatment of Chronic Wounds. Adv Wound Care (New Rochelle) 4: 560-582.
63. Jeffcoate WJ, Vileikyte L, Boyko EJ, Armstrong DG, Boulton AJM (2018) Current Challenges and Opportunities in the Prevention and Management of Diabetic Foot Ulcers. Diabetes Care 41: 645-652.
64. Monika P, Chandraprabha MN, Rangarajan A, Waiker PV, Chidambara Murthy KN (2022) Challenges in Healing Wound: Role of Complementary and Alternative Medicine. Front Nutr 20: 8.
65. Sanapalli BKR, Yele V, Singh MK, Thaggikuppe Krishnamurthy P, Karri VVSR (2021) Preclinical models of diabetic wound healing: A critical review. Biomedicine & Pharmacotherapy. 142: 111946.
66. Perez-Favila A, Martinez-Fierro ML, Rodriguez-Lazalde JG, Cid-Baez MA, Zamudio-Osuna M de J, et al. (2019) Current Therapeutic Strategies in Diabetic Foot Ulcers. Medicina (B Aires) 55: 714.