

Review

A Review on Development of Anti-Inflammatory Hydrogel Incorporating Tulsi and Indian Frankincense for Enhanced Wound Healing and Tissue Repairing

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Abstract:

The creation of hydrogels infused with herbal components for wound healing has surfaced as a potential direction in biomedical research and natural medicine. This research examines the composition and therapeutic efficacy of anti-inflammatory hydrogel systems using *Ocimum sanctum* (Tulsi) and *Boswellia serrata* (Indian Frankincense). These herbs are esteemed in traditional medicine for their powerful anti-inflammatory, antibacterial, antioxidant, and tissue-regenerative qualities. The review examines the physiological mechanisms of wound healing, emphasises the significance of inflammatory regulation, and offers comprehensive insights into the phytochemistry and pharmacodynamics of Tulsi and *Boswellia*. It also explores contemporary formulation methodologies, assessment criteria, and preclinical evidence, emphasising how these botanical medicines promote healing when integrated into hydrogel systems. Challenges and constraints are thoroughly assessed, and future opportunities for sophisticated hydrogel-based herbal formulations are delineated.

Keywords: Hydrogel, Tulsi, *Ocimum sanctum*, Indian Frankincense, *Boswellia serrata*, Wound healing, Anti-inflammatory, Herbal formulation, Polyherbal hydrogel

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1. Introduction

Wound healing is a complex biological process characterized by haemostasis, inflammation, proliferation, and remodeling stages. An imbalance in these phases, particularly persistent inflammation, may result in chronic wounds, delayed healing, or pathological scarring. Contemporary wound care approaches seek to safeguard the wound area while simultaneously fostering tissue regeneration and reducing infection and inflammation. Hydrogels have developed as a flexible wound care material due to their high water content, biocompatibility, and capacity to carry therapeutic chemicals. Hydrogels can establish a humid environment favorable for healing, safeguard against

microbial intrusion, and deliver active substances in a controlled way.

The use of herbal extracts into hydrogel compositions signifies a potential strategy, merging the biological efficacy of natural actives with the structural benefits of hydrogels. This review examines the integration of Tulsi (*Ocimum sanctum*) and Indian Frankincense (*Boswellia serrata*) into hydrogel matrices. Both herbs have been extensively utilized in Ayurveda and are corroborated by contemporary pharmacological research for their anti-inflammatory, antioxidant, and tissue-regenerative properties. Their combined application in hydrogel formulations is a burgeoning field of research with prospective uses in chronic wounds, diabetic ulcers, and surgical incisions. [1,2]

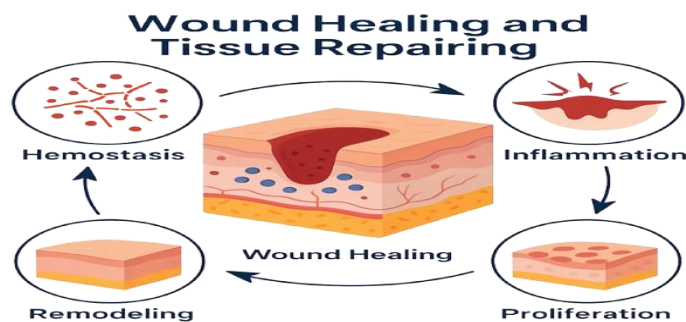


Figure1. The process of wound healing and tissue repairing

1.1 Wound Healing and Tissue Repairing [3-6]

Wound healing is an essential physiological process that reinstates the integrity of damaged tissues after injury. It is an intricate sequence of cellular and molecular processes comprising several overlapping yet separate phases:

1.1.1 Phases of Wound Healing

1. Hemostasis Phase

- Begins immediately after injury.
- Platelet aggregation and blood clot formation prevent further bleeding.
- Release of growth factors such as PDGF and TGF- β initiates the repair process.

2. Inflammatory Phase

- Occurs within hours to days post-injury.
- Neutrophils and macrophages migrate to the site.
- Pathogens are cleared, and inflammatory cytokines like IL-1 and TNF- α are released.

3. Proliferative Phase

- Fibroblasts produce extracellular matrix and collagen.
- Angiogenesis and granulation tissue formation occur.
- Re-epithelialization begins to cover the wound.

4. Remodeling (Maturation) Phase

- Lasts from weeks to months.
- Type III collagen is replaced by Type I collagen.
- Scar tissue forms and tensile strength is restored.

1.1.2 Key Aspects

Platelets initiate hemostasis and attract immune cells.

Neutrophils and **macrophages** clear debris and bacteria.

Fibroblasts synthesize collagen and ECM.

Endothelial cells promote angiogenesis.

Keratinocytes are involved in re-epithelialization.

1.1.3 Factors Affecting Wound Healing

- **Positive Influences:** Moist environment, growth factors, antioxidants
- **Negative Influences:** Infection, ischemia, diabetes, prolonged inflammation, oxidative stress

1.1.4 Desirable Properties in Wound Healing

Effective hydrogel wound dressings should possess the following:

- High water absorption to maintain wound moisture.
- Biodegradability and biocompatibility.
- Adequate mechanical strength and flexibility.
- Ability to support cellular migration and proliferation.
- Antimicrobial or anti-inflammatory properties when loaded with active agents.

1.1.5 Commercial Hydrogel Products

Examples include:

- **Intrasite Gel:** amorphous hydrogel used for necrotic and sloughy wounds.
- **Vigilon:** transparent gel sheet that allows wound observation.
- **DermaSyn:** hydrogel infused with silver for antimicrobial action.

Hydrogels also serve as platforms for tissue engineering, burn therapy, and transdermal drug

delivery.

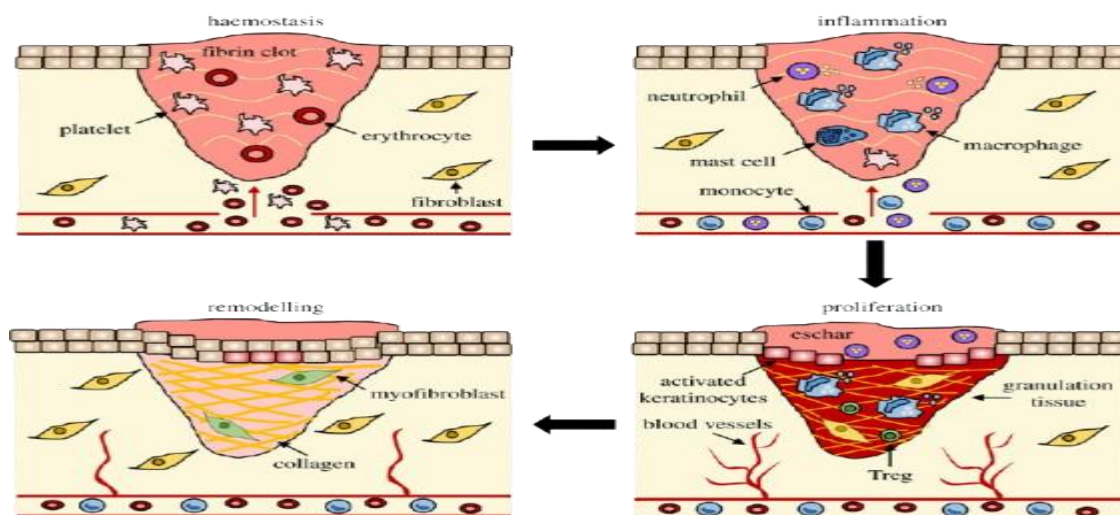


Figure 2: the stages of wound repair and their major cellular components. Wound repair begins with haemostasis, where a platelet plug prevents blood loss and a preliminary fibrin matrix is formed.

2. Hydrogels

Hydrogels have garnered significant attention over the past fifty years because to their exceptional potential in various applications. Hydrogels has the capacity to absorb water owing to the presence of hydrophilic functional groups linked to the polymeric backbone. Their resistance to disintegration is due to the cross-links established between network chains. [7].

2.1 Desired physicochemical properties of drug which required for formulation of topical hydrogels are

1. The medication must have adequate hydrophilicity.
2. The pH of a saturated aqueous solution of the drug must be between 5 and 9.
3. Drug solutions exhibiting elevated acidity or alkalinity are unsuitable for topical application. [8]

2.2 Applications of hydrogel

1. Wound healing: Hydrogels has the ability to retain water and medicines due to their linked structure. Due to their moisture retention capabilities, they may effectively collect and retain fluids exuded from wounds. The gel is composed of either polyvinyl pyrrolidone or polyacrylamide, including a water concentration of 70% to 95%. [9]

2. Medication delivery in the gastrointestinal tract:

Hydrogels provide targeted drug administration to specific regions inside the gastrointestinal tract (GIT). Colon-specific hydrogels including pharmaceuticals exhibit tissue specificity and undergo changes in pH or enzymatic activity, leading to the breakdown of the drug. [10, 11]

3. Transdermal Delivery: Various drug delivery systems employing hydrogels have been developed to enable medicine administration through the transdermal route. Researchers are now investigating hydrogel-based formulations for transdermal iontophoresis to improve the permeation of medicines such as hormones and nicotine.

4. Gene delivery: Altering the composition of hydrogels allows for the targeted transport of nucleic acids to specific cells, hence enhancing gene therapy. Hydrogels has considerable promise for the management of several inherited or acquired diseases. [12, 13]

5. Tissue Engineering: Micronised hydrogels are employed for the intracellular delivery of macromolecules into the cytoplasm of antigen-presenting cells. Agarose, methylcellulose, and other naturally derived materials serve as hydrogel polymers commonly utilised in tissue engineering. [14]

6. Ocular drug delivery: Ocular pharmaceutical delivery methods often utilise hydrogels. Hydrogels provide controlled or sustained release, hence decreasing dosage frequency and enhancing the medication's efficiency by accurately targeting its site of action. This minimises the required dosage and ensures reliable administration of the drug.

6. Function of polymers in hydrogel synthesis

Hydrogel administration techniques are favoured dosage forms that have several benefits, including ease of use, painlessness, enhanced efficacy due to extended rheological, swelling, and sorption properties, controlled drug release, and responsiveness to stimuli. Cellulose ether-derived hydrogels are significantly valued for their adjustable solubility, prolonged efficacy, and regulated release of active substances, in addition to their abundant availability, cost-effectiveness, and the flexibility to access raw ingredients from diverse origins. Hydroxypropyl methylcellulose (HPMC), commonly known as "hypromellose," is a widely used cellulose ether in pharmaceutical manufacturing, serving as a filler, coating, and carrier. The investigation of hydrogel carriers composed of polymer complexes and modified HPMC using acrylic, citric, and lactic acids, PVP, chitosan, Na-CMC, and gelatin is significantly relevant due to its essential rheological and swelling properties. This article aims to examine contemporary research and advancements in hydrogel systems derived from cellulose ethers, specifically HPMC, by assessing their characteristics, production techniques, and potential applications in medicine and pharmacy.

7. Formulation considerations of herbal hydrogel [15]

Hydrogels are three-dimensional polymeric networks that can hold significant amounts of water while maintaining their structural integrity. Hydrogels in herbal drug administration provide several benefits, such as sustained release, enhanced skin permeability, and heightened patient compliance. The incorporation of plant extracts like *Ocimum sanctum* and *Boswellia serrata* into hydrogel matrix requires careful consideration of formulation parameters to ensure efficacy and stability.

2.3. Hydrogels in Biomedical Applications

Hydrogels are cross-linked hydrophilic polymers capable of absorbing water several times their dry weight, resulting in a gel-like structure that resembles the natural extracellular matrix (ECM). This distinctive characteristic allows them to function as superior transporters for bioactive substances and frameworks for tissue regeneration. [16, 17]

2.4 Classification of Hydrogels

Hydrogels can be broadly categorized into:

- **Natural hydrogels:** derived from biopolymers like alginate, gelatin, chitosan, agarose, collagen.
- **Synthetic hydrogels:** prepared from polymers such as polyvinyl alcohol (PVA), polyethylene glycol (PEG), polyacrylamide.
- **Semi-synthetic hydrogels:** hybrids combining natural and synthetic polymers to enhance performance.

Advantages

- Hydrogel has superior elasticity and strength compared to other hydrogels of similar softness. The hydrogel implant material, composed of a copolymer of methyl acrylate and hydroxyethyl acrylate, demonstrates resilience and flexibility.
- Hydrogel-based microvalves provide several advantages over conventional microvalves, notably their intrinsic simplicity.
- The device has the following characteristics: it is manufactured by a specific technique, operates without an external power source, contains no electronic components, demonstrates a significant displacement of 185µm, and can create a substantial force of 22 mn.
- Researchers are now examining natural hydrogel polymers for potential in tissue engineering. The components consist of agarose, methylcellulose, and other polymers sourced from natural origins. [18, 19].

3. Pharmacological Profile of Tulsi (*Ocimum sanctum*)

Tulsi, or Holy Basil, holds a prestigious position in traditional medicine due to its extensive healing

qualities. It is a substantial source of phytochemicals with demonstrated effectiveness in regulating inflammation and oxidative stress—two essential aspects in wound pathophysiology.

Tulsi embodies the comprehensive lifestyle concept of well-being inherent in Ayurveda. Tulsi has a pungent and bitter taste and is said to penetrate deep tissues, dry secretions, and balance kapha and vata doshas. The consistent use of tulsi is said to prevent disease, improve general health, foster well-being, prolong life, and assist in coping with daily challenges. Tulsi is acknowledged for its ability to enhance complexion, improve vocal quality, and promote attractiveness, intellect, endurance, and emotional tranquility. Tulsi is recommended for the treatment of numerous conditions, such as anxiety, cough, asthma, diarrhoea, fever, dysentery, arthritis, ocular disorders, otalgia, indigestion, hiccups, vomiting, gastrointestinal, cardiovascular, and genitourinary issues, lumbago, dermatological problems, ringworm, and bites from insects, snakes, and scorpions, as well as malaria.[20,21]

3.1 Botanical classification

- **Family:** Lamiaceae
- **Parts used:** Leaves, seeds, essential oil

- **Cultivars:** Rama Tulsi, Krishna Tulsi, Vana Tulsi

3.2 Phytochemical Constituents

- **Phenolic compounds:** Eugenol, rosmarinic acid, gallic acid
- **Triterpenoids:** Ursolic acid
- **Essential oils:** Linalool, carvacrol
- **Flavonoids:** Orientin, vicenin

3.3 Pharmacological Activities

- **Anti-inflammatory:** Suppresses pro-inflammatory cytokines like TNF- α and IL-6, inhibits COX and LOX enzymes.
- **Antioxidant:** Increases glutathione levels and scavenges reactive oxygen species (ROS).
- **Antimicrobial:** Effective against *Staphylococcus aureus*, *Pseudomonas aeruginosa*, and fungal strains.
- **Wound healing:** Promotes angiogenesis, epithelialization, and fibroblast activity.

Experimental studies show that topical application of Tulsi extracts significantly accelerates wound contraction and collagen deposition.



Figure: 3 Holi Tulsi Leave

4. Pharmacological Profile of Indian Frankincense (*Boswellia serrata*)

Boswellia serrata resin, historically utilised as an anti-inflammatory substance, has attracted scientific attention due to its distinctive pharmacological

characteristics, especially in chronic inflammatory disorders.

Historically, preparations from the oleo-gum resin of *Boswellia serrata* Roxb. ex Colebr. (family Burseraceae), referred to as Indian frankincense or Salai Guggal, have been employed in traditional

Ayurvedic medicine to treat inflammatory conditions, including osteoarthritis and chronic gastrointestinal disorders. [22-24]

4.1 Botanical classification

- **Family:** Burseraceae
- **Active resinous exudate:** Oleo-gum resin
- **Geographic distribution:** India, North Africa, Middle East

4.2 Phytochemicals

- Boswellic acids: AKBA, KBA
- Other terpenoids: β -boswellic acid, acetyl-boswellic acid

4.3 Pharmacological Properties

- **Anti-inflammatory:** Inhibits 5-LOX, reducing leukotriene synthesis.
- **Anti-angiogenic and anti-proliferative:** Useful in psoriasis and abnormal scar formation.
- **Antimicrobial and analgesic effects.**
- **Wound healing:** Promotes fibroblast proliferation, angiogenesis, ECM remodeling, and collagen maturation.

Preclinical wound models have demonstrated improved tensile strength and tissue regeneration with topical *Boswellia* preparations.



Figure: 4 Indian Frankincense *Boswellia serrata*

5. Synergistic Effects of Tulsi and *Boswellia*

Combining Tulsi and *Boswellia* may amplify their individual therapeutic effects. Their phytoconstituents act on multiple pathways:

- Inhibition of both COX and LOX enzymes
- Combined antimicrobial action
- Enhanced collagen synthesis and angiogenesis
- Reduced oxidative stress via multiple antioxidant pathways

The potential for dual-action anti-inflammatory and regenerative effects makes them ideal for co-formulation in hydrogel systems.

6. Design and Development of Herbal Hydrogels

Formulating a hydrogel incorporating Tulsi and *Boswellia* requires careful consideration of solubility, compatibility, release kinetics, and physical properties.

6.1 Extraction and Preparation

- **Aqueous and ethanol extractions** of Tulsi leaves and *Boswellia* resin
- **Phytochemical standardization** using HPLC or UV-spectroscopy

6.2 Hydrogel Base Formulation

- Gelling agents: Carbopol, sodium alginate, PVA
- Crosslinkers: Glutaraldehyde, genipin, CaCl_2
- Plasticizers: Glycerol, propylene glycol

6.3 Evaluation [25]

- **Physical properties:** Clarity, viscosity, texture, spreadability
- **pH and swelling index:** Essential for compatibility with wound environment
- **Drug content and entrapment efficiency**
- **In vitro release studies:** Dialysis bag or Franz diffusion cell

- **Antibacterial studies:** Agar diffusion or MIC testing
- **Accelerated stability testing** as per ICH guidelines

7. Preclinical and Clinical Evidence

Numerous in vivo studies support the wound-healing efficacy of Tulsi and Boswellia:

- **Tulsi hydrogels:** Enhanced wound contraction, faster epithelialization in rat excision models
- **Boswellia gels:** Reduced wound area, increased hydroxyproline content (a collagen marker)
- **Combination studies:** Although limited, indicate enhanced healing synergy when both herbs are co-administered

Clinical studies remain sparse but suggest that herbal hydrogels are well tolerated and improve patient comfort.

8. Challenges and Limitations

- **Phytochemical variability:** Seasonal and geographic variation in plant actives
- **Formulation stability:** Sensitivity to heat, light, and pH
- **Regulatory issues:** Lack of standardized guidelines for herbal-medical hydrogels
- **Lack of human clinical trials:** Most data are preclinical
- **Patient acceptability:** Odor, color, and texture may affect usage

9. Future Prospects

- **Advanced delivery systems:** Liposome- or nanoparticle-loaded hydrogels
- **Smart hydrogels:** Responsive to pH, temperature, enzymes
- **Personalized formulations:** Tailored to wound type and patient condition
- **Combination therapies:** Herbal hydrogels with antibiotics or growth factors
- **Clinical translation:** Large-scale trials needed to confirm efficacy and safety

10. Conclusion

Hydrogels containing *Ocimum sanctum* and *Boswellia serrata* offer an innovative and advantageous approach for wound care. Their complimentary anti-inflammatory, antioxidant, and regenerative properties produce a synergistic combination that enhances healing while reducing adverse effects. Although existing preclinical data substantiates their efficacy, clinical validation and regulatory frameworks require enhancement. Ongoing multidisciplinary research may facilitate the incorporation of these polyherbal hydrogels into conventional wound care methodologies.

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