



Herbal Treatment of Mouth Ulcer: A Review

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ABSTRACT

Mouth ulcer is one of the common disorders caused due to variety of etiological factors. The two most common causes of oral ulceration are local trauma (e.g. Rubbing from a sharp edge on a filling) and aphthous stomatitis ("canker sores"), a condition characterized by recurrent formation of oral ulcers for largely unknown reasons.⁴ Ulcers are an open sore of the skin or mucus membrane characterized by removing of inflamed dead tissue. The mouth ulcer often caused pain and discomfort and can alter the person choice of food while healing occurs. The foremost common oral ulceration is Aphthous stomatitis. This review focuses on the causes of mouth ulcer and factors in charge of the mouth ulcer. There are various synthetic drugs which are available to treat mouth ulcer. As we all know herbal medicine is that the most stay of primary healthcare thanks to better culture acceptability, better computability with natural object and lesser side effects. And the literature also revealed that there are various medicinal plants which can be utilized within the treatment of mouth ulcers. Therefore, this review summarises about the medicinal plants which could be used for the treatment of mouth ulcer as drug.⁶

Index Terms - Mouth Ulcer, Herbal, Treatment, Stomatitis, Sores

I. INTRODUCTION

A mouth ulcer (also termed an oral ulcer, or a mucosal ulcer) is an ulcer that occurs on the mucous membrane of the oral cavity. It is defined as "a break within the mucosal surface of the oral cavity"⁶ They are painful round or oval sores that form in the mouth, mainly on the inside of the cheeks or lips.⁴ The two most common causes of oral ulceration are local trauma (e.g. Rubbing from a sharp edge on a filling) and aphthous stomatitis ("canker sores").⁴ Aphthous stomatitis or mouth ulcer is an ulcerative condition that is related to the oral mucosa and is characterised by repeating ulcers in the throat and oral cavity.³ The term aphthae is derived from the Greek word aphthi, which means "to set on fire" or "to inflame," and is thought to have been first used by the philosopher hippocrates to describe the pain associated with a common disorder of the mouth during his time (likely, aphthous stomatitis). Local trauma, genetic factors, nutritional deficiencies, viral and bacterial infections, and immune or endocrine disturbances have all been implicated as etiological factors of frequent oral ulcerations. In a subset of patients, no etiology can be identified and a diagnosis of exclusion must be made; such cases are referred to as recurrent aphthous stomatitis (ras). Three forms of ras exist: minor (>70% of cases), major (10%), and herpetiform (10%). These subtypes differ in morphology, distribution, severity, and prognosis (table 1). Despite their distinct characteristics, all forms of ras have a significant impact on quality of life and interfere with activities of daily living.⁵

Table 1: Clinical features of minor, major, and herpetiform recurrent aphthous stomatitis (RAS)

	MINOR RAS	MAJOR RAS	HERPETIFORM RAS
Gender predilection	Equal	Equal	Female
Morphology	Round or oval lesion Gray white pseudomembranes Erythematous halo	Round or oval lesion Gray white pseudomembranes Erythematous halo	Small, deep ulcers that commonly converge irregular contour
Distribution	Lips, cheeks, tongue, Floor of mouth	Lips, soft palate, pharynx	Lips, cheeks, tongue, floor of mouth, gingiva
Numbers of ulcers	1-5	1-10	10-100
Size of ulcers	<10mm	>10mm	2-3mm
Prognosis	Lesions resolve in 4-14 days No scarring	Lesions persist >6 weeks High risk of scarring	Lesions of resolve in <30 days Scarring uncommon

II. TYPES OF MOUTH ULCER:

Ulcers are categorized as major, minor, or herpetiform based on the size and number of ulcers. The following are the most common forms of mouth ulcers:

Minor ulcers: Minor aphthous ulcers are the most frequent type, accounting for around 80% of occurrences. These are approximately 2-8 mm in diameter and usually clear up in 10 to 2 weeks. These ulcers are often superficial, small in size (less than 1.0 cm in size), few in number, occur alone or in clusters, and heal without scarring.



Figure 1 : Minor ulcer

Major ulcers: Major aphthous ulcers, which affect roughly 10% of patients, are the second category. These are larger and deeper in shape, with a raised or uneven border with a diameter of over 1 cm. They might appear as a single lesion or as a group of lesions. Because of the level of necrosis, this form of the ulcer may take many days to recover and can cause complications inside the mouth.



Figure 3: Major Ulcer

Herpetiform ulcers: Herpetiform ulcers, the third category, is a term that refers to the clustered appearance of lesions. This ulcer consists of a cluster of dozens of tiny lesions the size of pinheads. It has nothing to do with the herpes virus. These appear in enormous numbers, ranging from 10 to 100 at a time, and are made up of several tiny lesions that eventually join to form larger plaques. They may heal with a scar in 7 to 30 days depending on the size and depth of the ulcer. 21



Figure 4: Herpetiform ulcer

III. CAUSES:

There is no definite etiology and pathology known for mouth ulcer; although some factors are considered important which include nutritional deficiencies such as iron, vitamins especially B12 and C, poor oral hygiene, infections, stress, indigestion, mechanical injury, skin disease etc. Some other factor include such as: 6

Nutritional deficiency

- Various nutritional deficiencies, including ferric, folic acid, b-complex, B1, B2, and B6, have been linked to a subset of aphthous ulcer patients. Nutritional deficits' role in aphthous ulcers is expected to vary by region, depending on diet and dietary supplementation.

Food allergies

- Allergies can be triggered by a variety of foods. Patients with recurrent aphthous stomatitis have antibodies to milk from cows and wheat protein. As a result, several typically allergenic foods have not been linked to recurrent aphthous stomatitis. Cacao, coffee, almonds, cereals, nuts, strawberries, cheeses, tomato, and flour may be linked to some patients' symptoms.

Genetic factors

- Patients with aphthous ulcers have a genetic component, with about 30 percent to 40 percent of patients having a family background. Some sufferers have a family background of recurrent aphthous ulcers. A common link is the start of symptoms at a young age and the severity of the symptoms. In identical twins, recurrent aphthous ulcers are substantially associated.

Chemical injuries

- Chemicals like aspirin or alcohol that are kept or came in contact with the mucous membranes can cause necrosis and sloughing, resulting in an ulcerated surface. There is little evidence to link sodium laurel sulfate (SLS), one of the key chemicals in most toothpaste to an increased risk of mouth ulcers.

Immune system

- Many researchers believe that aphthous ulcers are the result of a variety of disease processes, all of which are mediated by the immune system. Aphthous ulcers are hypothesized to emerge when the body becomes aware of compounds it doesn't recognize and assaults them.²¹

Physical or Psychological Stress

- There is a strong connection of aphthous ulcer occurrences with stressful life. Psychological stress may play a role in the appearance of recurrent aphthous stomatitis as a trigger or a modifying factor. No studies have convincingly proved stress as a causative or precipitating factor for recurrent aphthous stomatitis.

Trauma

- The most likely factors which bring about aphthous ulcers are local trauma and stress. Injury to the oral mucosa may give result from accidental self-biting, dental procedures, tooth brush bristles, and sharp-edged foods (e.g., potato chips), anesthetic injection. Apart from this environmental and emotional stress also result into aphthous ulcer. ⁶

Tobacco smoking

- The patients suffering from recurrent aphthous stomatitis usually are non-smokers, but there is a lower prevalence and severity of recurrent aphthous stomatitis among heavy smokers as critical moderate smokers. Some patients report an onset of recurrent aphthous stomatitis after smoking cessation, while others report control on re-initiation of smoking. The use of smokeless tobacco is expounded to a significantly lower prevalence of recurrent aphthous stomatitis. Nicotinecontaining tablets also appear to control the frequency of recurrent aphthous stomatitis. ⁶

Drugs

- Such medications as Nicorandil, nsoids, Ibuprofen, and nicotine replacement therapy induce mouth ulcers. ²⁸

IV. PATHOLOGICAL FACTORS WHICH CAUSES ULCER:

Table 2: Pathological factors of mouth ulcer

Microbial disease	Malignant neoplasms
• Chickenpox	Blood disorder
• Hiv infection	• Anaemia
• Fungal infection	• Leukaemia
• Tuberculosis	• Neutropenia
• Syphilis	Gastrointestinal disease
• Herpetic stomatitis	• Ulcerative colitis
• Herpes zoster	• Crohn's disease
• Hand, foot and mouth disease	• Coeliac disease

V. TREATMENT

A variety of gel lozenges, sprays and mouthwashes are used to treat ulcers. Mouthwashes with ingredients such as povidone iodine, chlorhexidine or chlorohexidine as well as homemade salt and warm water mouthwashes and Aloclair mouthwash without alcohol. Gel with a liquid phase that generally seems thicker than other compounds is an example of a semisolid material. To relieve discomfort and lower the risk of complications, topically applied therapies are suggested. Usually, paracetamols, steroids, gel, ointment, and antibiotics such (doxycycline) are recommended to treat infections and suppress the immune system. Due to the numerous side effects and negative consequences these synthetic and semi-synthetic pharmaceuticals have nowadays, herbal medications are used .27

VI. IMPORTANCE OF HERBAL MEDICINE

Traditional herbal medicines are naturally occurring plant-derived substances have been used to treat human illnesses from the beginning of time. It is no surprise that 1.42 billion people, or one-fourth of the world's population, rely on traditional medicines to treat a variety of maladies. Evidences shows that most of the world population is using herbal medicine since ancient times. The Indian flora contains a wide range of therapeutic plants and plant components. These plants can be used to discover effective alternatives to manufactured medications.²⁶ There are many herbal plants which are useful in medicinal purposes. Plants various parts are used for treating various diseases. Therefore there are some plant which will be useful in treating mouth ulcer. 6

VII. ADVANTAGES OF HERBAL MEDICINE:

- Medicines have a long history of use and better patient tolerance and public acceptance medical plants have a renewable source, allowing us to provide more affordable medicines to the world's rising population.
- Because of the rich agro-climatic, cultural, and ethnic biodiversity of developing countries like India availability of medicinal plants is not a problem.
- The cultivation and processing of medicinal herbs are eco-friendly.
- Prolonged and apparently uneventful use of herbal medicines is safe and efficacious.
- Some medicinal plants and dietary nutrients, such as Aloe, Terminalia chebula, Vetiveriaziziinoides, Ginseng, Capsicum, and others, have been shown to have antiulcer activity.²⁸
- They are economically cheap and less expensive.¹⁹

VIII. HERBAL REMEDIES USED IN TREATMENT OF MOUTH ULCER:

Phytogenic agents are traditionally used by herbalists and indigenous healers for the prevention and treatment of ulcer. This article reviews the anti-ulcer properties of the most commonly employed herbal medicines and their identified active constituents. Botanical compounds with anti-ulcer activity include flavonoids (i.e. Quercetin, naringin, silymarin, anthocyanosides, sophoradin derivatives) saponins (i.e. From Panaxjaponicus and Kochia scoparia), tannins (i.e. From Linderaeumbellatae), gums and mucilages (i.e. Gum guar and myrrh). Among herbal drugs, liquorice, aloe gel and capsicum (chilli) have been used extensively. Ethnomedical systems employs several plant extracts for the treatment of ulcer 4

1. Aloe vera

Common name: Aloe vera

Scientific name: Aloe Barbadensis

Biological source: Aloe is dried latex of leaves of aloe vera.

Family: Liliaceae

Chemical constituents: sterols, amino acids, enzymes, anthraquinones, lignins, vitamins, minerals, polysaccharides, monosaccharide, saponins, salicylic acid.



Figure 5 : Aloe vera

Mechanism of action: Through cell proliferation, aloe vera boosts the rate of wound closure and the tensile strength when applied to wounds this is due to aloe vera. Aloe vera speeds up blood flow to the areas that have been injured by increasing the amount of collagen and the level of collagen cross linking therefore promoting wound concentration and breaking of scar tissue. Antibacterial action of aloe vera helps in wound healing.

Uses: antiulcer, anti-inflammatory, anti-diabetic, antioxidant, anticancer, healing. Aloe Vera is used in the treatment of mouth ulcers, its anti-inflammatory property helps in reducing the pain of ulcer. Aloe vera shows soothing and wound healing activity on burn.

2. Guava leaves

Common name: Guava leaves (Amrood)

Scientific name: Psidium guava-java

Biological source: Psidium guajava L.

Family: Myrtaceae

Chemical constituents: Flavonoids, (Quercetin and its glycosides), tannis, saponin, oleanolic acid.

Fruit: Vitamins, iron, phosphorus & calcium.



Figure 6: Guava

Mechanism of action: It reduces the pain of ulcer and effectively decreases the size of ulcer and disinfects the wounds by rinsing affected areas with decoction of the leaves. The presence of flavonoids extracted from guava leaves, such as quercetin, morin-3-o-lyxoside, and morin-3-o-arabinoside, may shows a significant reduction in the size of aphthous ulcers.

Uses: Antimalarial, antiulcer, anthelmintic, analgesic, antispasmodic. Guava leaves. Guava leaves are used in the treatment of aphthous ulcers.

3. Ginger

Common name: Ginger

Scientific name: Zingiber officinale

Biological source: Ginger consists of the rhizomes of Zingiber officinale.

Family: Zingiberaceae

Chemical Constituents: Gingerol, shigaol, sesquiterpene, hydrocarbons, oleoresin.



Figure 7: Ginger

Mechanism of action: Anti-inflammatory effect of ginger reduce the pain of ulcer. With the help of mucoadhesive containing liquorice extract decrease the size of lesion and also reduce the pain. Yanoacrylate-2-octyle mucoadhesive which help in wound healing, decrease the time (duration) of healing and also decrease the size of lesion.

Uses: Anticancer, Antiulcer, Anti-inflammatory, Antioxidant, antimicrobial, anti-diabetic. Ginger is used in the treatment of Aphthous ulcers.

4. Honey

Common name: Madhu, Mel.

Scientific name: Honey

Biological source: Honey is a sugar secretion deposited in honey comb by the bees.

Family: Apidae

Chemical constituents: Glucose, Fructose, Sucrose, dextrin, formic acid, protins, enzymes, vitamins.



Figure 8: Honey

Mechanism of action: The rate of tissue regeneration is accelerated by honey and inhibition of edema, exudation, malodour, inflammation in wounds. Honey also reduced the severity of the pain, the size of the ulcer and the erythema in a safe and effective manner.

Uses: Antiseptic, Antibacterial, anti-inflammatory, immune boosting, antifungal. Honey is used in treatment of minor RAS.

5. Indian Jasmine

Common name: Chameli

Scientific name: Jasminum

Biological source: Jasminum Officinale

Family: Oleaceae

Chemical constituents: Benzyl Alcohol, Benzyl acetate, Linolool, Indol, Benzyl Benzoate, Cis jasmine, Geroniol, Methyl antrolinate.



Figure 9: Jasmine

Mechanism of action: Due to the anti-inflammatory, antibacterial activity the jasmine applied on ulcer so decrease the ulcer so automatically decrease the pain due to the ulcer.

Uses: It give anti- inflammatory action so it is used to decrease the inflammation due to the ulcer. It is used to decrease pain due the presence of ulcer in mouth and also used in the treatment of cancer as a pain removal. It is used to healing of canker in mouth. It is also used in treat constipation so automatically treat mouth ulcer.

6. Mint

Common name: Pepper mint

Scientific Name: Mentha

Biological source: It consists of the dried leaves and flowering tops of mentha piperita L.

Family: Lamiaceae

Chemical constituents: Vitamin A, Vitamin C, Iron, Calcium, Magnesium.



Figure 10: Mint

Mechanism of action: The mint leaves are applied on mouth ulcer so it give cooling effect on ulcer, so decrease the pain due to the ulcer and give fragrance in mouth.

Uses: It antibacterial effect against cryogenic bacteria. It gives antimicrobial effect, so it is used in the treatment of ulcer. The mint leaf is useful for fresh breath due to the presence of flavonoids. It also provides cooling effect in mouth.

7. Neem

Common name: Neem

Scientific name: Azadirachta indica

Biological source: It consists of leaves and other aerial parts of Azadirachta indica.

Family: Meliaceae

Chemical Constituent: Azadiractin, nimbin, DPPH, Azadiradione, salninin, Azadirone, gedunin, 2-pentadecanone, methyl starate, phytol, nimbidin, gueraceatin, ascorbic acid, amino acid, polyphenolic flavonoids



Fig 11: Neem

Mechanism of action: They improve the immune response in gum and tissue of the mouth, which are good remedies for mouth ulcers. Neem leaves act as pain reliever in mouth ulcer and toothache problems. Neem contain azadirachtin, nimbin, nimbidin, nimbolide, have antibacterial effect. Neem inhibit the growth of bacteria and fungi. Neem leaves show anti-inflammatory effect. Neem leaves play an important role in wound healing by tensile strength of the healing tissue. Azadirachta indica leaf extracts stimulates wound healing by triggering an inflammatory response and neovascularization.

Uses: Anti-inflammatory, Anti ulcer, Anticarcinogenic, Anti oxidant, anti mutagenic, Anti bacterial, Antiviral, Antifungal, Antihyperglycemic.

8. Turmeric

Common name: Haldi

Scientific name: Curcuma longa

Biological Source: It is the dried rhizome of Curcuma longa Linn.

Family: Zingiberaceae

Chemical constituents: Diarylheptanoids, curcumin, dimethoxycurcumin, bisdimethoxycurcumin.



Fig 12: Turmeric

Mechanism of action: Curcumin shows wound healing activity, so it also effective in the treatment of mouth ulcer by increasing cellular proliferation & collagen synthesis at the wound site as evidenced by increase in DNA and total protein & also shows increase in type-III collagen content of wound tissue, results in faster rate of epithelialization and wound contraction, it also shows increase in tensile strength.

Uses: Anti-inflammatory, antiulcer, anti-arthritic activity, antioxidant, anticarcinogenic, antimutagenic, anticoagulant, antifertility, antidiabetic, antiulcer, antibacterial. Turmeric is used in the treatment of RAS. Turmeric helps in reducing the pain of the ulcer.

9. Tulsi

Common name: tulsi

Scientific name: Ocimum sanctum.

Biological source: It consists of fresh and dried leaves of Ocimum sanctum Linn.

Family: Lamiaceae

Chemical Constituents: Fixed oil: Linoleic acid, Linolenic acid, oleic acid, Palmitic acid.

Essential oil: eugenol, cubenol, Linalial, carinene Minerals: Vitamin C, Vitamin A, calcium, Zink, iron.

Mechanism of action: The tulsi has immunomodulatory properties so it affects the hemopoetic tissues and skin. Thus, Tulsi can be applied to oral Lichen planus therapy. Tulsi helps in healing the sores of ulcers. Antiulcer effect of tulsi is due to cytoprotective effect.



Fig 13: Tulsi

Uses: Anti-cancer, antiulcer, antiarthritic, antibacterial, antifungal, antioxidant, antiinflammatory, anti-helminthic, antispasmodic, imunomodulatory. Tulsi is used in the treatment of different types of ulcers. Due to its anti-inflammatory, antibacterial, anti-oxidant and immuno-modulatory characteristics, tulsi can be promising herb in the treatment of various oral disorders. Tulsi leaves are effective in oral infection. Tulsi leaves include antibacterial like carracrol and terpene & sesquiterpene b carbophyline. Tulsi leaves can be chewed to maintain good dental hygiene.

10. Liquorice

Common name: Mulethi

Scientific name: Glycyrrhiza glabra

Biological source: It is obtained from peeled and unpeeled stolons and roots of Glycyrrhiza globra.

Family: Fabaceae

Chemical Constituents: Triterpene saponins, flavonoids, polysaccharides, pectin, simple sugars, amino acids.



Fig 14: Licorice

Mechanism of action: Licorice's mechanism of action involves anti-inflammatory and mucosal protective actions. Glycyrrhizin produces inflammation, while other compounds promote mucin production, forming a protective layer. These actions may contribute to soothing effects, aiding in the healing and alleviation of discomfort associated with mouth ulcers.

Uses: It used as Expectorent and Demulcent. Also used in peptic ulcer in the form of deglycyrrhized licorice. Some other activities like Antithrombotic, Anti-inflammatory, Antioxidative, Antiallergenic, Antimicrobial, Antidepressive, Antidiabetic and as a flavouring agent.

IX. CONCLUSION:

The whole discussion proved that the naturally occurring components of medicinal herbs can effectively treat and prevent mouth ulcers, regardless of the etiology. The anti ulcer activities probably due to the presence of flavanoids in herbal plants due to their better compatability with human body and lesser side effects. Plants which contain flavonoids are – guava leaves, licorice (mulethi), turmeric, aloe vera,neem, jasmine, tulsi . The potential of these herbs to treat the sickness holistically is owing to their medicinal characteristics as well as their ability to improve immunity.

X. REFERENCES:

1. Vorvick LJ, Zieve D. "Mouth ulcers on medlineplus". A.D.A.M., Inc. Retrieved 27 December 2016
2. Daddy S,Izzaty N,Khalik B,Taib H,Pohchi A,Hassan A,Novel material in the treatment of minor oral recurrent Aphthous stomatitis. International Medical Journal 2013;20:392- 4.
3. Shashy R, Ridley M. Aphthous ulcers: a difficult clinical entity. Am J Otolaryngol 2000;21:389-93.
4. Femanio f, lanz a, Buonaiuto a, et al. Guidelines for diagnosis and management of aphthous stomatitis. Pediatr Infect Dis J. 2007;26(8):728–732.
5. Belenguer-Guallar i, Jiménez-soriano Y, Claramunt-lozano a. Treatment of recurrent aphthous stomatitis. A literature review. J Clin Exp Dent. 2014;6(2):e168–e174.
6. Charde K, Upadhye KP, Gholse YN, Chaple DR. Current updates on recurrent aphthous stomatitis: etiology, pathogenesis and management. World J Pharm Pharm Sci. 2020;9(5):448–462.
7. Deshmane S. A review on oral mouth ulceration. Int J Pharm. 2014;1(1):216–29.
8. Mohd, Ad, Sakarkar DM, Kosalge SB, Shafiq S. " Formulation Development and Evaluation of Unit Moulded Herbal Semisolid Jelly useful in treatment of Mouth Ulcer. J Pharma Biomed Anal. 2011;3:1705–13.
9. Misal G, Dixit G. Formulation and evaluation of herbal gel. Indian J Nat Prod Resour. 2012;3(4):501–6.
10. Teresa A. Herbal Remedies for Mouth Ulcer: A Review. J Bio Innov. 2017;(4):521–7.
11. Woo SB, et al. Recurrent aphthous ulcers: a review of diagnosis and treatment. J Am Dent Assoc.1996;127:1202-13 11.

12. Mittal S, et al. A review: herbal remedies used for the treatment of mouth ulcer. *Int J Heal and Clin Res.* 2019;2:17-23.
13. Singh S, et al. Formulation and Evaluation of Herbal Gel From Different Parts of *Cyamopsis Tetragonoloba (L.) Taub.* For Wound Healing. *World J Pharm Pharm Sci.* 2015;5:740-752.
14. Purushotham K, et al. Formulation of topical oral gel for the treatment of oral sub mucous fibrosis (OSMF). *Pharm Lett.* 2011;3:103-102.
15. Felix DH, et al. Oral medicine: 1. Ulcers: aphthous and other common ulcers. *Dental update.*2012;39:513-519.
16. Redman RS. Recurrent oral ulcers. *Northwest Dent* 1972;51:232-4.
17. Abdullah, et al. Prevalence of recurrent aphthous ulceration experience in patients attending Piramird dental speciality in Sulaimani City. *J Clin Exp Dent.*2013;5:89.
18. Rezvaninejad R, et al. Herbal Medicine in Treatment of Recurrent Aphthous Stomatitis. *J Isla Dent Assoc IRAN* 2017;29:127-134.
19. Woo SB, et al. Recurrent aphthous ulcers: a review of diagnosis and treatment. *J Am Dent Assoc.*1996;127:1202-13
20. Kumar BR, et al. A Review on the Perspective of Peptic, Mouth and Corneal Ulcer and Their Treatment Facts. *Asian J Pharma Res Dev.* 2013:2-11.
21. Halaszynski TM, et al. Management of oral ulcers and burning mouth syndrome. *Inorofacial Pain.* 2014; 103-114.
22. Yamada T, et al. *Textbook of gastroenterol.* John Wiley & Sons.2011.
23. Mohsin J Jamadar, Rajmahammad Husen Shaikh. Preparation and evaluation of herbal gel formulation. *Journal of Pharmaceutical Research and Education* 2017;1(2):201-224.
24. Camila de Barros Gallo, Maria Angela Martins Mimura, Norberto Nobuo Sugaya. Psychological stress and recurrent aphthous stomatitis. *Clinics* 2009;64(6):645-648
25. Subiksha, P.S., 2014. Various remedies for recurrent aphthous ulcer-a review. *Journal of Pharmaceutical Sciences and Research*, 6(6), p.251.
26. Tilburt JC, Kaptchuk TJ. Herbal medicine research and global health: an ethical analysis. *Bulletin of the World Health Organization.* 2008;86:594-9.
27. Thube SA, Patil MJ. Evaluation of Wound Healing Potential of Some Indian Herbal Extracts and it's Formulation in *Acne Vulgaris*. *Pharmacognosy Journal.* 2014 Sep 1;6(5).
28. Mishra, P., Banweer, J., Tahilani, P., Samundre, P. And Shrivastava, S., Herbal chewing Gum to Treat Mouth Ulcer using Guava Leaf and Turmeric Rhizomes. *IJCMCR.* 2022; 21 (5), 1.
29. Sumitra singh, bhagwati devi rohilla. Formulation and evaluation of herbal gel from differents part of *cyamopsis tetragonoloba(L.) Taub.* For wound healing. *World journal of pharmacy and pharmaceutical sciences*, 2015; 5(3): 740-752.
30. Chun-Lei Li, He-Long Huang, Wan-Chun wang, Hong Hua, efficacy and safety of topical herbal medicine treatment on recurrent aphthous stomatitis: *Drug Desing, Development and Therapy*, 2016; 10: 107-115
31. Borelli F,Izzo A A.The plant kingdom as a source of anti-ulcer remedies.*Phytotherapy Research.*2000;14:581-91.