



Preparation of Herbal Gel Formulation for Mouth Ulcer

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ABSTRACTS

The current study aimed to formulate and evaluate a pharmaceutical herbal mucosal gel containing betel leaves for treating mouth ulcers. Mouth ulcers, characterized as sores on the mouth lining, are described as "a breach within the mucosal surface of the buccal cavity." Causes include nutritional deficiencies (e.g., iron, vitamins B12 and C), poor oral hygiene, infections, stress, indigestion, mechanical injury, food allergies, hormonal imbalances, and skin diseases. Mouth ulcers, commonly known as canker sores, can benefit from natural remedies due to their safer profile and fewer side effects compared to synthetic medicines. Herbal medicinal plants are recognized for treating skin diseases and promoting wound healing, along with possessing antifungal, antiviral, and antimicrobial properties.

Experimental formulations utilized varying concentrations of Carbopol 934, PEG 400, and methyl paraben as a preservative. Formulations underwent characterization for pH, viscosity, spreadability, extrudability, mucoadhesion time, and in-vitro drug release. Results demonstrated that herbal gel formulations containing Glycyrrhiza glabra, Aloe vera, and Curcumin were therapeutically effective. The combined dosage in the new herbal gel formulation exhibited good mucoadhesive properties, confirming its safety, stability, and efficacy in treating mouth ulcers.

Keywords: Mouth ulcer, Mucosal gel, Carbopol 934, Mucoadhesion, Drug delivery, Formulation, Evaluation, Betel leaves.

INTRODUCTION

The World Oral Health Report of 2003 underscored the importance of oral health as an integral component of overall well-being. Many chemical products contain antiseptics that play a crucial role in controlling plaque buildup (1). Mouth ulcers, also known as canker sores, are painful lesions that develop in the mouth, typically at the base of the gums, causing discomfort during talking and eating. Treatment of oral ulcers often involves antibiotic or analgesic semi-solid formulations, alongside antiseptic mouthwashes like chlorhexidine or povidone iodine (2).

Gels, characterized by a liquid phase that thickens with additional components, are beneficial for topical application on skin or mucosal surfaces for localized action or drug penetration (4). Numerous Indian medicinal plants are recognized for their pharmacological activities and are traditionally used for treating mouth ulcers (4). Combining multiple herbs into polyherbal oral mucosal gels can enhance therapeutic efficacy. These gels must have good mucoadhesive properties to ensure prolonged medication retention at the application site (5).

Common causes of mouth ulcers include nutritional deficiencies (such as iron, vitamins B12 and C), poor oral hygiene, infections, stress, indigestion, mechanical injury, food allergies, hormonal imbalances, and skin diseases. Mouth ulcers, also referred to as aphthous ulcers, can cause significant discomfort while eating, drinking, or brushing teeth (6). Oral health, inseparable from general health, influences speech, food choices, quality of life, and overall well-being due to the pain and suffering associated with oral diseases and the costs of their treatment (3).

DRUG & EXCIPIENTS

Betel leaves



Scientific Name: Piper betel L.

Common Name: Betel leaf or Paan

Family: Piperaceae

Chemical Constituents: Alkaloids, carbohydrates, amino acids, tannins, steroidal components. Major components include chavicol, eugenol, Piper betol, and betel oil containing cadinene, carvacrol, allyl catechol.

Phytochemicals: Piper betel contains a variety of biologically active compounds whose concentrations vary with plant variety, season, and climate. Essential oils contain safrole across leaf, stalk, stem, and root, alongside hydroxychavicol acetate, allylpyrocatechol, piperbetol, isoeugenol, anethole, steric acids, methyl eugenol, and other compounds contributing to its aroma.

Bio-active Components: Chavibetol (53.1%), chavibetol acetate (15.5%) are major constituents, with eugenol, α -pinene, β -pinene, limonene, safrole, and 1,8-cineole also present. Hexane fractions from leaf stalks yielded compounds like pentadecyl 6-hydroxytridecanoate, pentatriacontanol, methyl hexacos-7-enoate, and 6,9-heptacosadiene.

Geographical Source: Native to Southeast Asia, cultivated in various states including Assam, Andhra Pradesh, Bihar, Gujarat, Odisha, and Karnataka.

Plant Description: A perennial dioecious creeper with semi-woody stems climbing upwards. Leaves are 10-20 cm long, ovate, slightly heart-shaped, bluish-green, and pointed. Male spikes are cylindrical and tight, while female spikes are drooping.

Medicinal Uses: Betel leaf is utilized in traditional medicine for its broad range of therapeutic properties. It is employed for treating conditions such as bad breath, boils, conjunctivitis, constipation, headaches, gum swelling, cuts, and injuries. The leaf juice is administered for coughs, indigestion, and exhibits activities like anti-malarial, antibacterial, antifungal, insecticidal, antioxidant, anti-diabetic, gastroprotective, analgesic, cytotoxic, and anti-platelet effects.

Modern Medicinal Applications: Betel leaves are beneficial in pulmonary infections, childhood ailments, and for relieving cough and breathing difficulties when applied externally with mustard oil. Local applications treat sore throats, arthritis, orchitis, and boils due to its analgesic and cooling properties. It also aids in wound healing and lactation promotion.

Additional Uses: The plant parts are used in culinary applications, as fish baits and poisons, hallucinogens, oils, ornaments, perfumes, and for their pungent taste. They normalize digestive tract functions and are useful in treating indigestion, bronchitis, constipation, coughs, and asthma.

Traditional and Unani Medicine: According to Unani medicine, betel leaf enhances appetite and acts as a tonic for the brain, heart, and liver, attributed to its sharp taste and aroma.

This comprehensive overview highlights Piper betel's diverse medicinal and cultural significance across different disciplines and regions.

METHODS AND MATERIALS

MATERIALS

1. Plant Material:

- Source: Betel leaves (Piper betel L.), a perennial vine indigenous to Southeast Asia and cultivated extensively in regions like Assam, Andhra Pradesh, Bihar, Gujarat, Odisha, and Karnataka.

- Description: The leaves of Piper betel are harvested for their medicinal and aromatic properties.

2. Preparation of Extract:

- Method: The extraction process involves pulverizing betel leaves into a fine powder.
- Solvent: Typically, the powdered leaves are extracted using ethanol or water to yield a concentrated extract.
- Extraction Conditions: Extraction is conducted under controlled conditions of temperature and duration to optimize the extraction efficiency and preserve bioactive compounds.

3. Composition of Gel:

- Ingredients:
 - Betel leaves powder
 - Carbopol 934 (gelling agent)
 - Methyl Paraben (preservative)
 - Propyl Paraben (preservative)
 - Triethanolamine (pH adjuster)
 - Distilled water
- Preparation: The gel formulation is prepared by dispersing betel leaves powder into a solution containing Carbopol 934, methyl paraben, propyl paraben, triethanolamine, and distilled water. The mixture is then neutralized to achieve the desired pH and consistency.
- Purpose: This gel formulation integrates the therapeutic properties of betel leaves with a gel base, facilitating topical application while ensuring stability and effective delivery of active compounds.



METHODS

1. Chemicals Collection:

Chemicals such as triethanolamine, Carbopol 934, methyl paraben, and peppermint oil were sourced from the laboratory.

2. Preformulation Study:

Preformulation studies are essential to ensure the development of a stable, effective, and safe dosage form. During this stage, pharmacists characterize the physicochemical properties of the drug substance and its interactions with various formulation components.

- To determine the necessary physicochemical parameters of a new drug substance.
- To identify any incompatibilities with excipients used in the formulation.

3. Collection and Authentication:

Fresh betel leaves (*Piper betel*) were collected from a farmer's garden in Nashik, Maharashtra, for use in the study.

4. Organoleptic Characterization:

The color, odor, shape, and taste of the betel leaves were observed and documented.

5. Physicochemical Characteristics:

After botanical evaluation, the shade-dried plant material was reduced to a coarse powder and sieved through a No. 80 sieve to obtain a uniform powder. Standardization was performed using various parameters as per literature guidelines.

6. Extraction of Plant Material:

The extraction process involved cold maceration:

- 100 g of plant material was mixed with 200 mL of ethanol.
- The mixture was left at room temperature for 7 days with periodic shaking.
- The extract was filtered successively through muslin cloth, filter paper, and Whatman filter paper to obtain a clear liquid extract.

7. Preparation of Plant Material:

Different combinations of aqueous betel leaf extracts (1% and 2%) were tested with various polymers (Carbopol 934) using different formulations. The formulation that resulted in the smoothest and most stable gel involved Carbopol 934. Control samples also showed stability.

8. Preliminary Phytochemical Screening:

Various tests were conducted to screen for phytochemicals:

- ****Carbohydrates (Benedict's Test):**** The solution turned green upon heating.
- **Proteins (Millon's Test):** The solution turned brick red upon heating.
- **Glycosides (Baljet's Test):** A yellow to orange color was observed with sodium picrate.
- **Flavonoids (Shinoda Test):** The solution exhibited colors ranging from orange to purple.
- **Alkaloids (Mayer's Test):** Formation of a precipitate was observed with Mayer's reagent.
- **Tannins (Lead Acetate Test):** Addition of lead acetate solution resulted in a precipitate, indicating the presence of tannins.

Table no. 2. Formulation of gel formulation

Sr.No.	Name of ingredients	Properties
1.	Betel Leaves Extract	Anti – inflammatory cooling agent Antiulcer activity Antifungal
2.	Triethaloloamine	Neutrizer
3.	Methyl paraben	Preservatives
4.	Propyl paraben	Preservatives
5.	Carbopol934	Binder
6.	Pappermint oil	Soothe effect Cooling agent Relieve pain
7.	Distilled water	Solvent

Table no. 3. Formulation and Development Ingredients

Sr.No.	Ingredients	Quantity
1.	Betel leaves extract	1gm

2.	Tiethnoleomine	q.s+pH6.5-7
3.	Methyl paraben	0.01gm
4.	Propyl paraben	0.01gm
5.	Carbopol	1gm
6.	Pappermint oil	q.s
7.	Distilled water	100 ml

Preparation of Simple Herbal Gel

1. Carbopol 934 was dispersed in demineralized water.
2. 5 mL of distilled water was mixed with propyl paraben and methyl paraben.
3. The mixture was heated in a water bath, and propylene glycol was added after cooling.
4. The ingredients were combined, and Carbopol 934 was added slowly with continuous stirring.
5. Triethanolamine was added to adjust the pH to the desired level.

Composition of various gel formulations

Table no.4 . Composition of various gel formulations

Sr.No.	Ingredients	F1	F2	F3	F4
1.	Betel leaves extract	1gm	1.5gm	2gm	3gm
2.	Triethaloloamine	q.s+H6.5-7	q.s+pH6.5-7	q.s+pH6.5-7	q.s+pH6.5-7
3.	Methyl paraben	0.01gm	0.01gm	0.01gm	0.01gm
4.	Propyl paraben	0.01gm	0.01gm	0.01gm	0.01gm
5.	Carbopol	1gm	1gm	1gm	1gm
6.	Pappermint oil	q.s	q.s	q.s	q.s
7.	Distilled water	Upto100ml	Upto100ml	Upto100ml	Upto 100 ml

Evaluation Parameters

1. Physical appearance
2. pH
3. Homogeneity
4. Spreadability
5. Viscosity
6. Irritability
7. Extrudability
8. Stability

Characterisation of Gel

1. Physical Appearance:

- The prepared gels were examined for color, clarity, texture, transparency, and the presence of any grit.

2. pH Measurement:

- The pH of herbal gel compositions was measured using a digital pH meter. 1 g of gel was dissolved in 10 mL of distilled water and set aside for two hours. pH measurements were taken three times, and the average values were calculated to report on the pH of the gel composition.

3. Homogeneity:

- After the gels set in containers, visual inspection was conducted to check the homogeneity of all formulated gels. They were examined for the presence of aggregates and their appearance.

4. Spreadability:

- Spreadability was evaluated by measuring the time it took for two glass slides to separate under a specific load with gel placed between them. Improved spreadability was indicated by quicker separation time.

- Formula: $S = \frac{M \times L}{T}$

- (M): weight connected to the upper slide

- (L): length of the glass slides

- (T): time taken to separate the slides

5. Viscosity:

- The viscosity of all prepared formulations was analyzed using a Brookfield viscometer (LVDVE model) with helipath, using spindle number 96 at 10 rpm.

6. Extrudability:

- Extrudability was determined by measuring the time required for a sample to completely extrude from its container, i.e., sample amount divided by time required.

7. Skin Irritability:

- A small quantity of gel was applied to the surface of the skin and left for a few minutes to assess any irritability or adverse reactions.

8. Stability Study:

- The formulated gels were subjected to stability testing under various temperature conditions for 56 days. Parameters such as color, odor, pH, and consistency were evaluated periodically to assess stability over time.

RESULTS AND DISCUSSION

Preliminary phytochemical test

Table no. 5 Preliminary phytochemical test

Sr.no.	Quantity Test	Results
A	Test for Alkaloids	+ve
B	Test for Flavonoids	+ve
C	Test for Saponins	+ve
D	Test for Proteins	+ve
E	Test for Cardiac Glycosides	+ve

Table no.6 organoleptic characteristics

Sr.no	Evaluation Parameters	F1	F2	F3	F4
1	Colour	Light brown	Light brown	Light brown	Light brown
2	Odour	Characteristics	Characteristics	Characteristics	Characteristics
3	Homogeneity	Good	Good	Good	Good
4	Nature	Semi-solid	Semi solid	Semi solid	Semi solid
5	pH	6.7	6.8	6.8	6.8
6	Extrudability	Good	Good	Good	Good

7	Spreadability	Spreadable	Spreadable	Spreadable	Spreadable
8	Irritability	No irritable	No irritable	No irritable	No irritable
9	Viscosity	3714+0.21	3688+0.69	3671+0.58	E3671+0.58
10	Texture	Smooth	Smooth	Smooth	Smooth

The mouth ulcer gel formulation was developed and evaluated, with evaluation parameters meeting the required criteria. Stability studies revealed a slight pH change in formulations stored at 40°C, while no changes were observed at room temperature. Based on these results, the formulation from the fourth trial was identified as the optimal batch and selected for further consideration in large-scale manufacturing.

CONCLUSION

In the current study, a herbal gel formulation was developed and evaluated for various parameters, demonstrating successful results. The formulated herbal gel, devoid of toxic effects, is proposed for treating mouth ulcers. This form of treatment is widely embraced due to its cultural acceptance, natural compatibility, and minimal side effects. Dietary supplements and lifestyle adjustments can effectively treat or prevent canker sores. Homeopathic remedies offer another effective approach for managing mouth ulcers, with individualized treatment plans yielding promising outcomes. Homeopathic treatments are considered safe and demonstrate significant efficacy in resolving this condition over a few months.

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