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FORMULATION AND EVALUATION OF HERBAL AQUEOUS GELFOR MOUITH ULCER

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ABSTRACT

Background: Mouth ulcers often cause pain and irritation of the sores by salty, spicy and sour food items and may cause discomfort while healing occurs due to the use of chemical formulations. This project focuses on the preparation of a herbal mouth ulcer healing gel because of better cultural acceptability, better compatibility with human body and lesser side effects. The gel was prepared by using alcoholic extract of Psidium guajava, and aqueous extract of liquorice. **Objective:** The Present investigation was performed to formulate and evaluate the antiulcer activity of herbal gel containing guava leaves and liquorice root extract. **Method:** The Guava leaves collected and drying it by using hot air oven. Extraction was done by using soxhelet method by using ethanol as solvent. Liquorice root is collected dried in sunlight. Extraction was done by using soxhelet method by using ethanol as solvent.

Evaluation of Antiulcer of both extract was carried out by

1. Determination of clarity and color
2. Determination of Odor
3. Determination of Viscosity
4. Determination of the Ph
5. Determination of Spread ability

Result: Evaluation of antiulcer activity of the gel containing extract of guava leaves and liquorice root was evaluated by determining. **Conclusion**: We conclude that formation of liquorice root and guava leaves extract containing gel is effective in mouth ulcer.

KEYWORDS: Liquorice root, Guava Leaves, Piperment oil, Glycerine, Soxhelet Appratus.

INTRODUCTION[1]

MOUTH ULCERS[1,2]

Mouth ulcers are painful sores that can occur anywhere inside the mouth. This leaflet is about the most common type of mouth ulcers, which are aphthous mouth ulcers. At least 1 in 5 people can develop aphthous mouth ulcers at some stage in their lives. Women are affected more often than men.

Figure no. 1: Ulcer.

TYPES OF MOUTH ULCERS[1,3]

There are three types.

1. Minor aphthous ulcers are the most common (8 in 10 cases). They are small, round, or ovaland are less than 10 mm across. They look pale yellow but the area around them may look swollen and red. Only one ulcer may

develop but up to five may appear at the same time. Each ulcer lasts 7-10 days and then goes without leaving a scar. They are not usually very painful.

2. Major Aphthous ulcers occur in about 1 in 10 cases. They tend to be 10 mm or larger across. Usually only one or two appear at a time. Each ulcer lasts from two weeks to several months but will heal leaving a scar. They can be very painful and eating may become difficult.

3. Herpetiform ulcers occur in about 1 in 10 cases. These are tiny pinhead-sized ulcers, about 1-2 mm across. Multiple ulcers occur at the same time but some may join together and form irregular shapes. Each ulcer lasts one week to two months. Despite the name, they have nothing to do with herpes or the herpes virus.

CAUSES OF MOUTH ULCERS[1,4]

The cause is not known. They are not infectious and you cannot 'catch' aphthous mouth ulcers. In most cases, the ulcers develop for no apparent reason in people who are healthy. In some cases the ulcers are related to other factors or diseases.

- These include.
- Injury - such as badly fitting dentures, a graze from a harsh toothbrush, etc.
- Changes in hormone levels. Some women find that mouth ulcers occur just before theirperiod. In some women, the ulcers only develop after the menopause.
- Stopping smoking - some people find they develop ulcers only after stopping smoking.
- Rarely, a food allergy may be the cause.
- Mouth ulcers run in some families. So, a genetic factor may play a part in some cases.
- Stress or anxiety is said to trigger aphthous mouth ulcers in some people.

METHODS[2]

Gels are typically semi solid formulation having a liquid phase that has been thickened with other components .uses of topical gel preparations are for skin application or percutaneous penetration of medicament or local action to certain mucosal surfaces. A mouth ulcer is a break or breach in the mucous membrane, which is lines the inside of the mouth. It is usuallyhas yellow or white colour and usually looks like a depression in mouth that is mucous membrane.

Table no. 01: Ingredients used in herbal aqueous gel.

Sr. no.	Ingredients	F1	F2	F3
		Qty in %	Qty in %	Qty in %
1	Liquorice Root Extract	2 %	1 %	0.5 %
2	Guava Leaves Extract	2 %	1 %	0.5 %
3	Carbapol 934	1 %	1 %	1 %
4	Triethanolamine	Q.S pH 6.5-7	Q.S pH 6.5-7	Q.S pH 6.5-7
5	Methyl paraben	0.0015 %	0.0015 %	0.0015 %
6	Peppermint oil	Q.S	Q.S	Q.S

1. Liquorice Root :-(:Glycyrrhiza glabra)

Figure no. 2: liquorice root.

In traditional medicine, liquorice has been recommended as a prophylactic agent for gastric and duodenal ulcers. It is employed in dyspepsia as an anti-inflammatory agent during allergenic reactions. It is used as a contraceptive, laxative, anti-asthmatic, emmenagogue, galactagogue, antiviral agent in folk therapy . Glycyrrhiza roots are useful for treating cough because of its demulcent and expectorant property.

02. Guava leave

Figure no: 3 guava leaves.

Guava leaves are jam-packed with antioxidants, antibacterial, and anti- inflammatory properties that can benefit you. The various chemicals that guava leaves have are tannins, flavonoids, polyphenols, and carotenoids used to treat multiple diseases.

03. Carbapol 934

Admix has been mixing Carbopol, a polymer used as a thickener, suspending agent and stabilizer, for decades.

Carbopol is utilized in a wide variety of cosmetic and personal care products, pharmaceuticals and household cleaners. Most Carbopol polymers are high molecular weight acrylic acid chains usually crosslinked, and are available as powdersor liquids.

In the cosmetic industry, Carbopol is used as a thickener in lotions, creams and gels. It is also used to stabilize, suspend, and control the release of pharmaceutical products.

4. Methyl Paraben

Methylparaben is commonly used as a fungicide in Drosophila food media at 0.1%.[5] To Drosophila, methylparaben is toxic at higher concentrations, has an estrogenic effect (mimicking estrogen in rats and having anti-androgenic activity), and slows the growth rate in the larval and pupal stages at 0.2% .

5. Triethanolamine

It is a common ingredient in formulations used for both industrial and consumer products. The triethanolamine neutralizes fatty acids, adjusts and buffers the pH, and solubilizes oils and other ingredients that are not completely soluble in water.

6. Pipermint Oil

Peppermint oil has a wide variety of uses. For example, it can be used as.

- A treatment for a variety of conditions, including irritable bowel syndrome (IBS), nausea, and other digestive issues, as well as the common cold and headaches.
- A topical application for relief from itching, muscle pain, and headache.
- A flavoring agent in foods and in products such as mouthwashes.
- A fresh, pleasing scent added to soaps and cosmetic products.

Procedure[2,2]

1. METHODOLGY

Drying: Dehydration (or drying) is defined as the application of heat under controlled conditions to remove the majority of the water normally present in a food by evaporation (or in the case of freeze drying by sublimation).

Grinding: Once the leaves and seeds were properly dried, then the seeds and leaves grinded to make afine powder and used for making extract.

Percolation: Soxhlet extraction has been used widely for extracting valuable bioactive compounds from various natural sources. In this extraction, a small amount of dry sample is placed in a thimble, which is placed in a distillation flask containing the solvent of particular interest. After reaching an overflow level, the solution of the thimble-holder is aspirated by a siphon, which unloads the solution back into the distillation flask. This solution carries the extracted solutes into the bulk liquid. The solute remains behind in the distillation flask, and the solventpasses back to the solid bed of samples. The process is repeated until complete extraction takes place.

Figure no. 4: Soxhlet apparatus.

Procedure for development of formulation of herbal gel[2,3]

1. Specified amount of Carbopol 934 was dispersed in required amount of distilled water with continuous stirring.
2. 5ml of distilled water was taken and required quantity of methyl paraben and propyl paraben were dissolved by heating on water bath.
3. Further varying concentration of Guava leaves ethanolic extract and liquorice root aqueous extract were mixed to the above mixture.
4. Finally full mixed ingredients were mixed properly to the Carbopol 934 gel with continuous stirring and triethanolamine was added drop wise to the formulation for adjustment of required pH (6.8-7).
5. Volume was made up to 100 ml with distilled water

and few drops of Peppermint oil was added as flavourant.

6. The composition of herbal gel prepared from the powdered guava leaves and liquorice root extract coded as F1, F2, and F3 is tabulated in Table 1.

Evaluation[3,1]

Physical Appearance

1. Physical parameters such as appearance and colour were checked

Table 2: in vitro evaluation parameter.

Formulaition	Physical appearance	pH	Homogenei ty	Spread ability (gm.cm/sec)	Viscosity(Pa.S)	Extrudability
F1	Greenish	6.8±0.9	Good	5.70±0.1	3.174±0.01	Good
F2	Greenish	7±0.9	Good	5.86±0.15	3.073±0.049	Good
F3	Greenish	6.9±0.5	Good	6.52±0.05	2.334±0.012	Good

Measurement of Ph

The pH of herbal gel formulations were determined by using digital pH meter. 1gm of gel was taken and dispersed in 10ml of distilled water and keep aside for two hours. The measurement of pH of formulation was carried out in three times and the average values are reported. pH of gel formulation was reported in table 2.

Homogeneity

All developed gel formulations were tested for homogeneity by visual inspection after the gels have been set in to the container. They were tested for their presence and appearance of any aggregates. Homogeneity of gel formulation was reported in table 2.

Spreadability

Spreadability was determined by glass slide and wooden block apparatus. Weights about 20gm were added to the pan and the time were noted for upper slide to move to separate completely from the fixed slide. An excess amount of gel 2gm under study was placed on thisground slide. The gel was then sandwiched between this slide and another glass slide having the fixed ground slide and there is provided with the hook. A 1kg weighted was placed on thetop of the slides for 5 minutes to provide a uniform film of the gel and remove air between the slides. Excess of the gel was removed off from the edges. The top plate was then subjected to pull with the help of string attached to the hook and the time in seconds required by the top slide to cover a distance of 7.5cm be noted. A shorter or less interval indicates better Spreadability. Spreadability of gel was calculated using the following formula Spreadability of gel was reported in table no 2.

$S = M \times L / T$Where, S = Spreadability, M = Weight in the pan which is tied to the upper slide, L = Length moved by the glass slide T = Time in second taken to separate the slide completely each other.

Viscosity

Viscosity was determined by using Brookfield viscometer (DV-III programmable Rheometer). Formulated gels were tested for their rheological behaviors at 250C. The measurement was made over range of speed from 10rpm to 100rpm with 30seconds between2 successive speeds and then in a reverse orders.

Extrudability

The gel formulations were filled in standard capped collapsible aluminium tubes and sealed to the end. The extrudability was determined by pressing of the thumb.

Clarity

The clarity of all the three batches was determined by visual inspection.

Gel strength

Gel strength was determined by the time in seconds required by the weight to penetrate in the gel. A Sample amount of 5gm of each of the optimize batches was taken and 3.5gm weight was placed on the surface of gel. The time in seconds required by the weight to penetrate 0.5cm in the gel. The gel strength was then reported in table 3.

Bioadhesive Strength

Bioadhesive strength was determined by using glass slide and wooden block apparatus. Bioadhesive strength used to measuring the force required to detach the formulation from cellophane membrane. Specified amount that is 1 gm of prepared gel was taken on glass slide wrapped with cellophane membrane. Intimate contact was provided by the movable glass slide was placed on fixed slide. Two minute contact time was given to ensure intimate contactbetween formulation and membrane. The weight was added in the pan which is provided to apparatus until slides got detached. The bioadhesive force, expressed as the detachment stress in dyne/cm2 was determined by the formula. Bioadhesive strength was reported in table 3.

Detachment stress = $m \cdot g/A$

Where, m = Weight required to detach two glass slides from each other (gm). g = Acceleration due to gravity i.e 980 cm/s2. A = Area of membrane exposed (cm2).

Stability Study

Stability studies were done with open and close container. Here, by subjecting the product to room temperature for 1 month Stability study was reported in table 3.

Table 3: *In vitro* evaluation parameters.

Formulaition	Bioadhesive strength (dyne/cm2)	Gelling Strength (Sec)	Open Container	Closed Container
F1	4422.22 ± 18.82	42±0.75	Unstable	Stable
F2	3525.31 ± 31.09	36±0.07	Unstable	Stable
F3	2873.48 ± 18.25	27±0.5	Unstable	Stable

Antibacterial activity

The antifungal activity of all developed batches of formulation and without drug containing gel formulation i.e. blank formulation were carried out by Cup-plate method in comparison with marketed antifungal formulation (Zolef). There are two different bacteria cultures used were Aspargilious aureusand Candida Albicans. The Antibacterial test was performed using the agar well diffusion Prepared nutrient brought and poured in to sterile petri plates and kept for drying and cooling. After that each bacterial culture were spread by micron wire loop. A sterile cork borer 6mm diameter was used to drill holes 4 mm deep. Then 0.5gm of gel from each batches add in to this holes. Plates were then incubated at 27^0C for 48 hr. The zone of inhibition (diameter in mm) developed, if any, was then measured for the particular compound with each fungal strength. Antibacterial studies were reported in table 4.

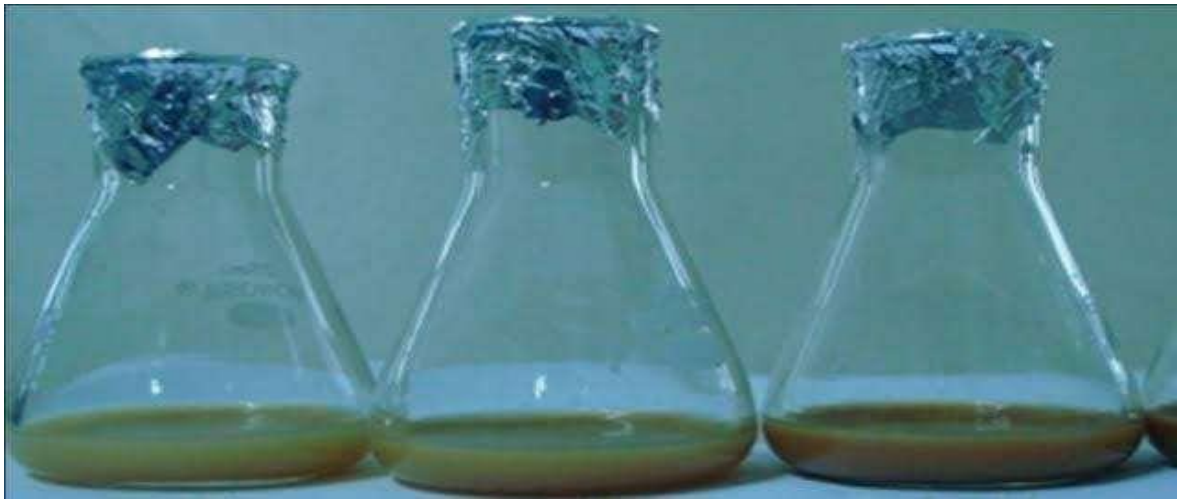
Table 4: in vitro Antibacterial study.

Formulation	Aspergillus aureus (mm)	Candida albicans (mm)
Blank	12	15
F1	22±0.4	20±0.4
F2	20±0.6	19±0.6
F3	19±0.4	18±0.5
Marketed Formulation	26±0.2	28±0.4

RESULTS

From the result it is clearly shown that all the prepared gel formulations having good homogeneity and gelling properties. The pH of all gel formulations was in the range of compatible with normal pH range of the skin. The rheological behavior also indicates that thegels were neither too thick nor too thin. The spreadability shows that with increasing viscosity of formulation, spreadability decreases and vice versa. Extrudability study was done by pressing thumb and it's easily extendable.

All three batches of developed formulation showed antibacterial activity against Aspargilious aureus and Candida Albicans this are main microorganism responsible for mouth ulcer and formulation it can also use to treat mouth ulcer infection.



F1 **F2** **F3**

Figure no 04: Three types of formulations.

Table no. 05: Antimicrobial evaluation of clindamycine, Herbal Aqueous gel , and Normal saline solution.

Sr.no	Zone of Inhibition		
	Marketed formulation (Clindamycine)	Herbal Preparation (aqueous gel)	Control (Normal saline)
F1	35	36	No Zone of Inhibition
F2	36	35	No Zone of Inhibition
F3	34	33	No Zone of Inhibition
F4	35	32	No Zone of Inhibition

Figure no. 05: Zone of Ihibition.

DISCUSSION

From the result it is clearly shown that all the prepared gel formulations having good homogeneity and gelling properties. The pH of all gel formulations was in the range of compatible with normal pH range of the skin. The rheological behavior also indicates that thegels were neither too thick nor too thin. The spreadability shows that with increasing viscosity of formulation, spreadability decreases and vice versa. Extrudability study was done by pressing thumb and it's easily extendable. The gelling and bioadhesive strength of all the batches was found in the suitable range. one Month stability study was done with open and close container and it's showed that open container containing gel was not stable and close container gel was stable. Formulated gel containing open container when expose to ambient room temperature then syneresis was observed it means liquid exudates separating. Syneresis occurs when the interaction between particles of the dispersed phase becomes so great that on standing. In that dispersing medium is squeezed out in droplets forms and the gel shrinks. Syneresis it means the form of instability in aqueous gels. In syneresis system separation of a solvent phase is occur only because of the elastic contraction of the polymer means polymeric molecules. Allthree batches of developed formulation showed antifungal activity against Aspargilious aureus and Candida Albicans this are main microorganism responsible for mouth ulcer and formulation it can also use to treat mouth ulcer infection

CONCLUSIONS

From the above study we can conclude that herbal gel can be prepared for topical administration.liquarice root can be used along with guava leaves in gel to provide antiulcer effect as well moisturising effect on skin. The extract taken in the present study can be replaced with other extract having more activity.

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ABBREVIATIONS

cm: Centimeter.
F1 : Formulation 1.
F2 : Formulation 2**F3 :** Formulation 3**F4 :** Formulation 4
gm: Gram **ml:** Miligram **mm:** Milimeter **um:** Micrometer**Qty:** Quantity.

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