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Review Article

A Review Article on Wound Healing Hydrogels: Formulation, Mechanisms and Therapeutic Applications

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Wound repair is a coordinated biological response in which hemostasis, inflammation, tissue formation, and remodeling occur in a sequential but overlapping manner. Damage caused by burns, trauma, surgery, infection, or chronic disease can interrupt this process and delay restoration of the skin barrier. Hydrogel dressings are increasingly considered useful for wound care because their hydrated polymer networks help maintain moisture at the wound surface and can provide a vehicle for local delivery of therapeutic substances. Medicinal plants are also of interest because their flavonoids, phenolics, alkaloids, tannins, terpenoids, and related constituents may provide antioxidant, antimicrobial, anti-inflammatory, and tissue-supporting effects. This review discusses the role of hydrogels in wound care and summarizes the reported relevance of Curcuma longa, Hibiscus rosa-sinensis, Carica papaya, Catharanthus roseus, Ampelopsis japonica, Psidium guajava, Azadirachta indica, and Ocimum tenuiflorum. The review further describes formulation ingredients, quality-control tests, release studies, antimicrobial and antioxidant evaluation, and stability assessment. Combining standardized botanical extracts with a suitable hydrogel matrix may provide a useful topical platform for wound care. Nevertheless, differences in plant material, extraction procedures, phytochemical composition, formulation behavior, and biological evidence make standardization essential. More detailed preclinical and clinical investigations are required before herbal hydrogel systems can be considered established therapeutic alternatives.

Keywords: Wound healing; Hydrogel; Herbal formulation; Curcumin; Antioxidant; Antimicrobial activity; Tissue regeneration; Topical drug delivery.

INTRODUCTION

The skin is the largest organ of the human body and provides a protective barrier against microorganisms, chemicals, physical injury, and excessive water loss. It also contributes to temperature regulation and immune defense. When the skin is damaged by burns, cuts, surgery, trauma, infection, or disease, the protective barrier is disrupted and a coordinated wound-healing response begins. Wound repair is a dynamic biological process involving overlapping phases of hemostasis, inflammation, proliferation, and remodeling. Failure or delay at any stage may result in prolonged inflammation, infection, poor tissue formation, or chronic wounds. Hydrogel-based wound dressings have received substantial attention because their three-dimensional hydrophilic networks can retain large quantities of water and create a moist environment at the wound surface. Such an environment can support cell migration and tissue formation while reducing adherence of the dressing to newly formed tissue. Hydrogels may also act as vehicles for drugs, antimicrobial agents, antioxidants, and plant extracts, thereby providing opportunities for controlled or sustained topical delivery. Medicinal plants contain numerous secondary metabolites that may contribute to wound repair through complementary mechanisms. Flavonoids and phenolic compounds can reduce oxidative stress, while selected alkaloids, tannins, terpenoids, and essential-oil constituents may provide antimicrobial or anti-inflammatory effects. The present review therefore considers the integration of medicinal plant extracts with hydrogel systems as a potential approach for wound care.

2. Classification of Wounds

Wounds are injuries involving disruption of the skin or underlying tissues. They can be classified according to the extent of tissue damage, whether the skin barrier is breached, and the duration of healing.

2.1 Open Wounds

Open wounds involve disruption of the skin and exposure of underlying tissues to the external environment. They may result from trauma, falls, sharp instruments, puncture injuries, abrasions, lacerations, penetrating injuries, or surgical procedures. Because the protective skin barrier is broken, open wounds have an increased risk of contamination and infection.

2.2 Closed Wounds

Closed wounds occur when the skin remains intact while tissues and blood vessels underneath are damaged. Blood and tissue fluid may accumulate beneath the skin, causing swelling, pain, and discoloration. Contusions, hematomas, and crush injuries are common examples.

2.3 Acute Wounds

Acute wounds are recent injuries that generally progress through the normal sequence of healing within an expected period. Cuts, surgical incisions, burns, and accidental trauma are common causes. Appropriate wound care, infection control, and protection of the wound environment generally support uncomplicated healing.

2.4 Chronic Wounds

Chronic wounds fail to progress through the normal healing sequence and may remain open for prolonged periods. Persistent inflammation, infection, impaired blood circulation, diabetes, pressure injury, and other underlying conditions can contribute to delayed healing. Chronic wounds frequently require specialized dressings, pharmacological treatment, repeated assessment, and long-term monitoring.

3. Wound-Healing Process

3.1 Hemostasis

Hemostasis begins immediately after tissue injury and limits blood loss. Vasoconstriction, platelet activation, and coagulation result in formation of a fibrin-rich clot. The clot provides temporary structural protection and forms a provisional matrix through which subsequent inflammatory and reparative events can occur.

3.2 Inflammatory Phase

The inflammatory phase follows hemostasis and is characterized by recruitment of immune cells and release of inflammatory mediators. Vasodilation and increased vascular permeability allow leukocytes and plasma proteins to enter the injured area. Neutrophils and macrophages help remove microorganisms, cellular debris, and damaged tissue. Controlled inflammation is essential for defense, whereas excessive or prolonged inflammation can delay repair.

3.3 Proliferative Phase

The proliferative phase involves formation of granulation tissue, fibroblast proliferation, extracellular matrix deposition, angiogenesis, wound contraction, and re-epithelialization. Fibroblasts synthesize collagen and other matrix components, while endothelial cells contribute to formation of new blood vessels. Keratinocyte migration and proliferation help restore the epithelial barrier.

3.4 Remodeling Phase

Remodeling may continue for weeks to months. Newly deposited collagen is reorganized and progressively strengthened through maturation and cross-linking. The scar gradually becomes flatter and more organized, although the mechanical strength of healed tissue generally remains lower than that of uninjured skin.

4. Hydrogels In Wound Management

Hydrogels are three-dimensional polymeric networks capable of holding substantial amounts of water or biological fluids. Their high water content and soft, flexible structure can resemble aspects of biological tissue. In wound care, hydrogels can maintain moisture, facilitate exchange at the wound interface, and provide a matrix for incorporation of therapeutic substances. Hydrogel dressings may be prepared from natural polymers, synthetic polymers, or combinations of both. Natural materials such as chitosan, alginate, gelatin, hyaluronic acid, and cellulose derivatives can provide biocompatibility and useful biological interactions, whereas synthetic polymers can improve mechanical strength, reproducibility, and control of swelling or drug release. Selection of the polymer system depends on the intended application and characteristics of the wound. For herbal formulations, the hydrogel can function as a carrier for standardized plant extracts or selected phytoconstituents. The formulation should provide adequate physical stability, acceptable skin compatibility, uniform distribution of the active material, suitable rheology, and controlled release where required.

5. Herbal Hydrogels for Wound Healing

Plant-derived wound-healing agents are of interest because their phytochemicals may act on multiple biological pathways. Antioxidant activity can reduce oxidative stress, antimicrobial activity can limit microbial contamination, and anti-inflammatory effects can help regulate excessive inflammatory responses. Other constituents may support fibroblast activity, collagen synthesis, angiogenesis, granulation tissue formation, and re-epithelialization. The selected plants discussed below were included in the submitted manuscript because of their reported traditional or pharmacological relevance to wound care. The evidence and exact contribution of individual constituents can vary according to plant part, extraction method, dose, formulation, and experimental model.

6. Medicinal Plants and Their Wound-Healing Significance

6.1 Curcuma Longa

Curcuma longa (turmeric) belongs to the family Zingiberaceae. Curcumin is its best-known bioactive constituent and has been extensively investigated for reported biological effects. The submitted manuscript describes curcumin as influencing inflammatory signaling and cellular responses and as potentially supporting fibroblast proliferation, granulation tissue formation, collagen synthesis, and tissue repair. These properties make Curcuma longa a promising candidate for incorporation into topical hydrogel systems, provided the extract is standardized and the formulation maintains suitable stability and release characteristics.

6.2 Hibiscus Rosa-Sinensis

Hibiscus rosa-sinensis belongs to the family Malvaceae and has traditional relevance in the management of skin disorders and wounds. Flavonoids such as quercetin and kaempferol, anthocyanins, and phenolic constituents may contribute antioxidant and anti-inflammatory effects. Such activities can help create a more suitable environment for tissue repair. The submitted material also associates the plant with processes including fibroblast proliferation, collagen synthesis, angiogenesis, granulation tissue formation, and re-epithelialization.

6.3 Carica Papaya

Carica papaya belongs to the family Caricaceae. Papain is an important enzyme associated with papaya and has been used traditionally in several therapeutic contexts. The submitted manuscript describes papaya as possessing antimicrobial, antioxidant, and anti-inflammatory properties and notes investigation of aqueous fruit extract in wound models. These activities suggest potential utility in topical herbal formulations, although standardized preparation and controlled studies are required to establish reproducible therapeutic benefit.

6.4 Catharanthus Roseus

Catharanthus roseus, commonly known as Madagascar periwinkle, belongs to the family Apocynaceae. It contains several alkaloids, including catharanthine, vindoline, vinblastine, and vincristine, together with flavonoids and phenolic compounds. The submitted manuscript discusses antioxidant, anti-inflammatory, antimicrobial, and tissue-protective potential and relates these activities to fibroblast activity, collagen deposition, granulation tissue formation, and re-epithelialization. Because some constituents have potent pharmacological actions, extract standardization and safety evaluation are particularly important.

6.5 Ampelopsis Japonica

Ampelopsis japonica belongs to the family Vitaceae and has traditional use in parts of East Asia for burns and skin-related conditions. The submitted material identifies flavonoids, phenolic compounds, and stilbenoid derivatives as relevant constituents and associates them with antioxidant and anti-inflammatory effects. These properties may contribute to a wound environment favorable to tissue repair, although formulation-specific evidence should be established before therapeutic claims are made.

6.6 Psidium Guajava

Psidium guajava (guava) belongs to the family Myrtaceae and is traditionally associated with wound and skin care. The plant contains flavonoids such as quercetin, guaijaverin, and avicularin, together with tannins and phenolic compounds. The submitted manuscript describes antioxidant, antimicrobial, and anti-inflammatory potential and relates these activities to fibroblast proliferation, collagen synthesis, granulation tissue formation, angiogenesis, and re-epithelialization. These characteristics make standardized guava extracts of interest for herbal hydrogel development.

6.7 Azadirachta Indica

Azadirachta indica (neem) belongs to the family Meliaceae and has traditional use in wound and skin-related conditions. Nimbidin, nimbin, azadirachtin, salannin, and quercetin are among the constituents described in the submitted manuscript. Their reported antimicrobial, antioxidant, and anti-inflammatory activities may help control microbial growth and oxidative stress and may assist tissue repair. A hydrogel may provide a convenient topical vehicle for standardized neem extracts.

6.8 Ocimum Tenuiflorum

Ocimum tenuiflorum, commonly called Tulsi or holy basil, belongs to the family Lamiaceae. Eugenol, ursolic acid, rosmarinic acid, flavonoids, and phenolic constituents contribute to its pharmacological profile. The submitted manuscript associates these constituents with antioxidant, antimicrobial, and anti-inflammatory effects and potential support for fibroblast activity, collagen synthesis, and granulation tissue formation. These properties support further investigation of Tulsi-based hydrogel systems.

7. Conventional Agents Used In Wound Care

8. Formulation Components Of Herbal Hydrogels

A topical herbal hydrogel generally contains a gelling or polymeric phase, aqueous medium, plant extract or active constituent, and suitable excipients. The polymer determines gel structure, viscosity, swelling, adhesion, and release behavior. Depending on the formulation, carbomers, cellulose derivatives, poloxamers, alginate, chitosan, gelatin, or other compatible polymers may be selected. Other components may include humectants to reduce drying, preservatives where appropriate, penetration or release modifiers, buffering agents, and purified water. The choice and concentration of each ingredient should be justified by compatibility, safety, stability, and intended therapeutic performance. Herbal extracts should be characterized for identity and, where possible, marker compounds or total phytochemical content.

9. Evaluation Parameters

9.1 Physical Appearance

Color, odor, clarity, homogeneity, consistency, and absence of visible lumps or phase separation should be examined. A uniform preparation supports consistent topical application and reproducible dosing.

9.2 PH

The pH is measured using a calibrated digital pH meter. A topical preparation should have a skin-compatible pH and should avoid unnecessary irritation. The submitted manuscript uses approximately pH 5.5–7.0 as a practical target range.

9.3 Viscosity

Viscosity can be measured using a Brookfield viscometer. Appropriate viscosity supports spreadability, retention at the application site, and ease of administration.

9.4 Spreadability

Spreadability indicates how readily the formulation can be distributed over the wound area. It can be evaluated using a suitable glass-slide or texture-based method. Good spreadability facilitates uniform coverage without requiring excessive force.

9.5 Extrudability

Extrudability describes the force required to expel the hydrogel from its container. A formulation should be sufficiently easy to dispense while maintaining adequate structural integrity during storage.

9.6 Extract/Drug Content and Uniformity

A known quantity of hydrogel can be diluted with an appropriate solvent or buffer and analyzed by a validated analytical method, such as UV-visible spectrophotometry when the marker compound is suitable. The purpose is to confirm uniform distribution and reproducible content.

9.7 Gel Strength

Gel strength evaluates the resistance of the gel structure to deformation. Adequate strength contributes to handling stability and retention at the application site.

9.8 Swelling Index

Swelling behavior can be studied by measuring the increase in mass or dimensions of the hydrogel after exposure to a selected aqueous medium. Swelling influences water uptake, mechanical behavior, and release of incorporated substances.

9.9 In Vitro Drug/Extract Release

In vitro release may be evaluated using a Franz diffusion cell or another validated diffusion system with an appropriate receptor medium. Samples are collected at predetermined intervals and analyzed using a suitable analytical method. Release data can be fitted to mathematical models such as zero-order, first-order, Higuchi, and Korsmeyer–Peppas models when appropriate.

9.10 Antimicrobial Activity

Antimicrobial activity can be investigated using agar diffusion or another validated microbiological method against relevant test organisms. Results should be interpreted with appropriate controls and standardized inoculum and assay conditions.

9.11 Antioxidant Activity

DPPH, ABTS, or other validated antioxidant assays may be used to estimate radical-scavenging activity. Such assays provide supportive evidence of antioxidant potential but should not be considered a direct substitute for wound-healing efficacy studies.

9.12 Stability Studies

Stability assessment should monitor physical appearance, pH, viscosity, extract or marker content, microbial quality, and other relevant attributes under defined storage conditions. Appropriate stability protocols should be selected according to the formulation, packaging, intended shelf life, and applicable guidelines.

10. Mechanistic Basis Of Herbal Hydrogel-Assisted Healing

The therapeutic rationale for herbal hydrogels is based on combining the physical benefits of a hydrogel matrix with the biological activity of plant-derived constituents. During inflammation, antioxidant and anti-inflammatory constituents may help control excessive inflammatory and oxidative responses. During proliferation, an appropriate moist environment can support cell migration, while selected phytochemicals may support fibroblast activity, collagen deposition, angiogenesis, and re-epithelialization. During remodeling, continued matrix organization and collagen maturation contribute to strengthening of repaired tissue.

A simplified sequence is: Wound injury → hemostasis → controlled inflammation → fibroblast proliferation and granulation tissue formation →

angiogenesis and re-epithelialization → collagen remodeling → restoration of tissue integrity. Hydrogel application can provide moisture and act as a local delivery platform throughout this process.

11. Advantages Of Herbal Hydrogels

Herbal hydrogels can offer several potential advantages: maintenance of a moist wound environment; localized delivery of plant-derived constituents; reduced need for repeated application when sustained release is achieved; protection of the wound surface; ease of spreading; cooling and soothing effects associated with high water content; and the possibility of combining antioxidant, antimicrobial, and anti-inflammatory activities in a single formulation. These advantages make hydrogels attractive for further pharmaceutical development.

12. LIMITATIONS AND CHALLENGES

The major challenges include variability in plant material, differences in extraction procedures, uncertain concentrations of individual phytochemicals, potential incompatibility between extracts and polymers, stability problems, microbial contamination, and batch-to-batch variation. In addition, in vitro antioxidant or antimicrobial activity does not automatically demonstrate clinical wound-healing efficacy. Standardized analytical methods, appropriate controls, reproducible manufacturing, toxicity assessment, and well-designed in vivo and clinical studies are required.

13. RECENT ADVANCES AND FUTURE PERSPECTIVES

Current research is increasingly focused on multifunctional wound dressings capable of providing moisture management together with controlled delivery of therapeutic agents. Natural and synthetic polymer combinations, stimuli-responsive systems, nanostructured carriers, antimicrobial materials, and bioactive scaffolds are being investigated. For herbal hydrogels, future work should prioritize standardized extracts, identification of marker compounds, improved control of release, compatibility studies, advanced packaging, and robust stability evaluation. For pharmacy-oriented development, the most important translational steps are reproducible raw-material authentication, validated extraction, formulation optimization, quality control, safety testing, and evidence from relevant animal and human studies. These steps can help bridge the gap between traditional use and scientifically supported wound-care products.

DISCUSSION

The reviewed material indicates that medicinal plant materials may contribute to wound care through multiple complementary activities, including antioxidant, antimicrobial, anti-inflammatory, and tissue-regenerative effects. The selected plants—Curcuma longa, Hibiscus rosa-sinensis, Carica papaya, Catharanthus roseus, Ampelopsis japonica, Psidium guajava, Azadirachta indica, and Ocimum tenuiflorum—contain diverse phytochemicals that may influence different aspects of tissue repair. A hydrogel matrix can complement these activities by maintaining a moist environment and providing a suitable vehicle for topical delivery. The submitted manuscript also emphasizes evaluation of appearance, pH, viscosity, spreadability, extract content, gel strength, extrudability, in vitro release, antimicrobial activity, and stability. These tests are useful for preliminary formulation development; however, the final evidence package should include validated analytical methods, appropriate controls, microbiological quality, skin compatibility, and efficacy studies. Therefore, herbal hydrogels should be regarded as promising pharmaceutical platforms rather than established substitutes for standard clinical wound care without adequate evidence.

CONCLUSION

Herbal hydrogel formulations represent a promising approach for topical wound care because they combine the moisture-retaining and drug-delivery characteristics of hydrogels with the reported biological effects of medicinal plant constituents. Selected plants such as Curcuma longa, Hibiscus rosa-sinensis, Carica papaya, Catharanthus roseus, Ampelopsis japonica, Psidium guajava, Azadirachta indica, and Ocimum tenuiflorum provide diverse phytochemicals with reported antioxidant, antimicrobial, anti-inflammatory, and tissue-repair potential. A successful formulation requires suitable polymer selection, standardized herbal material, uniform active-content distribution, skin-compatible pH, acceptable rheology, controlled release where required, and adequate stability. Further preclinical and clinical studies are necessary to establish long-term safety, reproducibility, therapeutic efficacy, and commercial feasibility.

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