

“A Systematic Review of Herbal Approaches for Mouth Ulcer Management”

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ABSTRACT:

The mouth ulcer is common disorder caused by various etiological factor. These oral ulcers, often referred to as tiny sores, are painful lesions that typically appear along the gum line inside the mouth. They frequently cause discomfort and pain. Which can influence a person's food choices during the healing process. The aim of this work is to evaluate the effectiveness and safety of different herbal remedies for treating and managing mouth ulcer. Numerous formulations, both synthetic and natural, are available on the market. Herbal remedies play a crucial role in primary healthcare due to its cultural acceptability. Better compatibility with the human body, and fewer side effects. This review summarizes herbs used in the treatment of mouth ulcers, such as guava, aloe vera, ivy gourd, pomegranate, and jasmine, discussing their biological sources, families, morphology, chemical constituents and uses.

KEYWORDS: Mouth ulcer, Herbs, Oral ulceration, Oral cavity, Anti-ulcer, Recurrent aphthous stomatitis

I. INTRODUCTION :

Mouth ulcers, also known as oral or mucosal ulcers, occur in the mucous membrane of the oral cavity, primarily on the inside of the cheeks or lips^[1, 2].it is most common oral condition, affecting 20-25% of the world's population^[3]. The mouth ulcer generally arises as a yellow or white colour, and they can be quite painful^[4]. The mouth ulcers, regardless of their cause, bring significant discomfort and pain to those affected. As they heal, individuals often need to adjust their diets, avoiding acidic, sugary, salty, or spicy food and drinks. This restriction is a practical measure to reduce the discomfort aggravated by this items in the sensitive healing environment of the mouth, consequently, the relationship between the causes, symptoms, and dietary changes paints a complex picture of oral ulceration^[5]. This type of ulceration

can develop in any area of the body with mucous membrane, including the gastrointestinal tract, mouth, throat, and genital regions, mucosal arise from several factor, such as infections (like H pylori in the stomach), trauma, inflammatory condition (such as Crohn's disease or ulcerative colitis), or specific medications. The severity, symptoms, and treatment of mucosal ulcers can vary based on their underlying cause and location^[6]. This sets ulcer apart from shallower lesions such as excoriations. Unlike these superficial injuries, ulcers extend deeper, impacting both the epithelium and the underlying lamina propria, This greater depth can results in more severe symptoms and complications, requiring careful evaluation and appropriate management to promote healing additional tissue damage^[7].The other name of them includes aphthae, apothosis, aphthous, aphthous stomatitis and cancer sores^[8]. The term 'aphthae' comes from the Greek word 'aphthae' meaning to set on fire or to infame. It is believed that the philosopher Hippocrates first used this term to describe the pain associated with a common disorder of the mouth^[9]. Aphthous ulcers are recurring round or oval sores that occur in the mouth, particularly under the tongue and in area where the skin is loosely attached to the underlying bone. They can affect both male and female^[10].mouth ulcer occurs due to the erosion or loss of the delicate tissue lining inside the mouth^[11].mouth ulcers, also known as aphthous ulcers, are relatively common and can results from various diseases and mechanism, though they usually don't indicate serious underlying issue. Common causes include nutritional deficiency particularly in iron, vitamin B12, and vitamin C, poor dental hygiene, infections, stress, indigestion, mechanical injuries, food allergies, hormonal imbalances, and skin conditions. These ulcers can lead to discomfort while eating, drinking, or brushing teeth^[12, 13, 14].

Types of mouth ulcers:

Minor ulcer:

The primary type is minor aphthous ulcers, which account for approximately 70-80% of cases. These ulcers appear as a small round or oval lesions covered by a greyish-white pseudo membrane, surrounded by a red halo. Each episode typically involves the emergence of 1 to 5 ulcers, each measuring under 1 cm in diameter. These episodes are self-limiting, resolving within 4 to 14 days without leaving scars^[15, 16].



Figure 1: Minor ulcer



Figure 2: Major ulcer



Figure 3: Herpetiform ulcer

Major ulcer:

Major aphthous ulcers, seen in about 10% of patients, are larger and deeper commonly affecting the lips, soft palate, and pharynx. They can persist for weeks and may leave scars^[17, 18, 19].

Herpetiform ulcer:

Herpetiform aphthous ulcers 1-10% cases involve recurrent outbreaks of small, painful ulcers 2-3 mm that may merge into larger, irregular lesions. Up to 100 aphthae can develop at once, more commonly in women and older patients^[20].

Causes of mouth ulcer:

Nutritional deficiencies:

Nutritional deficiencies such as those in iron, folic acid and vitamin B include (B1, B2, B6) have been associated with certain patients suffering from aphthous ulcers. The impact of these nutritional deficits on aphthous ulcers may differ by region. Influenced by local diets and supplementation practices^[21].

Physical or physiological stress:

Aphthous ulcer occurrences are closely linked to stressful life events. Physiological stress may act as a trigger or modifying factor for recurrent aphthous stomatitis. However, no studies have definitively established stress as a precipitating factor for this condition^[22, 23].

Genetic factor:

The genetic components in patients with aphthous ulcers is notable, with 30-40% reporting a family history. In some cases, a distinct family pattern emerges, characterized by early onset and more severe symptoms. Furthermore, RAS show a strong correlation among identical twins^[24].

Food allergies:

Allergies in patients with recurrent aphthous stomatitis can be triggered by various foods, with many showing antibodies to cows' milk and wheat protein. However, several common

allergens are not typically linked to this condition. Still, some patients may associate their symptoms with cocoa, coffee, almonds, cereals, nuts, strawberries, cheese, tomatoes, and flour^[25, 26].

Immune disorder:

Aphthous ulcers are more common and severe in patients with immune disorders, including cyclic neutropenia, inflammatory bowel disease, and HIV^[27].

Trauma:

Aphthous ulcers are mostly caused by local trauma and stress. Injuries to the oral mucosa can occur from accidental self-biting, dental procedures, toothbrush bristles, sharp foods like potato chips, and anaesthetic injections. Additionally, both environmental and emotional stress can contribute to the development of these ulcers^[28].

Drug

Medications like nicorandil, NSAIDs, ibuprofen, and nicotine replacement therapy can cause mouth ulcers^[29].

Tobacco smoking:

Patients with recurrent aphthous stomatitis are typically non-smokers, yet heavy smokers and moderate smokers experience lower prevalence and severity of the condition. Some individuals report

an onset of recurrent ulcers after quitting smoking, while others find relief upon resuming. The use of smokeless tobacco is associated with a significantly reduced prevalence of recurrent aphthous stomatitis. Additionally, nicotine-containing tablets seem to help control the frequency of these ulcers^[30].

Some other factor which causes mouth ulcer are:^[31]

- Hormonal changes
- Viral infection
- Toothpastes & mouthwashes that contain sodium lauryl sulphate
- Medical condition
- Bacterial & viral infections

Symptoms of mouth ulcer:^[31]

- The lining of the mouth.
- Inflamed and reddened mucous membrane surrounding the sore.
- Difficulty chewing or brushing teeth due to sensitivity.
- One or more painful lesions on the mucous membrane.
- Sores aggravated by salty, spicy, or acidic foods.

Treatment:

There is no definitive cure of RAS thus treatment primarily focuses on pain relief, promoting faster healing, and reducing the frequency and intensity of episodes^[32].

Table 1: Treatment of mouth ulcer

General measures	Topical Treatments			Systemic Treatments	
Topical Oral	Topical Anaesthetics & barrier Agents	Topical Antiinflammatory & antiseptic Agent	Topical Corticosteroids	First line	Second line
Oral Hygiene	Benzocaine gel	Diclofenac gel	Dexamethasone ointment	Prednisone	Colchine
Supplements	Sucralfate suspension	Chlorhexidine mouthwash	Aloedent gel	Aspirin	Clofazimine

Importance of herbal medicine:^[33]

The traditional herbal medicines derived from naturally occurring plants have been used to treat human illnesses since ancient times. It's not surprising that 1.42 billion people or one-fourth of the world's population. Rely on traditional medicine to treat a variety of maladies. Evidence shows that most of the world population is using herbal medicine since ancient times the Indian flora contains a wide range of therapeutic plant and plant components. The many developing countries still rely on herbal medicine as their main form of healthcare traditional medicine has been practiced for nearly a century before the advent of modern medicine. It is often regarded as one of the costliest forms of indigenous medicine utilized by

practitioners. Additionally traditional medicine is documented in the literature of various nations and consists of organic materials, minerals and medicinal plants. Many herbal plants have medicinal properties, and different part of these plants are used to treat various disease. Some of these plants can be particularly effective in treating mouth ulcers.

Advantages of herbal medicines:^[34]

- Easily available
- Eco-friendly
- Cost effective
- Used for long time
- Prolonged use is also safe and efficient

Table 2: Herbs used for treatment of mouth ulcer

Sr.no	Herbs	Biological name	Family
1	Ivy gourd	Cocciniagrandis	Cucurbitaceae
2	Aloe vera	Aloe barbandesis	Liliaceae
3	Tobacco leaves	Nicotianatabacum	Solanaceae
4	Chameli	Jasminum grandiflorum	Oleaceae
5	Guava	Psidiumguajava	Myrtaceae

6	Pomegranate	Punicagranatum	Punicaceae
7	Myrrh	Commiphora	Bursaceae

IVY GOURD:^[35, 36]

The biological source of ivy gourd is obtained from the dried leaves and fruits of *Cocciniagrandis*. It is belonging to the cucurbitaceae family. The synonyms of Ivy gourd

aretindora and kowai fruit. Ivy gourd contain lupeol, teraxerol, cucurbitacin, heptacosane, cephalandrol, lycopene, cryptoxanthin, xyloglucan, carotenoids, B-sitosterol.

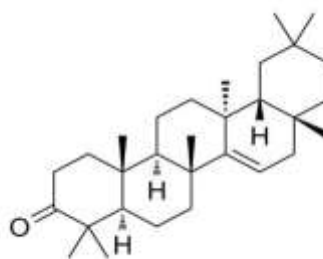
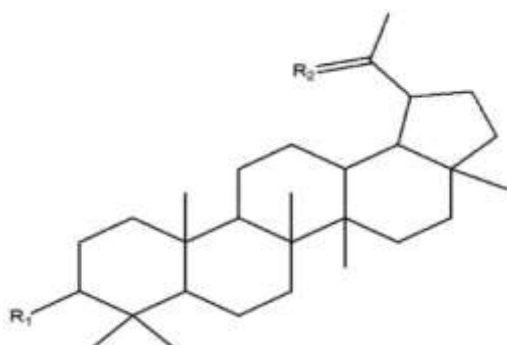


Figure 4: Structure of Lupeol^[37] Figure 5: Structure of Teraxerone^[38]

Uses: The ivy gourd is used as Anti-ulcer, anti-diabetic, anti-bacterial, anti-inflammatory, anti-pyretic, anti-fungal, and also used as analgesic.

Study: The study of Ivy gourd in-vivo study on Wister rats weighing 150-250 gm. The plant part used as ivy gourd fruits and extraction solvent used as water: ethanol(70:30). The results were found in the study on 20% w/w gel of *Cocciniagrandis* fruit extract showed an 83% reduction in ulcers within 9 days in animal, compared to a 76% reduction with diclofenac sodium gel over the same period^[39].

ALOE-VERA:^[40,41]

The biological source of aloe-vera is obtained from the dried juice of the leaves of *Aloe barbandesis miller*. It is belonging to the Liliaceae family. The synonyms of Aloe-vera are Aloe, musabbar, kumari. aloe-vera contain barbaloin, aloesin, isobarbaloin, choline, choline salicylate, aloetic acid, aloesone, hexuronic acid.

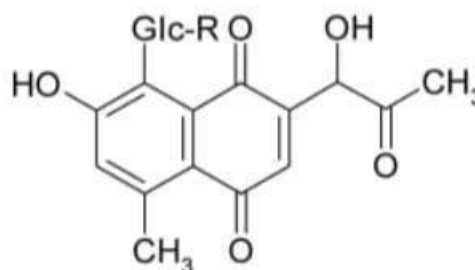
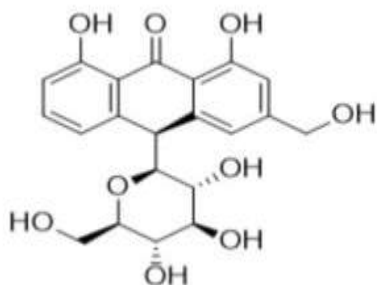


Figure6: Structure of Barbaloin^[42] Figure7: Structure of Aloesin^[43]

Uses: The Aloe-vera is used as Anti-ulcer, anti-inflammatory, anti-diabetic, anti-oxidant, anti-cancer and also used as healing.

Study: A randomized, single-blind clinical study (2019): In this type of study topical aloe vera gel are used in thirty for Individuals with clinical

manifestation of minor aphthous stomatitis divided into two groups with 17 patients each. Group A: Topical Aloe-veragel and Group B: Topical Triamcinolone acetonide (0.1%) oral paste and result was found to be triamcinolone acetonide oral paste was reported be beneficial than aloe-vera. On

the other hand, aloe-vera gel had a better impact in reducing pain and burning sensation^[44]. A randomized double-blind study. (2020): in this type of study Aloe-vera gel formulation are used in 46 patients' aloe-vera formulation gel (AA group) and chitosan gel (AC group). And result was found to be AA group had better effects on healing time than the AC group and AA group decreases the harmful oral bacteria^[45]. A Randomized double-blind vehicle-controlled study (2013): In this type of study Aloe-vera gel (0.5 %) are used in total three groups, each consisting of 30 patients: Group 1: mucoadhesive gel aloe-vera. Group 2: Mucoadhesive gel with myrrh extract. Group 3:

placebo (plain mucoadhesive gel). And result was found to be absolute ulcer healing was reported in 76.6% of patients using aloe vera gel. Erythema & exudation was subsided in 86.7% & 80% patients' recovery^[46].

TOBACCO:^[47,48]

The biological source of tobacco is consisting of dried leaves of *Nicotianatabacum*. It is belonging to the solanaceae family. The synonyms of tobacco are tamak and siah. Tobacco contains Nicotinic acid, nornicotine, nicotine, nicotimint, anabine, isoquercetin, lupeol.

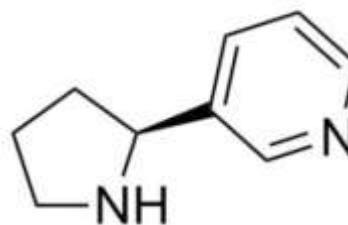
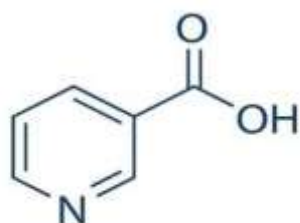


Figure 8: Structure of Nicotinic acid^[49] Figure 9: Structure of Nornicotine^[50]

Uses: The Tobacco leaves is used as Anti-ulcer, anti-microbial, anti-Alzheimer's, anti-bacterial, anthelmintic.

Study: The study of tobacco leaves in mouth ulcer in A randomized control trials in 60 patients with achieve or ever had aphthous ulcers for the past 1-5 years. In tobacco plant part used as leaves and extraction solvent used as ethanol and result was found to be current study indicated that a decoction of nicotianatabacum leaves, administrated as a mouthwash demonstrated a remarkable effect in

treating aphthous ulcer with a 92.1% reduction ulcer size within 5 days^[51].

CHAMELI:^[52]

The biological source of Chameli is obtained from the dried leaves of *Jasminum grandiflorum*. It is belonging to the family Oleaceae. The synonyms of tobacco are Jati and Chameli. Chamelicontains salicylic acid, benzyl acetate, indole, oleanolic acid, eugenol, benzyl alcohol, benzyl cyanide, benzyl acetate.

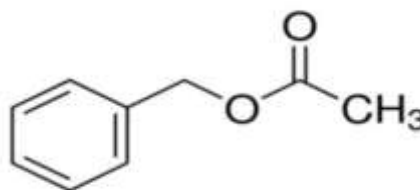
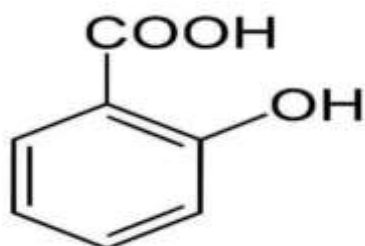


Figure 10: Structure of Salicylic acid^[53] Figure 11: Structure of Benzylacetate^[54]

Uses: The Chameli is used as ulcers, Toothache, Pain and ear, Healing, anti-septic, anti-depressant, and anti-inflammatory.

Study: A pilot open label, non-randomized clinical trials with 20 participants compared a trial and control group. The trial group showed a significant reduction in mucositis area, with six patients improving to grade 1 within 9.5 days, while no control patients improved to grade 1. One trial patient remained at grade 2 for 15 days, versus

three control patients for 14.6 days, compared to seven control patients in 8.28 days^[55].

GUAVA:^[56,57]

The biological source of guava is *Psidiumguajava* L., which belongs to the family Myrtaceae. It is commonly known by synonyms such as amrood, peru, and jama. Guava contains several chemical constituents, including quercetin, lycopene, limonene, caryophyllene, and humulene.

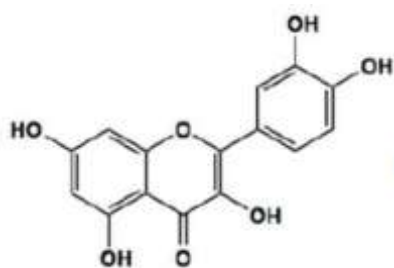


Figure 12: Structure of Quercetin^[58]

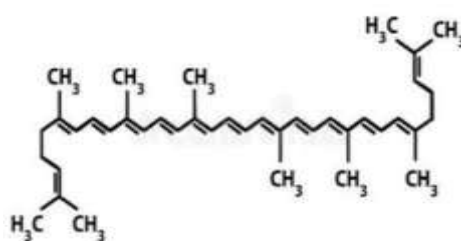


Figure 13: Structure of Lycopene^[59]

Uses: Guava exhibits various therapeutic uses, including anti-ulcer, anti-malarial, anti-plasmodic, and analgesic properties.

POMEGRANATE:^[60, 61]

The biological source of pomegranate is *Punicagranatum* L. which belongs to the family

Lythraceae. It is commonly known by synonyms such as anar, dadim, dadimah, and dalimba. Pomegranate contain several chemical constituents, including gallic acid, uroloic acid, quercetin, catechin, punicalin, punicalagin.

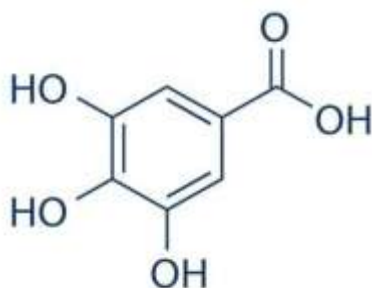


Figure 14: Structure of Gallic acid^[62]

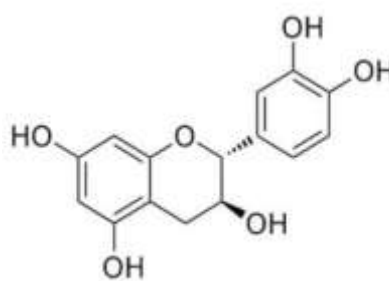


Figure 15: Structure of Catechin^[63]

Uses:The Pomegranate is used as anti-ulcer, anti-oxidant, anti-inflammatory, and wound healing.

MYRRH:^[64]

The biological source of Myrrh is *Commiphoramolmol*Engler. Which belongs to the family Burseraceae. It is commonly known by synonyms such as gum myrrh, bol, and myrrha. Myrrh containsm-cresol, cuminaldehyde, cumenic.

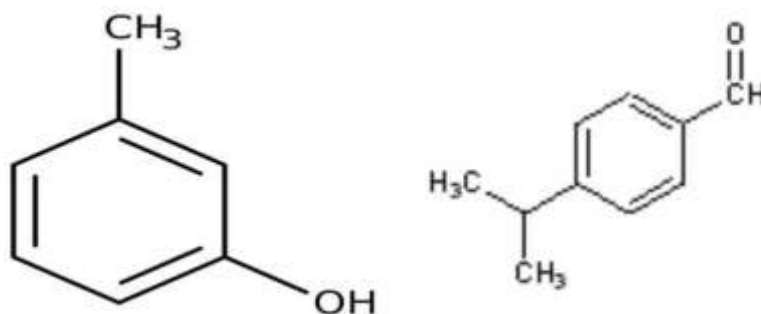


Figure 16: Structure of m-cresol^[65] Figure 17: Structure of Cuminlaldehyde^[66]

Uses: Myrrh is applied directly to the mouth of soreness and swelling, inflamed gums, loose teeth, canker sores, bad breath, and chapped lips.

Study: The combination study of Chameli, Guava, pomegranate, Myrrh for mouth ulcer

In-vivo study on male rats weighing 150-300 mg and plant part used as leaves, leaves, and flower. The extraction method solvent is used as 70% methanol, Dis. Water, Methanol, 90% Ethanol. The results were found to be in-vivo study on male rats with combination of Chameli, guava, pomegranate, and myrrh extract gel is decrease the period of ulcer within 14 days^[67].

II. CONCLUSION:

This review highlights the significant role medicinal plants play in the treatment of mouth ulcer. The antiulcer effect is likely attributed to the presence of flavonoids in these herbs, which offer better compatibility with formulations and fewer side effects. Herbal medicine emerges as a promising option for treating mouth ulcer due to the presence of naturally available chemical constituents with proven therapeutic and healing properties. Ayurveda, being the oldest medicinal system in the world, has contributed to identifying therapeutic valuable compounds from plants. Therefore, integrating ayurvedic knowledge with modern science is essential for isolating, characterizing, and standardizing the active constituents of herbal sources for anti ulcer activity. Combining traditional wisdom with modern research can lead to the development of more effective treatment for mouth ulcers with minimal side effects.

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ABBREVIATION:

RAS- Recurrent aphthous stomatitis

HIV- Human immunodeficiency virus

NSAIDS- Non steroidal anti-inflammatory drugs

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