Polyherbal Chewing Gum: A Comprehensive Exploration of Design and Quality for Mouth Ulcers Relief

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ABSTRACT: Gummies are mobile drug delivery systems. Extract from herbal medicines can be incorporated into chewing gum and can be used in the treatment of mouth ulcers. It was concluded that the gum is an excellent drug delivery system for self-medication as it is convenient and can be administered directly without water and contain one or more active substances that are released by chewing and are intended for use for local treatment of oral diseases or systemic administration after absorption through the buccal mucosa. Natural gum base that is economical, safe, environmentally friendly and used in the treatment of various oral diseases.

KEYWORDS: Medicinal gums, mouth ulcers, oral drug system.

1. INTRODUCTION:

Man is constantly waging a war against disease. Nature has endowed mankind with various powers weapons in the fight against the diseases they suffer from. In past years, a person was addicted to drugs of natural origin to fight against diseases, but for a period time invented drug synthesis as its own a weapon against the diseases they suffer from; late synthetic drugs became more popular than natural opposites, but there are still some areas natural drugs are preferred over their synthetic counterparts part, one such area is ulcer medication.

Mouth ulcer [(1)]

A mouth ulcer (also called a mouth ulcer or mucous ulcer) is an ulcer that occurs on the mucous membrane oral cavity. They are painful round or oval boils that forms in the mouth, mainly on the inside of the cheeks or lips. Mouth ulcers are very common and occur in association with many diseases and various mechanisms, but usually there is no serious basis cause. Common causes of mouth ulcers include: nutritional deficiencies such as iron, especially vitamins B12 and C, poor oral hygiene, infection, stress, digestive disorders, mechanical injury, food allergies, hormone imbalance, skin disease, etc. Mouth ulcers, also known as can be painful when eating, drinking or tooth brushing.

Fig 01: Mouth Ulcers

Types of mouth ulcer [(1)]

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

- **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.

- **Herpetiform ulcers:**

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

Causes of mouth ulcers: [2]

Mouth ulcers are not contagious. The exact cause of oral ulcers 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:**

Most common in teens, stress-related mouth ulcers will 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.

Herbal anti ulcer drugs: [3]

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

Mouth ulcer treatment:

Mouth ulcers 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 a new drug delivery system containing a chewing gum base with pharmacologically active ingredient and intended for use for the local treatment of oral or systemic diseases absorption through the oral mucosa. The MCG is considered to be vehicle or drug delivery system for administering the active substance principles that can improve health and nutrition. Medicated chewing gum is a solid or semi-solid dose in a form that consists of one or more active ingredients (water soluble or insoluble) incorporated into water insoluble base. Many scientific studies have investigated the role of chewing gum in supporting healthy teeth. Rubber chewing is a common habit in many countries.[8] Initially, sugar was used to sweeten chewing gum, which led to dental cavities. Today, however, sugar substitutes (polyols) are used to sweeten more than half of the chewing gum sold in Europe. Clinical data indicates that chewing gum without sugar does not cause caries because the polyols do not cause a clinically significant amounts of metabolic acids to be produced in tooth plaque. This systematic literature review aims to evaluate the available data about the potential therapeutic or anti-carcinogenic benefits of sugar-free chewing gum for individuals. With potential applications in pharmaceuticals, over-the-counter medications, and nutraceuticals, MCG is the newest system [10,11].

Fig 02: Medicated Chewing Gum

Merits of MCG [13-17]:

1. Does not require water to swallow. Hence can be taken anywhere.
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, diarrhoea.
3. Additives in gum like flavouring 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.

Types of Chewing Gum:

Chewing gums come in a variety of flavors, shapes and sizes. There is no standard type of gum, but mostly is a small stick or wad of gum. Chewing gum is basically made by combining a water-insoluble phase with a water-soluble phase of sweeteners, flavoring and food coloring. Several types of chewing gum are designed for dental hygiene. There are gums to whiten teeth, clean teeth and fresh breath. The most popular flavors are mint, spearmint, peppermint, wintergreen, cinnamon, licorice, sour apple, cherry, grape, orange, watermelon, strawberry, lemon, and blueberry(26).

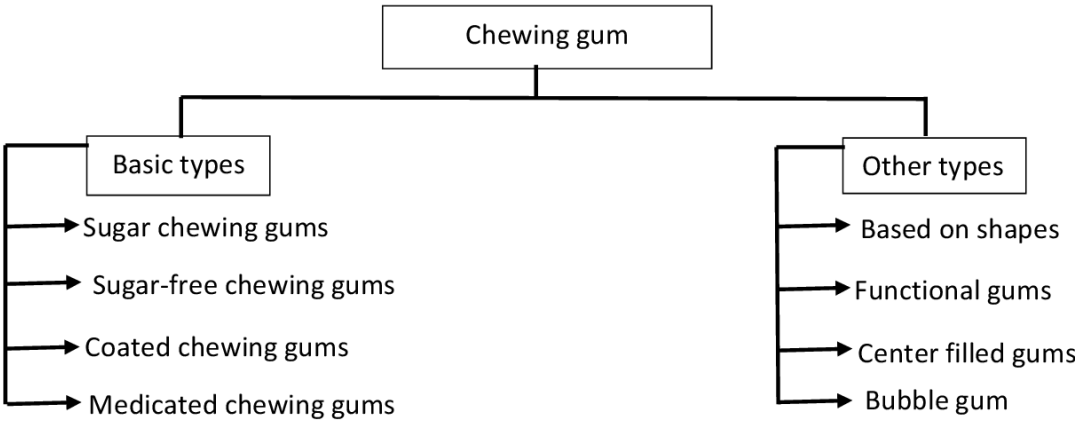

Fig 03: Classification of Chewing Gum

Fig 04: Types of Chewing Gum

2. Materials:

Gum Base

Gum base is an inert and insoluble nonnutritive product used as a support for the edible and soluble of the chewing gum (sugar and flavoring agent) other row materials. Gum base is made of a combination of food-grade polymers, waxes, and softeners. e.g., gum ghatti, chicle gum.

Sweeteners

Bulk Polyol Sweeteners are responsible for initial sweetness, whereas intensive sweeteners are intended for prolonging the sweetness effect. Intensive Sweeteners are often encapsulated to delay the release of flavor. The most important among these are that added sugar in chewing gum acts as a sweetener, preservative, texture modifier, fermentation substrate, flavoring and coloring agent, bulking agent. e.g., sugar.

Flavoring Agent

For taste and sensory appeal. Flavor components in gum exist in liquid, powder forms. A variety of flavoring agents are used to improve flavour in chewing gum. Carminative, Flavoring agent, Aromatic and stimulant. e.g., cardamom.

Coloring Agent:

For visual appeal [23-28].

Method of Preparation of Chewing Gum:

All ingredients were weight accurately as shown in formulation Table 1. Crush the gum base in the mortar pestle. Add adequate volume of distilled water and properly stir in the porcelain dish and add honey was mixed. The dish was kept in a water bath and temperature was maintained at about 35-45. The drugs jasmine leaves extract, mahonia aquafolium and white willow bark was then added to the above mass. Corresponding amount of sugar, coloring agent and flavoring agent was added to the above mixture with continuous stirring up to 30 min. finally the adequate amount of flavor was incorporated in the mixture. The mass was poured into the mould and was allowed to cool at room temperature. The gum pieces were removed [2].

Table 1: Formula of herbal chewing gum:

Sr.No	Ingredients	Batch 1	Batch 2	Batch 3
1	Gum base	1gm	1gm	1gm
2	Jasmine leaves extract	0.3 gm	0.6 gm	0.8 gm
3	Mahonia aquifolium	0.3 gm	0.6 gm	0.8 gm
4	White willow bark	0.3 gm	0.6 gm	0.8 gm
5	Honey	1 gm	1 gm	1 gm
6	sugar	q.s	q.s	q.s
7	Flavoring agent	q.s	q.s	q.s
8	Coloring agent	q.s	q.s	q.s

3. Physical Evaluation of Herbal Chewing Gum:

Stickiness: The formulated herbal chewing gum was placed on plane surface. A mass of 250gm was hammered on it up to 10min, after 10min, sticking of mass to hammered surface was observed[29].

Weight Variation Test:

Chewing gum from each batch were individually weighted on analytical balance. The average weight and standard deviation were calculated which was found in acceptable unit[(24)]

Plasticity/Hardness: The hardness of chewing gum was determined by Monsanto hardness tester and the average hardness and standard deviation were reported [(24)].

Table 2: Physical evaluation of herbal chewing gum:

Sr.No.	Batch	Color	Stickiness	Hardness
1	A	Light pink	sticky	4 kg/cm^2
2	B	Light pink	sticky	4 kg/cm^2
3	C	Light pink	sticky	4 kg/cm^2

4. METHOD DEVELOPMENT

Instrument: Double beam UV Spectrophotometer (UV SHIMADZU 1800)

- **Method**

A stock solution of 10 mg/ml of Jasmine leaves extract was made by dissolving 10 milligrams of the medication in 10 ml of water. This was done in order to determine the wavelength of maximal absorption of the herb.Using a spectrophotometer, several drug solutions in water were scanned against water as a blank in the 400–200 nm wavelength range. The final spectra were displayed in Figure 3, and the drug's absorption curve revealed a distinctive absorption maximum at 260 nm.

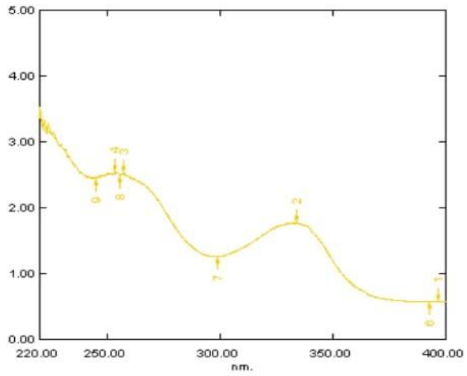

Figure 5: UV Spectrum of Jasmine leaves Extract in Water

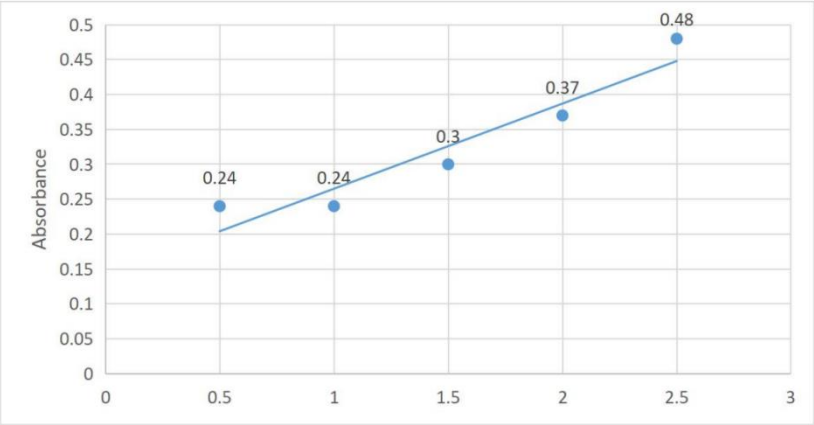

Figure 6:Standard curve of jasmine leaves

Concentration	Absorbance
0.5	0.24
1	0.24
1.5	0.30
2	0.37
2.5	0.48

Table 3: Data for standard curve of jasmine leaves

- **Preparation of standard stock solution of jasmine leaves extract:**
  The standard stock solution was prepared with weighed amount of jasmine leaves extract (10 mg). The stock solution was dissolved separately in 10mL of water in a volumetric flask. A series of dilutions of 0.5, 1, 1.5, 2 and 2.5 were prepared, and absorbance was measured at 260nm. These diluted solutions were analyzed for Linearity, Accuracy, Precision, Robustness, Limit of Detection (LOD) and Limit of Quantification (LOQ).
- **Linearity**
  The linearity of this method was determined at concentration levels ranging between 0.5 mg/ml and 2.5mg/ml. The plot of absorbance v/s concentration of jasmine leaves extract was found to be linear in the range Beer's law was obeyed over this concentration range.
- **Precision**
  The precision of the method was assessed by repeatability (intra-day) and intermediate precision (inter-day). Intra-day precision was determined by analysing 1microgram/ml jasmine leaves extract for three times within the day and average % RSD was calculated. Inter-day precision was determined by analysing the same concentration of solutions for three days and average % RSD was calculated.

Sr no.	Concentration (µg/ml)		Absorbance	Mean	SD	% RSD
1	10	Morning	0.69	0.68	0.01	1.47 %
2	10		0.67			
3	10		0.68			
4	10	Afternoon	0.59	0.58	0.01	1.72 %
5	10		0.58			
6	10		0.57			
7	10	Evening	0.79	0.78	0.01	1.28%
8	10		0.77			
9	10		0.78			

Table 4: Intraday (On same Day)

Sr No	Concentration(µg/ml)		Absorbance	Mean	SD	% RSD
1	10	Day 1	0.63	0.62	0.01	1.61 %
2	10		0.61			
3	10		0.62			
4	10	Day 2	0.54	0.53	0.01	1.89 %
5	10		0.53			
6	10		0.52			
7	10	Day 3	0.76	0.75	0.01	1.33 %
8	10		0.75			
9	10		0.74			

Table 5: Interday (On different day)

% RSD should not be more than 2 %

❖ **Accuracy:**

Accuracy is defined as closeness of agreement between the actual (true) value and analytical value and obtained by applying test method for a number of times. Accuracy may often be expressed as % Recovery by the assay of known, added amount of analyte. It is measure of the exactness of the analytical method. The recovery experiments were carried out in triplicate by spiking previously analyzed samples of with three different concentrations of jasmine leaves extract.

Sr No	Concentration (%)	Original level (µg/ml)	Amount Added (µg/ml)	Recovery %	Mean % Recovery	% RSD
1	80	10	8	99.12	99.43	1.06%
	80	10	8	98.57		
	80	10	8	100.6		
2	100	10	10	99.95	100.22	0.28%
	100	10	10	100.20		
	100	10	10	100.51		
3	120	10	12	100.20	99.07	1.03%
	120	10	12	98.82		
	120	10	12	98.21		

Table 6: Accuracy Determination

❖ **LOD & LOQ:**

LOD (k ¼ 3.3) and LOQ (k ¼ 10) of the method were established according to ICH definitions. LOD and LOQ of method are reported in Table 6. In this study, LOD and LOQ were based on the standard deviation of the response and the slope of the corresponding curve using the following equations:

LOD ¼ 3:3 S=M; LOQ ¼ 10 S=M

where S is the standard deviation of the absorbance of the sample and M is the slope of the calibrations curve.

5. RESULTS:

The Jasmine leaves extract was found to be soluble in Water. The Wavelength of drug was found to be 270 nm. From the result obtained it was found that Jasmine leaves extract obeys linearity within the concentration range of 0.5 mg/ml 2.5mg/ml and coefficient correlation was found to be 0.9513. The regression of the curve was y ¼ 0.314 x - 0.010. 2. The detection and quantitation limits as LOD (k ¼ 3.3) and LOQ (k ¼ 10) were calculated and these were found to be 2.788 mg/ml and 8.449 mg/ml respectively. The precision (measurements of intra-day and inter-day) results showed significant reproducibility with percent relative standard deviation (% RSD) is below 2.0. This

indicated that method is highly precised. The percent recovery value which was higher than 100%, indicates the accuracy of the method.

6.CONCLUSION:

It was discovered that the devised procedure was straightforward, sensitive, exact, accurate, repeatable, and above all cost-effective. When it comes to calculating commercial formulations without excipient involvement, the suggested procedure is precise.

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