

## Herbal chewing Gum to Treat Mouth Ulcer using Guava Leaf and Turmeric Rhizomes

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### Abstract

The aim of this study was to formulate and evaluate the herbal chewing gum containing extracts of powdered *Psidium guajava* leaf extract and *Curcuma longa* Linn rhizomes to treat mouth ulcer. Guava leaves have been usually used to govern several diseases such as diarrhea, diabetes mellitus, wound sore throat, cough and it also gives good soothing effect. Guava comprises some chemical compounds such as tannins, triterpenes, pentacyclic triterpenoid, guajanoic acid, saponins, carotenoids, ellagic acid, amritoside, betasitosterol, uvaol, oleanolic acid and ursolic acid while turmeric has anti-bacterial, anti-inflammatory, virucidal effects. Turmeric contains a large variety of phytochemicals such as curcumin, demethoxycurcumin, eugenol, tannins, alkaloids, saponins, terpenoids and curcumol. The herbal chewing gum was prepared by using guava leaf extract, turmeric rhizome extract and other ingredients required. After the crude preparation triethanolamine was added drop wise to maintain the pH (6.7-7.2) of oral mucosa. The physicochemical parameters were studied accordingly and noted for further assistance.

As we all know chewing gums are mobile drug delivery systems. As we know extract of the herbal medicines can be incorporated in the chewing gum and they can be used in the treatment of mouth ulcers. After the various studies done, we can conclude that chewing gum is an excellent drug delivery system for self-medication as it is convenient and can be administered directly without water and they contain one or more active substances which are released by chewing and are intended to be used for local treatment of mouth diseases or systemic delivery after absorption through the buccal mucosa. Natural gum base which is economical, safe, environment friendly used in the treatment of various mouth diseases.

**Keywords:** Herbal medicines, *Psidium guajava*, *Curcuma longa*, chewing gum, oral mucosa, environment friendly.

### Introduction

As a human being we all are constantly waging a war against disease, mother nature has gifted us with various powerful weapons to fight against the diseases we are suffering from. In the ancient times we were dependent on drugs of natural origin to combat diseases but over a period of time we had invented synthesis of drugs as our own weapon against diseases we are suffering from. Synthetic drugs have become more popular than the natural counter parts but still there are some areas where natural drugs are preferred to their synthetic counter parts, one such area is antiulcer drugs.

### Mouth Ulcer [1]

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. They are painful round or oval sores that form in the mouth, mainly on the inside of the cheeks or lips. Mouth ulcers are very common, and they occur in association with many diseases including different mechanisms, but usually there is no serious underlying cause. Some of the common causes of mouth ulcers are nutritional deficiencies such as iron, vitamins especially B12 and C, improper oral hygiene, infections, stress, constipation, mechanical injury, food allergies, hormonal imbalance, skin disease etc. Mouth ulcers, also known as aph-

thous ulcers as they can be painful while eating, drinking or brushing teeth.

### Types of Mouth Ulcer [1]

On the basis of ulcer size and number, mouth ulcer can be classified as Minor, major, and herpeticiform.

#### Minor ulcers:

These are around 2-8mm in diameter and they usually clear up in 10 days to 2 weeks.

#### Major ulcers:

These are bigger and deeper, often with a raised or irregular border. This type of ulcer can take several weeks to heal and may leave a scar in the mouth.

#### Herpeticiform ulcers:

This type of ulcer is a cluster of dozens of smaller sores about the size of pinheads.

### Causes of Mouth Ulcers [2]

As we know mouth ulcers are not contagious and their cause is not known, but there are several factors that are suspected of contributing to their appearance.

#### Trauma or Tissue Damage:

Damage to the mouth lining is common. Damage from vigorous brushing, orthodontic braces, ill-fitting dentures or biting

the inside of your mouth can cause a mouth ulcer to form.

### Infections:

Bacterial, viral or fungal infections may cause mouth ulcers.

Stress Related Mouth Ulcers, Aphthous Ulcers:

Stress is the main problem in teens, stress-related mouth ulcers can heal within a couple of weeks. Prevention is by resolving stress-related problems or using stress-busting relaxation strategies. Hormonal changes and allergic reactions may also cause mouth ulcers.

### Foods and Drinks:

Mouth ulcers may be triggered by acids in certain foods, including oranges, lemons, pineapples, strawberries, tomatoes, and others.

### Toothpaste or Oral Rinses:

Pastes or rinses that contain sodium lauryl sulfate may contribute to the appearance of mouth ulcers.

### Vitamin Deficiencies:

A deficiency of vitamins such as B-12, iron, folate or zinc could also be a cause of mouth ulcers.

### Quitting Smoking:

Immediately after quitting smoking, you may get mouth ulcers. This is usually temporary.

These are some of the causes for mouth ulcer and they can be treated accordingly by changing the habit and using herbal remedies.

### Herbal Remedies for Mouth Ulcer [1]

As from the ancient era photogenic agents are used by for the prevention and treatment of mouth ulcer. Some of the botanical compounds with anti-ulcer activity include flavonoids (i.e. quercetin, naringin, silymarin, anthocyanosides, sophoradin derivatives) saponins (i.e. from *Panax japonicus* and *Kochia scoparia*), tannins (i.e. from *Lin deraeumbellatae*), gums and mucilages (i.e. gum guar and myrrh). Among herbal drugs, liquorice, aloe gel and capsicum (chilli) can be used extensively having major effect in treatment of mouth ulcer. Ethno medical systems employ several plant extracts for the treatment of ulcer.

### Some of the Herbs that can be used as anti-ulcer drugs: [2,3]

1. **Harra (*Terminalia chebula*)** [4] chewed after dinner cures mouth ulcers.
2. **Basil leaves (*Ocimum sanctum*)** [5] and **Tomato juice (*Lycopersicon esculentum*)** are taken for mouth ulcers.
3. **Powder of nirgund (*Vitex negundo*)** and **Musli (*Chlorophytum borivilicum*)** is prepared and can be taken four times a day for mouth ulcers.
4. **Mulberry (*Morus Alba*)** juice is given to infants for this ailment.
5. **Akarkara (*Spilanthes calva*)** flower is chewed in mouth ulcers. It gives strength to the teeth.
6. Ash of burnt fruit bark of the water melon is also given.
7. Solanum and ginger oil are also used for mouth ulcer.

### Advantages of herbal medicines:

1. Herbal medicines have a long history of use and better patient tolerance and public acceptance.
2. Medical plants have a renewable source, so that we can have sustainable supplies of cheaper medicines for the worlds growing population.
3. Because of the rich agro-climatic, cultural and ethnic bio diversity of developing countries like India availability of me-

dicinal plants is not a problem.

4. The cultivation and processing of medicinal herbs are eco-friendly.

5. Prolong and apparently uneventful use of herbal medicines is safe and efficacious.

6. Some of medicinal plants and dietary nutrients have been shown to possess antiulcer activities such as Aloe, *Terminalia chebula*, *Vetiveriaziziinoides*, Ginseng, *Capsicum* etc.

### Mouth ulcer treatment:

One of the properties of mouth ulcers are that they can heal within 2 weeks without treatment but medicine and treatment may provide relief [6]. Treatment can numb the pain, protect the ulcer from further damage or decrease the chances of a bacterial infection; some medicines may speed up the healing if used early enough.

Paste treatments, gel treatments, mouth washes, liquid paint treatments, neutralizing acid and numbing of the pain, pain killers, corticosteroids [7].

### Medicated Chewing gum:

Medicated Chewing Gum (MCG) is identified as a novel drug delivery system containing masticatory gum base with pharmacologically active ingredient and intended to use for local treatment of mouth diseases or systemic absorption through oral mucosa. MCG is considered as vehicle or a drug delivery system to administer active principles that can improve health and nutrition. Medicated chewing gum is a solid or semisolid dosage form which consists of one or more active ingredient (water soluble or insoluble) incorporated in water insoluble base.

Many previous studies have explored the role of chewing gum in promoting healthy teeth; gum chewing is a common habit in many countries including India [8]. Chewing gum has been used for centuries to clean the mouth and freshen the breath. They usually contain Acetyl Salicylic Acid which was commercially introduced in 1928 [9]. Chewing gum was initially sweetened with sugar, which contributed to dental caries. Today, however, more than 50% of chewing gum sold in Europe is sweetened with sugar substitutes (polyols). Clinical evidence shows that sugar substituted chewing gum does not lead to caries, because the polyols do not lead to a clinically relevant production of metabolic acids in dental plaque. The objective of this systematic literature review is to appraise existing evidence concerning a possible therapeutic/anti-carcinogenic effect of sugar-free chewing gum for patients. MCG represents the newest system with potential uses in pharmaceuticals, over the counter medicines and nutraceuticals [10,11]. Unlike chewable tablets medicated gums are not supposed to be swallowed and may be removed from the site of application without resort to invasive means and MCGs are solid, single dose preparations. Preferring the patient convenience, it is discrete and easy administration without water promotes higher compliance. Since it can be taken anywhere, a chewing gum formulation is an excellent choice for acute medication. The advantages for children and for patients who find swallowing tablets difficult are obvious.

### History of Medicated Chewing Gum [12]

Over a decade ago, the Mayan Indians chewed tree resin from the sapodilla tree in order to clean their teeth and freshen the breath. As per previous literature the shortage of natural gum bases during World War II enhanced development of the syn-

thetic gum bases that are popular today. The first patent for the production of chewing gum was filed in 1869 and was issued to Mr. W. F. Semple in Ohio under U. S. Patent No. 98,304. The first medical chewing gum, Aspergum®, was launched in 1928. This chewing gum contains the analgesic substance acetylsalicylic acid known from Aspirin® tablets. Chewing gum did not gain acceptance as a reliable drug delivery system until 1978, when nicotine chewing gum became available. Another commercially available medical chewing gum is dimenhydrinate-containing chewing gum for motion sickness.

### Merits of MCG [13-17]

1. Does not require water to swallow, easy to carry.
2. Advantageous for patients having difficulty in swallowing.
3. Excellent for acute medication.
4. Counteracts dry mouth, prevents candidiasis and caries.
5. Highly acceptable by children.
6. Avoids first pass metabolism and thus increases the bioavailability of drugs.
7. Fast onset due to rapid release of active ingredients in buccal cavity and subsequent absorption in systemic circulation.
8. Gum does not reach the stomach. Hence G.I.T. suffers less from the effects of excipients.
9. Stomach does not suffer from direct contact with high concentrations of active principles, thus reducing the risk of intolerance of gastric mucosa.
10. Fraction of product reaching the stomach is conveyed by saliva delivered continuously and regularly. Duration of action is increased.
11. Aspirin, Dimenhydrinate and Caffeine show faster absorption through MCG than tablets.
12. Stimulates flow of saliva in the mouth.
13. Neutralizes plaque acids that form in the mouth after eating fermentable carbohydrates.
14. Helps whiten teeth by reducing and preventing stains.

### Demerits of MCG [18-22]

1. Risk of over dosage with MCG compared with chewable tablets or lozenges that can be consumed in a considerable number and within much shorter period of time.
2. Sorbitol present in MCG formulation may cause flatulence, diarrhea.
3. Additives in gum like flavoring agent, Cinnamon can cause Ulcers in oral cavity and Liquorice cause Hypertension.
4. Chlorhexidine oromucosal application is limited to short term use because of its unpleasant taste and staining properties to teeth and tongue.
5. Chewing gum has been shown to adhere to different degrees to enamel dentures and fillers.
6. Prolonged chewing of gum may result in pain in facial muscles and ear ache in children.

### Turmeric (Curcumin)

The most active constituent and major curcuminoid found in turmeric is curcumin. Various medicinal properties listed for curcumin are analgesic, antioxidant, antiseptic, antibacterial, anti-inflammatory and immuno modulatory. Clinical trials have proved its effectiveness in treating RAS as well as radiation-induced oral mucositis [23-26]. Curcumin inhibits biosynthesis of inflammatory prostaglandins, which is responsible for its anti-inflammatory properties. Daddy et al [27] compared turmeric with triamcinolone for the treatment of minor oral RAS and both were found to have similar effectiveness in alle-

viating pain and reducing the ulcer size. The authors concluded that turmeric can be used for treating minor RAS, meanwhile triamcinolone cannot be advocated for the long-term management of oral ulcers.

Deshmukh and Bagewadi [28] conducted a randomized clinical trial comparing the efficacy of curcumin with that of triamcinolone acetonide for the treatment of minor RAS. A significant difference was found in terms of reduction of size, pain intensity, duration and number of lesions in both the groups. No allergic reactions were reported for both of these gels. Manifar et al [29] in a similar randomized, placebo-controlled trial compared curcumin gel to placebo for the treatment of minor aphthous ulcers. It was found that the use of curcumin gel resulted in a definite reduction in the pain intensity and the size of the lesion as compared with the placebo. Pandharipande et al [30] concluded from their study that curcumin was slightly more effective than honey for the treatment of aphthous ulcers and that both honey and curcumin could be used as an alternative treatment modality in the management of RAS.

### Guava (*Psidium guajava*)

*Psidium guajava* has been used for the herbal management of various oral diseases such as toothache, sore throat, and inflamed gums, and ulcers. A decoction of guava leaves also has been used as mouthwash. [31] Shaikh et al and Thombre et al in two different studies formulated and evaluated aqueous gel of powdered guava leaves for mouth ulcer treatment and observed that powdered guava leaves contained flavonoids and showed a significant antioxidant effect. The herbal formulation was found to be stable, safe and effective as compared with synthetic formulations for the treatment of mouth ulcers [31,32]. Guintu and Chua [33] in their randomized prospective open label clinical study found that guava leaves mouthwash was effective in reducing the pain intensity and resulted in faster healing of aphthous ulcers [34].

### Conclusion

This review gives us the understanding that the naturally occurring constituents of medicinal herbs are surely able to resolve oral ulcers irrespective of their etiology and prevent their recurrence; healing ability of these herbs besides stepping up the immunity is responsible for their unmatched ability to cure the disease holistically.

Natural remedies are more acceptable in the belief that they are safer with lesser side effects than the synthetic medicines. Nowadays herbal formulations have increasing demand in the world market. It is very good attempt to establish herbal chewing gum of guava leaf extract with turmeric rhizome extract.

An herbal medicated chewing gum can be formulated with the ingredients that have been scientifically proved in the management of mouth ulcer. In this respect, traditional medicine has introduced good protocols for treatment of various disorders. Chemical substances derived from plants have been used to treat human diseases since the dawn of medicine. Roughly 50% of new chemical entities introduced during the past two decades are from natural products. Recent technological advances have renewed interest in natural products in drug discovery. Therefore, efforts should be directed towards isolation and characterization of the active principles and elucidation of the relationship between structure and activity.

## References

- Anjali Teresa, Krishnakumar K, Dinesh Kumar B, Anish John. *J.Bio.Innov*, 2017; 6(4): pp 521-527.
- Jerry Kennard, what to do about Ulcers in the Mouth, 2018.
- Deepak Acharya. Medicinal plants for curing common Ailments in India, listed in herbal medicine, 2004; 102.
- Praveen Sharma, et al, Antiulcerogenic activity of Terminalia chebula fruit in experimentallu induced ulcer in rats, *Journal of Pharmaceutical biology*, 2011; 49(3).
- Sai Krishna G. "Tulsi-the wonder Herb (Pharmacological Activities of Ocimum sanctum), *American Journal of Ethnomedicine*, 2014; 1(1): 089-095.
- Jenna Fletcher, everything you need to know about mouth ulcers, 2018.
- Mouth Ulcers, NHS, 2019.
- Edgar W, Geddes D. Chewing gum and dental health - A review. *Br Dent J*, 1990; 168: 173-177.
- Conway B. Chewing gum as a drug delivery system. *The Drug Delivery Companies Report Autumn/Winter*; 2003: 33-35.
- Patel PV, Desai TR, Dedakiya AS, Bandhiya HM. Medicated chewing gum: A review. *IJUPLS*, 2011; 1(1): 111-128.
- Biswal PK and Kumar A. An Updated Review on Medicated Chewing Gum. *IJAPBC*, 2013; 2(2): 351-359.
- Cloys L, Christen A, Christen J. The development and history of chewing gum. *Bulletin of the History of Dentistry*, 1992; 40: 57-65
- Morjaria Y, Irwin WJ, Barnett PX, Chan RS, Conway BR: In Vitro Release of Nicotine from Chewing Gum Formulations. *Dissolution Technologie*, 2004; 12-15.
- Chien YW. *Novel Drug Delivery Systems*, Marcel Dekker, New York, II edition, Revised and expanded, 1992; 139-140.
- Edgar W, Geddes D. Chewing gum and dental health -a Review, *Br Dent J*. 1990; 168: 173-177.
- Jacobsen J, Christrup LL, Jensen NH. Medicated Chewing Gum: Pros and Cons, *American Journal of Drug Delivery*, 2004; 2(2): 75-88.
- Conway B. Chewing Gum as a Drug Delivery System, *The Drug Delivery Companies Report Autumn/Winter*, 2003; 33-35.
- Jacobsen J, Christrup LL, Jensen NH. Medicated Chewing Gum. *American Journal of Drug Delivery*. 2004; 2(2): 75-88.
- Goldberg LD, Ditchek NT. Chewing gum diarrhea. *Am J Dig Dis*. 1978;23(6):568
- Addy M, Roberts WR. Comparison of the bisbiguanide antiseptics alexidine and chlorhexidine. II. Clinical and in vitro staining properties. *J ClinPeriodontol.*:8(3):1981,220-30.
- Munksgaard EC, Nolte J, Kristensen K. Adherence of chewing gum to dental restorative materials. *American Journal Dentistry*. 8(3); 1995:137-139.
- Weil AT. Coca leaf as a therapeutic agent, *American Journal Drug Alcohol Abuse*, 1978; 5(1): 75-86.
- Arun P, Sagayaraj A, Mohiyuddin M, Santosh D. Role of turmeric extract in minimising mucositis in patients receiving radiotherapy for head and neck squamous cell cancer: a randomised, placebo-controlled trial. *J Laryngol Otol* 2020;1-6. Doi: 10.1017/S0022215120000316
- Rao S, Dinkar C, Vaishnav LK, et al. The Indian spice turmeric delays and mitigates radiation-induced oral mucositis in patients undergoing treatment for head and neck cancer: an investigation-al study. *Integr Cancer Ther*. 2014; 13(3): 201–210.
- Francis M, Williams S. Effectiveness of Indian turmeric powder with honey as complementary therapy on oral mucositis: a nursing perspective among cancer patients in Mysore. *Nurs J India*, 2014; 105(6): 258–260
- Normando AGC, de Meneses AG, de Toledo IP, et al. Effects of turmeric and curcumin on oral mucositis: a systematic review. *Phytother Res*, 2019; 33(5): 1318–1329.
- Daddy S, Izzaty N, Khalik B, Taib H, Pohchi A, Hassan A. Novel material in the treatment of minor oral recurrent aphthous stomatitis. *Int Med J*, 2013; 20: 392–394.
- Deshmukh RA, Bagewadi AS. Comparison of effectiveness of curcumin with triamcinolone acetonide in the gel form in treatment of minor recurrent aphthous stomatitis: a randomized clinical trial. *Int J Pharm Investig*, 2014; 4(3): 138–141.
- Manifar S, Obwaller A, Gharehgozloo A, Boorboor S, Kordi R, Akhondzadeh S. Curcumin gel in the treatment of minor Aphthous ulcer: a randomized, placebo-controlled trial. *Faslnamah-i Giyahan-i Daruyi*, 2012; 11: 1–6.
- Pandharipande R, Chandak R, Sathawane R. Lanjekar A, Gaikwad R, Khandelwal V, et al. To evaluate efficiency of curcumin and honey in patients with recurrent aphthous stomatitis: a randomized clinical controlled trial. *Int J Res Rev*, 2019; 6(12): 449–455.
- Jaiarj P, Khoohaswan P, Wongkrajang Y, et al. Anticough and antimicrobial activities of *Psidium guajava* Linn. leaf extract. *J Ethnopharmacol*, 1999; 67(2): 203–212.
- Shaikh R, Raj Singh TR, Garland MJ, Woolfson AD, Donnelly RF. Mucoadhesive drug delivery systems. *J Pharm Bioallied Sci*, 2011; 3(1): 89–100.
- Thombre KP, Sharma D, Lanjewar M. Formulation and evaluation pharmaceutical aqueous gel of powdered *Cordia dichotoma* leaves with guava leaves. *Am J Pharm Res*, 2018; 8(2): 268–277.
- Guintu FZ, Chua AH. Effectivity of guava leaves (*Psidium guajava*) as mouthwash for patients with aphthous ulcers. *Philipp J Otolaryngol Head Neck Surg*, 2013; 28(2): 8–13.