

Available online on 15.09.2025 at <http://jddtonline.info>

Journal of Drug Delivery and Therapeutics

Open Access to Pharmaceutical and Medical Research

Copyright © 2025 The Author(s): This is an open-access article distributed under the terms of the CC BY-NC 4.0 which permits unrestricted use, distribution, and reproduction in any medium for non-commercial use provided the original author and source are credited



Open Access Full Text Article



Review Article

Therapeutic Strategies and Emerging Drug Delivery Systems for Oral Aphthous Ulcers

Ram Babu Sharma ^{*1}, Abhishek Dadwal ², Anjali Dixit ³

¹ Professor & Principal, Himalayan Institute of Pharmacy, Kala-Amb, Sirmour, Himachal Pradesh

² M. Pharm Scholar, Himalayan Institute of Pharmacy, Kala-Amb, Sirmour, Himachal Pradesh

³ Associate Professor, Himalayan Institute of Pharmacy, Kala-Amb, Sirmour, Himachal Pradesh

Article Info:



Article History:

Received 08 June 2025

Reviewed 19 July 2025

Accepted 17 August 2025

Published 15 Sep 2025

Cite this article as:

Sharma RB, Dadwal A, Dixit A, Therapeutic Strategies and Emerging Drug Delivery Systems for Oral Aphthous Ulcers, Journal of Drug Delivery and Therapeutics. 2025; 15(9):134-139 DOI: <http://dx.doi.org/10.22270/jddt.v15i9.7350>

*For Correspondence:

Ram Babu Sharma, Professor & Principal, Himalayan Institute of Pharmacy, Kala-Amb, Sirmour, Himachal Pradesh

Abstract

Aphthous ulcers, also known as canker sores, are painful mucosal lesions that occur on oral structures, including the cheeks, gums, lips, and tongue. Although their precise etiology remains unclear, contributing factors include nutritional deficiencies (vitamins B12, folate, C), stress, trauma, infections (viral, bacterial, fungal), chemical irritants like sodium lauryl sulfate, and heavy metal exposure. These ulcers significantly impair quality of life by causing pain during eating, brushing, and speaking. Treatment aims to manage pain, promote healing, and reduce the frequency of recurrence. Topical corticosteroids remain the mainstay of therapy, offering rapid resolution with minimal systemic effects. Adjunctive treatments include local analgesics, immunomodulators (e.g., thalidomide), NSAIDs (mesalazine), stem-cell therapy, and various herbal remedies such as extracts from *Psidium guajava*, *Curcuma longa*, *Glycyrrhiza glabra*, and *Punica granatum*, which demonstrate anti-inflammatory, antimicrobial, and wound-healing properties. Recent advances focus on novel mucoadhesive drug delivery systems—patches, gels, microneedles, nanosheets, hydrogels—to enhance drug residence time, bioavailability, and patient compliance. These innovative approaches target both symptomatic relief and accelerated healing, while minimizing systemic exposure and improving therapeutic outcomes. Moving forward, integrating molecular insights into disease mechanisms (microRNA dysregulation in OPMDs, microbial dysbiosis) with tailored delivery platforms may pave the way for precision interventions targeting recurrent aphthous ulcers.

Keywords: Aphthous ulcers, nutritional deficiencies, stress, trauma, infections

Introduction

Oral ulcers that develop in the mucosal layer of the oral cavity are also referred to as canker ulcers (aphthous ulcers). Ulcers come in a variety of forms, including vaginal, oesophageal, and mouth ulcers. These may appear inside the tongue, lips, gums, or cheeks. Round or oval in outline, ulcers are encircled by inflamed mucosa.¹ Although the exact cause of mouth ulcers is unknown, a number of factors, like nutritional deficiencies (vitamin B12, folate), stress, trauma, coeliac disease, genetics, medications, and microbiological factors, can contribute to their formation. They cause severe pain during eating, brushing teeth and may cause irritation.^{2,3}

The treatment for aphthous ulcer is primarily focused on symptomatic relief with three main objectives 1. Pain management 2. Enhance ulcer healing 3. Reduce the frequency of recurrences. Topical corticosteroids are the most frequently used anti-inflammatory medications for treating oral cavity inflammations, and their topical application is considered the primary treatment for mouth ulcers. This method minimises systemic negative effects while offering efficient relief.^{4,5} Because mouth

ulcers are located in the oral mucosa, mucosal medication delivery methods are recommended for their management. Topical gels, mouth washes, oral liquids, creams, ointments, patches, lozenges, and tablets are some of the formulations used to treat mouth ulcers.⁶ Approximately 80% of people worldwide use herbal remedies for their medical needs.

Causes⁷

Chemicals like Sodium Lauryl Sulphate (SLS), commonly found in numerous toothpaste formulations, have been associated with the development of mouth ulcers. These ulcers, also known as oral or aphthous ulcers, can occur as a result of the irritant effects of SLS on the delicate oral mucosa. Public health organizations such as the National Health Service (NHS) have acknowledged SLS as a potential risk factor for mouth ulcers due to its propensity to cause irritation and tissue damage.

Infections such as those caused by herpes viruses.

- Injuries to the oral mucosa can occur due to various factors, including accidental trauma such as chewing of the lip, tongue, or cheek, as well as mechanical irritation

from consuming hard foods that can scrape the delicate oral tissues.

Nutritional disorders, such as vitamin deficiencies, can contribute to the development of ulcers and erosions within the oral cavity. Essential vitamins, including vitamin B12, folate, and vitamin C, play crucial roles in maintaining the health and integrity of oral tissues. Deficiencies in these vitamins can compromise the body's ability to repair and regenerate oral epithelial cells, leading to increased susceptibility to oral mucosal lesions.

- For example, vitamin B12 deficiency can result in a condition known as pernicious anemia, which may manifest with symptoms such as glossitis (inflammation of the tongue) and oral ulceration. Similarly, folate deficiency has been associated with the development of oral mucosal lesions, including ulcers and erythema.
- Vitamin C deficiency, commonly known as scurvy, can cause widespread mucosal damage throughout the body, including the oral cavity. Oral manifestations of scurvy may include gingival bleeding, swelling, and ulceration.
- Overall, maintaining adequate nutritional status, including sufficient intake of vitamins and minerals, is essential for the health of oral tissues and can help prevent the development of ulcers and erosions associated with nutritional deficiencies. Individuals at risk of nutritional disorders, such as those with poor dietary habits, certain medical conditions, or malabsorption syndromes, should be vigilant about meeting their nutritional needs through dietary modifications or supplementation under the guidance of healthcare professionals.
- Potentially, heavy metals, among them cadmium found in phosphate rock, could be contributing factors

Infections Caused by Viruses

Whether the herpes virus contamination is primary or secondary affects the clinical aspects of the virus in the mouth. Primary herpetic gingivostomatitis refers to the initial infection. In very young children, it can be asymptomatic or extremely mild, but it is linked to increasingly severe general symptoms as the patient becomes older. Gingivitis is the first symptom, followed by the production of vesicles that easily rupture, causing excruciating ulcers covered in a yellowish film that usually clumps together after two to three days. The most frequent sites remain the palate, throat, mouth, tongue, and oral cavity.

- **Herpes simplex virus 1:** Numerous infections can result in oral ulcers. Main herpes simplex type 1 is the most common virus triggering ulcers (HSV-1). Those who are impacted may get widespread, small, shallow ulcers on their mouths. Similar to acute necrotising ulcerative gingivitis, the gingiva is often swollen and ulcerated. Previously believed to be a childhood illness, main HSV-1 infection typically happens in the second or third decade of life. Around five percent of those who have had an initial HSV-1 infection (cold sores) experience recurrent episode of herpes labialis. It includes ulcers at the mucocutaneous

junctions of the lips and/or nose, erythema, vesiculation, pustulation, and paraesthesia. Pregnancy, concurrent illness, and exposure to UV light are causes for herpes labialis.

- **Epstein-Barr Virus (EBV):** Although Epstein-Barr Virus (EBV) ulcers are rare, they may indicate infectious mononucleosis. The ulcers are composed of a few small, superficial lesions of the oral mucosa. The ulcers that accompany other non-lymphomas are more frequently associated with EBV. Tooth decay hairy leukoplakia (OHL), also known as Hodgkin's disease or white patches, can appear when the body's defence system is suppressed. OHL has been observed in intestinal inflammation patients taking immune-suppressive drugs.

Ulcers Caused by Fungal Infections

- **Candidiasis:** Ulceration is one of the many clinical manifestations of candidiasis, the most prevalent fungal infection of the oral cavity. Nearly forty percent of people without candidiasis symptoms have the common causal organism, *Candida albicans*, in their oral flora. However, when the oral flora is changed, this fungus can cause infection.
- Every instance of candidiasis requires an evaluation of risk factors. Examples include poorly fitted dentures and inadequate vertical dimension. Dentulous individuals and those with persistent problems require an examination of systemic factors. Rare genetic immune deficiencies and acquired immune deficiency syndrome are two immune deficiency illnesses that frequently cause intractable mucocutaneous candidiasis. Patients using immune-suppressive medications for autoimmune diseases, cancer, or to avoid organ rejection after transplants may develop candidiasis.

Ulcers Caused by Bacterial Infection

- **Acute necrotizing ulcerative gingivitis:** Acute destructive ulcerative periodontal is a nonspecific ulceration disease that affects the gingivae almost exclusively. Poorly controlled diabetes, tobacco smoking, immune deficiency, and possibly psychological stress are all associated contributing factors. Minor trauma, as well as cleaning and flossing, usually cause pain in the patient. Rubbing the gingiva can result in tissue desquamation or the creation of a blood-filled bulla. The illness is more common among postmenopausal women, but it is not exclusive to them. Erosive lichen planus, allergic stomatitis, and bullous pemphigoid are just a few of the disorders that might show clinically with comparable lesions.
- **Mycobacterial infection:** Sputum-borne *Mycobacterium tuberculosis* can infect the oral mucosa, causing non-healing indurated ulcers. Chronic ulcers are the most frequent source of ulcers. A granulomatous inflammation occurs, along with caseous necrosis. These lesions aren't easily distinguishable; hence tissue culture is required for diagnosis. Oral ulcers are persistent, indurated, and have an uneven undermined edge as well as thick

mucus material at the base. Tuberculous ulcers are usually painless and persistent, with overhanging or undermined borders and a pale floor; but they can also be ragged and uneven, which can be unpleasant. Secondary tuberculosis oral symptoms can occur anywhere in the mouth, with the tongue being the most usually afflicted site. The gingiva, mouth floor, palate, lip, and mucous membrane are the additional sites involved.

Pathophysiology Of Oral Ulcers

Oral Potentially Malignant Disorders (OPMD) also remain a great threat due to their high potential for malignant transformation. The pathophysiology of OPMD is associated with the dysregulation of some microRNAs at the cellular level, which are mainly involved in oral carcinogenesis. On a clinical basis, a timely diagnosis of malignancy in OPMD is significant because it relates to ulcers, which might be precancerous. The salivary microRNA changed in expression and observed as a potential biomarker will open up everything to a new horizon for research and practice⁸.

Oral Submucous Fibrosis is a disease of oral ulcers involving aberrant remodelling and fibrosis of the tissues. The pathophysiology of this OSF highlights the molecular mechanisms to be imparted because ulceration and restricted mouth opening have severe impacts on oral health and quality of life. Malignant potential in OSF further emphasizes the need for prevention and/or treatment measures. The main function of microbial interactions in the pathogenesis of oral ulcers is considered with chronic inflammatory diseases and malignant conditions as well. The dysbiosis,

or imbalance, in the systemic relationship of oral microbes can be a trigger mechanism for opportunistic infections that may eventually lead to ulcer formation. Pathogen-pathogen interactions, such as those of *Candida albicans* with streptococci, need to be discussed to have a comprehensive picture of infection mechanisms on the oral mucosa and their potentiality in ulcers of the same. Such microbial interactions should be explored in future studies to guide preventive and therapeutic strategies^{9,10}.

Despite the insights obtained from recent studies, there are still some gaps in knowledge regarding the pathophysiology of oral ulcers. For example, though immune dysregulation plays a key role in conditions like LP and Behçet's disease, the exact triggering factors for the development of ulcers are yet to be fully understood. Another point is that the relationship between dietary factors and the recurrence of oral ulcers is rather unexplored and should be looked into further for chronic diseases such as recurrent aphthous ulcers. And while there have been great strides in the discovery of biomarkers for early malignancy in OPMD, wider studies are needed that take those findings into action within clinics. Future research in that direction should seek therapeutic targets from the molecular mechanisms involved with OSF and OPMD to have an intervention that can actually work on oral ulcers.¹¹

The mechanism by which an oral ulcer heals is listed and described in Table 1. Phases of oral ulcer healing the process of wound healing involves multiple phases that are interrelated and distinct, such as haemostasis, inflammation, proliferation, and maturation stages.^{12,13}

Table 1: Stages of mouth ulcer heals

Phases	Description
Haemostasis	Initial response to blood vessel injury; exposure of subendothelial ECM activates platelets, initiating the hemostatic cascade.
Inflammation	Peaks intensity reaches within 24–48 hours after injury, persisting for several days; inflammation recruits immune cells and enhances vascular permeability.
Proliferation	Characterized by the replacement of fibrin clot with granulation tissue, driven by regenerative growth factors.
Maturation	Final phase, where granulation tissue remodels into a denser ECM, restoring homeostasis over time.

Management of Mouth Ulcer

Herbal Treatment

The majority of people on the planet have been using herbal medicine since ancient times, according to evidence. Several medicinal plants and plant parts can be found in Indian flora. Effective substitutes for produced drugs can be found using these plants. Numerous human ailments can be effectively treated by plants, and people increasingly turn to herbal remedies because they don't have the typical side effects of allopathic medications. Therefore, in order to improve patient acceptance, it is necessary to research these kinds of pharmaceuticals and

their effective mixtures. Since ancient times, herbal items and cures have been utilised in India to treat and cure a wide range of illnesses. Additionally, Indian folk medicine offers a wide range of treatments for a number of illnesses, such as snake bites, diarrhoea, scabies, leprosy, wound healing, inflammation, skin infections, and venereal disease. Over 80% of people worldwide still use traditional treatments for a variety of skin conditions. Herbal remedies in wound management include surgical intervention, debridement, disinfection, and keeping the area moist to promote the development of a favourable environment for natural healing. Therefore, it is clear that herbal remedies represent a significant part of treatment plans that are used all over the world.¹⁴

Herbal Medicine for Mouth Ulcers

Common Name	Scientific Name	Family	Chemical Constituents	Uses	Ref
Guava leaves, Amrood	Psidium guajava	Myrtaceae	Tannins and flavonoids (quercetin and its glycosides)	Antimalarial, anthelmintic, antiulcer properties	[15]
Indian cherry leaves, Lasoda, Tenti	Cordia dichotoma	Boraginaceae	Alkaloids, flavonoids, amino acids	Used for headaches and ulcers including decoction for sore throat	[16]
Liquorice, Mulethi	Glycyrrhia glabra L.,	Leguminoseae	Saponin, flavonoid, liquirtin, isoliquertin liquiritigenin and rhamnoliquirililn	Anti-inflammatory and expectorant, controls properties.	[15]
Turmeric	Curcuma longa	Zingiberceae	Diarylheptanoids, curcumin, dimethoxy curcumin,	Anti-inflamator, antiulcer and antiarthritic activity	[17]
Pomegranate flowers	flowers Punica m L.	Punicacea	Polyphenols, gallic acid, ellagic acid and ethyl brevifolincarboxylate, triterpenes oleanolic acid	Peptic ulcers, oral ulcers and, antimicrobial, antiinflammatory properties.	[18]
Betel leaves	Piper betle L.	Piperaceae	Alkaloids, carbohydrate, amino acids, tannins and steroids	Anti-ulcer, Anti- bacterial, Antifungal, Antiinflammatory activities,	[19]
Capsicum	Capsicum annum L.	Solanaceae	Capsaicin, paprika oleoresin, and dihydrocapsaicin	Among other things, gastrointestinal problems include gas in the stomach, cramps, stomach pain, diarrhoea, and mouth ulcers.	[20]
Noni Fruit	Morindacitrifolia Linn.	Rubiaceae	Anthraquinones, flavonoids and phenolics	Abnormal menstruation, acne/ boils, constipation, high blood pressure, gastric and other ulcers, arthritis, diabetes, fever, high blood pressure, gastric and other ulcers.	[20]

Local treatment agents²¹

The mainstay of local treatment for mouth ulcers is symptomatic therapy. Analgesia, pain relief, and tissue regeneration are the goals of local therapy.

Analgesics

Analgesics are important for symptom management even though they don't directly encourage recovery. Since major aphthous ulcers usually take a month or more to heal, patients frequently suffer from excruciating pain and have trouble eating. In therapeutic practice, lidocaine and dactinon hydrochloride are often used analgesics. Additionally, Zilactin (Zila Inc., Phoenix, AZ), an over-the-counter drug, has a hydroxypropyl cellulose covering that has long-lasting analgesic benefits in addition to mucosal adhesion qualities. However, the brief burning sensation

it produces on the skin and gums is a disadvantage of its use.

Corticosteroids

It is commonly acknowledged that the main treatment for oral ulcers is corticosteroids. Although corticosteroids are often effective in managing severe outbreaks and curing most mouth ulcers within a week, they are not very effective at preventing recurrence. Dexamethasone or triamcinolone acetonide by itself can accelerate ulcer healing, according to in vitro research. Additionally, a clinical study has shown that using triamcinolone with fluocinonide gel speeds up ulcer healing and lengthens the interval between recurrences. To minimise serious side effects, it is important to remember that long-term

usage of corticosteroids at high broad doses should be avoided.

Immunomodulators

Thalidomide is a glutamate derivative that has anti-inflammatory, immunomodulatory, and analgesic effects. Thalidomide is thought to reduce TNF levels, which lessens the immune system's assault on healthy membranes. The results of a clinical trial by Revuz *et al.* showed that thalidomide significantly improved patients' symptoms, but it did not stop relapses. Thalidomide is linked to a number of other negative side effects, including headache, constipation, dry mouth, and drowsiness, along with its well-known teratogenic side effects. Thus, thalidomide's popularity is hampered by its reputation.

Nonsteroidal anti-inflammatory drugs (NSAIDs)

The active ingredient of salazosulfapyridine (SASP), which is used to treat ulcerative colitis, is mesalazine (5-aminosalicylic acid). Collier *et al.* demonstrated that mesalazine can effectively alleviate discomfort, pain, and promote healing in patients with oral ulcers, with no significant occurrence of adverse effects. The mechanisms of action are proposed to involve the reduction of prostacyclin synthesis, suppression of oxygen metabolite generation by polymorphonuclear cells, and inhibition of leukotriene release from mucosal membranes.

Regenerative therapy

In cellular therapy, mesenchymal stem cells (MSCs) have been used to heal mucosal and cutaneous wounds. Through processes including cell differentiation and paracrine factor release, this treatment has proven to be beneficial. Adipose-derived MSC sheets were recently presented by Lee *et al.* as a possible substitute therapy that could speed up the healing of oral mucosal ulcers and possibly take the place of existing therapeutic approaches. The capacity of MSCs to differentiate into multiple cell types and perform paracrine actions, such as anti-apoptotic, pro-angiogenic, and stem cell activation functions at the site of damage, may be the possible mechanism of action.

Novel Drug Delivery Systems

Novel drug delivery systems enable patient-targeted therapy for each individual. The dosage forms such as mucoadhesive films, buccal patches, oral wafers, oral dissolving strips, liposomes, nanotechnology-based preparations and hydrogel are gaining importance in prevention and treatment of oral ulcers. A Swedish startup called Mucor has developed an intra-oral patch that absorbs tissue fluid containing inflammatory mediators, bacteria, and pathogens involved in ulcer formation. The patch absorbs tissue fluid up to 20-25 times its original weight and turns into a biodegradable gel within 3 to 4 hours. It is designed to reduce inflammation, stimulate healing and offer a hygroscopic effect to support oral ulcer recovery. Dissolving microneedle patches loaded with combination of betamethasone sodium phosphate and betamethasone dipropionate (BSP-BDP) along with hyaluronic acid was

reported to have therapeutic effect against mouth ulcers. BSP-BDP promotes cell proliferation whereas hyaluronic acid facilitates oral ulcer healing. Similarly, microneedle patches containing triamcinolone acetonide showed better bioavailability and physical properties when formulated with mesoporous polydopamine nanoparticles. It is a unique dressing for treating oral mucositis. Mucoadhesive gel, prepared using naturally obtained polynucleotides (from the fish tissues) and sodium hyaluronate, was explored as a novel approach in treating oral ulcer as a Class III CE0373 medical device. Polynucleotides restore the innervated oral tissues and hyaluronate promotes wound healing. Cuttlefish ink is reported to have antimicrobial, antioxidant, antiulcerogenic and anti-neoplastic properties. This natural bioactive ingredient was combined with nanoparticle based biopolymer in treating oral ulcers developed in diabetic patients. Dexamethasone loaded into HPC-based oral dissolving films was found to regulate PI3K/Akt signalling pathway to produce anti-oro-ulcerogenic action. Antimicrobial peptides-modified polycaprolactone-collagen nanosheets provide better adhesion and improve the healing of oral ulcers.²²

Conclusion

Oral aphthous ulcers are multifactorial mucosal lesions with diverse etiologies, encompassing nutritional deficiencies, mechanical injury, infections, chemical irritants, immune dysregulation, and genetic predispositions. Current treatment modalities prioritize symptomatic relief principally through topical corticosteroids and analgesics alongside emerging immunomodulators and NSAIDs to expedite healing. Herbal remedies, widely used globally, offer promising therapeutic adjuncts due to their anti-inflammatory, antimicrobial, and wound-healing effects, with several plant extracts demonstrating efficacy in promoting ulcer resolution. Notably, novel drug-delivery technologies are transforming ulcer management. Mucoadhesive films, dissolvable strips, microneedles, hydrogels, and nanoparticle-enhanced gels are being developed to improve local drug concentration, prolong mucosal residence time, and enhance patient adherence. Examples include biodegradable intra-oral patches (Mucort), hyaluronic acid-based dissolving films, and collagen nanosheets, which collectively show superior bioavailability and healing acceleration. Furthermore, cellular therapies leveraging mesenchymal stem cells present potential for regenerative treatment in chronic refractory cases. Despite these advances, knowledge gaps remain in understanding the molecular pathogenesis—particularly in OPMDs and oral submucous fibrosis as well as the role of microbial interactions and dietary influences in ulcer recurrence. Future research should prioritize translational clinical trials that integrate molecular biomarkers, microbiome profiling, and personalized drug delivery platforms. Such a multidimensional approach holds promise for more effective, targeted, and patient-centric management of recurrent oral aphthous ulcers.

Conflict of Interest: The authors declare no potential conflict of interest concerning the contents, authorship, and/or publication of this article.

Author Contributions: All authors have equal contributions in the preparation of the manuscript and compilation.

Source of Support: Nil

Funding: The authors declared that this study has received no financial support.

Informed Consent Statement: Not applicable.

Data Availability Statement: The data supporting this paper are available in the cited references.

Ethical approval: Not applicable.

References

1. Yogarajah S, Setterfield J. Mouth ulcers and diseases of the oral cavity. *Medicine*. 2021;49(7):407-413. <https://doi.org/10.1016/j.mpmed.2021.04.003>
2. Burley V, Biyani D, Umekar M, Naidu N. Medicinal plants for treatment of ulcer: A review. *Journal of Medicinal Plants Studies*. 2021;9(4):51-59. <https://doi.org/10.22271/plants.2021.v9.i4a.1312>
3. Öner Ü, Özdemir Ş, Öner F, Akdeniz N. Do Heavy Metals Accumulated in Saliva Involve in the Etiopathogenesis of Recurrent Aphthous Stomatitis? *Biological Trace Element Research*. 2020;198(1):46-50. <https://doi.org/10.1007/s12011-020-02058-2> PMID:32030633
4. Pan Z, Zhang X, Xie W, Cui J, Wang Y, Zhang B, et al. Revisited and innovative perspectives of oral ulcer: From biological specificity to local treatment. *Frontiers in Bioengineering and Biotechnology*. 2024;12:1335377. <https://doi.org/10.3389/fbioe.2024.1335377> PMID:38456005 PMCid:PMC10917957
5. Nishad SR, Narwade SS, Naik PR, Patil VP. Nature's Shield for Oral Ulcer Management: A Comprehensive Review. *Research Journal of Pharmacognosy and Phytochemistry*. 2025;17(1):49-55. <https://doi.org/10.52711/0975-4385.2025.00009>
6. Suharyani I, Fouad Abdelwahab Mohammed A, Muchtaridi M, Wathoni N, Abdassah M. Evolution of Drug Delivery Systems for Recurrent Aphthous Stomatitis. *Drug Design, Development and Therapy*. 2021;15:4071-4089. <https://doi.org/10.2147/DDDT.S328371> PMID:34616142 PMCid:PMC8489189
7. Yadav RK. A review on mouth ulcer and its various treatment. *Journal of Pharmaceutical Sciences and Research*. 2021;10:28-40.
8. Tan Y, Wang Z, Xu M, Li B, Huang Z, Qin S, Nice EC, Tang J, Huang C. Oral squamous cell carcinomas: state of the field and emerging directions. *International Journal of Oral Science*. 2023;15. <https://doi.org/10.1038/s41368-023-00249-w> PMID:37736748 PMCid:PMC10517027
9. Maheswari TN Uma, Venugopal A, Sureshababu N Malli, Ramani P. Salivary micro RNA as a potential biomarker in oral potentially malignant disorders: A systematic review. *Tzu-Chi Medical Journal*. 2018;30:55-60.
10. Abati S, Bramati C, Bondi S, Lissoni A, Trimarchi M. Oral Cancer and Precancer: A Narrative Review on the Relevance of Early Diagnosis. *International Journal of Environmental Research and Public Health*. 2020;17. <https://doi.org/10.3390/ijerph17249160> PMID:33302498 PMCid:PMC7764090
11. Choudhari S, Chaudhary M, Gadail A, Sharma A, Tekade S. Oxidative and antioxidative mechanisms in oral cancer and precancer: a review. *Oral Oncology*. 2014;50(1):10-8. <https://doi.org/10.1016/j.oraloncology.2013.09.011> PMID:24126222
12. Pan Z, Zhang X, Xie W, Cui J, Wang Y, Zhang B, et al. Revisited and innovative perspectives of oral ulcer: from biological specificity to local treatment. *Frontiers in Bioengineering and Biotechnology*. 2024;12:1335377. <https://doi.org/10.3389/fbioe.2024.1335377> PMID:38456005 PMCid:PMC10917957
13. Maver T, Kurečić M, Smrke DM, Stana Kleinschek K, Maver U. Plant-Derived Medicines with Potential Use in Wound Treatment. *Herbal Medicine*. 2018; <https://doi.org/10.5772/intechopen.72813>
14. Thube SA, Patil MJ. Evaluation of Wound Healing Potential of Some Indian Herbal Extracts and its Formulation in Acne Vulgaris. *Pharmacognosy Journal*. 2014;6(5). <https://doi.org/10.5530/pj.2014.5.8>
15. Bandana K, Kumar S, Sagar MK, Tyagi H. Formulation and evaluation of herbal gel of guava leaves and liquorice roots extract for using mouth ulcer. *Journal of Critical Reviews*. 2020;7(18):3097-110.
16. Thete M, Shimpi P. Review on Role of Herbs in Management of Oral diseases. *Asian Journal of Pharmaceutical Research*. 2020;10(4). <https://doi.org/10.5958/2231-5691.2020.00055.6>
17. Sing R, Bansal S, Kumar Mishra M. Formulation and evaluation of herbal oral gel containing extracts of powdered Psidium guajava linn leaves with Curcuma longa linn rhizomes to treat mouth ulcer. *International Journal of Drug Development and Research*. 2020;12(2):1-7.
18. Jadhav TS. Formulation and evaluation pharmaceutical aqueous gel of powdered guava, aloe vera and acacia leaves for treatment of mouth ulcer. *International Journal of Science and Research*. 2018;8(5):1693-1697.
19. Jain NK, Roy R, Pathan HK, Sharma A, Ghosh S, Kumar S. Formulation and evaluation of polyherbal aqueous gel from Psidium guajava, Piper betel and Glycyrrhiza glabra extract for mouth ulcer treatment. *Research Journal of Pharmacognosy and Phytochemistry*. 2020;12(3):145-148. <https://doi.org/10.5958/0975-4385.2020.00024.2>
20. Mittal S, Nautiyal U. A review: herbal remedies used for the treatment of mouth ulcer. *International Journal of Health and Clinical Research*. 2019;2(1):17-23.
21. Pan Z, Zhang X, Xie W, Cui J, Wang Y, Zhang B, Du L, Zhai W, Sun H, Li Y, Li D. Revisited and innovative perspectives of oral ulcer: from biological specificity to local treatment. *Frontiers in Bioengineering and Biotechnology*. 2024;12:1335377. <https://doi.org/10.3389/fbioe.2024.1335377> PMID:38456005 PMCid:PMC10917957
22. Yashaschandra P, Madhavi BL. Current Treatments and Strategies for Management of Oral Ulcers: A Review. 2025;16(90).