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(RESEARCH ARTICLE)

Formulation and evaluation of herbal *Aegle marmelos* anti – diarrheal lozenges

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Abstract

Aegle marmelos is considered as the most sacred or holy plant which is grown by the sides of Hindu temples. *Aegle marmelos*, commonly known as Bael, is a medicinal plant with a wide range of pharmacological properties. Besides this, the plant is associated with a great medicinal value whose medicinal description is also mentioned in the ancient treatise like Vedas, Puranas, Charaka Samhita and Brihat Samhita and has also been portrayed in the paintings of Ajanta caves. Every part of the Bael plant is used to treat various diseases. In Ayurveda, the plant is used in Punching form to treat diarrhea, dysentery and ulcer. In folklore, the plant parts are used to treat diabetes, skin diseases and typhoid, wound healing, ulcer, stomach-ache, jaundice, high BP, malaria, cancer and other diseases. The fruit of the plant is edible and carries great medicinal value because of the presence of vitamins, minerals and various antioxidants. The pulp of the fruit is aromatic, sweet, pale orange and resinous. The unripe fruit pulp of the plant is used to prepare murabba, pudding and juice. The plant is associated with ethnomedicinal uses and possesses various therapeutic and pharmacological properties including antioxidant, anti-diabetic, antihistamine, radio protective, antiulcer, anticancer, cardio-protective, antidiarrheal, antibacterial, antimicrobial, hepatoprotective, anti-inflammatory and antiviral.

Keywords: *Aegle marmelos*; Medicinal Value; *Rutaceae*; Lozenges; Antidiarrheal

1. Introduction

Lozenges are palatable unit dosage form administrated in the oral cavity, which is the most common route and easiest way of administering a drug and have a bright future as novel method of delivering drugs for local and systemic effect. However, Pediatric, geriatric patients show less compliance in swallowing tablets and capsules due to difficulties in swallowing and bitter taste of many drugs when formulated as liquid dosage form. The benefit of the medicated lozenges is they increase the retention time of the dosage form in the oral cavity which increases bioavailability and reduces first pass metabolism. Lozenges are the flavored medicated dosage forms intended to be sucked and held in the mouth or pharynx containing one or more medicaments usually in the sweetened base [1,2]. Lozenges are used for patients who cannot swallow solid oral dosage forms as well as for medications designed to be released slowly to yield a constant level of drug in the oral cavity or to bathe the throat tissues in a solution of the drug [3]. They can be prepared by molding (gelatin and/or fused sucrose and sorbitol base) or by compression of sugar-based tablets. Molded lozenges are sometimes referred to as pastilles, whereas compressed lozenges may be referred to as troches. They are used for patients who cannot swallow solid oral dosage forms well as for medications designed to be released slowly to yield a constant level of drug in the oral cavity or to bathe the throat tissues in a solution of the drug. One of the more popular lozenges for pediatric use is the chewable lozenge, or "gummy type" candy lozenge. The dosage forms were then "punched out" using various shaped punches.

1.1. Advantages of Lozenges [4].

- It is easy to administer to both pediatric and geriatric patients.

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- It has a pleasant taste and will extend the time a quantity of drug remains in the oral cavity to elicit local activity.
- It very well may be given to those patients who experience issues in gulping.
- It can decrease dosing recurrence.
- No disintegration.
- Do not require water for intake.
- Less production times.
- Less production cost.
- Lozenge can be withdrawn if dose is not needed.

1.2. Disadvantages of Lozenges

- Possible draining of drug from oral cavity to stomach along with saliva.
- The lozenges dosage form could be used as candy by children mistakenly.
- A hard candy lozenge is a high temperature required for their preparation.
- Heat stable drugs are suitable.
- Children having above 6 years of age can use lozenges safely.
- Drugs having minimum bitter taste are suitable.

1.3. Classification of Lozenges

- According to the site of action:
  - Local effect Ex. Germicides, Decongestants
  - Systemic impact. Ex. Nutrients, Nicotine.
- According to texture and composition:
  - Compressed tablet lozenges.
  - Soft lozenges.
  - Hard sweets lozenges.

1.3.1. Chewy or caramel based medicated lozenges:

These are the dosage form in which medicament is incorporated into a caramel base which is chewed instead of being dissolved in mouth. Most formulations are based on the glycerinated gelatin suppository formula which consists of glycerin, gelatin, and water. These lozenges are often highly fruit flavored and may have a slightly acidic taste to cover the acrid taste of the glycerin [5].

1.3.2. Compressed tablet Lozenges

When the active ingredient is heat sensitive, it may be prepared by compression. The granulation method is similar to that used for any compressed tablet. These tablets differ from conventional tablets in terms of organoleptic property, non-disintegrating characteristics and profiles slower dissolution [6,7].

1.3.3. Soft Lozenges

They are either meant for chewing or for slow drug release in mouth. They can be made from PEG 1000 or 1450, chocolate or sugar-acacia base while some soft candy formulations can also contain acacia and silica gel. Acacia is used to provide texture and smoothness and silica gel is used as a suspending agent to avoid settling of materials to the bottom of the mold cavity during the cooling. The formulation requires heating process at about 50 0C, hence is only suitable to heat resistant ingredients [8,9,10].

1.3.4. Hard Candy Lozenges

These are mixtures of sugar and other carbohydrates in an amorphous (non-crystalline) or glassy state. They can also be regarded as solid syrups of sugars. The moisture content and weight of hard candy lozenge should be in between, 0.5 - 1.5% and 1.5-4.5 g respectively. These should undergo a slow and uniform dissolution or erosion over 510 min., and they should not disintegrate.

Disadvantage: The temperature required for their preparation is high hence heat labile materials cannot be prepared [11,12].

1.4. Objectives

- Provide natural relief for sore throat and cough symptoms.
- Vanilla flavor offers a palatability and sugar syrup provides preservative effect.
- Bael leaf lozenges are cost effective & safe.
- Deliver a convenient and portable solution for on-the-go relief.
- Promote overall wellness by boosting immunity by plant-based ingredients.
- Ensure efficacy and safety through rigorous quality control and testing processes.
- Cater to specific preferences and needs by offering a variety of flavors and formulas.
- Educate consumers about the benefits of herbal remedies and their role in health practices.

2. Material and Methodology

2.1. Extract *Aegle marmelos* Powder

- English Name: Beal fruit, Bengal quince, Golden apple.
- Tamil Name: Vilvam, Vilva-pazham, Bilvam
- Telugu: Bilvamu.
- Kingdom: Plantae.
- Order: Sapindales.
- Family: *Rutaceae.*
- Sub family: Aurantioideae
- Genus: *Aegle*.
- Species: *A. marmelos* habitat [13].

Aegle marmelos treating fever, nausea, vomiting, swellings, dysentery, dyspepsia, seminal weakness, and intermittent fever. Anti-diarrhoea and Anti-dysentery. marmelos unripe fruit pulp is traditionally used to cure diarrhea and dysentery. Both root and leaf extracts of Bel show gastroprotective and antidiarrheal activities against oil induced diarrhea in animal models. Unripe fruit reduces rapid flush and limit sensation to defecate, blood, and mucus. The dry powdered leaves and fruit pulp is specially recommended in sub-acute, chronic, and amoebic dysentery. For quick results and to combat diarrhea dried fruit or its powder is found a better remedy. For this purpose, unripe green fruits are sliced and dried in the sun. These dried fruit slices are milled to convert into powder and preserved in air-tight bottles [14].

Figure 1 *Aegle marmelos* Powder

2.2. Sugar

Sugar is used for coating, adding volume or texture, and flavoring medicine. It can also act as antioxidant helps in caramel formation and hardens the lozenges.

Figure 2 Sugar

2.3. Sugar Syrup

It helps to the formulation for thicken and preserve the formulation. It acts as a preservative.

Figure 3 Sugar Syrup

2.4. Flavor

Flavoring agents are addictive substances that give a Lozenges an additional taste or flavor.

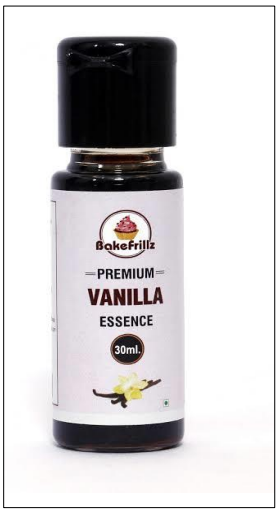

Figure 4 Flavor

Tables 1 Formulation of Hard Lozenges

Sr. No.	Ingredients	Quantity	Activity
1.	Extract *Aegle marmelos* powder	9 gm	Anti – Diarrheal
2.	Sugar	33.75 gm	Antioxidant
3.	Sugar Syrup	1-2 Drop	Preservative
4.	Flavour	q. s.	Taste
		Total 42.75 ≈ 43gm	

2.5. Methodology

The lozenges were prepared using silicon Mold Method.

↓

The Herbal Lozenges composition formula is illustrated in table no.1.

↓

Aegle marmelos leaves are extracted by maceration process.

↓

The sugar, macerated extract mixture is prepared then the vanilla flavour & sugar syrup added in adequate quantity.

↓

For preparation of individual lozenges mixture is poured into the silicon Mold.

↓

Dry it at room temperature.

↓

Evaluation is carried out.

Figure 5 Pouring in mould

Figure 6 Hard Lozenges

3. Result and Discussion

3.1. Macroscopic evaluation

Refers to the assessment of sensory properties such as taste, odor, and appearance of a product. Herbal lozenges can be evaluated using the following organoleptic parameters [15].

- Appearance: The color, size, and shape of the lozenges should be assessed. The surface texture, presence of any speckles, and uniformity of shape should also be checked.
- Taste: The taste of the lozenges should be evaluated for sweetness, sourness, bitterness, and saltiness. The aftertaste and mouth feel should also be assessed.
- Odour: The herbal aroma of the lozenges should be assessed for intensity, quality, and pleasantness.
- Texture: The texture of the lozenges should be assessed for hardness, chewiness, and stickiness. It should also be checked if the lozenges dissolve easily in the mouth [16].

Table 2 Organoleptic Properties

Parameter	Observation
Colour	Brown
Odour	Pleasant
Taste	Sweet & Slightly acrid
Shape	Round

Formulation developed was sampled and evaluated for different parameters such as organoleptic properties, weight variation, friability, hardness, dissolution test, disintegration test.

3.2. Organoleptic parameters:

The lozenges were found to be round in shape with smooth texture. This round shape was due to molds used for preparation. The taste of the lozenges was determined using human volunteer panel of 10 people and was sweet and acrid in taste. The sweet taste could be attributed to the use of sugar as base and acrid taste due to *Aegle marmelos* macerated extract.

3.3. Weight variation test

The USP weight variation test is done by weighing 20 lozenges individually and then by taking average comparing it as follows [17].

Table 3 Weight Variation

SR, NO	Weight of Lozenges
1	3.16
2	3.29
3	3.60
4	3.45
5	3.72
6	3.75
7	3.15
8	3.21
9	3.45

10	3.05
11	3.29
12	3.75
13	3.16
14	3.45
15	3.15
16	3.60
17	3.75
18	3.45
19	3.05
20	3.21

Total Weight of Lozenges = 67.66 ÷ 20 = 3.383

Average Weight = 3.383

3.4. Friability

These is carried out for same as hardness testing. Friability testing is carried out by using Roche Friabilator operated at specific speed for specific time such 25 rpm for 4 min.

Table 4 Friability test

Sr.no	Friability test (%)
1.	≤1

Initial Weight = 33.83

Final Weight = 33.49

Formula =

$$\text{Friability} = \frac{\text{Initial weight} - \text{Final Weight}}{\text{nitial Weight}} \times 100$$

3.5. Hardness

The resistance of lozenges to shipping, storage conditions breakage, Transportation and handling, depending upon the hardness. hence it becomes necessary to measure hardness for checking its threshold capacity which can be measured by using Monsanto hardness tester in terms of kg/cmsq [18].

Table 5 Hardness value

SR .NO	Hardness ($kg/cm^{2)}$
1	5±0.5 kg /cm^2

3.6. Dissolution time

Dissolution time is an important parameter to evaluate in herbal lozenges as it can affect the release of active ingredients and the efficacy of the product. The dissolution time of herbal lozenges can be influenced by factors such as the size and shape of the lozenge, the type and number of excipients used, and the environmental conditions during storage [19].

The dissolution time of herbal lozenges can be determined by placing a lozenge in a beaker of water at a specified temperature and measuring the time it takes for the lozenge to completely dissolve. The acceptable dissolution time for herbal lozenges depends on the specific product and its intended use [20,21].

Table 6 *In-vitro* dissolution time

Sr .no	Dissolution time (min)
1	8 Min

3.7. Disintegration time

Ideally this test is not official for the formulation expected to be dissolved slowly in the mouth and hence the limits are not specific. Still the test was performed to find whether the lozenge dissolves in mouth and how much time it takes to dissolve completely so that the faster and localized onset of action can be obtained. The test was performed as per the procedure given in the monograph for uncoated tablets. The medium used was phosphate buffer pH 6.2 to simulate the pH of oral fluid. Sampled six lozenges revealed average disintegration time of 4±0.5 min.

Table 7 Disintegration time

Sr .no	Disintegration time (min)
1.	4±0.5 min

3.8. Measurement of PH

PH is an important parameter to evaluate in herbal lozenges. PH is a measure of the acidity or alkalinity of a solution and can have an impact on the stability, efficacy, and sensory properties of the product. The pH of herbal lozenges can be determined using a pH meter or pH paper. A small amount of the lozenge is dissolved in water, and the pH of the resulting solution is measured. The acceptable pH range for herbal lozenges depends on the specific product and its intended use. Typically, a pH range of 5.5 to 7.5 is acceptable for most herbal lozenges [22].

Table 8 PH value

Sr. no	Dosage Form	PH
1.	Hard Lozenges	5-6

3.9. Stability

Stability testing is an important part of product development for herbal lozenges. Stability testing is used to evaluate the chemical, physical, and microbiological characteristics of the product over time and under various storage conditions.

The stability of herbal lozenges can be affected by factors such as temperature, humidity, light, and oxygen exposure. 6 months stability study as per ICH guidelines was performed and conclude that it completely stable at room temperature [23].

3.10. Packaging

Hard candies are hygroscopic and frequently prone to absorption of atmospheric moisture. (Considerations must include the hygroscopic nature of the candy base, storage conditions of the lozenges, length of time they are stored and the potential for drug interactions.) (These products should be stored in tight containers to prevent drying. This is especially true of the chewable lozenges that may dry out excessively and become difficult to chew.) If a disposable Mold with a cardboard sleeve is used, it is best to slip this unit into a properly labelled, sealable plastic bag. Packaging should be proper and attractive or colorful [24].

4. Conclusion

Herbal lozenges show potential for addressing various health issues due to their natural ingredients, their efficacy and safety for specific diseases remain inconclusive. Further research is needed to determine their effectiveness, appropriate dosage, and potential interactions with medications to use as an effective against various disease such as anti-diarrheal activity. Lozenges show promising potential for anti-diarrheal activity, offering convenience and potential targeted delivery. Future studies could explore novel ingredients, enhance taste, and conduct clinical trials to validate their effectiveness and safety, ultimately leading to practical applications in heal.

Compliance with ethical standards

Disclosure of conflict of interest

No conflict of interest to be disclosed.

References

[1] Sastry SV, Stidham JR. Review of formulation used in oral cavity. Pharm Sci and Techno Today. 2000; (3): 138-145.

[2] Mohan H. Text book of Pathology – The oral cavity and salivary glands. 4th ed. New Delhi: Jaypee Brothers Medical Publishers (P) Ltd; 2000: 494-496.

[3] The Pharmaceutics and compounding Laboratory, Lozenges and medication sticks. Available from: http://pharmlabs.unc.edu/labs/lozenge/lozenges.htm

[4] Reddy RM, Ragabhoina T. Lozenges Formulation and Evaluation: A Review. International Journal of Pharmaceutical Sciences and Research.2021;6(6):678-684.

[5] Sastry SV, Nyshdham JR. Review of formulation used in oral cavity. Pharm Sci and Techno Today. 2000; (3): 138-145.

[6] Allen LV. Troches and lozenges, Secundum Artem. Current & Practical Compounding Information for the Pharmacist. 2001;4(2): 23-25.

[7] Peters D. Medicated lozenges. In: Lieberman HA, Lachman L, Schwartz JB editors. Pharmaceutical Dosage Forms: Tablets, 2nd ed. New York: Marcel Dekker, Inc. 2005: 419-577.

[8] Batheja P, Thakur R, Muchnik B. Basic biopharmaceutics of buccal and sublingual absorption, enhancement in drug delivery. London, New York: Touitou E, Barry BW editors. CRC Press, Taylor and Francis Group. 2006; 1: 189.

[9] The Pharmaceutics and compounding Laboratory, Lozenges and medication sticks. Available from: http://pharmlabs.unc.edu/labs/lozenge/lozenges.htm.

[10] Mendes RW, Bhargava H. Encyclopaedia of Pharmaceutical Technology. 3rd ed. North California, USA: Informa Healthcare Inc. In: Swayback J editor; 2006: 2231-2235.

[11] Allen LV. Troches and lozenges, Secundum Artem. Current & Practical Compounding Information for the Pharmacist. 2001;4(2): 23-25.

[12] Peters D. Medicated lozenges. In: Lieberman HA, Lachman L, Schwartz JB editors. Pharmaceutical Dosage Forms: Tablets, 2nd ed. New York: Marcel Dekker, Inc. 2005: 419-577.

[13] Journal of Complementary and Alternative Medical Research 7(2): 1-10, 2019; Article no. JOCAMR.48068 ISSN: 2456-6276 A Review of Anti – Diarrheal Activity of *Aegle marmelos* R. Rakulini1* and S. Kalaichelvi1 1 Unit of Siddha Medicine, University of Jaffna, Sri Lanka

[14] Sekar DK, Kumar G, Karthik L, Rao KB. A review on pharmacological and phytochemical properties of Aegle maemelos (L.) Corr. Serr. (Rutaceae). Asian Journal of Plant Science and Research. 2011;1(2):8-12.

[15] Jagadeesh P, Ashamed DA, Devi GG, Mohiuddin YK, Naveen R, Lakshmi BP, et al. Review on medicated lozenges. Int J Inova Pharm Sci Res., 2019; 7: 11-25.

[16] Rao KP, Kumar CA, Afshanlaheji AK, Manjunath P, Babura NC. Formulation and evaluation lozenges. Int J Pharm Sci., 2011; 3: 125-8.

[17] Kini R, Rathnanand M, Kamath D. Investigating the suitability of Isomalt and liquid glucose as sugar substitute in the formulation of Salbutamol sulphate hard candy lozenge. J Chem Pharm Res. 2011; 3(4): 69-75.

[18] Shohei H.A. Development of medicated Lozenges. J Pharm Sci. 1998; 1(1): 15-30.

[19] Sastry SV, Nyshadham JR, Fix JA. Recent technological advances in oral drug delivery-a review. Pharm Sci Tech Today, 2000; 3: 138 45.

[20] Ghosh PK, Sharma HK, Boruah N. Different methods used in solid dispersion. J Pharm., 2018; 8: 28-38.

[21] Dahiya J, Jalawla P, Arora S, Singh B. Formulation and evaluation of polyherbal lozenge Pharma Inova, 2015; 4: 97.

[22] Alton ME. Pharmaceutics: the science of dosage form design. Churchill Livingstone. 2000.

[23] McElhanney LF. Education, training, and evaluation of hospital compounding personnel. Int J Pharm Comp'd, 2006; 10: 361.

[24] Chandrawanshi MJ, Sakhare RS. Review on medicated lozenges . wjpr .2019.vol 8, issue 2, 392-412.