A Novel Herbal Approach Formulating and Assessing Antiulcer Gel for Mouth Ulcers

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Abstract- **This study focuses on the formulation and evaluation of an antiulcer gel for the treatment of mouth ulcers using herbal compounds. Mouth ulcers, characterized by painful sores in the oral cavity, can be caused by various factors such as injury, poor oral hygiene, nutritional deficiencies, allergies, hormonal changes, stress, and underlying medical conditions. The prevalence of mouth ulcers varies with age, sex, and geographic location, affecting 20% to 60% of the population. The formulated antiulcer gel incorporates herbal extracts known for their antiulcer and medicinal properties, Carbopol is used as a thickening agent, triethanolamine for pH adjustment, sodium benzoate as a preservative, and clove oil with potential anti-inflammatory and anesthetic effects. The gel was systematically developed, considering the selection of polymer concentration and various evaluation parameters, demonstrating the safety of the gel. The herbal compounds, along with carefully selected excipients, offer a potential solution for the management of mouth ulcers. The study provides valuable insights into the development of an antiulcer gel, presenting a promising alternative for individuals suffering from recurrent mouth ulcers.**

Keywords: **Gel, Herbal, Mouth Ulcers, Drug.**

INTRODUCTION

Gels are mainly semi-solid formulations having a liquid phase that has been thickened with some other components. Topical gel preparations are used for the skin application orpercutaneous penetration of medicament or local action to certain mucosal surfaces.[1] A mouth ulcer is a painful sore or lesion that develops in the mouth, on the inner cheeks, lips, tongue, gums, or roof of the mouth. Mouth ulcers can be quite common, and they usually heal on their own within a week or two. However, they can be quite uncomfortableand may interfere with your ability to eat or talk. There are several different types of mouth ulcers, including canker sores, cold sores, andoral thrush. Canker sores are small, shallow ulcers that appear on the inside of the mouth, while cold sores are caused by the herpes simplex virus and usually appear on the lips or around the mouth, oral thrush is a fungal infection that can cause white patches in the mouth.[2]

The causes of mouth ulcers can vary, but they are often related to stress, injury to the mouth, certain foods, or underlying medical conditions. Treatment for mouth ulcers may include over-the-counter pain relievers, topical medications, or in some cases, prescription drugs.

The exact cause of mouth ulcers is not fully understood, but there are several potential factors that can contribute to their development.[3] Some common causes of mouth ulcers include, Injury to the inside of the mouth, such as accidental biting, aggressive brushing, or dental procedures, can cause mouth ulcers to form. Poor oral hygiene, including inadequate brushing and flossing, can lead to the development of mouth ulcer. Deficiencies in certain vitamins and minerals, such as vitamin B12, iron and folic acid can increase the risk of mouth ulcers. Some people may develop mouth ulcers as a result of sensitivity or allergies to certainfoods, such as acidic or spicy foods. Hormonal changes during menstruation or pregnancy can sometimes triggers the development of mouth ulcers. Psychological stress and emotional factors, such as anxiety and tension, can weaken the immune system and increase the risk of mouth ulcers. Certain immune system disorders, such as auto immune diseases like Crohn's diseaseor lupus, can increase the risk of mouth ulcers. There may be a genetic predisposition to developing mouth ulcers, as they tend to run in families. Some viral infections, such as herpes simplex virus (HSV), can cause mouth ulcers to form. Certain medical conditions, such as Behcet's disease or HIV/AIDS, can be associated with an increased risk of mouth ulcers. It's important to note that mouth ulcers can also occur without an identifiable cause, and triggers may vary from person to person. If you frequently experience mouth ulcers or if they are severe, persistent, or accompanied by other symptoms, it's recommended to consult with a healthcare professional for proper evaluation and management.

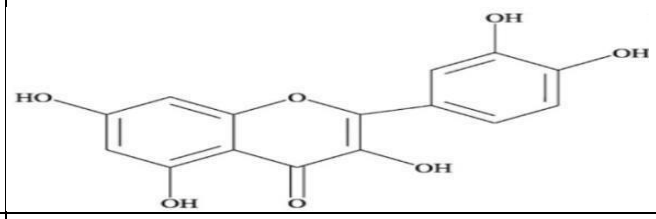
Epidemiology of mouth ulcer

Mouth ulcers are a common condition that affects a significant portion of the world's population. The epidemiology of lesion, sores varies with age, sex, and geographiclocation. Here is some general information on the epidemiology of canker sores. Mouth ulcers are a common condition, with prevalence ranging from 20% to 60% of thepopulation,

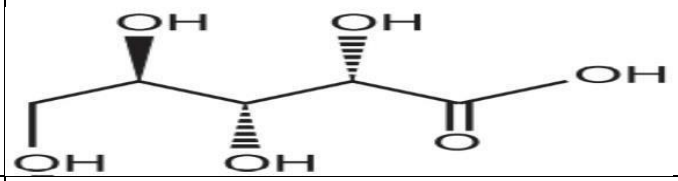
depending on the population studied and the criteria used to make the diagnosis. Canker sores can occur at any age, but they most commonly occur in young people between the ages of 10 and 40. There was no significant gender difference in the incidence of canker sores. Mouth ulcers have been reported in all geographic regions of the world. There may be differences in the incidence and prevalence of canker sores in different regions, possiblyrelated to environmental factors, dietary habits and cultural practices. Mouth ulcers can occur as a symptom of certain underlying medical conditions, such asinflammatory bowel disease, celiac disease, and HIV infection. The prevalence of canker sores in these populations may be higher than in the general population. Mouth ulcers can recur frequently in some people, with some people having multiple episodes per year. Recurrent mouth sores can be a chronic and uncomfortable condition that can significantly affect quality of life.[4]

DRUG PROFILE

1. Guava Leaves [5]

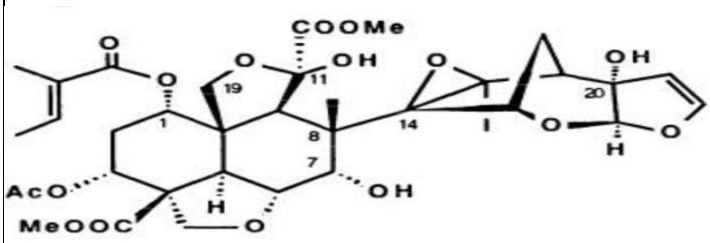
Botanical Name	Psidii Guajavae Folium
Biological Source	Small tropical tree or shrub
Chemical Constituents	Myricecetin, Guavijaverin
Family	Myrtaceae
Molecular Formula	$C_{20}H_{18}O_{11}$
Structure	
Category	Antiulcer, Antimicrobial
Uses	Treatment of mouth ulcer, Reduction of symptoms of pain and faster reduction of ulcer size.

2. Acacia Leaves [6]

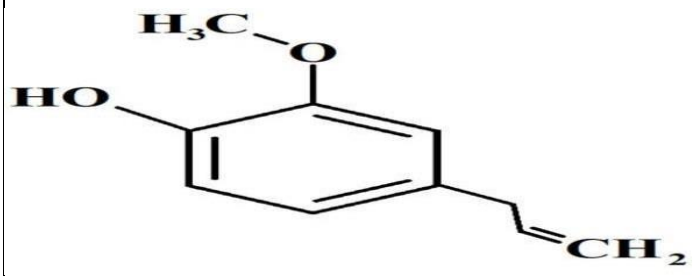
Botanical Name	Acacia Arabica
Biological Source	Incision of trunk and branches of AcaciaArabica
Chemical Constituents	Arabin and Arabic acid
Family	Leguminosae
Molecular Formula	$C_{24}H_{34}O_5$
Structure	
Category	Antiulcer
Uses	Reduce inflammation, wound healing, healingof acid peptic disease, used as film forming agent.

3. Neem [7]

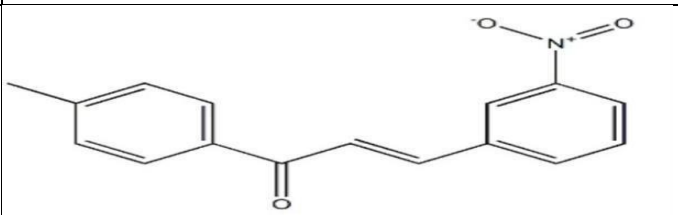
Botanical Name	Azadirachta Indica

Biological Source	Fresh or Dried leaves seed oil of azadirachtaindica
Chemical Constituents	Azadirachitin, salannin.
Family	Meliacea
Molecular Formula	$C_{35}H_{44}O_{16}$
Structure	
Category	Antiseptic
Uses	Treatment of inflammation, treat wounds andulcers, treatment of ulcerative colitis.

4. Clove Oil [8]

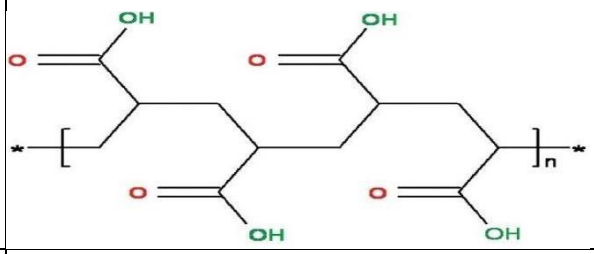
Botanical Name	Clove bud
Biological Source	Dried flower buds of clove
Chemical Constituents	Eugenol
Family	Myrtaceae
Molecular Formula	$C_{10}H_{12}O_2$
Structure	
Category	Carminative
Uses	Local Anesthetics, Stimulant, Flavoring agent.

5. Aloe vera [9]

Botanical Name	Aloe barbadensis miller
Biological Source	Dried juice of leaves of aloe vera
Chemical Constituents	Aloe emodin and various lectins, Barbalion.
Family	Asphodelaceae
Molecular Formula	$C_{16}H_{13}NO_3$
Structure	
Category	Antioxidant, Antimicrobial, Anticancer Anti-inflammatory.
Uses	Heals psoriasis lesions, Antibacterial activity,Anti-inflammatory agent.

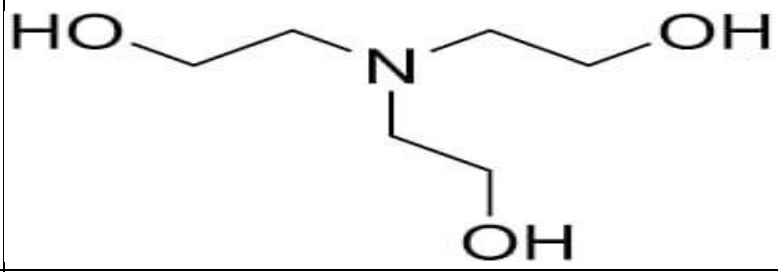
EXCIPIENTS

A. Carbopol 934 [10]

Chemical Name	Polyacrylic acid
IUPAC Name	Poly (acrylic acid), poly (1-Carboxyethylene)
Molecular Formula	$C_3H_4O_2$
Structure	
Category	Emulsifying agent, stabilizing agent, thickening agent
Uses	Use as viscosity enhancer, gelling agent and suspending agent

B. Triethanolamine [11]

Chemical Name	Trolamine
IUPAC Name	2-[bis(2-hydroxyethyl) amino] ethanol
Molecular Formula	$C_6H_{15}NO_3$
Molecular weight	149.19 gm/mol

Structure	
Uses	It is use in pH adjuster, gelling agent and thickening agent.

MATERIALS

The Materials are obtained from the following sources.

Sr.No.	Ingredients	Sources
1	Guava Leaves	Tropical Gardan
2	Acacia Leaves	Tropical Gardan
3	Neem Leaves	IOPR Herbal Gardan
4	Aloe Vera	IOPR Herbal Gardan
5	Carbopol 934	IOPR Laboratory store
6	Triethanolamine	IOPR Laboratory store
7	Sodium Benonate	IOPR Laboratory store
8	Clove oil	Local Market

TABLE 1:- Procurement of Ingredients

1. Guava leaves: Guava leaves have been traditionally used in many cultures as a natural remedy for various ailments, including stomach ulcers. Scientific studies have also investigated the anti-ulcer potential of guava leaves and have shown promising results. The anti-ulcer activity of guava leaves is attributed to the presence of several bioactive compounds, including flavonoids, tannins, and triterpenoids. These compounds possess various pharmacological activities such as antioxidant, anti-inflammatory, and antimicrobial properties that help in the prevention and treatment of stomach ulcers.[12]

2. Acacia leaves: Acacia leaves have also been traditionally used in some cultures as a natural remedy for various ailments, including stomach ulcers. Scientific studies have investigated the anti-ulcerpotential of Acacia leaves and have shown promising results as well. The anti-ulcer activity of Acacia leaves is attributed to the presence of several bioactive compounds, including tannins, flavonoids, and phenolic acids. These compounds have various pharmacological activities such as antioxidant, anti-inflammatory, and antimicrobial properties that help in the prevention and treatment of stomach ulcers.[13]

3. Neem leaves: Neem leaves have been traditionally used in Ayurvedic medicine for their various medicinal properties, including antiulcer activity. Several scientific studies have also supported the antiulcer properties of neem leaves through invitro and in vivo experiments.Neem leaves contain numerous bioactive compounds such as flavonoids, alkaloids, triterpenoids, and glycosides, which exhibit various pharmacological activities, including antiulcer effects. Here are some ways in which neem leaves may exert their antiulcer activity.[14]

4. Aloe Vera: Aloe vera, a succulent plant with thick, fleshy leaves, has been traditionally used for its medicinal properties, including its potential antiulcer activity. Several studies have investigated the effects of aloe vera on ulcers, and evidence suggests that aloe vera may possess antiulcer properties through various mechanisms.[15]

5. Carbopol 934: Carbopol 934 is a type of synthetic high molecular weight polymer that is commonly used as a thickening and suspending agent in pharmaceutical and cosmetic formulations, including gel formulations. When used in gel formulations, Carbopol 934 can provide a unique texture and consistency that is desirable for various applications. Here are some key features of Carbopol 934 in gel formulations**.**

A. Thickening agent: Carbopol 934 is known for its excellent thickening properties, which can help increase the viscosity of liquid formulations and transform them into gels. This can be beneficial in creating gels with a desired consistency, texture, and spread ability for topical or oral applications.

B. Suspending agent: Carbopol 934 can also act as a suspending agent, helping to uniformly disperse solid particles or other ingredients in the liquid matrix of the gel formulation. This can be usefulfor formulations that require the suspension of insoluble or poorly soluble active ingredients to ensure their even distribution.[16]

6. Triethanolamine: Triethanolamine (TEA) is a commonly used ingredient in the formulation of gels for various applications, including pharmaceuticals, cosmetics, and personal care products. TEA is a clear, colorless, and viscous liquid that can serve multiple functions in gel formulations. Triethanolamine can promote gelation in some formulations by enhancing the viscosityand consistency of the gel. It can work synergistically with other gel-forming agents, such as polymers or gelling agents, to create a stable and desirable gel texture.[17]

7. Sodium benzoate: Sodium benzoate is used to preserve food products with an acidic pH, such as fruit pulp and purees, jams, pickles, pickled herring and mackerel, margarine, olives, beer, fruit yogurts, canned vegetables, and salads. Sodium benzoate is most commonly added to sauces, tomato paste, fruit preserves, mayonnaise, margarines, and carbonated beverages. Conversely, in its unprocessed state, it may be found in a variety of foods, including cloves, cranberries, blueberries, mushrooms, and cinnamon. [18]

8. Clove oil: Clove oil, derived from the dried flower buds of the clove tree (Syzygium aromaticum),has been traditionally used for various medicinal purposes, including its potential antiulcerproperties. Clove oil contains several bioactive compounds, such as eugenol, which has been shown to possess antioxidant, anti-inflammatory, and antimicrobial properties, among others. Due to these properties, clove oil has been investigated for its potential use in antiulcer gel formulations. Clove oil has a strong, distinct odor and flavor that may impact the sensory characteristics of the gel formulation. Formulators should carefully consider the potentialimpact of the strong aroma and taste of clove oil on the overall sensory experience of the gel product, especially if it is intended for oral use. Clove oil has been shown to possess anti-inflammatory properties, which may help reduce inflammation and irritation associated with ulcers. This may contribute to its potential antiulcer activity by mitigating inflammation and promoting ulcer healing, also mainly used in the preparation for local anesthetic activity.[19]

METHODOLOGY

Objective

1. Formulation of Antiulcer gel for treatment of ulcer
2. To develop antiulcer gel using different herbal compound by direct dispersionmethod
3. To optimize prepared Antiulcer gel formulation
4. To evaluate prepared antiulcer gel

Plan of work

1. Literature Survey
2. Procurement of Drug and Excipients
3. Formulation of gel using different polymers
4. Evaluation of Herbal Antiulcer gel - Physical Appearance, Homogeneity, pH measurement, Viscosity, Washability, Extrudability, Spread ability, Skin Irritation Test
5. Completion of work

Formulation of blank gel for the selection of polymer

The gel can be formulated by using two different types of gelling agent, Carbopol 934 and Carbopol 940

Sr. No.	Ingredients	Formulations 1	Formulations 2
1	Carbopol 934	0.250gm	-
2	Carbopol 940	-	0.250 gm
3	Triethanolamine	0.25 ml	0.25 ml
4	Distilled water	25 ml	25 ml

TABLE 2:- Formulation of blank gel for the selection of polymer

Selection of Polymer Concentration: The “Carbopol 934” polymer is best chosen because it gives excellent stability, high viscosity, and a light skin feel. The “Carbopol 934” polymer is generally used in creams, gels, lotions, ointments, and hair removal creams.

Carbopol 940 has a high carbon cross-link density; because of that, it has greater gel viscosity and makes gel more tortuous. Along with that, it has a high molecular weight,molecular size, and density. As a result, due to its greater

molecular weight and size, it cannot absorb into the skin, hence Carbopol 934 is chosen.

Batch No.	Carbopol 934	Triethanolamine	Distilled water
1	0.250 gm	0.25 ml	19 ml
2	0.280 gm	0.28 ml	19 ml
3	0.300 gm	0.30 ml	19 ml
4	0.320 gm	0.35 ml.	19 ml

TABLE 3:- Selection of Polymer Concentration

Extraction Procedure

Acacia extract: 75 gm of fresh dried acacia leaves were taken in 200 ml of water in conical flask. Themixture was heated for 2 hours and reduced up to 50 ml.

Neem extract: 75 gm of fresh dried Neem leaves were taken in 200 ml of water in conical flask andboiled for 2 hours and reduced up to 50 ml.

Guava extract: 75 gm of fresh dried guava leaves were taken in 200 ml of water in conical flask andboiled for 2 hours and reduced up to 50 ml.

Aloe vera powdered extract: 150 ml of Aloe Vera gel were equally spreaded on 24×24inch ceramic tile and heatedin hot air oven at 80° C for 60 minutes and scratch from ceramic tile and obtained powderedform of Aloe Vera.

Preparation of antiulcer gel

Sr. No.	Ingredients	Quantity (for 100 gm)
1	Guava extract	8 ml
2	Acacia extract	8 ml
3	Neem extract	8 ml
4	Aloe vera gel powder	0.60 gm
5	Carbopol 934	1.12 gm
6	Triethanolamine	1.2 ml
7	Sodium benzoate	0.12 gm
8	Clove oil	3 ml
9	Distilled water	76 ml

TABLE 4:- Ingredients and their Quantity used in the formulation

- Accurately weigh 1.2 gm of Carbopol 934 polymer by using butter paper and transferredslightly little amount of Carbopol 934 to the preparation with continuous stirring.
- Guava extract, Acacia extract, and Neem extract Each 2 ml taken in 100 ml beaker to it 0.60 gm Aloe vera gel powder was added and shaken vigorously. Apart from that 0.12gm sodium benzoate was added as a preservative and mix all of them until they completely mix.
- Beaker of 250 ml was taken and add 76 ml of distilled water to it by using measuring cylinder.
- Now place the distilled water containing beaker under the electronic stirrer and slowly add the Carbopol 934 polymer with Mixture of API (Guava extract, Acacia extract, Neem extract and aloe vera gel powder) and preservative (Sodium Benzoate) at regularinterval of 15 Seconds at 1000 RPM.
- Once the Carbopol completely dissolved in distilled water add 2 ml clove oil in a formulation and add Triethanolamine in small small quantity as the viscosity of gel is achieved.

Evaluation parameters of the gel

1. **Physical appearance:** The gel formulation was evaluated for physical characteristics like color, odor, consistency. The antiulcer gel was yellowish brown with which on application found to besmooth. It was observed that gel has passed all the parameters of Physical appearance test.
2. **Homogeneity:** The prepared antiulcer gel was tested for homogeneity by placing the gel on a transparent plate

(cuvette) and simply spread the gel by finger and visually observe the presence of course particle in a gel.

3. **pH:** The pH of a gel formulation is measured by using digital pH meter at constant temperature was found to be 6.90.
4. **Washability:** The prepared antiulcer gel formulation was applied on the skin and then ease extent of washing with tap water was checked normally.
5. **Viscosity**: Brookfield viscometer was used for the measurement of viscosity of the prepared gel. The Brookfield viscometer was rotated at 100 rpm. Spindle no. 3 was used Each reading was taken after the equilibrium was attained by the sample at the end of two minutes. The studywas repeated three times and average value is calculated. The Viscosity of gel was found to be 4.37 poise. Percent torque was found to be 7.3%.
6. **Extrudability**: The prepared antiulcer gel formulation was filled in a collapsible tube, the tube was pressed and the material was extruded out from the tube was checked.
7. **Spread ability**: Approximately 2 gm of gel was sandwiched between 2 glass slides. About 500 mg of weight was applied on the glass slide for 5 minutes. Then the weight was removed and thediameter of the spread circle was measured at different point.
8. **Skin irritation test:** An area of (1 sq cm) was marked on the left-hand dorsal surface. A small amount of gel was applied on that area and Irritancy, Edema, Erythema was checked at a regular intervalof 45 minutes of interval.

RESULT AND DISCUSSION

1. **Selection of polymer concentration:** The herbal antiulcer gel was formulated using two different gelling agents Carbopol 934 and Carbopol 940.The concentration 0.300 gm of Carbopol 934 was considered suitable in terms of stability, viscosity and spreadability. Thus Carbopol 934 was used for further optimization and development of formulation batches.
2. **Physical appearance:** It was observed that the color of all the herbal antiulcer gel was yellowish brown with translucent look which on the application was found to be smooth.
3. **Homogeneity:** By visual examination of the appearance and the presence of any lumps, Flocculates or aggregates. The produced herbal antiulcer gel was checked for homogeneity. The homogeneity of prepared gel has been shown to be fine.
4. **pH:** The pH of formulated herbal antiulcer gel was found to be 6.83 which corresponds to the value of saliva pH (5.5–8.0).
5. **Skin Irritation Test:** The formulation showed no redness, edema, inflammation and irritation during irritancy studies.
6. **Washability:** The prepared herbal antiulcer gel was applied and then wash with tap water, after washing no trace of gel was found to be present.
7. **Spreadability**: The spreadability of prepared herbal antiulcer gel has been shown to be fine.
8. **Viscosity:** The viscosity of prepared herbal antiulcer gel are measured by the Brookfield viscometerand viscosity was found to be 4.37 poise and 7.3 % torque.

CONCLUSION

In conclusion, the formulated herbal antiulcer gel, comprising guava, acacia, neem extracts, aloe vera, Carbopol 934, and other excipients, demonstrated favorable physical characteristics, including a smooth and translucent appearance. The optimized polymer concentration was determined to be 0.300 gm of Carbopol 934, ensuring stability, viscosity, and spreadability. The pH of the gel was found to be within the range of saliva pH. Skin irritation tests revealed no adverse effects, and washability was effective. The gel exhibited satisfactory homogeneity, and its spreadability and viscosity were deemed suitable for topical application. Overall, the developed antiulcer gel presents a promising formulation for the treatment of mouth ulcers, utilizing natural herbal ingredients with potential antiulcer properties.

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