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Oral ulcer and associated herbal pharmacological activities

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Abstract
The mouth ulcer typically induced agony and distress and may influence the individual's selection of foods while recovery takes place. Local trauma and aphthous stomatitis are the two most frequent causes of oral ulceration. The objective of this evaluation is on the mouth ulcer's etiology and contributing elements. Traditional remedies, as we all know, is the foundation of basic treatment due to higher cultural acceptance, greater compatibility with the human body, and less adverse effects. This article highlights the herbal medications used to treat mouth ulcers.

Keywords: mouth ulcer, herbal medications, inflammation, open sores

Introduction

Plants have an essential role in the healing of a wide range of human ailments, and herbal approaches are acquiring appreciation amongst patients because of their devoid side effects that are commonly involved in allopathic drugs [1]. A large variety of medicinal plants and plant constituents can be found in the Indian flora. As a result, there is a necessity to research such medications and their optimal formulations in order to improve patient compliance [2]. Wound healing, inflammation, skin infections, leprosy, dysentery, scabies, venerealillness, ulcers of any form, snake bites, etc. are among various disorders covered by Indian traditional medicine. More than 80% of the world's population already uses conventional treatments to treat various forms of skin ailments [3].

Oral ulcers are a type of oral mucosa membrane condition that is highly frequent. Mouth ulcers are open sores of the skin or mucus membrane lining characterised by shedding of inflammatory damaged tissue [4]. Recurrent Aphthous Stomatitis is amongst the most common pathologic conditions affecting ulcers in the oral mucosal membrane. Recurrent Aphthous Stomatitis develops an excruciating and erythematous aura on a single or several chronic ulcers in the oral mucosa [5]. Aphthous stomatitis is treated with antiseptics, anti-inflammatory drugs, analgesics, lasers, and herbal medicine [6].

Mouth ulcers can affect people of any age or inhabitants and can develop for a variety of reasons, including diseases, sicknesses, disorders, and symptoms that can be serious, even life-threatening. Oral cancer and leukoplakia are the two examples [7]. Mouth ulcers are lesions on the gums and within the mouth that are distressing. They are also known as canker sores. Although most mouth ulcers are innocuous, they can be rather painful for certain individuals, affecting eating, drinking, and brushing their teeth problematic. A mouth ulcer's size and symptoms vary based on the form of ulcer [8].

Roots of Mouth Ulcer [9]

Mouth ulcers are formed by a number of reasons that differ from one individual to another. However, there are a few typical factors:

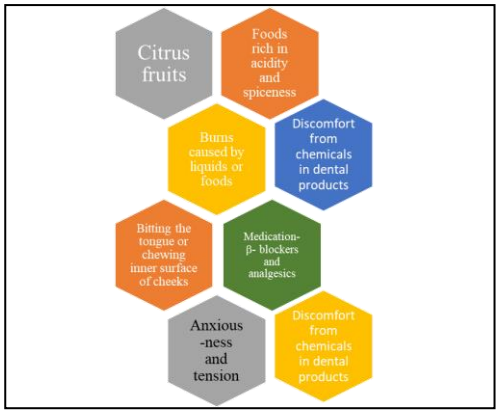

Fig 1: Roots of Ulcer

Types of Mouth Ulcer [10]
Mouth ulcer has been categorised into following three types-

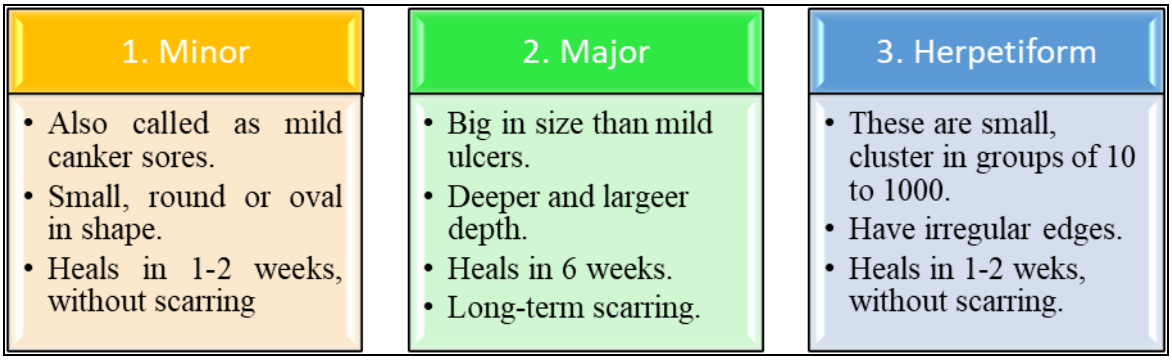

Fig 2

This article highlights the characteristics of certain of the plants that have been found to have antiulcer and ulcer-healing abilities. The plants are discussed in the following paragraphs:

***Ocimum sanctum Linn.* (Tulsi)**
The religious shrub Ocimum sanctum, also referred as Tulsi in Hindi, pertains to the Labiatae family. The plant is made up of several synthetic components that consolidate in a sophisticated approach to produce pharmacodynamic consequences [11]. During experimenting with fixed oil of tulsi plant, Singh and Majumdar (1999) [12] discovered that the plant had a powerful antiulcer efficacy towards ulcers caused by aspirin, indomethacin, histamine, serotonin, alcohol, reserpine, and aggravation. Hence, speculated that the powerful antiulcer activity has been probably attributed by blocking of 5-lipooxygenase in ulcer models generated by aspirin, indomethacin, and alcohol [12].
Dharmani P *et al*. (2004) [13], carry forwarded the work of Singh and Majumdar and investigated the antiulcer efficacy of an ethanolic extract of leaves of Ocimum Sanctum in rats with ulcer generated by cold restraint (CRU), alcohol (AL), aspirin (ASP), and pyloric ligation (PL), and in guinea pigs with histamine (HST) produced duodenal ulcers and found that the ethanolic extract have a mucoprotective action in addition to reducing acid secretion. They also investigated the therapeutic efficacy of plant in a chronic gastric ulcer model generated by acetic acid [13].
Ayesha *et al*. (2017) [14], suggested some key outcome of that was the dose-dependent nature of OS action, with the highest significant doses being 100 mg/kg body weight. The efficiency of OS extract in all five scenarios, therefore, was the greatest noteworthy evidence of this investigation, demonstrating that OS extract has antiulcerogenic activity via various routes. A further theory is that OS extracts include many active components that are beneficial towards numerous ulcer-inducing processes. Ulcer recovery is a multi-step procedure that includes wound shrinkage and re-epithelialization. Different variables, including as growth regulators and angiogenesis, are also involved. After 10 days of medication, OS dramatically minimized the extent of the ulcer [14].

Allophylus serratus Kurz
Allophylus serratus Kurz also called as Allophylus cobbe Raeuschel is a big Sapindaceae genus with a significant ethno pharmacological history. The existence of distinct chemical components in multiple regions of the Allophylus serratus (AS) plant has been revealed through pharmacognostic investigations and phytochemical analysis. Sitosterol is found in the plant's leaves. Phenacetamide, a molecule with antiulcer properties, is also present. Two flavonoid glycosides found in crude extract have been proved to be beneficial treating ulcers [15].
Kero Jemal (2019) [16] investigated the anti-ulcerogenic efficacy of AS by comparing the ethanolic extract of its dried, pulverized leaves for various ulcer variants. He investigated biochemical measures like as basic and gross acidity, peptic reactivity, and mucin formation to back up our findings. In all of the trials, AS provided large and considerable prophylaxis towards stomach ulcers. The main mechanisms behind the protection seen in the PL model were a decrease in acid output and peptic action, as well as an enhancement in mucin secretion. In the CRU model, decreased acid outflow was the primary cause, whereas in the AL and ASP versions, a massive rise in mucus composition and possibly an enhancement in prostaglandin concentration might be the defensive approach [16].

Desmodium gangeticum
Desmodium gangeticum DC (Leguminosae) is a well-recognized Indian medicative species referred as "Shaparni" in Hindi and has a high curative potential [17].
Agarwal V.S. (1997) [18] during testing the antiulcerogenic capability of DG's ethanolic extract in four different inducement variants, including CRU, ASP, PL, and AL, discovered that a dose of 200 mg/kg has been the greatest efficacious in all of them. The antioxidant action of DG could explain its potency in the CRU model.

This is consistent with previous findings on DG's antioxidant function, implying that DG has a free radical scavenging action. These actions could also be to contribute for DG's antiulcer properties. The efficacy of the extract's defensive framework on the gastric mucosa, inducing a suppression of gastric outflow, is indicated by the lower acid outflow assessed post pyloric ligation. Elevated mucin production in the AL and ASP generated ulcer models demonstrated the cytoprotective efficacy. DG's antiulcerogenic potency has been mostly owing to its superior cytoprotective action in respect to its antisecretory action, as opposed to OS and AS. Natural medications have been shown to enhance protective qualities and are much more trustworthy and secure than synthetic medications, despite their slower action. As a result, using DG individually or in conjunction with certain medicines should be closely considered [18].

Azadirachta indica

Azadirachta indica A. Juss, popularly referred as "Neem," is a naturopathic medication widely utilized in India to alleviate ailments such as leprosy, intestinal helminthiasis, and respiratory issues in infants.

The gastroprotective ability of dried Azadirachta indica bark extract in ulcer models caused by mercapto-methylimidazole, PL, CRU, indomethacin, AL, and HST has been stated by Rastogi R.P. *et al.* (1995) [19], It primarily works by preventing oxidative injury to the stomach mucosa and decreasing acid secretion. H+K+AT Pase functioning has been inhibited to validate the control of acid secretion, and lipid peroxidation and endogenous hydroxyl radical scavenging showed that the limitation of oxidative damage to the gastric mucosa (OH.). In the PL and stress ulcer models, they also contrasted the bark extract with two well-known antiulcer medications, ranitidine and omeprazole, and discovered that it was nearly equally effective and the antioxidant efficacy of the bark extract was higher than that of many other well-known antioxidants [19]. Bandyopadhyay *et al*. identified a phenolic glycoside as an active component; its characterization and mechanism are currently being researched [20].

The leaf extract has also been shown to have antiulcer properties, with the avoidance of mucus depletion and mast cell degranulation being suggested as potential mechanisms by Garg *et al*. As a result, Azadirachta indica provides a different choice for a more secure and efficient antiulcer medication [21].

Asparagus racemosus

Rastogi R.P *et al*, (1990) [22] examined that the methanolic extract of fresh roots of AR have antiulcerogenic effect in both the cysteamine-induced duodenal ulcer model and the gastric ulcer models caused by CRU, AL, ASP, and PL. The CRU, AL, and cysteamine-induced ulcer models all showed success with AR, however the PL and ASP models did not. However, the plant significantly enhanced mucin production, revealing cytoprotective ability as a potential strategy, while having no discernible impact on acid and peptic behavior. On acid secretion, the herb had no impact. Except for its impact on protective mucosal components, its efficacy in the CRU model was linked to its adaptogenic potential, respectively. In the PL induced model, this defensive system exhibited resistance [22].

Aegle marmelos

The plant that is most usually found growing on land in India is Aegle marmelos, popularly recognized as a "bael tree" and a member of the Rutaceae family. Domestically, it is referred to as "vilvam." Flavonoids, tannins, and saponins are the chemical components of this plant [23].

Ilavarasan *et al*, (2002) [24] in their findings revealed that in Kanyakumari district, Tamil Nadu, India, the kani tribes have long utilised the fruit of A. marmelos to cure ulcers. Rigorous Findings determined that Aspirin combined with pylorus ligation causes stomach ulcers in rats, and aqueous leaf extract must be taken orally for 21 days at a rate of 1 gm/kg every day. When compared with reference, the results showed a considerable decrease in the number of ulcer lesions. Active Ingredient investigated is luvangetin, a pyranocoumarin isolated from the seeds [24].

Allium Sativum

The plant Allium sativum, a member of the Liliaceae family, is also known as "vellapundu" in several parts of the world. It is grown throughout India. The active ingredient in this plant is an acrid volatile oil, which also contains starch, mucilage, albumen, and sugar as its chemical components. Seeds produce fragrant oil. In addition to crucial nutrients and supportive materials comprising vitamins, the juice, and especially its oil contents, is rich in combinations of salicylic acid, iodine, and sulphur that are naturally coupled [25].

Applying fried garlic in mustard or coconut oil is a great way to get rid of maggots that are permeating wounds, ulcers, and ulcerated areas, according to R. Rezvaninejad *et al*, (2017) [27]. An ointment made of garlic juice and three to four parts of ordinary or distilled water has been used to wash wounds and treat nasty ulcers. Rats were given oral doses of the A. sativum bulb juice extract against cysteamine-induced stomach ulcers of 250 and 500 mg/kg. The extract greatly speeds up the healing of gastric ulcers in rats and inhibits the growth of experimentally produced duodenal and gastric ulcers [26].

Aloe Vera

The term "aloe gel" refers to the Liliaceae family member aloe vera. It is known as "kattalai" domestically, and it is common throughout India. This plant contains the chemicals aloin, isobarbaloin, and emodin [27].

Mohsin *et al*., (2017) [8, 28] revealed through their experiment that when Aloe vera powder and gum acacia were combined, and the resulting solution was given orally to rats at a rate of 200 mg/kg to treat a stomach ulcer brought on by indomethacin, remarkable antiulcer efficacy equivalent to control has been demonstrated by the extract [28].

Annona squamosa

Custard apple is the conventional term for Annona squamosa (Annonaceae). In India, it is grown in gardens and is known there as "sitapalam." Alkaloids, flavonoids, saponins, and tannins are some of this plant's chemical components. Seeds produce oil and resin, and young fruit, leaves, and seeds all have an acerbic characteristic [29]. Saleem *et al*., (2012) [30] performed an experiment and resulted that ulcers have been treated with leaves by grounding them into a slurry without the use of water. The aqueous leaf extract safeguarded rats' abdomen from ethanol-induced gastric ulcers and pylorus ligation [30].

Balsamodendron mukul

The botanical name for Balsamodendron mukul (Burseraceae) is "gum-gugul." Formerly known as "gukkulu," it is prevalent in Sind, Rajputana, Eastern Bengal, Berars, Assam, Khandesh, and Mysore. This plant contains acerbic elements, volatile oil, and gum-resin as chemical components. In order to treat indolent ulcers, guggul gum is combined with lime juice or coconut oil and administered as a paste or ointment [31].

Bauhinia variegate-

The Sub-Himalayan region, as well as the woods of India and Burma, are home to Bauhinia variegate, a member of the Caesalpiniaceae family. Domestically, it is referred to as "shemmandarai" and is more widely recognized as "orchid tree." Quercetin, rutin, apigenin, and apigenin 7-0-glucoside are the chemical components identified in this plant. Tannic acid, glucose, and a brownish gum are all found in the bark [32].

The bark's decoction works well as a wash for ulcers. The following substances are used in a remedy called "kanchanara guggula," which is beneficial for ulcers: Take 10 parts of the Bauhinia variegate bark, 3 portions of each of the three myrobalans, ginger, black pepper, long pepper, Crataeva nurvala bark, cardamoms, cinnamon, and Tejpatra leaves. To create a pill masses, blend them altogether and add guggula (15 parts). Half a tola of this is used each morning together with a decoction of Sphaeranthus mollis, Triphala, or catechu. In order to treat pylorus ligation, ethanol, and aspirin-induced stomach ulcers in rats, oral dosages of 200 and 400 mg/kg of the ethanolic and aqueous root extract of B. variegate were given. The extract considerably lowered basal stomach acid yield and prevented gastric mucosal injury [33].

Berberis aristata

Mostly on Nilgiris and throughout the temperate Himalayas, from Bhutan to Kunawer, Berberis aristata (family Berberidaceae) is cultivated. Its regional name is "kasturimanjal," while its popular name is "Indian or Nepal barberry." This plant's roots and wood are claimed to have high concentrations of the bitter yellow alkaloid "berberine," that mixes in acids to generate salts of the alkaloid. The root also includes two other alkaloids [34].

Rasaut, a crude extract has been made from the roots and bark of the plant and mixed with honey, and applied onto the ulcerated skin, the method has been proposed by ayurvedic literature and has been used as a traditional medicine for healing of ulcers [35].

Beta vulgaris

The botanical family Chenopodiaceae member Beta vulgaris is popularly referred to as "beetroot." It is commonly called to as sugar-beet and is a native of the Mediterranean seacoasts. For the purpose of its fleshy roots and leaves, it is also grown in gardens over most of India. There are two varieties: red and white. The chemical components contain “betin” and is an active ingredient of the plant. This has been used as a conventional medicine for treating ulcers and running sores. By preparing a decoction of the root and a little amount of vinegar has been added to it and was then given to patients suffering from ulcers [36].

Careya arborea

The Myrtaceae plant Careya arborea is frequently referred to as the "slow match tree." Domestically, it is referred to as "pailacputatammi"and occurs frequently in the Sub-Himalayan region. The plant have thick red bark that contains 8% of tannins. Enormous modest crystals of calcium oxalate are also present.

Obstinate ulcers can be quickly healed by applying a poultice comprised of pulped leaves three to four times each day. The alcohol-based stem and bark extract of C. Arborea has been given orally to rats for 5 days at doses of 300 and 600 mg/kg to treat ethanol, cold-restraint-, and pylorus-ligation-induced ulcer models. In comparison to controls, the extract dramatically speeds up the healing of stomach ulcers [37].

Carica Papaya

Papaya is the popular name for the Carica papaya (Caricaceae). Locals refer to it as "papali-pazham." It thrives in all tropical nations and numerous subtropical areas worldwide. This plant contains papain, chymopapain, pectin, carposide, carpaine, carotenoids, and antheraxanthin as active compounds. The fruit can be eaten in a both way, riped and unriped in the healing of ulcer.

Rats were given oral doses of 50 and 100 mg/kg of the aqueous seed extract of C. papaya to treat ethanol-induced stomach ulcers. Against the effects of ethanol, the extract shielded the stomach mucosa. The amount of gastric juice and stomach acidity were dramatically lowered by C. papaya extract [38].

Euphorbia neriifolia

The popular name for the Euphorbia neriifolia (Eurphorbiaceae) plant is "common milk hedge." Domestically, it is known as "ilaikkalli." This leafless plant is grown in Bengal and can be found throughout Central India. This plants possess euphorbon, resin, gum, caoutchouc, calcium malate, and other chemicals. For unhealthy ulcers and scabies plant juice along with melted butter has been given [39].

Ficus Religiosa

The term "holy fig" refers to Ficus religiosa (Urticaceae). "Arasha-maram" is the term used natively. Hindus nurture this holy Peepal, a big tree that grows in the habitat all across India. This plant's bark contains tannin, caoutchouc (cochtone), and wax as chemical components. Rats have been tested against absolute ethanol, aspirin, and pylorus ligation-induced stomach ulcers using two dose intervals of the hydro alcoholic extract from the leaves of F. religiosa (250 and 500 mg/kg, oral). As contrasted to reference, the extract dramatically lowers the ulcer benchmark level [40].

Hibiscus rosa sinensis

The term "changing rose" refers to the plant Hibiscus rosa sinensis (Malvaceae). "Chembaruthi" is the indigenous name for it. It is a native of China and is frequently cultivated as a decorative plant in India. This plant contains hydrocitric acid, flavonoids, anthocyanins, quercetin, cyanidin, kaempferol, and cyaniding [41].

The kani communities of Kanyakumari region, Tamil Nadu, India, have historically utilised the root of H. rosa sinensis to cure ulcers. At dosages of 250 and 500 mg/kg, the aqueous and alcohol extracts of plant roots significantly reduced ulceration in rats with pylorus ligation. It has therefore been demonstrated experimentally that such extracts have adequate potency as an antiulcerogenic substance [42].

Mangifera indica

The popular name for Mangifera indica (Anacardiaceae) is "mango tree." Locally, it is known as "mangaai." It is raised all over India. This plant has alkaloids, sterols, saponins, tannins, and flavonoids among its chemical components. To treat ulcers, rice bran oil was mixed with leaf extracts, then given orally. According to mythology, the plant has antiulcer properties. Rats with gastric lesions received oral dosages of 250, 500, and 1000 mg/kg of the flower decoction in a dose-dependent approach. As a result, the extract dramatically decreased both gastric acidity and volume of gastric liquid [43].

Mimosa pudica

The Fabaceae plant Mimosa pudica is also referred to as "touch me not." Traditionally, it is known as "thottal sinungee."It flourishes throughout the globe's temperate and tropical climates. Flavonoids, quercitin, naringin, saponins, tannins, gums, and mucilage are some of the plant's chemical components. For intestinal ulcers, fresh leaves and seeds are made into a decoction and ingested. Mimosa pudica leaf extracts in ethanol have been found to have antiulcer action in a dose-dependent approach, suggesting that they could be used as a biological antioxidant for the healing of ulcers [44].

Conclusion

It has been extrapolate from such a review that investigations incorporating organic resources could lead to a fresh and efficient structure of care. Conventional medications is increasingly being studied in light of the contemporary impasses that mainstream treatment faces in treating a variety of disorders. In this regard, conventional medicine has developed effective procedures for the management of a variety of gastrointestinal illnesses.

The effectiveness of each of the cures discussed here was sufficiently supported by both older and newer scientific sources. The old theory held that acid secretion was the only factor contributing to ulcer development, and that reducing acid production was the only therapeutic strategy. But this idea has modified in light of current research.

Today, reducing acid secretion and strengthening the defence system are the main goals of ulcer treatment. In order to clarify the link between configuration and function, attempts must be focused on isolating and characterizing the dynamic components. Therapeutic relevance should be taken into account when conducting a thorough analysis of the active ingredients in natural medicines. To ensure consistent reliability in biological assessment, standardization is essential. Although there has been a quite astonishing amount of experimental research on herbal medicines for the treatment of gastric ulcers, very few have made it to clinical trials, and even fewer have been released onto the market. This demonstrates that the advantages of research are not reaching the target population for medical research, and as a result, time, personnel, and resources are not being used effectively. In order for herbal medicines to be clinically successful and commercially accessible, specialists require to exhibit a deeper prominent consideration in evaluating herbal medicines for possible antiulcer action.

Abbreviations

Al- alcohol, ASP- aspirin, CRU- Cold restraint ulcer, PL- Pyloric ligation, HST- Histamine.

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