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Review on Hydrogel-Based Herbal Oral Ulcer Patches

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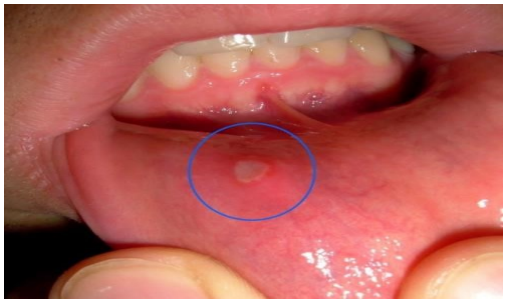
Abstract: ***Oral ulcers are a common and painful condition affecting the mucosal lining of the oral cavity. They can result from a variety of causes, including mechanical trauma, nutritional deficiencies, infections, or underlying systemic diseases. Conventional treatments, such as corticosteroids and antiseptics, often provide temporary relief but are associated with side effects and limited patient compliance. In recent years, there has been growing interest in herbal therapies due to their natural origin, safety profile, and multifunctional therapeutic actions. Herbal ingredients such as aloe vera, licorice, gotu kola, and honey possess anti-inflammatory, antimicrobial, and wound-healing properties, making them ideal candidates for oral ulcer management.***

The development of herbal oral ulcer patches offers a promising approach by enabling localized, sustained delivery of active phytoconstituents directly to the ulcer site. These patches not only provide therapeutic benefits but also protect the affected area from mechanical irritation and secondary infection. This review aims to explore various herbal ingredients commonly used for oral ulcers, discuss formulation strategies for herbal patches, and highlight key evaluation parameters such as mucoadhesive strength, drug release, and stability. By compiling current findings and advancements, this paper emphasizes the potential of herbal oral patches as an effective, patient-friendly alternative in the management of oral ulcers.

Keywords: Oral ulcers, hydrogel patches, herbal medicine, aloe vera, honey, gotu kola, licorice, wound healing, biocompatible materials, targeted drug delivery, antiinflammatory, antibacterial, collagen synthesis, natural wound care

I. INTRODUCTION

Oral ulcers, also known as aphthous ulcers, Are a frequent clinical condition affecting individualities across all age groups.Characterized by painful pustules on the mucosal stuffing of the mouth, lingo, or lips, they significantly vitiate quotidian functions analogous as eating, speaking, and swallowing. intermittent oral ulcers not only reduce quality of life but may also gesture bolstering systemic conditions,including autoimmune conditions, gastrointestinal disturbances, or nutritional deficiencies. The global frequency of oral ulcers is estimated to be around 20, with advanced frequence observed In immature grown- ups and immunocompromised Individualities(1,2). conventional treatments for oral ulcers include topical corticosteroids, antiseptics, anaesthetics , and antimicrobial agents. while these phrasings give temporary symptom relief, they constantly have downsides Analogous as mucosal vexation, unpleasant taste, frequent dosing conditions, and implicit systemic side goods upon long- term use(3). Also, utmost synthetic specifics only Address symptoms without promoting Complete mucosal healing(4). In distinction, herbal medicines have gained Considerable attention in oral healthcare due To their safety, biocompatibility, and broad Remedial spectrum. Natural ingredients Like aloe vera, licorice, turmeric, and clove Paradeanti- seditious, antimicrobial, Analgesic, and crack- mending parcels, Making them suitable for oral ulcer Operation(5,6). The use of oral patches as a delivery system For herbal actives offers distinct advantages Over conventional capsule forms. These Patches give localized, dragged drug Release, reduce dosing frequency, enhance Mucosal adhesion, and form a protective Barricade over the ulcerated area(7,8). As a Result, herbal oral ulcer patches have surfaced As a promising volition in the development Of effective and patient-friendly remedial Systems.



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II. PATHOPHYSIOLOGY AND TYPES OF ORAL ULCERS

Oral ulcers develop as lesions on the mucous membrane and are often accompanied by pain, inflammation, and a burning sensation. Their pathogenesis involves a combination of epithelial disruption, immune response, and secondary infection. The causes can be broadly classified into mechanical (e.g., trauma from braces or accidental biting), chemical (e.g., acidic foods), infectious (e.g., viral, bacterial, fungal), nutritional deficiencies (e.g., vitamin B12, iron, folate), and systemic diseases (e.g., Behcet's disease, Crohn's disease) (9,10).

Oral ulcers are commonly categorized into several types. The most frequent are recurrent aphthous stomatitis (RAS), which can be minor (small, shallow lesions), major (larger and deeper), or herpetiform (clustered pinpoint ulcers) (11). Traumatic ulcers result from physical or chemical irritation. Infectious ulcers arise from pathogens such as herpes simplex virus or Candida albicans. Systemic-associated ulcers are linked to autoimmune or gastrointestinal disorders (12).

The biological process of ulcer formation involves epithelial injury followed by an inflammatory cascade. Cytokines such as TNF-α and IL-1β are released, attracting immune cells and increasing vascular permeability (13). Healing begins with epithelial regeneration, fibroblast activity, angiogenesis, and reepithelialization, often influenced by growth factors and extracellular matrix remodeling (14).

III. HERBAL REMEDIES USED IN ORAL

A. Ulcers

The use of herbal remedies for oral ulcer management has roots in traditional medicine and is supported by modern pharmacological studies. Many plant-derived compounds exhibit properties such as anti-inflammation, antimicrobial activity, antioxidant action, and tissue regeneration, making them valuable alternatives or complements to conventional drugs.

1) Aloe vera is one of the most studied herbs for oral ulcers. Its gel contains polysaccharides and glycoproteins that exert anti-inflammatory and wound-healing effects by modulating cytokine activity and promoting collagen synthesis (15,16). Clinical trials have shown that aloe vera gel reduces ulcer size and pain duration in aphthous stomatitis patients (17).



2) Licorice (Glycyrrhiza glabra) contains glycyrrhizin and flavonoids, which possess strong antiinflammatory, antibacterial, and mucoprotective effects. It inhibits prostaglandin and leukotriene pathways, promoting mucosal healing (18). Licorice-based gels and mouthwashes have demonstrated efficacy in reducing ulcer symptoms in both in vitro and clinical studies (19).



3) Centella asiatica (Gotu kola) enhances wound repair by stimulating collagen production, angiogenesis, and fibroblast proliferation. Triterpenoids present in the plant activate antioxidant defenses and modulate the inflammatory response (20). Its traditional use in Ayurveda and modern formulations supports its application in oral ulcer care (21).

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4) Honey, a natural bioactive agent, offers antimicrobial protection and accelerates tissue regeneration. Its high osmolarity, hydrogen peroxide content, and flavonoids contribute to microbial inhibition and healing promotion (22). Topical application of honey has shown pain relief and faster ulcer resolution in clinical settings(23).



Together, these herbs serve not only as natural anti-ulcer agents but also reduce side effects commonly seen with synthetic drugs. Their incorporation into mucoadhesive oral patches further enhances localized delivery, retention, and therapeutic efficiency.

IV. FORMULATION OF HERBAL ORAL ULCER PATCHES

The development of effective herbal oral ulcer patches involves careful selection of polymers, incorporation of herbal extracts, and appropriate fabrication techniques to ensure optimal mucoadhesion, drug release, and patient compliance. These patches are typically designed for local application, adhering to the oral mucosa and delivering herbal actives directly to the site of the ulcer, minimizing systemic exposure and enhancing therapeutic efficiency.



A. Selection of Polymers

The choice of polymer plays a critical role in determining the mechanical strength, bioadhesiveness, flexibility, and drug release profile of oral patches. Commonly used mucoadhesive polymers include hydroxypropyl methylcellulose (HPMC), polyvinyl alcohol (PVA), chitosan, and sodium alginate (24).

HPMC is a widely used hydrophilic polymer known for its excellent film-forming and swelling properties, making it ideal for sustained drug release (25).

PVA provides flexibility and transparency to the patch and acts as a film-forming base (26).

Chitosan, a natural cationic polymer, offers mucoadhesion, biocompatibility, and antimicrobial properties, making it highly suitable for herbal formulations (127.
Sodium alginate, derived from brown algae, forms gels upon contact with calcium ions and contributes to mucoadhesive and woundhealing effects (28).
These polymers can be used alone or in combination to modulate the patch's physical and functional characteristics.

B. Incorporation of Herbal Extracts

Herbal extracts are incorporated into patches using several preparation methods depending on the nature of the plant material and the target bioactive components. The most common methods include:
Infusion – Soaking the plant material in hot water to extract water-soluble constituents.
Decoction – Boiling tough plant parts like roots or barks to extract active compounds.
Gel incorporation – Mixing herbal extracts with gel bases like carbopol or aloe vera to enhance viscosity and retention in the polymer matrix (29).
The resulting extracts are often filtered, concentrated, and then mixed with the polymer solution before casting.
Standardization of these extracts ensures consistency in phytochemical content and therapeutic activity.

C. Types of Herbal Oral Patches

Herbal oral patches can be classified based on their intended performance:
Mucoadhesive patches adhere to the mucosal surface, enabling prolonged contact and controlled release of herbal actives (30).
Fast-dissolving patches are designed to disintegrate quickly in the oral cavity, releasing herbal constituents rapidly for immediate symptom relief (31).
Bilayer patches can be formulated with a drug-loaded mucoadhesive layer and an impermeable backing layer to ensure unidirectional release and prevent saliva washout (32).
The choice depends on the therapeutic goal— whether prolonged exposure or rapid relief is desired.

D. Fabrication Techniques

The most commonly used fabrication method is solvent casting, in which the polymer and herbal extract mixture is poured into a mold and allowed to dry under controlled conditions to form a thin film. The process typically includes:

1) Dissolving polymers in suitable solvents (e.g., water, ethanol, acetic acid for chitosan).
2) Adding plasticizers like glycerol or propylene glycol to improve flexibility.
3) Incorporating the herbal extract under gentle stirring.
4) Casting the solution into molds and drying at controlled temperatures to avoid phytochemical degradation
(33).

Other fabrication techniques include lyophilization, hot melt extrusion, and electrospinning, though these are more complex and used less frequently for herbalbased patches (34).
Overall, the formulation strategy must balance herbal extract stability, polymer compatibility, mucoadhesion, and patient acceptability to ensure therapeutic efficacy and ease of use.

V. EVALUATION PARAMETERS OF HERBAL ORAL ULCER PATCHES

A thorough evaluation of herbal oral ulcer patches is essential to ensure their safety, efficacy, and patient acceptability. The following parameters are commonly assessed during formulation development.

A. Physicochemical Evaluation

Physical parameters such as thickness, weight variation, folding endurance, and surface pH are crucial indicators of uniformity and mechanical integrity. Consistent thickness and weight ensure dose uniformity, while folding endurance reflects flexibility and mechanical strength (35). Surface pH should be close to neutral (6.5– 7.0) to prevent mucosal irritation and ensure compatibility with the oral environment (36).

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B. Mucoadhesive Strength and Swelling Index

Mucoadhesive strength determines how well the patch adheres to the oral mucosa, which is essential for localized and prolonged drug delivery. This is often measured using texture analyzers or modified balance techniques (37). The swelling index indicates the hydration capacity of the patch, which affects drug diffusion and adhesion; an optimal swelling rate enhances comfort and effectiveness (38).

C. In vitro Drug Release and Permeation Studies

In vitro release studies provide insights into the release kinetics of herbal actives from the patch matrix. These are usually conducted using Franz diffusion cells or USP dissolution apparatus with simulated saliva as the medium (39). Permeation studies evaluate the ability of herbal actives to penetrate the mucosal tissue, which is crucial for systemic absorption or local action (40).

D. Stability Studies

Stability testing under different temperature and humidity conditions assesses the shelf life and formulation robustness. Parameters such as drug content, pH, appearance, and mechanical properties are monitored over time according to ICH guidelines (41).

E. Microbial Testing and Safety Profiles

Herbal formulations are susceptible to microbial contamination; hence, microbial load testing ensures compliance with pharmacopeial standards. Additionally, cytotoxicity studies using cell lines like human gingival fibroblasts help evaluate biocompatibility (42). Safety testing is particularly important for herbal patches due to the variability of plant extracts.

VI. ADVANTAGES AND LIMITATIONS

Herbal oral patches offer numerous advantages, including targeted delivery, prolonged drug retention, sustained release, and enhanced patient compliance, especially for patients who have difficulty swallowing pills or prefer natural therapies (43). The noninvasive nature and localized action also reduce systemic side effects.

However, there are limitations. The standardization of herbal extracts remains a challenge due to variability in phytochemical composition based on geographical, seasonal, and processing factors (44). Formulation challenges such as polymer–drug incompatibility, extract solubility, and patch disintegration in the moist oral environment can also hinder product development (45).

VII. FUTURE PROSPECTS AND CHALLENGES

The growing demand for herbal therapeutics highlights the need for standardized herbal ingredients with well-defined bioactive profiles and consistent pharmacological effects. Advancements in analytical techniques, such as HPTLC and LC-MS, can help in better standardization and quality control (46).

Furthermore, clinical trials are necessary to validate the safety and efficacy of herbal oral patches in larger populations. Regulatory guidelines for herbal drug delivery systems are still evolving, requiring harmonization to facilitate commercial development (47). With increased R&D and supportive policies, herbal oral patches have strong potential to enter mainstream oral care markets.

VIII. CONCLUSION

Herbal oral ulcer patches represent a promising and patient-friendly approach to managing oral mucosal lesions. By combining the benefits of natural healing agents with innovative drug delivery systems, these patches address many limitations of conventional therapies. Continued research into standardization, formulation techniques, and clinical validation will pave the way for their broader application and commercialization in oral healthcare.

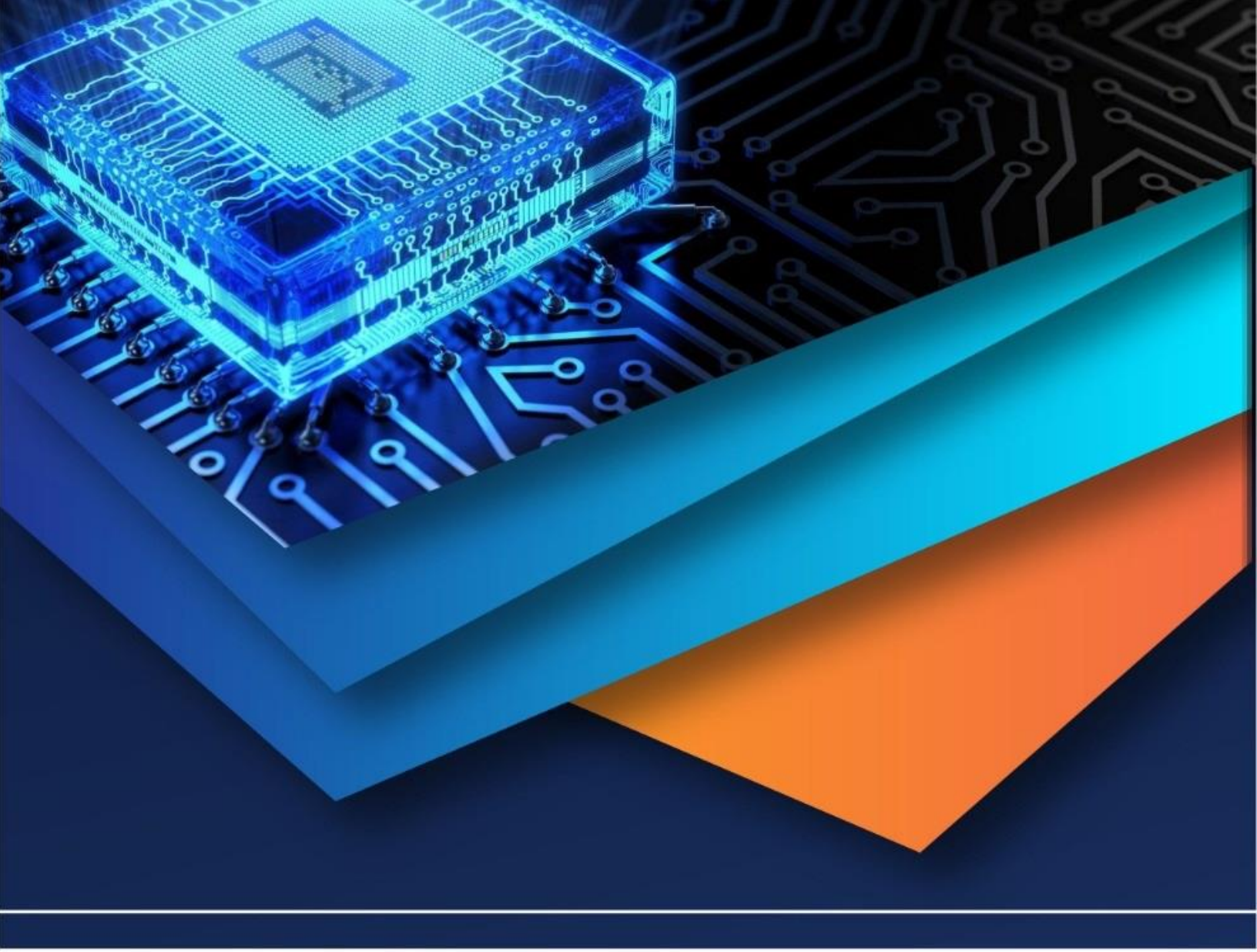
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