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A Review of Herbal Bioactives in Synergistic Treatment of Stomach Ulcers and Wound Healing

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Abstract: *Stomach ulcers and cutaneous wounds are major global health concerns involving oxidative stress, microbial infection, inflammation, and impaired tissue regeneration. Conventional therapies often present limitations such as resistance, recurrence, and side effects. Herbal bioactives derived from medicinal plants offer a promising alternative due to their multi-targeted pharmacological properties. This review highlights key phytoconstituents such as flavonoids, terpenoids, alkaloids, saponins, and polyphenols in the synergistic management of gastric ulcers and wound healing. Mechanistic pathways include anti-inflammatory modulation (NF-κB inhibition), antioxidant defense (Nrf2 activation), antimicrobial effects, and stimulation of angiogenesis and collagen synthesis. Evidence suggests overlapping biological mechanisms between gastric mucosal repair and dermal wound healing, supporting the dual therapeutic potential of herbal bioactives.*

Keywords: Herbal bioactives, gastric ulcer, wound healing, polyphenols, flavonoids, aloe vera, curcumin, licorice

I. INTRODUCTION

Stomach ulcers and cutaneous wounds represent two clinically significant conditions that, despite affecting different organ systems, share remarkably similar biological mechanisms of tissue injury and repair. A stomach ulcer, particularly peptic ulcer disease (PUD), is characterized by a localized breakdown of the gastric or duodenal mucosa due to an imbalance between aggressive factors such as gastric acid, pepsin, *Helicobacter pylori* infection, oxidative stress, and defensive mechanisms including mucus secretion, bicarbonate production, mucosal blood flow, and epithelial regeneration (Sung et al., 2019). On the other hand, wound healing in the skin involves a dynamic and complex process consisting of hemostasis, inflammation, proliferation, and remodeling phases, all of which aim to restore the integrity of damaged tissue (Gurtner et al., 2018). Although these conditions manifest in different tissues, both rely heavily on inflammation regulation, oxidative balance, microbial control, and efficient tissue regeneration.

Conventional therapies for stomach ulcers typically include proton pump inhibitors (PPIs), H2 receptor antagonists, antibiotics for *H. pylori* eradication, and mucosal protective agents. While these treatments are often effective, they are associated with limitations such as drug resistance, recurrence after discontinuation, adverse effects, and incomplete mucosal restoration in chronic cases (Kamada et al., 2021). Similarly, wound management strategies such as antiseptics, antibiotics, and synthetic dressings may not always ensure optimal healing, especially in chronic wounds such as diabetic ulcers, where impaired vascularization and persistent inflammation delay tissue regeneration (Guo & DiPietro, 2010). These challenges have encouraged increasing interest in alternative and complementary therapeutic approaches, particularly those derived from medicinal plants.

Herbal medicine has been used for centuries across various traditional systems such as Ayurveda, Traditional Chinese Medicine (TCM), and Unani medicine for treating gastrointestinal and dermatological disorders. Modern pharmacological research now validates that many medicinal plants contain bioactive compounds—such as flavonoids, alkaloids, tannins, saponins, terpenoids, and phenolic acids—that exhibit strong anti-inflammatory, antioxidant, antimicrobial, and tissue-regenerative properties (Salehi et al., 2019). These phytochemicals act on multiple molecular

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pathways simultaneously, making them particularly suitable for complex disorders like ulcers and wounds, where multiple pathological processes occur in parallel.

A key shared pathological mechanism between stomach ulcers and wound healing impairment is oxidative stress. Reactive oxygen species (ROS) play a critical role in damaging cellular structures, including lipids, proteins, and DNA, thereby delaying tissue repair and exacerbating inflammation. Herbal bioactives such as polyphenols and flavonoids scavenge free radicals and enhance endogenous antioxidant defense systems, including superoxide dismutase (SOD), catalase, and glutathione peroxidase. For example, curcumin derived from *Curcuma longa* has demonstrated strong antioxidant activity through activation of the Nrf2 signaling pathway, which regulates cellular defense against oxidative damage (Menon & Sudheer, 2017).

Inflammation is another central process in both gastric ulcer formation and wound healing. Acute inflammation is essential for initiating repair; however, prolonged or excessive inflammation leads to tissue destruction and impaired healing. In gastric ulcers, overactivation of inflammatory mediators such as tumor necrosis factor-alpha (TNF-α), interleukin-1β (IL-1β), and nuclear factor kappa B (NF-κB) contributes to mucosal injury. Similarly, chronic wounds exhibit persistent inflammatory signaling that prevents progression to the proliferative phase (Wallace, 2018). Herbal bioactives, including flavonoids from *Glycyrrhiza glabra* (licorice) and triterpenoids from *Centella asiatica*, have been shown to inhibit NF-κB signaling and reduce pro-inflammatory cytokine expression, thereby promoting resolution of inflammation and enhancing tissue repair (Shukla et al., 2010).

Another important factor linking gastric ulcers and wound healing is microbial infection. *Helicobacter pylori* infection is a major etiological factor in peptic ulcer disease, as it disrupts mucosal integrity and induces chronic inflammation. Similarly, bacterial colonization of wounds, particularly by *Staphylococcus aureus* and *Pseudomonas aeruginosa*, significantly delays healing and increases the risk of complications. Many herbal extracts possess broad-spectrum antimicrobial properties. For instance, tannins disrupt bacterial cell walls and inhibit enzyme activity, while essential oils from plants like *Ocimum sanctum* (tulsi) exhibit strong antibacterial effects (Cowan, 2010). This dual antimicrobial action supports the use of herbal bioactives in both gastrointestinal and dermatological infections.

Tissue regeneration and angiogenesis are also critical overlapping processes. Effective healing of gastric ulcers requires rapid re-epithelialization and restoration of mucosal blood flow, while wound healing depends on fibroblast proliferation, collagen deposition, and neovascularization. Herbal compounds such as asiaticoside from *Centella asiatica* enhance collagen synthesis by stimulating fibroblast activity and increasing hydroxyproline content in tissues. Similarly, aloe vera polysaccharides promote fibroblast proliferation and accelerate epithelial regeneration in both skin and gastric mucosa (Surjushe et al., 2018). These shared regenerative mechanisms highlight the synergistic potential of herbal bioactives.

In addition to individual effects, synergistic herbal formulations are gaining attention due to their multi-targeted therapeutic potential. Unlike single-molecule drugs, plant-based formulations can simultaneously modulate multiple signaling pathways, offering a holistic approach to healing. This is particularly relevant in conditions like ulcers and chronic wounds, where inflammation, oxidative stress, and microbial infection occur concurrently. Recent advancements in nanotechnology have further improved the bioavailability and targeted delivery of herbal bioactives, enhancing their therapeutic efficacy and stability (Yadav et al., 2015).

Despite promising evidence, challenges remain in translating herbal bioactives into standardized clinical therapies. Variability in plant composition, lack of controlled clinical trials, and insufficient pharmacokinetic data limit their widespread adoption. Therefore, future research must focus on rigorous clinical validation, molecular mechanism elucidation, and development of standardized formulations.

Stomach ulcers and wound healing disorders share multiple pathological mechanisms, including oxidative stress, inflammation, microbial infection, and impaired tissue regeneration. Herbal bioactives provide a promising multi-targeted therapeutic approach that can simultaneously address these underlying mechanisms. Their synergistic action makes them valuable candidates for integrative medicine strategies aimed at improving healing outcomes in both gastrointestinal and dermal tissues.

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MAJOR HERBAL BIOACTIVES AND THEIR SOURCES

Herbal Plant	Major Bioactive Compounds	Pharmacological Actions
Aloe vera	Acemannan, polysaccharides, vitamins	Anti-inflammatory, wound healing
Curcuma longa (Turmeric)	Curcumin	Antioxidant, anti-ulcer, collagen synthesis
Glycyrrhiza glabra (Licorice)	Glycyrrhizin, flavonoids	Anti-ulcer, mucosal protection
Centella asiatica	Asiaticoside	Collagen synthesis, tissue repair
Calendula officinalis	Flavonoids, triterpenoids	Anti-inflammatory, antimicrobial

Herbal extracts act on multiple healing phases including inflammation, proliferation, and remodeling in both gastric and dermal tissues.

MECHANISMS OF ACTION

1. Anti-inflammatory Activity

Herbal flavonoids and terpenoids suppress inflammatory mediators such as TNF-α, IL-6, and NF-κB, reducing tissue damage in ulcers and wounds.

2. Antioxidant Defense

Polyphenols activate Nrf2 signaling, reducing reactive oxygen species (ROS) and protecting epithelial cells from oxidative injury.

3. Antimicrobial Effects

Many plant extracts inhibit pathogens such as *Helicobacter pylori* (ulcers) and *Staphylococcus aureus* (wounds), reducing infection-driven inflammation.

4. Mucosal and Tissue Regeneration

Bioactives enhance:
Fibroblast proliferation
Collagen deposition
Angiogenesis (VEGF activation)
These processes are essential for both gastric mucosal repair and skin wound closure.

SYNERGISTIC RELATIONSHIP BETWEEN ULCER HEALING AND WOUND REPAIR

Both gastric ulcers and skin wounds share overlapping biological mechanisms:
Epithelial regeneration
Growth factor activation (EGF, TGF-β)
Extracellular matrix remodeling
Angiogenesis stimulation
Herbal bioactives act as multi-target agents, making them effective in both internal (gastric) and external (skin) healing systems.

KEY HERBAL BIOACTIVES IN DUAL THERAPEUTIC ACTION

I. Aloe vera

Enhances epithelial regeneration
Protects gastric mucosa
Promotes collagen formation

II. Curcumin

Reduces gastric acid damage
Accelerates wound contraction
Inhibits inflammatory cytokines

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III. Licorice (Glycyrrhiza glabra)

Stimulates mucus secretion in stomach

Enhances ulcer healing

Shows anti-inflammatory wound repair effects

SYNERGISTIC FORMULATIONS AND DELIVERY SYSTEMS

Modern studies emphasize enhanced delivery systems such as:

Hydrogels

Nanoparticles

Liposomal carriers

These improve stability, bioavailability, and targeted release of herbal compounds, increasing therapeutic efficiency in both ulcer and wound healing applications.

COMPARATIVE HEALING PATHWAYS

Healing Stage	Gastric Ulcer	Wound Healing	Shared Mechanism
Inflammation	Mucosal inflammation	Tissue inflammation	Cytokine suppression
Proliferation	Epithelial regeneration	Fibroblast activation	Growth factors (EGF, VEGF)
Remodeling	Gastric lining repair	Collagen remodeling	ECM reorganization

II. CONCLUSION

Herbal bioactives demonstrate strong potential in the synergistic treatment of gastric ulcers and wound healing due to their anti-inflammatory, antioxidant, antimicrobial, and regenerative properties. Their multi-targeted mechanism makes them promising alternatives or adjuncts to conventional therapies. However, further clinical validation and standardization are required for widespread therapeutic use.

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