



A brief review on poly-herbal medication for oral ulceration.

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Article History	Abstract
<p>Received: 20 Nov 2023 Revised: 10 Dec 2023 Accepted: 25 Dec 2023</p> <p>CC License CC-BY-NC-SA 4.0</p>	<p>Oral ulcers, also known as mouth sores or canker sore can be quite painful and can affect our ability to eat and speak comfortably. It is caused by various Etiological factor such as Chemical, Dental injury, Nutrition deficiency, Hormones, Genetically, Acidic food etc. Traditional medicine often utilizes a combination of different herbal remedies to address various health issues, and oral ulceration is no exception. The review highlights the effectiveness of using multiple herbal medicines in treating oral ulcers. These poly-herbal formulations typically consist of a combination of different medicinal plants, each chosen for its specific therapeutic properties. The article discusses the potential benefits of these formulations, such as reducing inflammation, promoting wound healing, and providing pain relief. This review emphasizes the importance of evidence-based research in assessing the safety and efficacy of these poly-herbal medications. While traditional medicine has a long history of using herbal remedies, it is crucial to conduct rigorous scientific studies to validate their effectiveness and ensure their safety for use.</p> <p>Key words: Oral Ulceration, Canker sore, Herbal medication, catechu, liquorice, Betel leave.</p>

Introduction:

Ulcers on the mucous membranes of the mouth cavity are referred to as oral ulcers. Nutritional deficiencies, local trauma, thermal and electrical burns, chemical traumas, irradiation, aphthous stomatitis, infections like Herpes labialis, chicken pox, HIV, etc., medications like cytotoxic treatments, non-steroidal anti-inflammatory drugs, etc. may all contribute to the development of these ulcers. [1] Most frequently occurring on the non-keratinized oral mucosa, such as the labial mucosa, buccal mucosa, and ventral surface of the tongue, minor aphthous ulcers make up around 80% of all aphthous ulcers.

They typically measure 4-6 mm, or less than 1 cm. They are distinguished by an oval or round region of ulceration with a yellowish fibrin covering that is encircled by an erythematous ring within 7–10 days, they often recover without leaving scars. Major Aphthous ulcers are bigger and can reach a diameter of more than

1 cm. They may leave scars after they have healed, which might take 4-6 weeks. A cluster of 10–100 small to medium-sized oral ulcers, known as cluster form ulcers, may appear. Lesions may combine to form larger, atypical ulcers. It is healed in 10-14 days. [2]



Fig: oral ulcers [2]

Varieties of mouth sores

There are minor, major, and herpetiform canker sores.

Minor: Mild canker sores are small round or oval ulcers that heal in one to two weeks without leaving any scars. **Major canker sores:** are larger and deeper than smaller ones in both size and depth. The time it takes to fix these jagged edges can reach six weeks. With severe mouth ulcers, there is a danger of long-term scarring. **Herpetiform:** Small, 10 to 100-strong clusters of herpetiform canker sores most frequently affect adults. This form of mouth ulcer has uneven margins and often heals within one to two weeks without leaving any scars. [3] To treat mouth ulcer, a variety of synthetic and semi-synthetic medication including anti-biotic, antiseptics, local anaesthetics, local analgesics, steroidal and NSIDs. The most commonly used treatments for topical steroids, triamcinolone and prednisolone, have significant side effects when used continuously including adrenal insufficiency, immunosuppression osteoporosis, hyperglycaemia, gastrointestinal disturbance, etc. The inclusion of some organic compounds and the high alcohol concentration in commercially available formulation with synthetic and semi-synthetic active ingredients have also been linked to complaints of local irritation, tooth discoloration, burning and other side effects. [3] Given these negative effects and the need for improved patients compliance, and use of plant-based medication is gaining acceptance around the world. Several research have reported the usage of herbal plant or extracts for the treatment of oral ulcer, extracts in the form of mouthwash, paste, or muco-adhesive gels are used. [4]

Merits of herbal medication:

Herbal medicines work as reversible sources, which is our only hope to provide a steady supply of affordable medications for the growing global population. Herbal medicine has supplied many of the world's most advantageous, practical, and diverse medicines to modern medicine. The cultivation and processing of medicinal plants and herbal products are environmentally benign and eco-friendly. [5]

Poly-herbal medication:

Ayurveda medications are categorized into three groups based on the source material: herbal, mineral, and animal. Among these, herbal formulation has recently grown in significance and received increasing global attention. This situation is clear-cut because a significant rise in the use of herbal formulations has been seen over the past few years in the developed world, where market expansion happened in European nations and the USA. [6] The two guiding concepts for Ayurvedic medication formulation are the use of many drugs (PHF) and the use of a single drug. Known as polypharmacy or polyherbalism, this important traditional therapeutic herbal approach makes use of the blending of various therapeutic plants to produce increased therapeutic effectiveness. The concept of polyherbalism in this antiquated medical system was underlined in the Ayurvedic book "Sarangdhar Samhita" from centuries ago in 1300 A.D. [7] Herbal remedies, which are mentioned in texts like the Vedas and Samhita, are among the most potent therapeutic components in the Indian Ayurvedic system. The early 19th century saw the development of synthetic pharmaceuticals from raw plants as a result of the development of chemical analysis techniques, which allowed scientists to extract and manipulate active components from the herbals. The usage of herbal remedies began to decrease around this time. [6] Knowledge of the separation, purification, characterization, and kind of preparation of herbals is an additional benefit to their discovery. The word "herbal drug" designates the parts of a plant (leaves, flowers, seeds, roots, barks, stems, etc.) used for making medications. A variety of herbal preparations, such as Kwatha (Decoction), Churna (Powders), Guggul (Resins and Balsams), Taila (Medicated Oil), and others, employ each and every portion of the herbs to the fullest extent possible for the many pharmacological actions they may create. [8]

Because of synergism, polyherbalism offers various advantages that are not present in single herb formulations. A single multi-constituent formulation can clearly produce a better therapeutic impact. In this case, a lesser dose of the herbal product would be required to have the desired pharmacological effect, lowering the probability of harmful side effects. Additionally, PHFs improve patient convenience by removing the need to take multiple herbal formulations at once, which in turn improves compliance and the therapeutic result. When compared to a single herbal formulation, all these advantages have increased the appeal of PHF on the market. [6]

These are dosage form used for the treatment of oral ulcer: Paste, Pharmaceutical gel, buccal patch, buccal tablet, Medicated chewing gum are used for treatment of oral Ulceration.

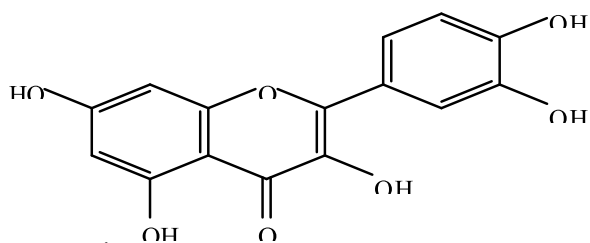
Material and method:

Some examples of allopathic and poly herbal medication:

Allopathic medication	Poly-Herbal medication
<ul style="list-style-type: none"> • Brand name– Curasil • Composition– Choline Salicylate, Lignocaine [9] 	<ul style="list-style-type: none"> • Brand name – HiOra – SG • Composition Jasmine Liquorice Triphala [11]
<ul style="list-style-type: none"> • Brand name– OraSore • Composition– Riboflavin Folic acid Niacin amide Lactic acid bacillus [10] 	<ul style="list-style-type: none"> • Brand name – HerboPearl •Composition Acacia catechu Valeriana Vallichi Cinnamomum Camphor's [12]
<ul style="list-style-type: none"> • Brand name– Dent gel • Composition– Benzalkonium chloride, Choline Salicylate, Lignocaine [9] 	<ul style="list-style-type: none"> • Brand name Oracare oral Gel •Composition: AloeVera Curcumin Menthol Ginger Ajwain Clove Oil [13]
<ul style="list-style-type: none"> • Brand name– Hexigel • Composition– Chlorhexidine Gluconate [9] 	<ul style="list-style-type: none"> • Brand name HERBOSMILE GEL • Composition Clove Ajwain Camphor Mint Cinnamon zeylianicum NaCl salt and glycerine [14]

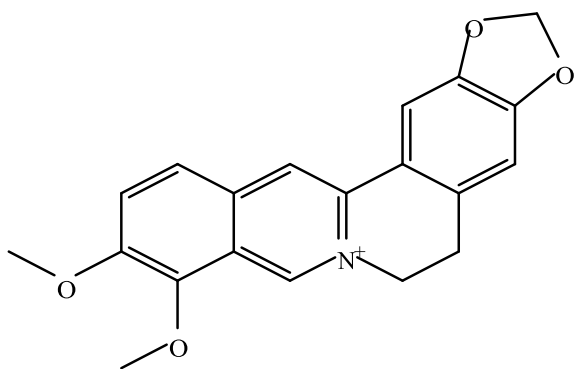
These are some examples of herbs which are used in treatment of oral ulcers:

1. Guava leaves: It is obtained from *Psidium guava* belonging from Myrtaceae family. It contains Flavonoids like quercetin and its Glycosides, tannins. It is used as Anti material, Anti-ulcer, Anthelmintic, and Anti spasmodic. [15]



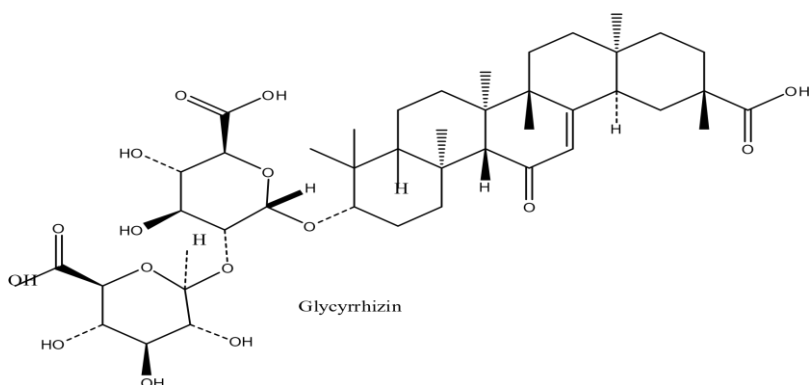
Quercetin

2. Indian Cherry leave: It is obtained from *Cordia dichotoma* belonging from Boraginaceae family. It contains Alkaloids (Tannins and berberine), flavonoids and Amino acid (proline, glycine, and arginine). [16]



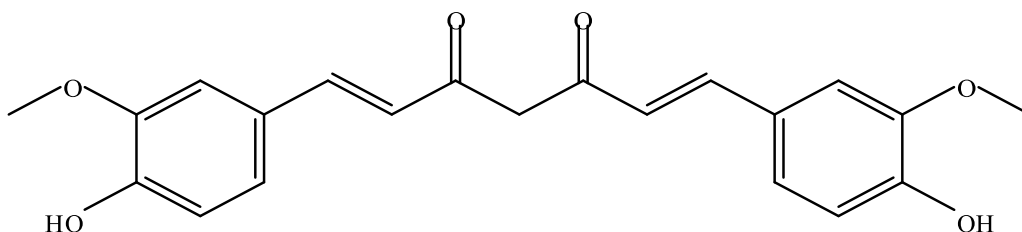
Berberine

3. Liquorice (Mulethi): It is obtained from *Glycyrrhiza glabra* L, belonging from Leguminoceae family. It contains Glycyrrhiza which is used as anti-ulcer. [17]



Glycyrrhizin

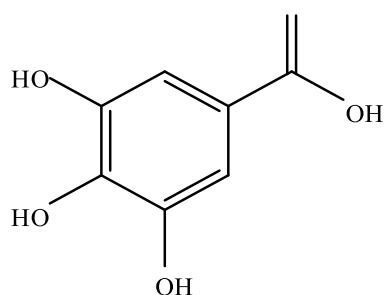
4. Turmeric (Haldi): It is obtained from *Curcuma longa* belonging from Zingiberaceae. It contains Curcumin, dimethoxycurcumin, and bisdemethoxycurcumin. It is used as antiseptic, Anti- Inflammatory [18]



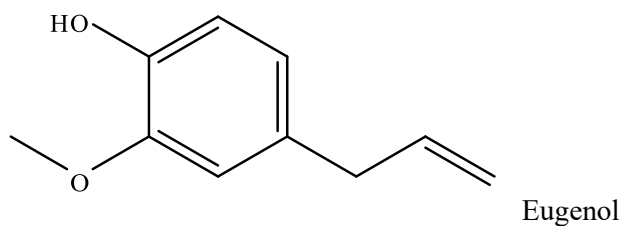
Curcumin

5. Pomegranate flowers: It is obtained from *Punica granatum* belonging from Punicaceae family. It contains Polyphenols like Gallic acid, ellagic acid and ethyl brevifolincarboxy-late, triterpenes Oleanolic acid. [19]

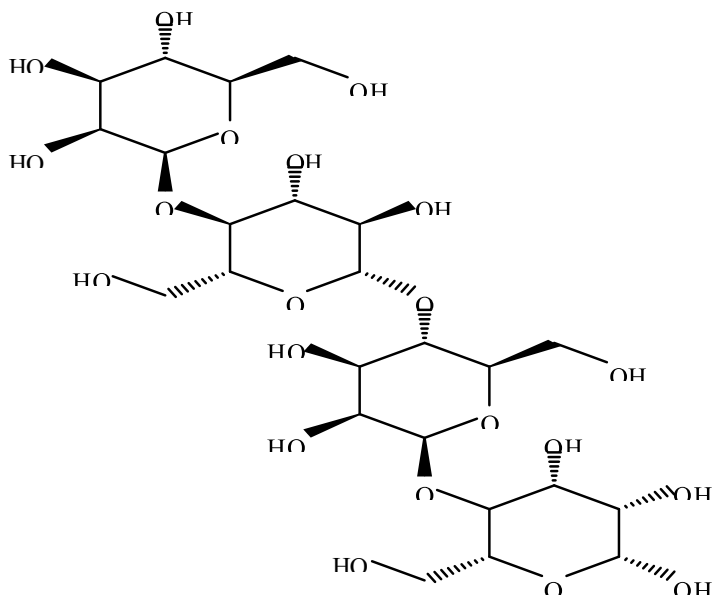
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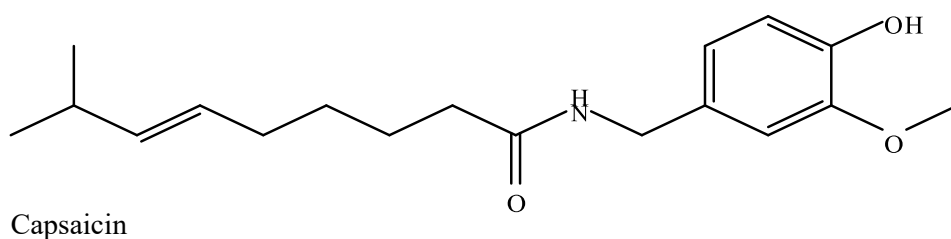
6. Betel leaves: It is obtained from Piper betle L belonging from Piperaceae l family. It contains Betel oil, Eugenol, amino acids, tannins and steroids, Vitamin A, Vitamin B2, Iodine, and Chavichol. It is use as Anti-ulcer, Anti-bacterial, Anti-fungal, Antioxidant, Anti-inflammatory. [20]



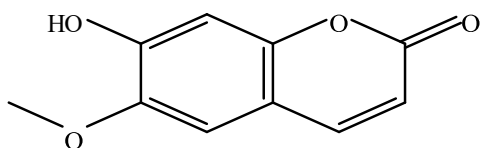
7. Aloe Vera: It is obtained from Aloe Bar-badensis Miller belonging from Liliaceae family. It contains Amino acids, anthraquinones, enzymes, minerals, Vitamins, lignins, Monosaccharide's, Polysaccharides. [21]



8. Capsicum: It is obtained from Capsicum annum L belonging from Solanaceae. It contains Capsaicin, paprika oleoresin, and dihydrocapsaicin. [22]

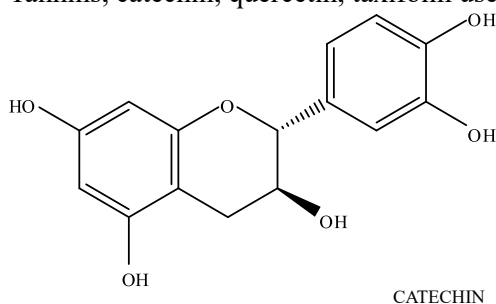


9. Noni fruit (Mulberry): It is obtained from *Morinda citrifolia* Linn, belonging From Rubiaceae. It contains Anthraquinones, Flavonoids and phenolic the antimicrobial effect of noni fruit is due to the presence of phenolic compounds such as L-asperuloside, acubin, scopoletin, alizarin, and other anthraquinones. [22]



Scopoletin

10. Accacia catechu (Katha): It is obtained from *Accacia catechu* belonging from Fabaceae family. It contains Tannins, catechin, quercetin, taxifolin used as Astringent and Anti- inflammatory. [23]



CATECHIN

Pharmaceutical gel: In semi-rigid systems known as gels, the mobility of the dispersing medium is constrained by an interlacing three-dimensional network of particles or solvated macromolecules of the dispersed phase. Both "gel" and "jelly" can be traced back to the Latin words *gelu* for "frost" and *gel* are, meaning "freeze" or "congeal." The term "gel" is derived from "gelatin." This origin illustrates the fundamental concept of a liquid setting to a solid-like substance that does not flow but is elastic and preserves some liquid properties.[24] Having at least two components, a gel is a solid or semisolid structure that comprises a condensed mass and is permeated by a liquid. In order to create gels and jellies, has a solid-like consistency rather than a liquid-like one, consisting of a small number of solids dispersed across a large amount of liquid. A defining characteristic of jelly and gel is the existence of some sort of epidermal structure, which gives them their solid-like properties. [25]

Simple method for preparation of Poly-herbal gel:

Combined with carbopol 934 and demineralized water. Add methyl paraben and propyl paraben to 5 ml of distilled water. In a water bath, warming when it has cooled, add propylene glycol. Next, add various concentrations of various types of powdered herbs or extracts. Add carbopol 934 after combining all components. Triethanolamine should be added gradually while stirring continuously to get the required pH. [26, 27]

Literature Review:

In a clinical study, NSS vs. Guava Leaves Mouthwash (no. of subjects = 16) There was a significant difference in size after 7 days ($p = 0.004$). The mean size of ulcers in those given guava mouthwash was significantly smaller than that in those with NSS. The size reduced was 0.8 mm from 1.44 mm. [28] Clinical study was performed by using control (Placebo gel) group and A. V. Gel. Control & A. V. Treated group, respectively which were not significantly different. The duration of complete wound size reduction and inflammation zone diameter was significantly lower than control group on specific time point after treatment. [29] Clinical trial was done and applied the mouth wash to six patients suffering from oral ulcer. 5 of them healed within three days, and 1 healed within four days. [30] In clinical study, reported that A. Vera polysaccharides could increase the level of blood TNF- α , IL-2 and IgG of the immune Inhibited mice. In this study, administration of A. Vera polysaccharides showed a significant increase in the plasma IgG, IgA and IgM Levels in polysaccharides treatment groups (I, II) when compared to ulcer model group. Moreover, there were higher plasma IgG, IgA and IgM levels in polysaccharides-treatment groups. [31] *Psidium guajava*, betel, and liquorice extracts with anti-mouth ulcer action were combined in various formulations. Exalcoholic *Psidium Guava* to create the gel, betel leaves, liquorice aqueous extract, and tract were all employed. Formulations that were developed may be used to treat mouth ulcers. [32] Natural medications advised using natural remedies for tooth discomfort. The herbal dental gel is a special composition that contains three crucial when administered locally, several oils

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specifically clove oil, camphor, and menthol—play a part in the treatment of dental discomfort. [33] If liquorice extract is used to treat a mouth ulcer using an adhesive oral patch that distributes the medication for at least 30 minutes and the patches are utilized for at . The approach reduces the healing times from usually 10 to 14 days to usually 2 hours if at least two or more hours per day. [34] For boils, ulcers, and skin eruptions, Acacia catechu bark powder is administered externally. A wonderful treatment for relaxing is to hold a small bit in your mouth and let it slowly melt. Pharyngitis and simple uvulitis. Due to its potent astringent and antioxidant properties, Acacia catechu willd is extremely valuable. [35] It is advised to use herbal products that are widely available in rural India to maintain good oral hygiene and prevent oral infections. For mouthwash to reduce gum discomfort, mixtures of peppermint, sage, clove oil, eucalyptus (*Eucalyptus globulus*) oil, and salt have been used.

Instead of using commercial mouthwashes, which could have negative side effects like teeth and tongue discoloration with prolonged usage, such as irritation and poor breath. Chewing tulsi (*Ocimum sanctum*) leaves and miswak (*Salvadora persica*) roots can help heal common mouth infections and keep teeth clean. [36] An important part of treating oral ulcers is using herbal lozenges. Because flavonoids have better compatibility with the human body and fewer adverse effects, their anti-ulcer properties are likely a result of their presence in herbal plants. Due to the presence of naturally occurring chemical components, as well as their many beneficial applications and curative effects, herbal medicine is the ideal option for the treatment of mouth ulcers. [37] Herbal medicine extracts can be used to treat mouth ulcers and can be integrated into chewing gum. The study came to the conclusion that chewing gum is a great drug delivery system for selfmedication because it is convenient, can be taken without water, contains one or more active ingredients that are released when chewed, and is designed to be used for either local treatment of mouth conditions or systemic delivery after absorption through the buccal mucosa. [38] Solid or semi-solid, single-dose formulations known as medicated chewing gums must be chewed, not ingested. They do include a chewable foundation for masticatory gum that contains one or more phytoconstituents. A medicated chewing gum is designed to be chewed for a specific amount of time in order to deliver the dose. Typically, the chewing gum is spit out once the medication has been released. They are designed for the local treatment of oral disorders. [39] Mouth ulcers can be treated with chewable tablets that include Acacia catechu extract. The chemical is also anticipated to aid in the healing of mouth ulcers. The fruit *Garcinia mangostana* (Gm.) contains a range of flavonoids, benzophenones, and tannins that have therapeutic qualities. GM has strong antibacterial and antioxidant properties as one of the traditional therapeutic herbs. [40] Gels for mucobioadhesion may contain herbs used in conventional Iranian medicine. One of these herbs is ginger extract, which is used to treat RAS ulcer discomfort, and Curcumin 5%, which has antibacterial properties. Using tragacanth gum, alcohol, sodium benzoate, and distilled water, mucobioadesive bases are created [41]

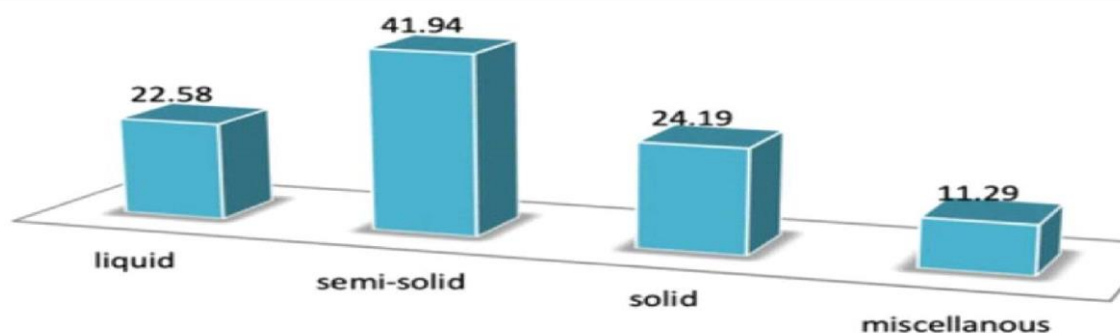


Fig: No of formulation used in treatment of Recurrent Aphthous Stomatitis (RAS) [41]

In treating chronic generalized gingivitis, a mouthwash containing 20% Acacia catechu has nearly equalled the effectiveness of a mouthwash containing 0.2% chlorhexidine. This was demonstrated by considerable decreases from the starting condition in a number of gingivitis-related clinical measures and microbiological analysis. [42] The created poly-herbal gel formulation, which contains Liquorice root, Guava leaves, and Betel leaves together with additives, has high therapeutic efficacy and works well as a low-cost medication delivery method. The novel herbal gel formulation for the treatment of oral ulcers shows promising. Its clinical usefulness is being determined through ongoing clinical investigations. The potential of herbal plants for treating ulcers in cancer patients has also been covered in other research. [43] Najafi and colleagues showed that the aqueous extract of glycyrrhizin could help those with head and neck cancer who are getting

radiotherapy by lessening the severity of oral mucositis.[44] A topical herbal gel created by Rimjhim Sahu et al. is intended to heal mouth ulcers. They focused on herbal extracts in their study that had potential advantages including pain alleviation, anti-inflammatory effects, antioxidant characteristics, wound healing properties, antibacterial attributes, and local anaesthetic properties. In the research they conducted, these extracts from *Glycyrrhiza glabra*, *Acacia catechu*, *Punica granatum*, *Curcuma longa*, and *Mentha piperita* shown substantial antibacterial effectiveness. [45] Shital Rajad et al. prepared a poly herbal gel including the extracts of *Bombax ceibathorn*, *Psidium guajava* leaf, and additives, and carried out an in vitro experiment. According to in vitro studies, polyherbal gel made of *Bombax C.* extract and *Psidium guajava* leaf extract is useful to heal Oral sores. And the improved batch persisted. Steady with the maximum medication dispersion for three months. [46] In their study, Shital Rajad et al prepared the Nano gel formulation using a combination of *Jasminum Officinale* and *Cynodon Dactyl* on extracts. They then assessed the physical properties, such as viscosity and pH, as well as the drug release characteristics of the Nano gel. Additionally, the researchers conducted in vitro studies to evaluate the antimicrobial activity of the formulation. [47] In order to cure mouth ulcers, this study set out to develop and test an herbal chewing gum that contained powdered *Psidium guajava* leaf extract and *Curcuma longa* Linn rhizomes. Guava leaves are frequently used to treat a variety of ailments, including diarrhoea, diabetes, sore throats, coughs, and wounds. They also have a calming effect. Turmeric includes a wide range of phytochemicals, including Curcumin, dimethoxycurcumin, Eugenol, tannins, alkaloids, saponins, terpenoids, and curcuma. Guava leaf extract, turmeric rhizome extract, and other necessary ingredients were used to produce the herbal chewing gum. [48] Plants like karpooravalli, cinnamon, and mint possess anti-inflammatory properties. Recent research on cinnamon reveals that it has anti-inflammatory effects in the nervous system by reducing the expression of cyclooxygenase-2, inducible nitric oxide synthesis, and nitric oxide production. In this performing study of poly herbal gel against microbes and measuring zone of inhibitions. [49, 50]

Conclusion:

This article provides a brief overview of the use of poly-herbal medication for oral ulceration. It highlights the potential benefits of these formulations but also emphasizes the need for further research to establish their efficacy and safety. Poly-herbal medication for oral ulcers shows promise in providing relief and promoting healing. This review highlights the effectiveness of such treatments. By combining various herbs, these medications target multiple factors involved in oral ulcer development. They have been found to reduce pain, inflammation, and promote tissue repair. However, more research is needed to fully understand their mechanisms and determine optimal dosages. Overall, poly-herbal medications offer a natural and potentially effective alternative for managing oral ulcers.

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Note: All structures are drawn in chemdraw.