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REVIEW ARTICLE

Phytotherapeutic Hydrogels for the Management of Chronic Wounds

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Abstract: Chronic wound management is a significant clinical hurdle due to the persistent inflammatory state, localized hypoxia, and microbial colonization that characterize non-healing ulcers. Conventional treatments frequently fail to address the complex biochemical environment of diabetic and pressure-induced wounds. Herbal-integrated hydrogels represent a sophisticated intersection of material science and pharmacology, utilizing the intrinsic biocompatibility of cross-linked polymers alongside the therapeutic diversity of plant-derived secondary metabolites. These systems facilitate a moist wound environment while enabling the sustained release of bioactive compounds such as flavonoids, terpenoids, and alkaloids. These biomaterials address the root causes of healing arrest by modulating the oxidative stress within the wound bed and promoting the transition of macrophages from the pro-inflammatory M1 to the pro-healing M2 phenotype. Advanced formulations incorporating natural gums and polyphenolic extracts show superior efficacy in stimulating neovascularization through the upregulation of pro-angiogenic markers like CD31 and alpha-smooth muscle actin. The inherent antimicrobial properties of specific phytochemicals provide a non-antibiotic strategy to disrupt bacterial biofilms, mitigating the risks associated with multi-drug-resistant pathogens. The synergy between the hydrogel matrix and encapsulated phytoconstituents optimizes epithelialization and collagen deposition, ultimately restoring tissue integrity. These cost-effective and safe biomimetic platforms offer a viable alternative to synthetic dressings, promising improved patient outcomes in the treatment of refractory cutaneous lesions and chronic skin injuries.

Keywords: Cutaneous regeneration; Bioactive phytoconstituents; Polymeric scaffolds; Oxidative stress mitigation; Angiogenic stimulation

1. Introduction

The physiological process of tissue repair is a highly orchestrated sequence of biological events intended to restore the structural and functional integrity of the skin. Under normal conditions, this progression involves a delicate balance between cellular signaling and extracellular matrix production. However, chronic wounds emerge when this sequence is interrupted, typically resulting in a state of pathological inflammation and impaired cellular response [1]. In these stalled wounds, the environment is characterized by an overabundance of proinflammatory markers and proteolytic enzymes that degrade neo-tissue as quickly as it is formed. This arrest in the inflammatory phase prevents the recruitment of fibroblasts and the deposition of new collagen, leading to stagnant lesions that pose a severe risk of secondary infection and systemic complications.

These refractory wounds, often associated with systemic conditions such as diabetes mellitus and vascular insufficiency, impose a substantial economic and psychosocial burden on global healthcare systems [2]. The epidemiological shift toward an aging population and the increasing incidence of metabolic syndrome have exacerbated the frequency of diabetic foot ulcers and venous stasis ulcers. Beyond the direct medical costs, patients suffer from chronic pain, social isolation, and significant mobility limitations. The failure of standard care to manage the biochemical complexity of the chronic wound bed has necessitated the development of advanced wound dressings that do more than provide a simple physical barrier. Conventional dressings, such as dry gauze, frequently adhere to the wound bed, causing trauma upon removal and failing to address the localized hypoxia or microbial colonization that prevents healing. Herbal hydrogels have surfaced as a potent therapeutic modality, merging the moisture-retentive properties of hydrophilic polymer networks with the multi-target pharmacological actions of plant extracts [3]. These polymeric scaffolds can absorb large quantities of exudate while maintaining the hydration levels necessary for optimal cellular activity. The cooling effect of the hydrogel also provides symptomatic relief for patients suffering from inflammatory pain. Unlike synthetic drugs that often target a single molecular pathway, herbal bioactives offer a holistic approach, addressing inflammation, infection, and tissue ischemia simultaneously [4]. Plant-derived compounds such as terpenoids and alkaloids provide a broad pharmacological spectrum,

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stimulating cellular proliferation while concurrently suppressing the oxidative stress that characterizes the chronic wound microenvironment.

Recent advancements in bio-nanocomposites and self-assembling peptide-herbal systems have further expanded the potential for localized, controlled delivery of these compounds [5]. It is possible to achieve a responsive release mechanism that triggers the delivery of phytochemicals in response to specific cues like pH changes or the presence of bacterial enzymes by engineering the hydrogel at the molecular level. Utilizing naturally derived materials not only reduces the probability of adverse allergic reactions but also addresses the escalating global concern regarding antimicrobial resistance, as many plant-derived compounds possess intrinsic antibacterial mechanisms that differ from conventional antibiotics [6]. These natural agents often target the bacterial cell wall or interfere with quorum sensing, providing a robust defense against biofilm-forming pathogens that are otherwise resistant to standard clinical interventions.

2. Physiology of Human Integument

The skin serves as the primary immunological and physical barrier of the human body, maintaining internal homeostasis against a variety of environmental stressors. Its complex structure is divided into three primary layers, each contributing specific mechanical and biological properties necessary for effective defense and repair.

2.1 The Epidermis and Barrier Function

The epidermis constitutes the outermost superficial layer, primarily composed of stratified squamous epithelium. Its primary cellular constituents, keratinocytes, undergo a continuous process of differentiation from the basal layer to the stratum corneum, creating a tough, cornified envelope that prevents desiccation and pathogen entry. In the stratum basale, melanocytes contribute to ultraviolet radiation protection through melanin production, while Langerhans cells provide a sentinel immune function by detecting foreign antigens. The absence of a direct vascular supply in the epidermis requires a reliance on the diffusion of nutrients and oxygen from the underlying dermal layer, a process that is frequently compromised in chronic wound scenarios.

2.2 The Dermal Layer and Mechanical Integrity

Beneath the epidermis lies the dermis, a dense connective tissue matrix that provides the skin with its characteristic tensile strength and elasticity. This layer is populated by fibroblasts, which are responsible for the biosynthesis of the extracellular matrix (ECM), including collagen and elastin fibers. The dermis is anatomically divided into the papillary region and the deeper reticular region. The papillary dermis contains an extensive network of capillaries and sensory nerve endings, facilitating thermoregulation and tactile sensation. In contrast, the reticular dermis is characterized by thick collagen bundles that provide structural support. During the wound healing process, the recruitment and activation of dermal fibroblasts are critical for the formation of granulation tissue and the eventual closure of the wound.

2.3 The Hypodermis and Metabolic Support

The hypodermis, or subcutaneous tissue, functions as the interface between the skin and underlying musculoskeletal structures. Composed largely of adipose tissue and loose connective tissue, it serves as a thermal insulator and an energy reservoir. From a wound healing perspective, the hypodermis provides the necessary padding to protect deeper structures from mechanical trauma and houses the larger blood vessels that supply the cutaneous layers. Impairment in the perfusion of these subcutaneous vessels is often a primary factor in the development of chronic pressure ulcers and diabetic foot complications.

3. Pathophysiology of Wound Healing

The restoration of skin integrity requires the seamless integration of cellular and biochemical activities. In a healthy physiological state, this progression follows a predictable timeline; however, in chronic pathology, the biological sequence is disrupted, leading to a non-healing state [1].

3.1. Phases of Normative Tissue Repair

Healthy wound healing is traditionally categorized into four overlapping stages: hemostasis, inflammation, proliferation, and remodeling. Hemostasis occurs immediately following injury, where platelet activation and fibrin clot formation provide a temporary scaffold and release growth factors [3]. This is followed by the inflammatory phase, where neutrophils and macrophages infiltrate the wound bed to clear debris and pathogens. During the proliferative phase, fibroblasts synthesize new extracellular matrix (ECM)

while endothelial cells initiate angiogenesis to supply the metabolic demands of the regenerating tissue [5]. Finally, the remodeling phase involves the maturation of collagen fibers to restore the skin's tensile strength.

3.2. Molecular Drivers of Chronic Healing Arrest

Chronic wounds, such as those associated with vascular insufficiency or metabolic disease, typically become stalled in a persistent inflammatory state [2]. This arrest is characterized by an excessive production of reactive oxygen species (ROS) and a high concentration of pro-inflammatory cytokines, such as TNF-α and IL-1β. These biochemical imbalances trigger the upregulation of matrix metalloproteinases (MMPs), which indiscriminately degrade growth factors and essential ECM proteins, effectively preventing the transition to the proliferative phase [4]. Localized hypoxia and the formation of bacterial biofilms create a hostile microenvironment that impairs cellular migration and suppresses the activation of regenerative pathways.

3.3. Therapeutic Intervention via Herbal Hydrogels

Phytotherapeutic hydrogels are specifically engineered to intervene in this pathological state by modulating the wound microenvironment [3]. Thereby protecting viable cells from oxidative damage and reducing localized inflammation by incorporating plant-derived antioxidants, these dressings can actively scavenge excess free radicals. The hydrophilic matrix of the hydrogel mimics the natural ECM, providing a moisture-rich scaffolding environment that encourages the migration of keratinocytes and fibroblasts [6]. Moreover, the controlled delivery of pro-angiogenic herbal constituents facilitates the re-establishment of the vascular network, effectively overcoming the localized ischemia that contributes to chronicity. This multi-target approach allows the wound to bypass the inflammatory stall and progress toward successful tissue remodeling.

4. Classification and Structural Diversity of Hydrogel Scaffolds

Hydrogels are three-dimensional, cross-linked polymeric networks capable of imbibing large volumes of water or biological fluids without dissolving. Their high-water content and soft consistency closely mimic the natural extracellular matrix, making them ideal for cutaneous applications [7]. The classification of these systems is essential for determining their suitability for specific wound environments.

4.1. Categorization by Polymeric Origin

The selection of the polymer backbone significantly influences the degradation rate, mechanical stability, and bioactivity of the dressing. Natural hydrogels are derived from proteins such as collagen, gelatin, and fibrin, or polysaccharides like chitosan, alginate, and hyaluronic acid. These materials offer superior biocompatibility and often possess inherent signaling molecules that promote cell adhesion. Conversely, synthetic hydrogels, including poly(ethylene glycol) (PEG) and poly(vinyl alcohol) (PVA), provide precisely tunable mechanical properties and reproducible architectures, though they typically lack intrinsic biological cues [8].

Table 1. Comparison of Polymeric Scaffolds for Hydrogel Synthesis

Polymer Type	Common Examples	Advantages	Limitations
Natural Polysaccharides	Chitosan, Alginate, Hyaluronic Acid	Inherent antimicrobial activity, superior biocompatibility, biomimetic ECM properties.	High batch-to-batch variability, rapid biodegradation, lower mechanical strength.
Natural Proteins	Collagen, Gelatin, Silk Fibroin	Promotes cell signaling, excellent cell adhesion, high enzymatic degradability.	Potential for immunogenicity, higher production cost.
Synthetic Polymers	PVA, PEG, PEO, Pluronics	Highly tunable mechanical properties, predictable degradation rates, consistent batch quality.	Lack of intrinsic bioactivity, often requires chemical modification for cell attachment.
Hybrid Systems	Chitosan-PVA, Alginate-PEG	Synergistic combination of bioactivity and structural resilience.	Complexity in cross-linking chemistry.

4.2. Mechanisms of Cross-linking and Network Stability

The structural integrity of a hydrogel is maintained through either physical or chemical cross-links. Physical hydrogels are formed through reversible interactions such as hydrogen bonding, hydrophobic associations, or ionic interactions. These are often responsive to external stimuli like pH or temperature, allowing for "in-situ" gelation within irregular wound cavities. Chemical

hydrogels are established via covalent bonds through methods such as photopolymerization or Michael addition. These networks are generally more robust and provide a more controlled release profile for encapsulated herbal bioactives [9].

4.3. Ionic and Structural Variations

The charge density of the polymer network plays a critical role in its interaction with wound exudates and cellular membranes. Nonionic hydrogels remain neutral and are often used for simple moisture retention. Ionic hydrogels, which may be anionic, cationic, or amphoteric, can actively interact with charged proteins and ions in the wound bed. For instance, cationic hydrogels like chitosan exhibit intrinsic mucoadhesive and antimicrobial properties through their interaction with negatively charged bacterial cell walls [10]. Structurally, hydrogels can be engineered as amorphous matrices, semi-crystalline films, or spherical microparticles, depending on whether the clinical objective is immediate coverage or deep-tissue delivery.

Table 2. Technical Specifications of Characterization Techniques

Analytical Technique	Evaluated Parameters	Scientific Significance for Wound Care
SEM / Cryo-SEM	Pore size and interconnectivity	Ensures gas exchange and facilitates cellular infiltration.
FTIR Spectroscopy	Functional group analysis	Confirms successful encapsulation of herbal bioactives and polymer compatibility.
Swelling Kinetic Analysis	Equilibrium Swelling Ratio	Determines the capacity to absorb wound exudate and maintain a moist environment.
Rheological Profiling	Storage (G) and Loss (G) Moduli	Assesses mechanical stability and "injectability" for deep wound cavities.
TGA / DSC	Thermal stability	Evaluates the integrity of the material during sterilization and shelf storage.

5. Usage of Phytotherapeutics

The development of herbal hydrogels requires a precise integration of phytochemical extraction and material engineering to ensure the stability of fragile plant metabolites.

5.1. Phytochemical Extraction and Standardization

To obtain high-purity bioactive fractions, such as flavonoids from *Nelumbo nucifera* (lotus) leaves or sea buckthorn oil, advanced extraction techniques are employed. Solvent-assisted extraction using ethanol-water mixtures is frequently combined with ultrasonic treatment to disrupt plant cell walls and maximize the yield of phenolics and terpenoids. Following extraction, centrifugation and vacuum filtration are utilized to isolate the flavonoid-rich supernatants, which are then standardized to ensure consistent pharmacological activity across different batches [11].

Table 3. Functional Role of Major Phytoconstituents in Wound Pathophysiology

Bioactive Class	Representative Compounds	Primary Therapeutic Target	Mechanism
Flavonoids	Quercetin, Puerarin, Epicatechin	Anti-inflammatory & Antioxidant	Scavenging of reactive oxygen species (ROS) and inhibition of TNF-α
Terpenoids	Asiaticoside, Lupeol	Tissue Proliferation	Stimulation of collagen biosynthesis and fibroblast proliferation.
Alkaloids	Berberine, Piperine	Antimicrobial	Disruption of bacterial peptidoglycan layers and inhibition of efflux pumps.
Steroids	Ergosterol, β-Sitosterol	Re-epithelialization	Modulation of keratinocyte migration and barrier restoration.
Phenolic Acids	Gallic acid, Ferulic acid	Angiogenesis	Upregulation of VEGF and HIF-1α signaling pathways.

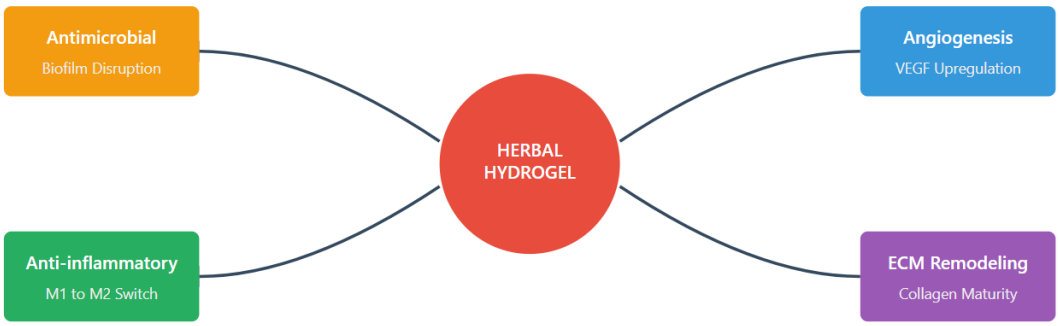

Figure 1. Multi-target Biological Mechanism of Action

5.2. Physicochemical and Morphological Characterization

The efficacy of a hydrogel dressing is dependent on its porosity and surface characteristics. Scanning electron microscopy (SEM) is utilized to visualize the interconnected pore structure, which must be large enough to allow for gas exchange and nutrient transport while remaining small enough to prevent bacterial infiltration. Spectroscopic techniques, such as Fourier-transform infrared spectroscopy (FTIR) and X-ray diffraction (XRD), confirm the chemical compatibility between the herbal extracts and the polymer matrix, ensuring that the bioactive compounds are successfully loaded without losing their functional groups [12].

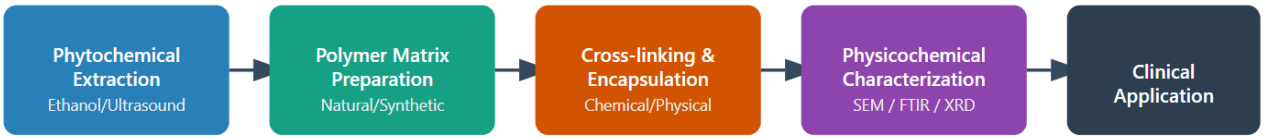

Figure 2. Fabrication and Characterization of Herbal Hydrogels

6. Therapeutic Mechanisms in Chronic Wound Repair

Herbal hydrogels function as active participants in the healing process by modulating the biochemical signals within the wound microenvironment.

6.1. Hemostatic Regulation and Early Clot Stabilization

Effective wound management begins with the control of hemorrhage. Advanced hydrogels, particularly those based on chitosan and augmented with bioactive glass or herbal hemostats, facilitate rapid coagulation. These materials promote vasoconstriction and enhance the recruitment of platelets. The porous architecture of the hydrogel serves as a template that concentrates clotting factors, thereby accelerating the formation of a stable fibrin clot and providing a foundation for subsequent tissue growth [13].

Table 4. Key Performance Indicators (KPIs) for Experimental Validation

Evaluation Metric	Target Value/Range	Clinical Rationale
WVTR (Water Vapor Transmission Rate)	2000 - 2500 g/m^2/day	Prevents fluid accumulation (maceration) while avoiding wound desiccation.
Antimicrobial Inhibition	> 99.0% ($\log_{10} \geq 3$)	Clinically significant reduction in localized bacterial load and biofilm prevention.
Hemostatic Time	< 180 seconds	Necessary for immediate stabilization of acute or surgical trauma.
Wound Contraction Rate	≥90% (by Day 14)	Indicator of accelerated healing kinetics in full-thickness injury models.
Porosity Percentage	60% - 90%	Required for efficient nutrient transport and vascular ingrowth.

6.2. Antimicrobial Efficacy and Biofilm Disruption

Infection is a primary cause of healing arrest in chronic ulcers. Herbal hydrogels address this through the sustained release of antimicrobial agents like puerarin or essential oils. These compounds disrupt the integrity of bacterial cell membranes, causing leakage of intracellular contents and inhibiting DNA replication. The hydrogel prevents the formation of biofilms complex bacterial communities that are highly resistant to conventional antibiotics. These dressings help the body's innate immune system clear localized pathogens more effectively by shifting the local environment toward an M2 macrophage phenotype [14].

6.3. Mitigation of Pathological Inflammation and Oxidative Stress

Chronic wounds are characterized by an overabundance of reactive oxygen species (ROS), which damage healthy cells and degrade the ECM. Phytotherapeutic hydrogels rich in polyphenolics act as potent antioxidants, scavenging free radicals and reducing the expression of pro-inflammatory cytokines such as TNF-alpha and IL-6. This antioxidant action protects migrating fibroblasts and keratinocytes, facilitating the transition from a chronic inflammatory state to the proliferative phase of healing [15].

6.4. Promotion of Angiogenesis and Revascularization

The restoration of blood supply is vital for delivering oxygen and nutrients to the regenerating tissue. Bioactive hydrogels can be engineered to deliver pro-angiogenic herbal components, such as *Panax notoginseng* saponins or salvianolic acids. These agents stimulate the proliferation of endothelial cells and the formation of new capillary networks, evidenced by the increased expression of vascular endothelial growth factor (VEGF) and CD31 markers. This neovascularization is essential for supporting the metabolic demands of the newly formed granulation tissue [16]

7. Experimental Evaluation of Herbal-Integrated Materials

The performance of a phytotherapeutic hydrogel is validated through a series of standardized *in-vitro* assays that simulate the biochemical and physical environment of a chronic wound.

7.1. Quantitative Antimicrobial and Viability Assays

The efficacy of herbal-treated scaffolds against common wound pathogens, such as *Staphylococcus aureus* and *Escherichia coli*, is determined through a combination of traditional culture methods and modern imaging [17].

7.1.1. Colony Enumeration and Inhibition Kinetics

The bactericidal activity is primarily quantified using the spread-plate method. Bacterial suspensions are exposed to the hydrogel matrix for specific intervals, after which the surviving populations are cultured on nutrient agar. The resulting colony-forming units (CFUs) are compared against control groups to calculate the percentage of microbial inhibition. This data provides critical information regarding the release kinetics of the herbal bioactives and their ability to maintain a sterile environment over extended periods.

7.1.2. Fluorescence-Based Viability Profiling

To visualize the mechanism of bacterial cell death, SYTO-9 and propidium iodide (PI) staining are employed. SYTO-9 is a small molecule that penetrates all bacterial membranes, labeling nucleic acids with green fluorescence. In contrast, PI is a larger, membrane-impermeant dye that only labels cells with compromised structural integrity, emitting red fluorescence. High-resolution fluorescence microscopy allows for the real-time quantification of membrane disruption, providing a direct measurement of the material's ability to eradicate localized infections without the use of systemic antibiotics.

7.2. Assessment of Water Vapor Transmission and Permeation

A critical function of any wound dressing is maintaining a balanced moisture level to prevent both tissue maceration and desiccation [18].

7.2.1. Standardized Evaporation Kinetics

The water vapor transmission rate (WVTR) is measured according to ASTM E96 standards. Hydrogel samples are sealed over vials containing a known volume of deionized water and placed in a controlled environmental chamber (37 °C, 30 ± 5% humidity). By monitoring the weight loss periodically, researchers can determine the rate at which moisture escapes the wound bed. An optimal WVTR ensures that the hydrogel acts as a "breathable" barrier, mimicking the natural transpiration of the skin.

7.2.2. Regulatory Effects on Cellular Migration

Maintaining an ideal moisture balance is essential for the metabolic activity of keratinocytes and the regulation of matrix metalloproteinases (MMPs). If the hydrogel is too occlusive, the resulting moisture accumulation can lead to the breakdown of healthy periwound skin. Conversely, a hydrogel that dries too quickly will cause the wound bed to crust, trapping inflammatory markers and halting the inward migration of epithelial cells. Fine-tuning the polymer cross-linking density allows for the precise control of these permeation characteristics.

8. *In-Vivo* Efficacy

The ultimate validation of herbal hydrogels occurs in animal models, typically utilizing Sprague-Dawley rats with full-thickness posterior skin wounds to assess systemic safety and local regeneration.

8.1. Wound Contraction and Healing

Progress in wound closure is monitored over a 14-day period, providing a temporal map of the healing trajectory [19].

8.1.1. Digital Planimetry and Area Analysis

The physical dimensions of the wound are recorded at regular intervals (Days 0, 3, 7, 10, and 14) using high-resolution digital photography. Image analysis software, such as ImageJ, is utilized to calculate the remaining wound area by converting pixel data into metric units. This quantitative approach allows for the calculation of the "Healing Rate Index," providing a statistically significant comparison between herbal-loaded hydrogels and conventional treatments like silver-impregnated gauze or commercial petroleum dressings.

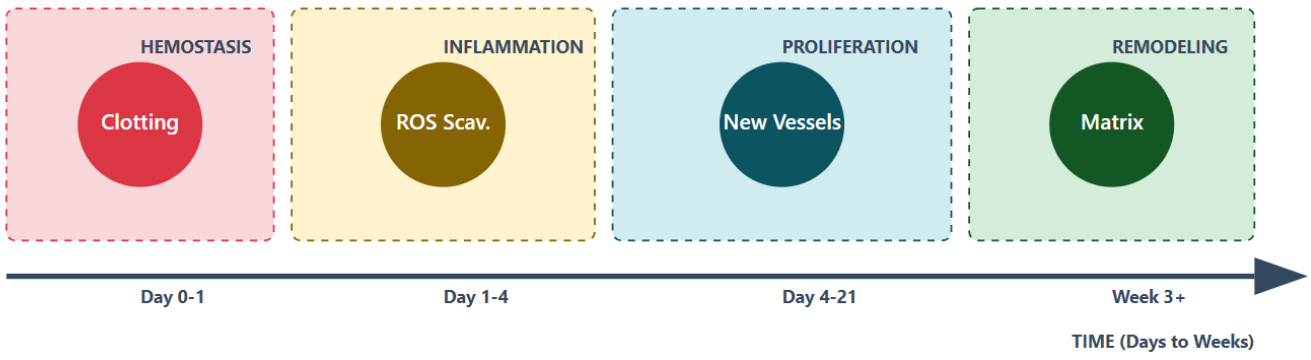

Figure 3. Temporal Stages of Wound Repair

8.1.2. Phytochemical Stimulation of Myofibroblasts

The accelerated contraction observed in herbal-treated wounds is largely attributed to the influence of terpenoids and flavonoids on myofibroblast differentiation. These compounds appear to upregulate the expression of alpha-smooth muscle actin (α-SMA),

the protein responsible for the contractile force that pulls the wound edges together. The hydrogel minimizes the time the internal tissue is exposed to potential environmental contaminants by facilitating faster physical closure.

8.2. Microscopic Tissue Analysis and Collagen Maturation

Histological examination of the regenerated tissue offers definitive evidence regarding the quality and maturity of the new skin [20].

8.2.1. Histomorphological Staining Protocols

On specific sacrifice days, skin samples are fixed in paraformaldehyde and processed into paraffin sections. Hematoxylin and eosin (H&E) staining is the gold standard for evaluating general tissue architecture, allowing researchers to observe the re-epithelialization process and the density of the inflammatory infiltrate. A successful herbal intervention is typically marked by a visible reduction in polymorphonuclear leukocytes and an increase in the thickness of the newly formed epidermis.

8.2.2. Collagen Realignment and Granulation Quality

Masson's trichrome staining is employed to specifically visualize the deposition of collagen within the dermis. In chronic wounds, collagen is often disorganized and fragmented due to high protease activity. However, wounds treated with bioactive hydrogels show a shift from haphazardly arranged Type III collagen to mature, bundled Type I collagen. This realignment is a hallmark of successful tissue remodeling, ensuring that the healed skin regains its original tensile strength and structural resilience.

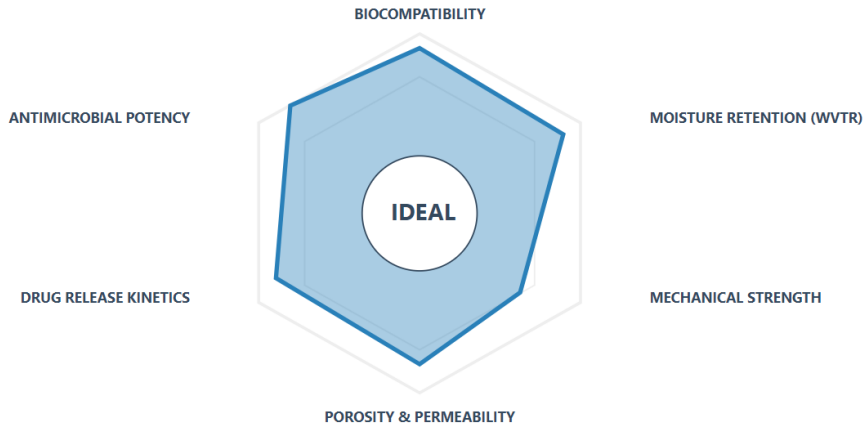

Figure 4. Critical Quality Attributes (CQAs) of an Advanced Herbal Hydrogel

9. Current Challenges and Future Perspectives

Despite the therapeutic potential of herbal hydrogels, several hurdles remain in bridging the gap between laboratory research and clinical application.

9.1. Limitations

9.1.1. Constraints of Short-Term Follow-up

The majority of current preclinical studies are limited to a 14-day observation window. While this is sufficient to observe initial wound closure, it does not allow for the assessment of long-term outcomes such as hypertrophic scarring or the functional recovery of sensory nerves and sweat glands. Future research must extend observation periods to several months to ensure that the regenerated tissue remains stable and does not undergo pathological fibrosis.

9.1.2. Challenges in Phytochemical Standardization

The chemical composition of herbal extracts can vary significantly based on the plant's geographical origin, harvest season, and extraction method. This variability poses a major challenge for the mass production of hydrogels. Establishing strict fingerprinting

protocols using UHPLC-MS/MS is necessary to ensure that every batch of the herbal hydrogel contains the exact concentration of bioactive steroids or flavonoids required for a consistent therapeutic effect.

9.1.3. Translational Hurdles in Clinical Scaling

Transitioning from small-scale laboratory fabrication to large-scale industrial manufacturing requires the development of cost-effective sterilization methods that do not degrade the sensitive plant metabolites. The regulatory pathway for "combination products" which involve both a medical device (the hydrogel) and a pharmacological agent (the herbal extract) is more complex than for standard dressings, necessitating rigorous clinical trials to prove multi-target safety and efficacy.

10. Conclusion

Herbal hydrogels represent a significant advancement in the management of chronic wounds by providing a multifunctional platform that addresses the biological complexities of non-healing ulcers. These systems effectively mitigate inflammation, eradicate microbial colonization, and stimulate neovascularization by combining the moisture-retention capabilities of polymeric networks with the diverse pharmacological profiles of plant-derived metabolites. Experimental evidence shows that these bio-nanocomposites outperform conventional dressings in terms of wound closure rates and histological quality. The safety, cost-effectiveness, and therapeutic versatility of these materials position them as a primary candidate for future wound care management. The development of these refined phytotherapeutic scaffolds offers a promising route toward restoring patient quality of life and reducing healthcare complications.

References

[1] Sen CK. Human Wounds and Its Burden: An Updated Compendium of Estimates. Adv Wound Care (New Rochelle). 2019;8(2):39-48.

[2] Lindley LE, Stojadinovic O, Pastar I, Tomic-Canic M. Overcoming the Barriers to Wound Healing: Are We There Yet?. Adv Wound Care (New Rochelle). 2016;5(11):479-500.

[3] Zhu Y, Cankova Z, Iatrou M, et al. Stage-Responsive Delivery of Therapeutic Agents for Wound Healing. Front Chem. 2022;10:1038839.

[4] Boateng JS, Matthews KH, Stevens HN, Eccleston GM. Wound healing dressings and drug delivery systems: a review. J Pharm Sci. 2008;97(8):2892-2923.

[5] Wang W, Lu KJ, Yu CH, et al. Nano-drug delivery systems in wound healing and regeneration. World J Biol Pharm Health Sci. 2021;7(2):27-40.

[6] Saghazadeh S, Hafizi C, Hosseinzadeh S, et al. Drug delivery systems in wound care: Recent developments and future prospects. Adv Drug Deliv Rev. 2018;127:138-166.

[7] Garg S, Garg A. Hydrogel: Classification, Properties, Preparation and Technical Features. Chem Biomol Eng. 2017;2(3):163-170.

[8] Ahmed EM. Hydrogel: Preparation, characterization, and applications: A review. J Adv Res. 2015;6(2):105-121.

[9] Rosiak JM, Ulanski P. Synthesis of hydrogels by irradiation of polymers in bulk and in solution. Radiat Phys Chem. 1999;55(2):139-151.

[10] Sahiner N. One step preparation of chitosan-based micro-and nanogels. Carbohydr Polym. 2006;64(2):171-183.

[11] Chen X, Wang G, Zhang X, et al. Extraction and characterization of flavonoids from lotus leaves and their antioxidant activity. Int J Biol Macromol. 2020;154:1124-1133.

[12] Singh B, Sharma S. Design of antibiotic containing hydrogel wound dressings: evaluation of network characteristics and drug release. Mater Sci Eng C Mater Biol Appl. 2021;120:111756.

[13] Huang Y, Zhao X, Ma PX. Injectable hydrogels as a delivery system for wound healing. Chem Eng J. 2022;433:133503.

[14] Zhao X, Wu H, Guo B, et al. Antibacterial anti-oxidant electroactive injectable hydrogel as self-healing wound dressing with hemostasis and adhesiveness for cutaneous wound healing. Biomaterials. 2017;122:34-47.

[15] Liang Y, Zhao X, Hu T, et al. Adhesive Hemostatic Antioxidant Conductive Injectable Composite Hydrogels for Wound Healing. Acta Biomater. 2019;97:151-167.

[16] Li S, Xu J, Xu Z, et al. Injectable and biodegradable hydrogels for local and sustained delivery of Panax notoginseng saponins to promote angiogenesis in diabetic wound healing. Bioact Mater. 2020;5(3):525-535.

[17] Zhang L, Zhao X, Guo B. Injectable antibacterial conductive hydrogels with adhesive and self-healing properties as wound dressings. J Colloid Interface Sci. 2023;630:571-584.

[18] ASTM International. ASTM E96/E96M-22: Standard Test Methods for Gravimetric Determination of Water Transmission Rate of Materials. West Conshohocken, PA: ASTM International; 2022.

[19] Masson-Meyers DS, Andrade TAM, Caetano GF, et al. Experimental models and methods for cutaneous wound healing assessment. Int J Exp Pathol. 2020;101(1-2):21-37.

[20] Masson P. Some improved methods for staining in histology. J Tech Methods Bull Int Assoc Med Mus. 1929;12:75-90.