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*RESEARCH ARTICLE*

# WOUND HEALING AND TISSUE REGENERATION: AN NARRATIVE REVIEW REVIEW OF MOLECULAR MECHANISMS, THERAPEUTIC ADVANCES, AND EVIDENCE-BASED AYURVEDIC APPROACHES

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## *Abstract*

**Background:** Wound healing is a tightly regulated, multicellular proce ss through which tissue continuity, barrier function, and, to a variable extent, physiological function is restored after injury. Repair requires coordinated haemostasis, inflammation, cellular proliferation, extracell ular matrix (ECM) formation, angiogenesis, re-epithelialisation, contrac ction, and remodelling. Disturbance of the timing or coordination of these events may result in delayed closure, persistent inflammation, infection, tissue loss, functional disability, and, in severe cases, amputat ion. Chronic wounds are particularly challenging because they frequent ly coexist with ischaemia, neuropathy, metabolic dysfunction, oedema, mechanical loading, and microbial biofilm.

**Objective:**This review aims to explain the principal cellular and molec ular events involved in cutaneous wound repair; examine local and syst emic determinants of delayed healing;summarise contemporary wound-assessment principles and established or emerging therapeutic intervent ions; and critically consider the scientific and clinical position of Ayurvedic wound-care concepts and formulations within an evidence-informed framework.

**Methods:** A narrative synthesis was prepared from PubMed-indexed mechanistic reviews,clinical reviews, systematic reviews, clinical trials, and practice guidelines addressing wound biology, chronic wounds, dia betic foot ulcers, negative pressure wound therapy (NPWT), regenerati ve technologies, wound infection, and Ayurvedic wound care interventi ons.

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Particular attention was given to the 2023 International Working Group on the Diabetic Foot (IWGDF) guideline updates and published clinical and experimental studies of Jatyadi-based preparations. This article is a narrative

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review, not a registered systematic review or meta-analysis; it did not employ an exhaustive reproducible search, duplicate independent screening, or formal risk-of-bias assessment.
**Discussion**: Physiological repair depends on the timely transition from clot formation and inflammatory defence to granulation-tissue development, epithelial coverage, and matrix maturation. Diabetes, peripheral arterial disease, venous hypertension, infection, biofilm, repetitive pressure, ageing, malnutrition, smoking, and selected medications can disturb this sequence. Current management is therefore aetiology-directed and includes assessment of perfusion and infection, appropriate debridement, moisture-balanced dressings, off-loading or compression when indicated, glycaemic and nutritional optimisation, and revascularisation where required. NPWT and selected advanced products may be considered for defined wound types when best standard care is insufficient; they should not be regarded as universal treatments. Ayurvedic principles such as Vrana Shodhana and Vrana Ropana provide a traditional framework for wound preparation and healing. Preliminary clinical findings involving Jatyadi tulle are of research interest, but the available clinical evidence is limited by small samples, open-label methods, short follow-up, and restricted wound populations. These preparations should be evaluated as potential adjuncts and must not replace essential contemporary care.
**Conclusion:** Safe and effective wound management requires accurate diagnosis of the underlying cause, correction of reversible barriers to healing, and use of treatments supported by evidence appropriate to the wound type. Standardised, quality-controlled Ayurvedic formulations may merit further evaluation as complementary interventions. Future studies should use adequately powered designs, concealed allocation, blinded outcome assessment, reproducible product specifications, systematic adverse-event monitoring, and patient-important outcomes such as sustained wound closure, recurrence, function, quality of life, and limb preservation.

## Introduction:-

Wound healing is a dynamic biological response that restores tissue continuity after trauma, surgery, burns, pressure-related injury, ulceration, or other forms of tissue damage. Although the skin is the most frequently studied model, many of the principles of repair—including haemostasis, inflammation, cell migration and proliferation, matrix deposition, vascular growth, and remodelling—are shared by other tissues. The final result may involve regeneration, in which the original tissue architecture and function are substantially re-established, or repair, in which a portion of the damaged tissue is replaced by connective tissue and scar. In adult skin, repair commonly produces a scar and does not fully restore the normal arrangement of appendages or the tensile strength of uninjured tissue [1-4].

The clinical burden of wounds extends beyond the visible defect. Acute wounds may be complicated by infection, dehiscence, excessive scarring, or delayed epithelial closure. Chronic wounds, including diabetic foot ulcers, venous leg ulcers, and pressure injuries, may persist for prolonged periods, limit mobility, cause pain and social isolation, and require repeated healthcare encounters. Their economic and service burden is substantial [5,6]. Importantly, chronic wounds are not simply acute wounds that have remained open for a longer period. They frequently exist in a persistent pathological microenvironment characterised by unresolved inflammation, altered protease activity, cellular senescence, impaired perfusion, recurrent mechanical trauma, and microbial communities that may include biofilm [1,5].

Diabetic foot ulceration illustrates the multifactorial nature of chronic wound disease. Peripheral neuropathy reduces protective sensation and permits repetitive unrecognised trauma; peripheral arterial disease compromises oxygen and nutrient delivery; altered biomechanics concentrate plantar pressure; and hyperglycaemia can impair immune and reparative responses. Infection may further increase tissue destruction and the risk of hospitalisation or amputation [7,8]. Similar interactions occur in other chronic wound types, although the dominant mechanisms differ according to aetiology.

A contemporary approach to wound care must therefore connect biological understanding with clinical assessment and correction of the cause. Dressing selection alone cannot compensate for critical ischaemia, persistent pressure, uncontrolled infection, venous hypertension, or untreated metabolic disease. Alongside established wound-care strategies, there is growing interest in advanced biomaterials, cell-based approaches, bioactive dressings, oxygen-based interventions, and traditional formulations. These interventions require evaluation according to study quality, reproducibility, safety, clinical relevance, and cost-effectiveness [9,16].

This review integrates current concepts in wound biology with practical management principles and examines the potential place of Ayurvedic wound-care approaches. The intention is not to equate traditional terminology directly with modern molecular pathways, but to identify areas of conceptual overlap, distinguish experimental promise from established clinical benefit, and outline priorities for safe integrative research.

**Review Approach**:-
This article was prepared as a narrative review using a selected body of PubMed-indexed literature on cutaneous wound repair, cellular and molecular mechanisms, chronic wound pathophysiology, diabetic foot ulcer management, wound infection, NPWT, regenerative technologies, and Ayurvedic wound-care interventions. The evidence base included mechanistic and clinical reviews, systematic reviews and meta-analyses, practice guidelines, one randomised clinical trial of topical tulle dressings, and an experimental animal study of Jatyadi Taila [1-19]. The 2023 IWGDF guideline updates were considered particularly relevant to diabetic foot ulcer management because they use systematic evidence appraisal and a GRADE-based recommendation process [8-12].

The purpose of the review was to provide a clinically oriented synthesis rather than calculate a pooled treatment effect. No protocol was prospectively registered. The review did not involve an exhaustive search across all databases, duplicate independent title/abstract or full-text screening, or a formal risk-of-bias assessment. Consequently, the discussion should be interpreted as a narrative appraisal and not as a comprehensive systematic evaluation of all available evidence. Before journal submission, the authors should document the actual search dates and terms if required by the target journal, verify every bibliographic record, and update the evidence base close to submission.

**Biology of wound healing:-**
Cutaneous wound repair is conventionally described in four overlapping phases: haemostasis, inflammation, proliferation, and remodelling. Angiogenesis and re-epithelialisation occur chiefly during the proliferative period but begin earlier and continue across phase boundaries. These stages are useful for teaching; in living tissue, they overlap and are influenced by wound depth, anatomical location, perfusion, microbial burden, systemic health, and mechanical environment [1-4].

**Haemostasis:-**
Haemostasis begins immediately after tissue disruption. Transient vasoconstriction, platelet adhesion and aggregation, and activation of the coagulation cascade limit blood loss. Platelets bind to exposed subendothelial structures and support the formation of a fibrin-rich clot. This clot provides more than mechanical haemostasis: it forms a provisional matrix through which inflammatory cells can migrate and acts as a reservoir for signalling molecules, including platelet-derived growth factor (PDGF) and transforming growth factor beta (TGF-β). These mediators contribute to leukocyte recruitment, fibroblast chemotaxis, and initiation of the reparative response [1,3,4].

The quality of the initial haemostatic response affects subsequent repair. Persistent bleeding, haematoma formation, poor perfusion, or impaired coagulation may interfere with wound stability and create conditions that favour infection or delayed healing. Conversely, the provisional clot must later be remodelled as granulation tissue and organised matrix develop.

**Inflammation:-**
The inflammatory phase provides early defence against microbial contamination and removes damaged cells and matrix. Neutrophils are among the first recruited leukocytes. They migrate in response to chemotactic signals and contribute to microbial killing and debris clearance through phagocytosis, reactive oxygen species (ROS), proteolytic enzymes, and neutrophil extracellular traps. Monocytes subsequently enter the wound and differentiate into macrophages, which participate in phagocytosis, cytokine regulation, efferocytosis, angiogenic signalling, and the transition toward tissue repair [1,2,4].

Inflammation is essential but must be appropriately regulated. A timely reduction in inflammatory activity permits keratinocyte migration, fibroblast function, angiogenesis, and matrix deposition. In chronic wounds, continued recruitment or activation of inflammatory cells, excess cytokine signalling, oxidative stress, and increased protease activity may injure viable tissue and degrade matrix proteins and growth factors. This can create a self-perpetuating cycle in which tissue damage sustains inflammation and inflammation perpetuates tissue damage [1,3,5].
The commonly used M1/M2 macrophage terminology describes broad inflammatory and reparative tendencies, respectively, but should not be interpreted as two discrete or fixed macrophage populations. Wound macrophages demonstrate diverse, context-dependent functional states that change over time and in response to local signals [1,2].

**Proliferation, granulation tissue, and re-epithelialisation:-**
The proliferative phase is characterised by restoration of the epidermal barrier, formation of granulation tissue, new vessel growth, and wound contraction. Keratinocytes at the wound edge and from surviving epidermal appendages

alter their adhesion and migratory behaviour, move across the wound surface, and subsequently proliferate and differentiate to re-establish epidermal continuity. Successful epithelial migration depends on an appropriate wound surface, adequate perfusion, controlled inflammation, and the absence of persistent mechanical disruption [1,2].
Fibroblasts migrate into the provisional matrix and synthesise collagen, fibronectin, proteoglycans, and other ECM constituents. Some fibroblasts acquire a contractile myofibroblast phenotype, contributing to wound contraction and matrix organisation. The balance between matrix production, contraction, and degradation influences the quality of the repair tissue. Insufficient fibroblast activity may delay closure, whereas excessive or prolonged activity can contribute to fibrosis, hypertrophic scarring, and contracture [1,4].

Angiogenesis is required to supply oxygen and nutrients to the metabolically active repair tissue. Endothelial cells proliferate and migrate in response to vascular endothelial growth factor (VEGF), angiopoietins, and other signals, while pericytes and surrounding cells contribute to vessel maturation and stability. The newly formed capillary network, fibroblasts, inflammatory cells, and provisional ECM collectively form granulation tissue. Adequate perfusion, oxygen availability, nutritional substrate, and metabolic control are therefore important for the development of healthy granulation tissue [1-4].

**Remodelling and scar maturation:-**
Remodelling begins while granulation tissue is still developing and may continue for months. During this period, collagen is reorganised, matrix composition changes, cellularity and vascular density decline, and the repair tissue gradually acquires greater tensile strength. Matrix metalloproteinases (MMPs) regulate degradation and turnover of ECM components, while tissue inhibitors of metalloproteinases (TIMPs) constrain their activity. A balanced MMP/TIMP relationship is necessary: excessive proteolysis can destroy newly deposited matrix and signalling molecules, whereas inadequate matrix turnover can contribute to abnormal fibrosis [1,3,4].

The mature scar generally remains mechanically and structurally different from uninjured skin. It may contain fewer normal epidermal appendages and does not ordinarily regain the full tensile strength of intact tissue. Excessive matrix accumulation can produce hypertrophic scars or contractures, while inadequate matrix deposition or poor remodelling can leave the wound fragile and susceptible to breakdown [1,2].

Figure 1. Overlapping phases of cutaneous wound healing. The figure should illustrate haemostasis, inflammation, proliferation, angiogenesis, re-epithelialisation, and remodelling as overlapping rather than strictly sequential events. The timeline is schematic; duration varies according to wound characteristics and host factors.

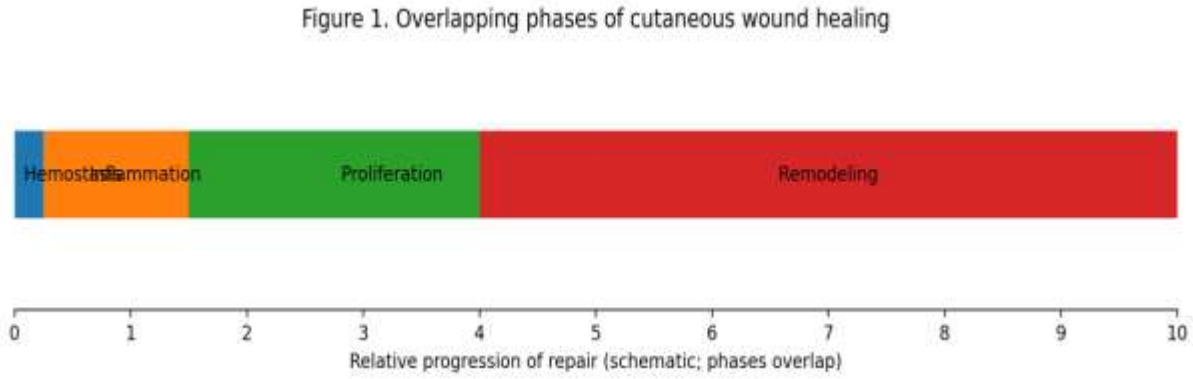



**Figure 1. Overlapping phases of cutaneous wound healing. The timeline is schematic; actual duration varies by wound type, depth, site, perfusion, infection, and host factors.**

**Cellular and molecular regulation of wound repair:-**
Wound repair depends on communication among platelets, neutrophils, monocytes/macrophages, mast cells, keratinocytes, fibroblasts, endothelial cells, pericytes, sensory nerves, adipocytes, and stem/progenitor-cell populations. These cells respond to growth factors, cytokines, chemokines, oxygen tension, mechanical forces, and the composition and stiffness of the ECM. Modern single-cell and spatial methods have demonstrated substantial heterogeneity within wound-cell populations and are refining the understanding of how these cells coordinate normal repair and pathological scarring [1,2].

**Table 1. Principal cellular and extracellular components involved in wound repair, their biological roles, mediators, and clinical implications**.

| Cellular component | Principal role in repair | Important mediators/processes | Clinical relevance |
|---|---|---|---|
| **Platelets and fibrin** | Haemostasis; formation of a provisional scaffold; initiation of repair signalling | Coagulation cascade, PDGF, TGF-β | Inadequate clot formation or persistent bleeding can destabilise the wound environment. |
| **Neutrophils** | Early antimicrobial defence and removal of cellular debris | Phagocytosis, ROS, proteases, chemokines, extracellular traps | Persistent activation can damage viable tissue and sustain inflammation. |
| **Monocytes/macrophages** | Debris clearance, immune coordination, inflammatory resolution, and reparative signalling | Cytokines, growth factors, efferocytosis | Dysregulated macrophage responses may prevent transition from inflammation to repair. |
| **Keratinocytes** | Migration and proliferation to restore the epidermal barrier | EGF-family signalling, integrins, cell-migration programmes | Ischaemia, infection, and repeated trauma can impair epithelial advancement. |
| **Fibroblasts/myofibroblasts** | ECM synthesis, wound contraction, and matrix organisation | Collagen, fibronectin, TGF-β, MMP/TIMP balance | Deficient activity delays closure; excessive activity may contribute to fibrosis. |
| **Endothelial cells/pericytes** | Angiogenesis and microvascular stabilisation | VEGF, angiopoietins, nitric oxide | Adequate perfusion is essential for oxygen delivery and granulation tissue formation. |
| **Extracellular matrix** | Structural scaffold and biochemical/mechanical signalling environment | Collagens, fibronectin, proteoglycans, MMPs/TIMPs | Abnormal degradation, composition, or stiffness can alter cell migration and repair. |

**Growth factors, cytokines, and intracellular signaling:-**

Growth factors coordinate cell recruitment, proliferation, migration, angiogenesis, and matrix formation. PDGF contributes to chemotaxis and fibroblast activity; TGF-β regulates inflammatory responses, fibroblast activation, ECM synthesis, and fibrosis; VEGF promotes endothelial-cell responses and angiogenesis; and epidermal growth factor (EGF)-family signalling supports keratinocyte migration and proliferation. Their biological effects depend on local concentration, timing, receptor expression, tissue perfusion, and susceptibility to proteolytic degradation [1,2,4].

These relationships help explain why applying an isolated growth factor may not be sufficient to heal a chronic wound. If the wound remains ischaemic, infected, mechanically overloaded, or excessively proteolytic, the local environment may continue to prevent a sustained reparative response. Therapeutic strategies must therefore address the underlying pathological conditions as well as the signalling pathways involved in tissue repair.

Inflammatory signalling networks, including nuclear factor kappa B (NF-κB) and several cytokine pathways, regulate leukocyte recruitment and host defence. Hypoxia-inducible pathways can promote angiogenic responses under reduced oxygen tension; however, prolonged or severe ischaemia limits cellular energy production and survival. ROS similarly have dual effects: controlled production contributes to antimicrobial defence and intracellular signalling, whereas excessive or persistent oxidative stress damages proteins, lipids, DNA, and ECM components [1-4]. These mechanisms provide plausible therapeutic targets, but molecular activity observed in cultured cells or animal models should not be interpreted as proof of clinical effectiveness.

**Extracellular matrix as a structural and signalling environment:-**

The ECM is an active component of the wound microenvironment rather than a passive support structure. Collagens provide tensile support, fibronectin supports cell adhesion and migration, and proteoglycans influence hydration and the availability of signalling molecules. Matrix fragments generated during tissue injury can also modify cellular behaviour. The composition, organisation, stiffness, and turnover of the ECM influence how fibroblasts, keratinocytes, endothelial cells, and immune cells respond to the wound environment [1,2,4].

In chronic wounds, excessive protease activity may degrade newly formed matrix and growth factors before they can exert their effects. Altered matrix stiffness and prolonged inflammatory signalling may further disrupt cell migration and reparative-cell function. These changes underscore the importance of controlling the aetiological factors that perpetuate tissue injury rather than focusing exclusively on topical wound products.

**Microbiome, biofilm, and persistent inflammation:-**

An open wound is exposed to microorganisms, but microbial presence or colonisation is not equivalent to clinically significant infection. Infection is a clinical diagnosis based on the overall presentation, including local inflammatory changes, tissue involvement, systemic manifestations, perfusion, and host susceptibility. A superficial swab may identify organisms present on the wound surface without proving that they are causing invasive infection. When microbiological investigation is indicated, the sampling method should be selected according to the clinical situation and local guidance; tissue specimens obtained after appropriate cleansing and debridement may be more informative in selected infected wounds [12,13].

Biofilms are structured microbial communities embedded in an extracellular matrix. They may increase tolerance to host immune responses and antimicrobial exposure and can contribute to persistent inflammation and delayed healing. However, routine clinical identification of biofilm remains difficult, and its presence should not be assumed solely because a wound is chronic or fails to close. Appropriate wound cleansing, debridement when indicated, management of the underlying cause, and targeted antimicrobial therapy for clinically infected wounds form a more defensible approach than routine antimicrobial treatment of every open wound [12,13].

**Acute and chronic wounds: pathophysiology and determinants of delayed healing:-**

Acute wounds generally progress through the phases of repair in an orderly manner when the initial injury is controlled and the patient has adequate physiological reserve. Chronic wounds, by contrast, are often maintained by one or more persistent local or systemic drivers. These may include repetitive pressure or shear, neuropathy, venous hypertension, arterial insufficiency, oedema, infection, retained foreign material, repeated trauma, poor glycaemic control, smoking, malnutrition, anaemia, immunosuppression, and medication-related effects [3,5,7].

Figure 3. Conceptual self-reinforcing cycle in chronic wound non-healing

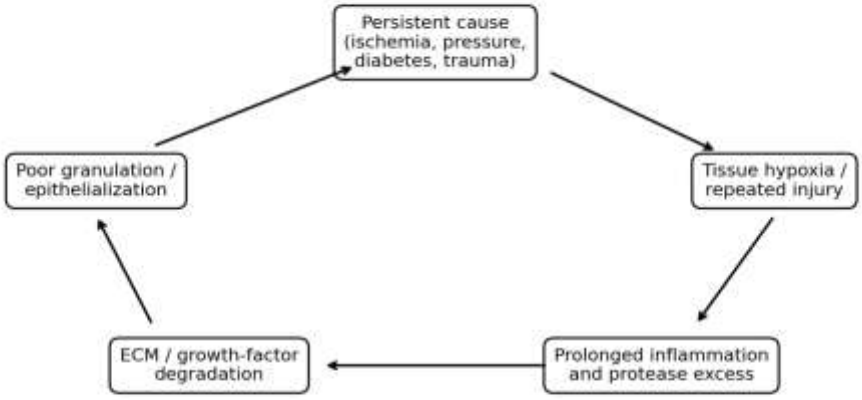



**Figure 2. Conceptual feedback loop contributing to chronic wound non-healing. The diagram is a mechanistic synthesis, not a quantitative model**

The distinction between acute and chronic wounds is not determined by duration alone. A wound that fails to demonstrate meaningful progress should prompt reassessment of its diagnosis, aetiology, perfusion, infection status, mechanical environment, and systemic contributors. Simply changing the dressing without addressing a persistent cause may not alter the biological trajectory of the wound [5].

**Table 2. Local and systemic factors associated with delayed wound healing and recommended clinical assessment.**

| Contributing factor | Mechanism of impaired healing | Clinical assessment and response |
|---|---|---|
| **Peripheral arterial disease/ischaemia** | Reduced oxygen and nutrient delivery; impaired immune-cell function; reduced granulation and epithelial repair. | Assess pulses and limb perfusion; obtain Doppler and ankle-brachial or toe-pressure testing as appropriate; seek vascular assessment when indicated. |
| **Diabetes/hyperglycaemia** | Neuropathy, microvascular dysfunction, altered leukocyte activity, and impaired matrix turnover. | Assess glycaemic control, protective sensation, foot structure, footwear, and need for multidisciplinary diabetic-foot care. |
| **Pressure and shear** | Repeated tissue deformation and microvascular compromise produce recurrent injury. | Institute pressure redistribution, off-loading, repositioning, footwear review, and mobility support. |
| **Infection/biofilm** | Persistent inflammatory stimulation, tissue destruction, and possible extension into deeper structures. | Diagnose clinically; obtain appropriate specimens when indicated; perform source control and targeted antimicrobial treatment. |
| **Venous hypertension/oedema** | Increased venous pressure, oedema, and altered microcirculation impair tissue oxygenation and repair. | Determine venous and arterial status; consider compression only after assessing perfusion and contraindications. |
| **Malnutrition, anaemia, smoking** | Reduced availability of substrates or oxygen and altered immune and fibroblast function. | Assess nutritional status and relevant deficiencies; treat anaemia when present; offer smoking-cessation support. |
| **Age, comorbidity, and medicines** | Changes in inflammatory responses, cell senescence, mobility, or medication-related effects. | Review comorbidities and medicines; individualise risk-benefit decisions rather than discontinuing treatment without clinical review. |

**Clinical assessment and wound-bed preparation:-**

A comprehensive assessment should establish the cause of the wound before selecting a treatment. Documentation should include the duration and anatomical location; length, width, and depth; wound-bed tissue; edge characteristics; undermining or tunnelling; amount and character of exudate; odour after cleansing; pain; periwound skin; and clinical evidence of infection. Serial measurements should be performed using a consistent method. Standardised photographs may support monitoring, provided informed consent and appropriate privacy safeguards are in place [5,7,8].The clinician should determine whether the lesion is primarily arterial, venous, neuropathic, pressure-related, traumatic, postoperative, inflammatory, or mixed. Assessment should also consider systemic contributors such as diabetes, renal disease, nutritional compromise, smoking, immunosuppression, and reduced mobility. In suspected diabetic foot disease, validated classification and communication tools may be used according to the clinical context; the IWGDF guidance discusses the role of systems such as SINBAD and WIfI, while emphasising that the component clinical findings should also be recorded [8].Perfusion assessment is essential when arterial disease is possible. It may include pulse examination, Doppler assessment, ankle-brachial pressure index, toe pressure, and vascular imaging or specialist evaluation as appropriate. In diabetes, medial arterial calcification can make the ankle-brachial index less reliable; toe pressure and other perfusion measures may therefore be helpful. A wound that is ischaemic cannot be expected to heal reliably through topical therapy alone, and revascularisation should be considered when clinically indicated [11].

Infection should be assessed clinically rather than inferred from a positive surface culture alone. When diabetic foot infection is suspected, severity classification, appropriate specimen collection, antimicrobial selection, and consideration of surgical source control should follow recognised guidance [12]. If osteomyelitis, deep abscess, foreign body, or other deep pathology is suspected, imaging and specialist assessment may be required. Laboratory investigations should be guided by the clinical question rather than applied indiscriminately.

Wound-bed preparation is often organised around the TIME framework: tissue management, control of infection or inflammation, moisture balance, and advancement of the epithelial edge. Debridement may remove devitalised tissue, reduce local barriers to repair, and assist in management of selected infected or sloughy wounds. The method and timing should be determined by wound type, perfusion, pain, bleeding risk, patient condition, and clinician expertise. Dry, stable eschar in a severely ischaemic limb should not be indiscriminately debrided before vascular assessment because removal may expose non-viable tissue and worsen the defect [5,8,11].

Dressings should maintain an appropriate moist environment, absorb or manage exudate, protect the surrounding skin, and minimise trauma during removal. No single dressing is best for every wound. Selection should be individualised according to wound depth, exudate, tissue type, infection status, anatomical site, comfort, availability, and cost. Unnecessarily frequent dressing changes may disrupt fragile granulation tissue and newly migrating epithelium.

**Established and advanced therapeutic approaches:-**

The foundation of wound treatment is correction of the underlying cause and delivery of appropriate local care. Advanced modalities should be considered only after the wound has been assessed and essential measures—such as perfusion management, infection treatment, pressure relief, or compression for suitable venous disease—have been addressed. The evidence and indications differ substantially among wound types and products [5,8,9].

**Table 3. Established and emerging wound interventions, their potential roles, evidence considerations, and practical safeguards.**

| Intervention | Potential clinical role | Evidence considerations | Practical safeguards |
|---|---|---|---|
| **Cleansing and moisture-balanced dressings** | Support a clean wound environment, manage exudate, and protect viable tissue. | Dressing selection is wound-specific; no single product is universally superior. | Avoid irritating or cytotoxic products unless specifically indicated; protect the periwound skin. |
| **Sharp or surgical debridement** | Remove devitalised tissue and selected barriers to healing. | Useful in appropriately selected wounds, but not suitable for indiscriminate removal of stable dry eschar in an ischaemic limb. | Assess perfusion, bleeding risk, pain, and operator competence before intervention. |
| **Off-loading and pressure redistribution** | Reduce repetitive mechanical injury, particularly in neuropathic plantar foot ulcers. | A core component of diabetic foot ulcer care; non-removable knee-high devices are first choice for many uncomplicated neuropathic plantar forefoot/midfoot ulcers when appropriate. | Individualise device choice; assess contraindications, infection/ischaemia, balance, mobility, and adherence. |
| **Compression therapy** | Reduce venous hypertension and oedema in appropriately selected venous ulcers. | An established treatment for venous disease when arterial perfusion is adequate. | Assess arterial status and contraindications before applying standard compression. |
| **Negative-pressure wound therapy** | Manage exudate, support granulation, and assist selected complex or postoperative wounds. | Guideline support is wound-specific; IWGDF gives a conditional recommendation for NPWT in selected postsurgical diabetic foot wounds, not routine use for all ulcers. | Not a substitute for revascularisation, infection source control, or off-loading; assess bleeding and other contraindications. |
| **Skin substitutes and placental-derived products** | Provide biological or structural support in selected hard-to-heal wounds. | Conditional recommendations exist for selected diabetic foot ulcers; certainty, cost, availability, and product- | Use alongside best standard care and within approved indications. |

| | | | |
|---|---|---|---|
| | | specific evidence vary. | |
| **Topical or hyperbaric oxygen** | Potential adjunct in selected wound populations. | Recommendations differ by indication; these are not routine treatments for every chronic wound. | Assess eligibility, contraindications, access, cost, and the evidence for the specific wound type. |
| **Growth factors, cell-based products, and scaffolds** | Attempt to support regenerative signalling or provide a matrix environment. | Biologically promising, but clinical evidence is heterogeneous and product-specific. | Do not extrapolate routine clinical effectiveness from preclinical findings alone. |

**Negative-pressure wound therapy:-**

Negative-pressure wound therapy applies controlled subatmospheric pressure to a sealed wound interface. Depending on the device and clinical setting, the system may help manage exudate, reduce oedema, support wound-edge approximation, and promote granulation tissue formation. It is used in selected complex wounds and postoperative defects, including some diabetic foot wounds. Its suitability depends on wound characteristics, perfusion, infection control, bleeding risk, exposed structures, and the overall treatment plan.

Systematic reviews and meta-analyses of NPWT in diabetic foot ulcers have reported favourable findings for selected outcomes, including complete healing and wound-area reduction. However, interpretation is limited by differences in study design, wound severity, co-interventions, and study quality [14,15]. The IWGDF 2023 update makes a conditional recommendation for NPWT in selected postsurgical diabetic foot wounds, while distinguishing this indication from routine use in all non-surgical diabetic foot ulcers [9]. The appropriate conclusion is that NPWT may be useful in selected patients and wound types; it is not a replacement for perfusion restoration, infection source control, or pressure off-loading.

**Guideline-supported adjunctive treatments:-**

The IWGDF 2023 guideline on interventions to enhance healing used a structured evidence-to-decision process and issued conditional recommendations for selected products and technologies, including sucrose octasulfate dressings, NPWT for postoperative wounds, placental-derived products, an autologous leucocyte/platelet/fibrin patch, topical oxygen, and hyperbaric oxygen in specified clinical contexts. The guideline emphasises that such interventions should be considered when best standard care alone has not achieved healing and when resources are available. It also notes that the certainty of evidence remains limited for many interventions [9].

These recommendations should not be generalised beyond the populations and indications considered by the guideline. A product supported for a particular type of diabetic foot ulcer may not have equivalent evidence in venous ulcers, pressure injuries, burns, or traumatic wounds. Similarly, improvements in wound area or selected surrogate markers should not be assumed to establish durable closure, reduced recurrence, improved function, or limb preservation.

**Aetiology-specific principles:-**

Diabetic foot ulcers require a coordinated approach that combines wound assessment, glycaemic management, evaluation of neuropathy and perfusion, infection diagnosis and treatment, pressure off-loading, footwear review, and long-term recurrence prevention. For neuropathic plantar forefoot or midfoot ulcers, the IWGDF off-loading guideline recommends a non-removable knee-high off-loading device as the first-choice option when appropriate and not contraindicated; alternatives are selected according to patient and wound characteristics [10].

For venous leg ulcers, management generally addresses venous hypertension and oedema, often through compression after arterial sufficiency and contraindications have been assessed. For arterial ulcers, restoration of blood flow is central and may require vascular intervention. Pressure injuries require pressure redistribution, repositioning, support surfaces, and management of contributing factors such as immobility and moisture. These approaches are not interchangeable: the dominant aetiology should guide the treatment plan [5,8,11].

**Regenerative medicine and emerging technologies:-**

Regenerative approaches seek to modify the wound microenvironment and support restoration of tissue rather than simply covering the defect. Areas of investigation include engineered biomaterial scaffolds, hydrogels, bioactive dressings, cell-derived secretomes, extracellular vesicles, stem and progenitor cell strategies, gene delivery systems, antimicrobial peptides, nanomedicine, organoid models, and three-dimensional bioprinting. Smart dressings may be designed to monitor pH, temperature, moisture, or selected biomarkers, while digital imaging and machine-learning approaches may assist with wound measurement, classification, and prediction of healing trajectories [2,16].

These developments are scientifically promising, but their level of clinical maturity varies. Many remain preclinical or are supported by small early-phase studies. Translation into routine practice is challenged by manufacturing reproducibility, product stability, sterilisation, immune effects, regulatory classification, long-term safety, affordability, and the need to identify the patient groups most likely to benefit [2,16].

A central translational principle is that biological plausibility does not equal clinical effectiveness. Regenerative products should be evaluated using outcomes that matter to patients and clinicians: complete and sustained wound closure, time to healing, recurrence, infection, pain, function, quality of life, amputation, adverse events, and cost-effectiveness. Changes in wound area, collagen content, angiogenic markers, or other laboratory measures may be informative secondary outcomes but should not replace clinically meaningful endpoints.

**Ayurvedic perspectives and wound care:-**

Classical Ayurveda describes wound management under the broad concept of Vrana. Two frequently discussed principles are Vrana Shodhana, referring to cleansing or preparation of the wound, and Vrana Ropana, referring to the promotion of wound healing. The Shashti Upakrama framework attributed to Sushruta describes a range of therapeutic measures for different wound presentations. In contemporary discussion, these principles may be considered alongside wound cleansing, removal of devitalised tissue when appropriate, management of local infection, maintenance of a suitable wound environment, and support of tissue repair. Such comparisons should remain interpretive: traditional categories should not be presented as direct equivalents of specific molecular pathways unless this relationship has been directly investigated.

A systematic review of grey literature on Ayurvedic wound-healing formulations documented a broad range of clinical and research activity involving preparations such as Jatyadi Taila, Jatyadi Ghrita, Nimba-based formulations, honey, and other topical interventions [17]. This literature is useful for mapping the scope of traditional practice and identifying research priorities. However, the number of publications or reports concerning a formulation is not a measure of therapeutic efficacy. Differences in formulation, indication, preparation method, patient population, comparator, and outcome measurement limit direct comparison across studies.

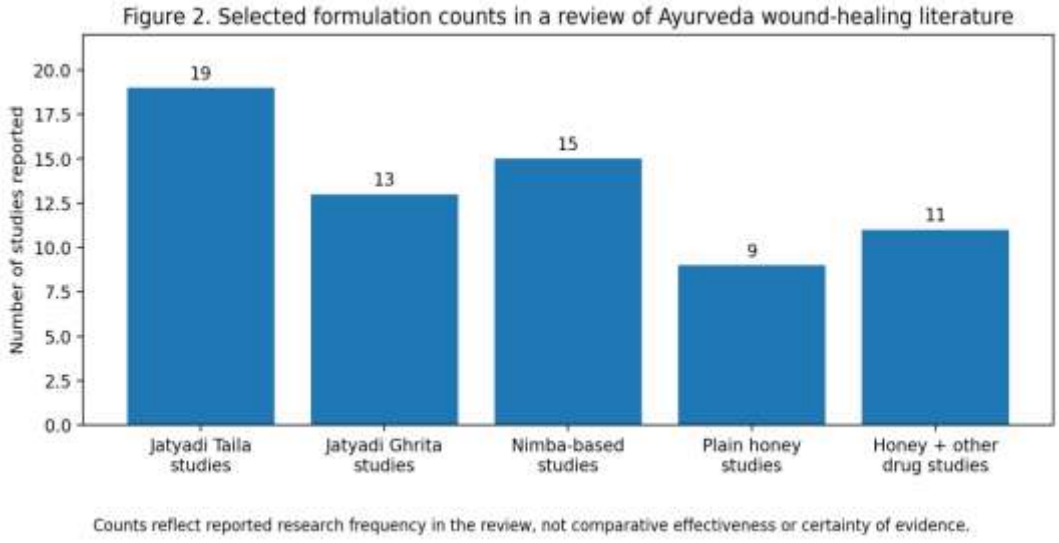



**Figure 3. Selected counts reported in a review of Ayurvedic wound-healing literature. These are counts of studies/formulation reports, not pooled treatment effects or proof of superiority [8].**

**Clinical evidence for Jatyadi-based wound preparations:-**

A three-arm, randomised, parallel-group, active-controlled, open-label clinical trial evaluated Jatyadi tulle, Madhughrita tulle, and honey tulle in 45 patients with clean wounds. Participants received the assigned dressing for 10 days, with assessment on days 5 and 10. Wound status was assessed using the Bates-Jensen wound assessment tool, while dressing-related characteristics were evaluated with a tissue-viability dressing assessment form. Within-group improvements were observed over the study period, while between-group outcomes were broadly comparable.

Jatyadi and Madhughrita tulle received favourable assessments for ease of application, removal, and patient comfort; no adverse drug events were identified during the short trial [18].

The findings provide preliminary clinical information about the use of these dressings in clean wounds. They do not establish that Jatyadi tulle is superior to the active comparator, nor do they establish effectiveness in deep, ischaemic, infected, diabetic, or long-standing chronic ulcers. The small sample, open-label design, short follow-up, and restricted wound population limit conclusions about comparative efficacy, recurrence, and longer-term safety [18].An experimental study investigated Jatyadi Taila in a rat excision-wound model and examined phytochemical markers and dermal absorption. The investigators identified marker constituents including β-sitosterol, lupeol, and karanjin using chromatographic methods, assessed local irritation in an animal model, and reported faster reduction in wound area in treated animals than in comparator groups [19]. These findings support further formulation research but remain preclinical. Animal wound models cannot establish effectiveness in human chronic wounds, and the results should not be used as a basis for substituting the formulation for established clinical care.

**Interpretation and limitations of Ayurvedic evidence:-**

The evidence relating to Ayurvedic wound formulations is heterogeneous. Preparations may differ in botanical identity, ingredient ratios, processing, extraction or heating conditions, vehicle, concentration, storage, and application frequency. Clinical studies may also vary in wound aetiology, baseline severity, comparator treatment, follow-up period, and outcome definition. These differences complicate replication and make it difficult to attribute observed effects to a specific ingredient or mechanism [17-19].

Accordingly, Ayurvedic formulations should be considered potential adjuncts only when the product is appropriately characterised, quality-controlled, and judged suitable for the particular wound. Their use must not delay vascular assessment, indicated debridement, treatment of clinical infection, pressure off-loading, glycaemic optimisation, or surgical management. Particular caution is required in deep wounds, critically ischaemic limbs, rapidly spreading infection, systemic illness, exposed vital structures, and immunocompromised patients. Preparations intended for application to open wounds require appropriate microbial quality and safety testing; traditional use or herbal origin alone does not establish sterility or safety.

**Proposed integrative clinical framework:-**

An integrative approach should preserve the primacy of diagnosis and guideline-based care while permitting carefully selected traditional adjuncts to be evaluated under defined conditions. The framework below is intended as a clinical and research model rather than a validated treatment algorithm.

**Table 4. Proposed integrative framework for evaluating Ayurvedic adjuncts alongside contemporary standard wound care.**

| Clinical step | Contemporary wound-care priority | Potential Ayurveda-integrative consideration and decision rule |
|---|---|---|
| **1. Diagnose** | Establish wound aetiology, depth, perfusion, infection status, neuropathy, mechanical factors, and systemic contributors. | Traditional wound descriptors may be recorded as additional context, but should not replace accepted diagnostic assessment. |
| **2. Stabilise** | Treat sepsis or spreading infection, address threatened perfusion, and protect the wound from further injury. | No traditional intervention should delay urgent medical, vascular, or surgical treatment. |
| **3. Prepare the wound bed** | Cleanse, debride when indicated, manage moisture, and institute appropriate off-loading or compression. | Vrana Shodhana may be discussed as a conceptual parallel to wound preparation, not as a direct biomedical equivalence. |
| **4. Support repair** | Optimise nutrition, glycaemic status, perfusion, and dressing strategy; consider evidence-supported adjuncts for selected indications. | A standardised topical formulation may be evaluated as an adjunct only after identity, quality, stability, and safety are established. |
| **5. Measure outcomes** | Record wound area and depth, complete closure, infection, pain, function, recurrence, adverse | Use the same validated outcomes for traditional and conventional treatment groups; avoid conclusions |

| | | |
|---|---|---|
| | events, and patient experience. | based solely on photographs or subjective impressions. |
| **6. Prevent recurrence** | Address footwear, pressure, oedema, vascular risk, mobility, metabolic control, and patient education. | Supportive traditional practices may be considered only when safe and compatible with long-term preventive care. |

**Safety, quality assurance, and research priorities:-**

Products intended for application to open wounds require a higher level of quality assurance than products applied to intact skin. Relevant considerations include botanical and chemical identity, ingredient concentration, batch-to-batch consistency, microbial contamination, sterility where appropriate, stability, local irritation, sensitisation, and compatibility with dressings or antiseptics. Depending on the product and its supply chain, testing may also need to address contaminants and adulterants. Herbal origin does not guarantee that a formulation is sterile, non-irritant, or safe for every wound type.

For research reproducibility, investigators should report the identity and source of each ingredient, authentication methods, formulation procedure, concentration, vehicle, application frequency, storage conditions, batch number, and quality-control specifications. The comparator should be clinically credible, and both treatment arms should receive the same best standard care. This is essential to determine whether an Ayurvedic adjunct provides additional benefit beyond the effects of cleansing, dressing, off-loading, compression, or other concurrent interventions.

Future clinical trials should be prospectively registered and should include an adequate sample-size calculation, random allocation with allocation concealment where feasible, blinded outcome assessment, clearly defined wound aetiology and severity, prespecified primary and secondary outcomes, intention-to-treat analysis, complete adverse-event reporting, and follow-up sufficient to assess sustained closure and recurrence. Where participant or practitioner blinding is not practical, blinded photographic or central wound assessment can reduce detection bias. Studies should also report adherence, co-interventions, treatment discontinuation, and cost-effectiveness.

For animal experiments, ethical approval and appropriate reporting standards, including ARRIVE principles, should be followed. For clinical studies, institutional ethics approval, informed consent, trial registration, and transparent reporting are essential. Future investigations should prioritise clinically meaningful outcomes rather than relying solely on wound-area reduction or biochemical markers.

Important research questions include: (i) which cellular and molecular signatures reliably predict delayed healing; (ii) how clinically significant infection and biofilm-associated disease can be identified more accurately; (iii) which patients benefit from specific advanced wound technologies; (iv) whether a standardised Ayurvedic formulation produces additional benefit when added to guideline-based care; (v) which patient-centred outcomes best capture treatment value; and (vi) whether digital monitoring improves timely escalation and continuity of care without increasing inequity.

**Limitations of the review:-**

This article is a narrative review and should not be interpreted as a systematic review or meta-analysis. It does not provide exhaustive database coverage, duplicate independent screening, a formal risk-of-bias assessment, or quantitative synthesis of treatment effects. The included literature spans mechanistic research, animal experiments, small clinical trials, systematic reviews, and clinical guidelines; these forms of evidence are not interchangeable. The Ayurvedic evidence is particularly heterogeneous with respect to formulation composition, preparation, clinical indication, comparator, and outcome measurement. The review therefore adopts a cautious interpretation and does not claim that any single conventional, advanced, or traditional intervention is universally effective.

## Conclusion:-

Wound healing is a coordinated biological process involving haemostasis, inflammation, cellular proliferation, angiogenesis, re-epithelialisation, ECM deposition, remodelling, and scar maturation. Chronic wounds arise when local and systemic drivers disrupt this coordinated response, particularly through persistent inflammation, impaired perfusion, infection, repetitive mechanical stress, neuropathy, and metabolic dysfunction. Effective management begins with accurate diagnosis and correction of remediable barriers to healing. Debridement, dressings, off-loading, compression, infection management, revascularisation, and advanced products should be selected according to wound aetiology and the strength of available evidence.

Ayurvedic wound-care principles, including Vrana Shodhana and Vrana Ropana, and formulations such as Jatyadi tulle are of legitimate clinical and research interest. However, the current clinical evidence is preliminary and does not justify replacing essential contemporary wound care. Integrative wound management should be evidence-informed, transparent about uncertainty, and based on standardised and safety-tested interventions. Well-designed clinical trials are needed to determine whether specific Ayurvedic formulations provide reproducible additional benefit in defined wound populations.

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