

## Wound Healing in Diabetes: Challenges, Mechanisms, and Emerging Therapeutic Approaches

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**ABSTRACT:** Wound healing is a dynamic biological process involving a series of overlapping and highly regulated phases, including hemostasis, inflammation, proliferation, and tissue remodeling. In patients with diabetes mellitus, this process is significantly impaired, resulting in chronic wounds such as diabetic foot ulcers that are difficult to heal and highly susceptible to infection. The global prevalence of diabetes continues to rise, and with it, the incidence of chronic wounds, contributing to increased morbidity, mortality, and healthcare burden. Hyperglycemia, oxidative stress, neuropathy, vascular insufficiency, and impaired immune response are the key factors that compromise healing capacity in diabetic individuals. Conventional management strategies such as glycemic control, wound debridement, infection management, and dressings remain the mainstay of care, but they often fail to achieve complete wound closure. Recent advances in biotechnology and regenerative medicine, including growth factor therapy, stem cell therapy, skin substitutes, nanotechnology-based dressings, and gene therapy, hold promise for improving outcomes. This review article provides a comprehensive overview of the normal wound healing process, the pathophysiological alterations in diabetes, current clinical management, and novel therapeutic approaches aimed at enhancing wound repair in diabetic patients.

### KEYWORDS:

Diabetes mellitus, Diabetic wounds, Diabetic foot ulcers (DFUs), Impaired wound healing, Hyperglycemia, Advanced glycation end products (AGEs)

### I. INTRODUCTION

Diabetes mellitus is a chronic metabolic disorder characterized by hyperglycemia due to defects in insulin secretion, insulin action, or both [1].

The International Diabetes Federation (IDF) has reported that more than 540 million adults worldwide were living with diabetes in 2021, and the number is projected to rise significantly in the coming decades [2]. Among its many complications, impaired wound healing represents one of the most debilitating and challenging outcomes. Diabetic wounds, especially diabetic foot ulcers (DFUs), are associated with delayed closure, recurrent infections, and increased risk of lower limb amputation. It is estimated that up to 25% of individuals with diabetes will develop a foot ulcer during their lifetime, and nearly 50% of these ulcers become infected, leading to further complications [3]. The process of wound healing is typically efficient in healthy individuals. However, in diabetes, the interplay of hyperglycemia-induced molecular changes, microvascular dysfunction, neuropathy, and impaired immune responses significantly disrupts normal tissue repair [4]. These factors not only prolong healing time but also predispose wounds to chronic inflammation, biofilm formation, and recurrent infections [5]. From a clinical perspective, diabetic wounds pose substantial economic and social burdens. Prolonged hospital stays, frequent dressing changes, antibiotic therapy, and surgical interventions contribute to rising healthcare costs [6]. Moreover, the psychological impact of chronic wounds such as pain, reduced mobility, and social isolation further diminishes quality of life in affected patients [7]. In recent years, intensive research has been directed toward understanding the molecular mechanisms underlying impaired wound healing in diabetes. Simultaneously, novel therapeutic strategies, such as regenerative medicine, nanotechnology, and growth factor delivery systems, have shown promising outcomes in preclinical and clinical studies [8]. However, the translation of these therapies into routine clinical practice remains limited due to cost, safety concerns, and regulatory challenges [9].

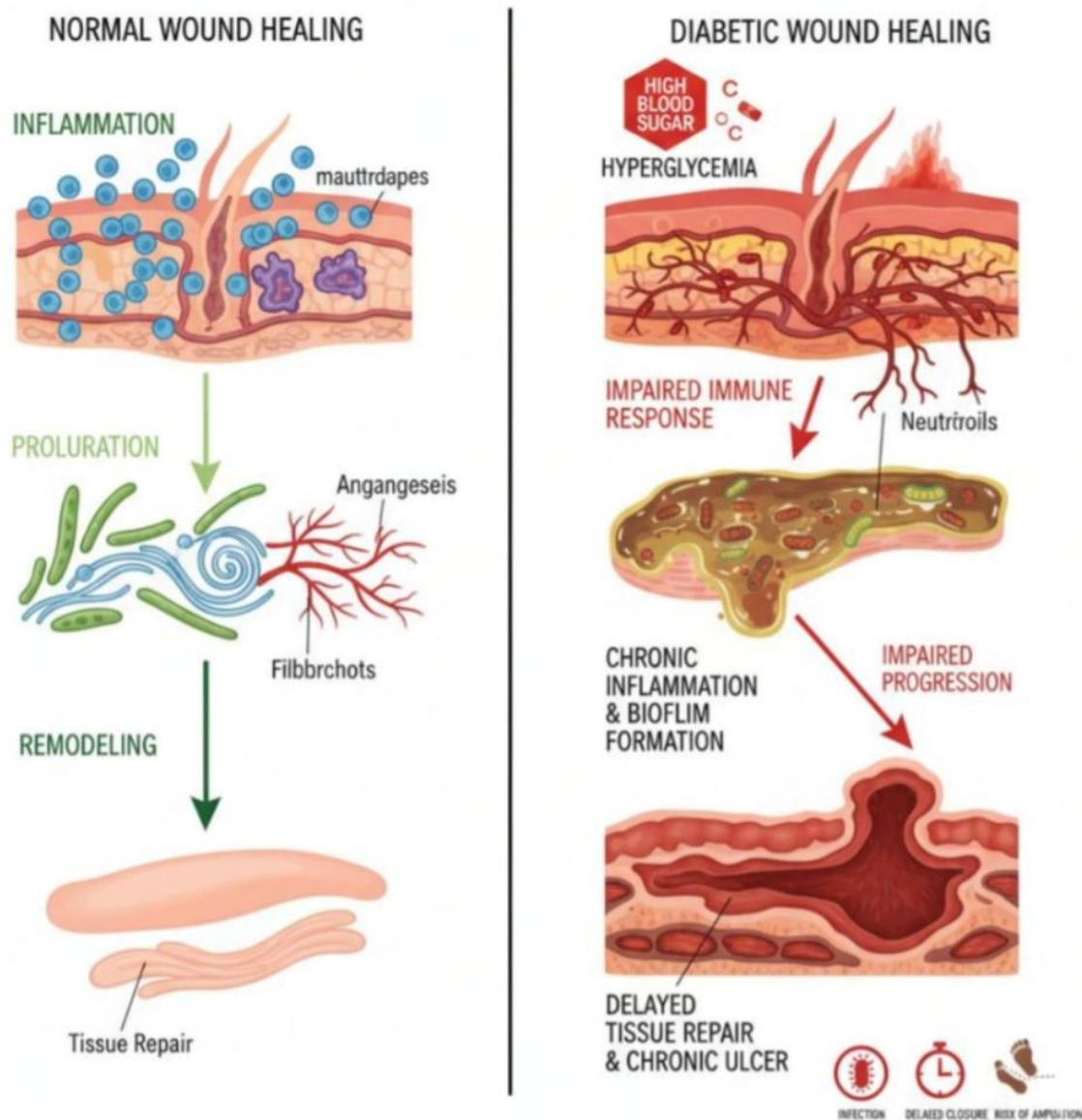


Figure 1: Normal Wound Healing Vs Diabetic Wound Healing

The objective of this review is to present a detailed overview of wound healing in diabetes by

Discussing:

1. The physiological phases of wound healing.
2. The pathophysiological mechanisms responsible for delayed healing in diabetes.
3. The clinical presentation of diabetic wounds.
4. Conventional treatment options and their limitations.
5. Advanced and emerging therapeutic strategies.

6. Future perspectives and challenges in improving diabetic wound healing.
7. By compiling the latest knowledge in this field, this review aims to highlight the critical gaps
8. In current management practices and identify potential directions for future research and Therapeutic innovations [10].

## II. Normal Wound Healing Process

Wound healing is a highly coordinated and complex physiological response to tissue injury. It involves a sequence of overlapping yet distinct phases: hemostasis, inflammation, Proliferation, and remodeling (or maturation) that restore the integrity and function of Damaged tissue [11]. Each phase is orchestrated by the interaction of various cell types, Extracellular matrix (ECM) components, growth factors, and signaling molecules. The Successful completion of these stages is essential for timely wound closure, and disturbances In any phase may lead to chronic or non-healing wounds [12].

### 2.1 Hemostasis Phase

The first and most immediate response to tissue injury is hemostasis. Within minutes of Vascular injury, platelets aggregate at the wound site, forming a temporary clot to stop bleeding [13]. Activated platelets release a variety of bioactive molecules, such as platelet-derived Growth factor (PDGF), vascular endothelial growth factor (VEGF), and transforming growth Factor-beta (TGF- $\beta$ ), which not only reinforce clot formation but also recruit immune cells to The wound bed [14]. The fibrin matrix generated during this phase provides the initial scaffold For cellular migration and serves as a provisional ECM [15].

### 2.2 Inflammatory Phase

Following clot formation, the inflammatory phase begins and typically lasts for 48–96 hours. Neutrophils are the first immune cells to infiltrate the wound, where they play a critical role in Clearing debris, pathogens, and necrotic tissue [16]. They secrete proteolytic enzymes and Reactive oxygen species (ROS) to combat infection. Subsequently, monocytes migrate to the Wound site and differentiate into macrophages, which are essential for regulating the transition From inflammation to repair [17]. Macrophages exhibit functional plasticity, with the Proinflammatory M1 phenotype promoting pathogen clearance and the anti-inflammatory M2 Phenotype supporting tissue repair [18]. An appropriate balance between these

phenotypes is Crucial for successful wound healing. Dysregulation at this stage may prolong inflammation And delay subsequent repair phases [19].

### 2.3 Proliferative Phase

The proliferative phase generally occurs from day 4 to day 21 post-injury. During this stage, Fibroblasts, keratinocytes, and endothelial cells dominate the wound environment. Fibroblasts Are recruited to the wound site, where they synthesize collagen, fibronectin, and Glycosaminoglycans that form the granulation tissue [20]. Angiogenesis, driven largely by VEGF and fibroblast growth factor (FGF), is a hallmark of this phase and ensures adequate Oxygen and nutrient supply to the regenerating tissue [21]. Simultaneously, keratinocytes at the Wound edges undergo proliferation and migration to re-epithelialize the wound surface [22]. The cross-talk between fibroblasts, keratinocytes, and endothelial cells is mediated by multiple Signaling pathways, including PI3K/AKT, MAPK, and Wnt/ $\beta$ -catenin, all of which are Essential for tissue regeneration [23].

### 2.3 Remodeling (Maturation) Phase

The final stage of wound healing, known as the remodeling or maturation phase, can last for Weeks to months depending on the extent of the injury. During this stage, granulation tissue is Remodeled into scar tissue, characterized by a more organized collagen network and reduced Vascularity [24]. Fibroblasts differentiate into myofibroblasts, which generate contractile forces That facilitate wound contraction [25]. Collagen type III, initially deposited during the proliferative phase, is gradually replaced by the stronger type I collagen, thereby enhancing Tensile strength [26]. Matrix metalloproteinases (MMPs) and tissue inhibitors of Metalloproteinases (TIMPs) regulate ECM turnover to maintain balance between degradation And synthesis [27]. Although the wound achieves closure, the remodeled tissue rarely attains The full strength and function of uninjured skin [28].

### III. Pathophysiology of Impaired Wound Healing in Diabetes

In diabetes mellitus, the normal and highly coordinated process of wound healing is disrupted

By a variety of metabolic, vascular, and immunological abnormalities. Hyperglycemia-induced biochemical changes alter cellular signaling, impair growth factor activity, and lead to persistent inflammation, resulting in chronic non-healing wounds [32]. The following mechanisms collectively contribute to the impaired wound healing observed in diabetic patients.

#### 3.2 Oxidative Stress and Reactive Oxygen Species (ROS)

In diabetic wounds, hyperglycemia enhances mitochondrial superoxide production and activates NADPH oxidase, leading to elevated levels of ROS [38]. While moderate ROS levels are beneficial for cell signaling and pathogen clearance, excessive ROS induces oxidative damage to DNA, proteins, and

lipids [39]. This oxidative stress impairs angiogenesis, disrupts fibroblast function, and promotes apoptosis of keratinocytes [40]. Moreover, ROS inactivates nitric oxide (NO), reducing vasodilation and further limiting blood flow to the wound [41].

#### 3.3 Chronic Inflammation and Immune Dysfunction

Diabetic wounds are characterized by prolonged and dysregulated inflammation. Neutrophils remain excessively activated and release proteases and ROS that damage healthy tissue [42]. Macrophage polarization is impaired, with a predominance of pro-inflammatory M1 macrophages and insufficient transition to the pro-healing M2 phenotype [43]. This imbalance prevents the resolution of inflammation and reduces secretion of repair-promoting cytokines like IL-10 and TGF- $\beta$  [44]. Additionally, impaired chemotaxis and phagocytic activity of immune cells compromise bacterial clearance, leading to recurrent infections [45].

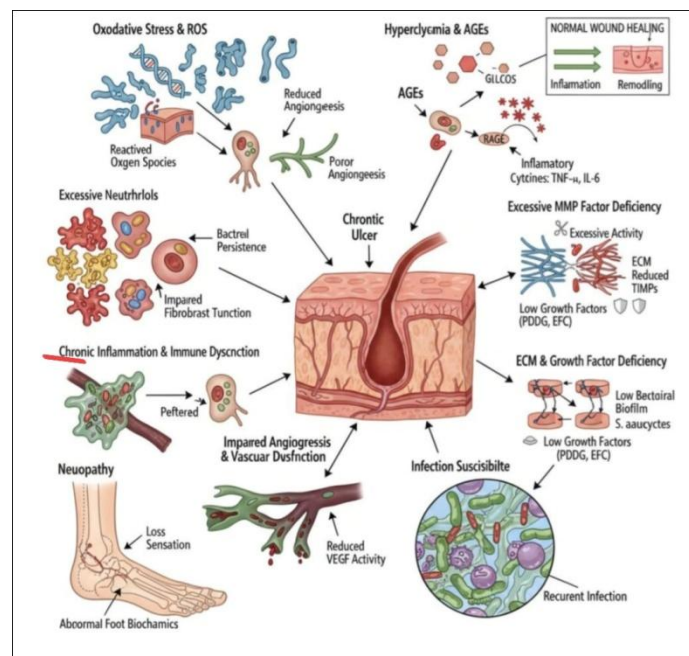


Figure 2: Pathophysiological mechanisms contributing to impaired wound healing in diabetes.

#### 3.4 Impaired Angiogenesis and Vascular Dysfunction

Adequate angiogenesis is essential for supplying oxygen and nutrients to regenerating

tissue. In diabetes, endothelial cell dysfunction and reduced expression of angiogenic factors such as VEGF impair new blood vessel formation [46]. Capillaries in diabetic wounds are often leaky and structurally abnormal, further limiting tissue

perfusion [47]. Peripheral arterial disease, Which commonly coexists with diabetes, exacerbates ischemia at wound sites and contributes To poor healing outcomes [48].

### 3.5 Neuropathy and Loss of Protective Sensation

Peripheral neuropathy is one of the most common complications of diabetes, affecting up to 50% of long-term patients [49]. Sensory neuropathy reduces the perception of pain and Pressure, making patients more prone to unnoticed injuries, repetitive trauma, and ulcer Formation [50]. Autonomic neuropathy further compromises wound healing by impairing sweat Gland function, leading to dry and cracked skin that is vulnerable to infection [51]. In addition, Motor neuropathy alters foot biomechanics, increasing the risk of pressure points and chronic Ulcers [52].

#### 3.6 Infection Susceptibility

Diabetic wounds have a high risk of infection due to impaired immune defenses.

Hyperglycemia promotes bacterial growth by providing a nutrient-rich environment [53]. Neutrophil dysfunction, impaired phagocytosis, and reduced cytokine response make it Difficult for the host to eliminate pathogens [54]. The presence of bacterial biofilms, Particularly by *Staphylococcus aureus* and *Pseudomonas aeruginosa*, further delays healing by Creating a persistent inflammatory environment and resisting antibiotic therapy [55]. Infected Diabetic wounds often progress to osteomyelitis or systemic sepsis if not managed Appropriately [56].

### 3.7 Extracellular Matrix (ECM) and Growth Factor Deficiency

The diabetic wound microenvironment is characterized by excessive degradation of ECM Components due to overexpression of matrix metalloproteinases (MMPs) and reduced activity of tissue inhibitors of metalloproteinases (TIMPs) [57]. This imbalance prevents the formation Of stable granulation tissue. Moreover, growth factors such as PDGF, VEGF, and EGF are either deficient or functionally impaired in diabetic wounds, leading to reduced fibroblast Proliferation, angiogenesis, and keratinocyte migration [58].

### 3.8 chronic Summary of Pathophysiology

The interplay of hyperglycemia, oxidative stress,

vascular dysfunction, neuropathy, and Immune impairment creates a hostile wound environment in diabetes. Instead of progressing Smoothly through the stages of healing, diabetic wounds remain trapped in a cycle of chronic Inflammation, poor angiogenesis, and repeated infection [59]. This multifactorial pathology Highlights the need for comprehensive management strategies that address both systemic Metabolic control and local wound care.

## IV. Clinical Manifestations of Impaired Wound Healing in Diabetes

The clinical presentation of impaired wound healing in diabetes is diverse, ranging from Delayed closure of minor cuts to severe chronic ulcers that may necessitate limb amputation. Among these, diabetic foot ulcers (DFUs) represent the most common and devastating Complication. The manifestations are primarily a result of the combined effects of Hyperglycemia, neuropathy, ischemia, and infection [60].

### 4.1 Diabetic Foot Ulcers (DFUs)

DFUs are one of the most frequent chronic complications of diabetes and are estimated to affect 15–25% of patients during their lifetime [61]. They typically occur on weight-bearing areas of The foot, such as the plantar surface, metatarsal heads, and heel, due to repetitive trauma and Pressure points. Neuropathy reduces protective sensation, while peripheral arterial disease Limits blood supply, making these wounds highly susceptible to breakdown [62].

Clinically, DFUs present as deep, non-healing ulcers with surrounding callus formation. They May show necrotic tissue, purulent discharge, or exposed tendons and bones in advanced cases [63]. Chronic DFUs are often colonized by bacteria, particularly *Staphylococcus aureus* and *Pseudomonas aeruginosa*, which complicate healing and increase the risk of systemic infection [64].

### 4.2 Delayed Wound Closure

Minor wounds and surgical incisions in diabetic patients tend to heal slowly compared to Nondiabetic individuals. Delayed closure is attributed to impaired keratinocyte migration, Reduced fibroblast proliferation, and defective angiogenesis [65]. Even small injuries may Persist for weeks or months,

increasing the risk of secondary infection [66].

#### 4.3 Chronic Non-Healing Wounds

A hallmark of diabetic wound pathology is the development of chronic, non-healing wounds that remain stuck in the inflammatory phase of healing [67]. These wounds often exhibit excessive exudate, foul odor, slough, and biofilm formation, reflecting persistent infection and poor tissue regeneration. Non-healing wounds frequently require advanced interventions, including negative pressure wound therapy, skin grafts, or amputations [68].

#### 4.3 Risk of Amputation

Diabetic patients with chronic ulcers face a significantly higher risk of lower limb amputation. It is estimated that more than 80% of non-traumatic lower extremity amputations are associated with diabetes [69]. Once an amputation is performed, the prognosis remains poor, with five-year mortality rates approaching 50%, which is comparable to many cancers [70]. Early detection and aggressive management of DFUs are therefore critical to preventing amputation and reducing mortality [71].

#### 4.5 Secondary Complications

Chronic wounds in diabetic patients predispose them to several secondary complications, including cellulitis, osteomyelitis, and sepsis [72]. Infections can spread rapidly due to impaired immune function, often requiring hospitalization and intravenous antibiotic therapy [73]. Osteomyelitis, an infection of the underlying bone, is a common and severe complication of DFUs, associated with poor healing outcomes and increased risk of limb loss [74].

#### 4.4 Quality of Life and Psychosocial Impact

Beyond physical manifestations, diabetic wounds profoundly affect quality of life. Patients experience chronic pain, reduced mobility, and limitations in daily activities [75]. Social isolation, depression, and anxiety are common among individuals with chronic wounds, particularly when long-term hospitalization or repeated surgical interventions are required [76]. The financial burden of ongoing wound care, frequent dressing changes, and hospital visits adds to the psychosocial stress of affected individuals and their families [77].

#### 4.7 Summary of Clinical Manifestations

In summary, diabetic wounds range from minor delayed-healing injuries to severe chronic ulcers with life-threatening complications. DFUs represent the most critical clinical manifestation, often leading to infections, osteomyelitis, and amputations. The combination of physiological impairments and clinical outcomes underscores the urgent need for effective management and innovative therapeutic approaches to reduce morbidity and mortality in

diabetic patients [78].

### V. Conventional Treatment Approaches for Diabetic Wounds

The management of diabetic wounds relies heavily on conventional therapeutic strategies that

target both systemic metabolic control and local wound care. These approaches aim to reduce infection risk, promote granulation tissue formation, and prevent complications such as amputation. Although advances in biotechnology are emerging, conventional therapies remain the first line of treatment in most clinical settings [79].

#### 5.1 Glycemic Control

Strict glycemic control is a cornerstone of wound management in diabetes. Hyperglycemia impairs neutrophil activity, angiogenesis, and fibroblast proliferation, thereby delaying wound healing [80]. Clinical studies have demonstrated that maintaining hemoglobin A1c (HbA1c) levels below 7% significantly improves wound healing outcomes and reduces the risk of infection [81]. Both oral hypoglycemic agents and insulin therapy are employed, depending on the severity of diabetes and patient-specific needs [82]. Lifestyle modifications, including dietary regulation and exercise, also contribute to improved glucose control and better wound repair [83].

#### 5.2 Wound Care and Dressings

Appropriate wound care is critical for maintaining a moist environment that facilitates tissue regeneration. Conventional dressings include gauze, foam, hydrocolloids, alginates, and hydrogels, each selected based on wound characteristics such as exudate levels and presence of infection [84]. Moist wound healing has been shown to accelerate epithelialization and reduce scarring compared to dry wound environments [85]. Regular wound

cleaning with Sterile saline and application of protective dressings help reduce microbial contamination and Support granulation tissue development [86].

### 5.3 Debridement

Debridement is the removal of necrotic, infected, or non-viable tissue from the wound bed to Promote healing. It can be performed surgically, mechanically, enzymatically, or biologically Using maggot therapy [87]. Surgical debridement is considered the gold standard, particularly For extensive necrosis or infected ulcers, as it allows rapid removal of devitalized tissue [88]. Regular debridement not only reduces bacterial load but also stimulates angiogenesis and Growth factor release, creating a healthier wound bed [89].

### 5.4 Offloading and Pressure Relief

Mechanical stress on wounds, especially foot ulcers, delays healing by causing repetitive Trauma and ischemia. Offloading techniques such as total contact casting (TCC), removable Cast walkers, and specialized footwear are widely used to redistribute pressure and protect the Ulcer site [90]. Clinical studies have shown that TCC significantly improves healing rates of Diabetic foot ulcers compared to conventional dressings alone [91]. Patient adherence to Offloading interventions is crucial, as inconsistent use can reduce therapeutic benefits [92].

## VI. Advanced and Emerging Therapies for Diabetic Wound Healing

While conventional treatments remain the backbone of diabetic wound care, many patients fail To achieve complete healing due to persistent inflammation, impaired angiogenesis, and Microbial colonization. To address these challenges, several advanced and emerging therapies Have been developed that focus on molecular, cellular, and bioengineering strategies [104]. These therapies aim to accelerate tissue regeneration, reduce infection risk, and improve Longterm outcomes in diabetic patients.

### 6.1 Growth Factor Therapy

Growth factors play a central role in wound healing by regulating angiogenesis, fibroblast Migration, and extracellular matrix (ECM) remodeling. In diabetes, the impaired release of Growth factors such as vascular endothelial growth factor (VEGF) and

platelet-derived growth Factor (PDGF) contributes to delayed wound closure [105]. Recombinant human PDGF (becaplermin gel) has been approved for diabetic foot ulcers and Demonstrated improved granulation tissue formation and wound closure [106]. VEGF-based therapies and basic fibroblast growth factor (bFGF) formulations have also shown Promise in preclinical and clinical studies [107]. However, limited bioavailability and high cost remain major barriers to widespread application [108].

### 6.2 Stem Cell Therapy

Stem cell-based interventions have emerged as a promising option for chronic diabetic wounds. Mesenchymal stem cells (MSCs) derived from bone marrow, adipose tissue, or umbilical cord Possess angiogenic, anti-inflammatory, and regenerative properties [109].

Transplantation of MSCs enhances neovascularization and collagen deposition, leading to Faster wound closure [110]. Adipose-derived stem cells (ADSCs) are particularly attractive due to their ease of isolation And abundance [111]. In addition, exosomes derived from stem cells have been investigated as cell-free alternatives, Providing growth factors and microRNAs that promote healing [112].

### 6.3 Immunomodulatory Therapies

Persistent inflammation is a major barrier to wound healing in diabetes. Targeting immune Dysregulation through cytokine modulation and anti-inflammatory agents represents an Emerging strategy [134]. Agents such as tumor necrosis factor-alpha (TNF- $\alpha$ ) inhibitors and interleukin modulators are Under investigation for their potential to restore immune balance [135]. Topical application of anti-inflammatory peptides has also shown promise in experimental Studies [136].

### 6.4 Future Trends in Advanced Therapies

The integration of biomaterials, nanotechnology, and regenerative medicine holds significant Potential for the future of diabetic wound management [137]. Personalized approaches Combining gene editing, patient-derived stem cells, and bioengineered scaffolds may transform The treatment landscape. However, large-scale clinical trials and cost-effective technologies are Required before these therapies can become standard practice [138].

## VII. Future Perspectives and Challenges in Diabetic Wound Healing

Despite significant advancements in understanding and managing diabetic wounds, multiple Challenges continue to hinder effective healing. Chronic wounds in diabetes remain a major Clinical and economic burden worldwide. Future therapeutic strategies must address both Systemic and local factors, integrate novel technologies, and provide personalized care [139].

### 7.1 Limitations of Current Treatments

Conventional therapies, while effective in some cases, often fail in chronic or complicated Wounds. Challenges include:

Persistent hyperglycemia that continues to impair cellular function and angiogenesis [140]. Limited efficacy of growth factor therapies due to short half-life and poor bioavailability [141]. High cost and technical demands of advanced therapies such as stem cell transplantation, Bioengineered skin substitutes, and gene therapy [142].

Inadequate patient adherence to offloading devices, dressing changes, and lifestyle Modifications [143].

These limitations underscore the need for multi-modal and integrative treatment strategies.

### 7.2 Personalized Medicine

Individual variability in wound biology, comorbidities, and response to therapy necessitates a Personalized approach [144]. Precision medicine, using patient-specific cellular or molecular profiling, can identify which Therapies are most likely to succeed [145]. Biomarkers such as growth factor levels, inflammatory cytokines, and gene expression patterns Could guide treatment selection and predict healing outcomes [146]. Integration of digital monitoring tools, such as smart wound dressings and wearable sensors, Can track healing progress and adjust therapy dynamically [147].

### 7.3 Combination Therapies

Future strategies are likely to rely on combination therapies that target multiple deficits Simultaneously. Examples include: Stem cell therapy combined with growth factor delivery to enhance angiogenesis and fibroblast Function [148]. Nanoparticle-based dressings that simultaneously provide antimicrobial action and controlled Release of bioactive molecules

[149]. Hyperbaric oxygen therapy combined with topical growth factors or stem cell applications for Ischemic diabetic wounds [150]. These multi-target approaches may overcome the limitations of single interventions and Accelerate wound closure.

### 7.4 Integration of Artificial Intelligence and Digital Health

Artificial intelligence (AI) and machine learning are emerging as powerful tools in diabetic Wound management [151]. AI-driven wound imaging can quantify wound size, depth, and healing progression more Accurately than manual assessment [152].

Predictive algorithms can identify high-risk patients, optimize treatment protocols, and Improve early intervention strategies [153].

Mobile applications and telemedicine platforms facilitate remote monitoring, patient education, And adherence tracking, reducing the need for frequent hospital visits [154].

### 7.5 Economic and Accessibility Challenges

Advanced therapies often come with high costs and limited availability, particularly in low and Middle-income countries [155]. Accessibility issues may prevent patients from receiving stem cell therapy, bioengineered skin Substitutes, or HBOT, even when clinically indicated [156]. Health policy and reimbursement strategies must evolve to make cutting-edge treatments Feasible for a broader patient population [157].

### 7.6 Research Gaps and Future Directions Key

Areas for future research include: Long-term safety and efficacy of stem cell and gene therapies in large patient populations [158]. Development of cost-effective, off-the-shelf regenerative products [159]. Exploration of immunomodulatory therapies to restore normal inflammatory resolution in Chronic diabetic wounds [160]. Integration of omics technologies (genomics, proteomics, metabolomics) to uncover novel Molecular targets [161].

Use of 3D bioprinting and tissue engineering to create personalized skin substitutes [162].

### 7.7 Summary of Future Perspectives

Addressing the complex pathophysiology of diabetic wounds requires innovative, Multidisciplinary, and personalized strategies. Integration of regenerative medicine, Nanotechnology, digital health, and AI has the potential to transform wound care, reduce Chronicity, and improve patient outcomes.

Overcoming economic, accessibility, and technical Barriers will be essential to translating these

### VIII. CONCLUSION

Diabetic wounds represent a significant clinical challenge due to their chronicity, high risk of Infection, and potential for serious complications such as amputations. Impaired wound healing In diabetes results from a complex interplay of hyperglycemia, oxidative stress, neuropathy, Vascular insufficiency, immune dysfunction, and extracellular matrix abnormalities. Conventional treatment approaches including glycemic control, wound care, debridement, Offloading, infection management, and surgical interventions remain the mainstay of therapy But often fail in chronic or complicated wounds.

Recent advances in regenerative medicine, growth factor therapy, stem cell transplantation, Gene therapy, bioengineered skin substitutes, nanotechnology-based dressings, hyperbaric Oxygen therapy, and immunomodulation offer promising avenues for improving healing Outcomes. Furthermore, integration of artificial intelligence, digital health tools, and Personalized medicine has the potential to optimize treatment strategies and monitor healing Progression more accurately.

Despite these innovations, challenges such as high costs, limited accessibility, technical Complexity, and safety concerns continue to hinder widespread clinical adoption. Future Research must focus on developing cost-effective, safe, and easily deployable therapies while Bridging the gap between laboratory research and real-world clinical practice.

Overall, a multi-disciplinary, personalized, and integrative approach that addresses both Systemic and local factors will be essential for advancing diabetic wound care, reducing Morbidity, improving quality of life, and lowering the economic burden associated with chronic Wounds. Continued investment in research, technology, and patient education is critical to Transforming the landscape of diabetic wound management worldwide.

advances into routine clinical practice [163].

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