

FORMULATION AND EVALUATION OF HERBAL GEL FOR TREATMENT OF RECURRENT APHTHOUS STOMATITIS (RAS)

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ABSTRACT

Herbal formulation have growing demand in the world market. Herbal medicines are the oldest form of health care known to mankind. The objectives of present investigation were to formulate and evaluate herbal gel for treatment of Recurrent aphthous stomatitis(RAS). Herbal gel was prepared by using aqueous extracts of guava, neem, tulasi and different concentration of Carbopol 940, Guargum as a gel base. Formulations were evaluated for various parameters like physical appearance, pH, homogeneity, spreadability, viscosity, extrudability. However, the Carbopol 940 based F3 Herbal gel proved to the formula of choice, since it showed the highest percentage of good spreadability, extrudability, and rheological properties. Formulation F3 with 1 % leaves extract herbal gel showed best results because all the parameter showed satisfactory results.

KEYWORDS: Guava, Neem, Tulasi, herbal formulation, herbal gel, ulcer treatment.

I. INTRODUCTION

Herbal medicine is still the mainstay of about 75–80% of the world population, mainly in the developing countries, for primary health care because of better cultural acceptability, better compatibility with the human body and lesser side effects. However, the last few years have seen a major increase in their use in the developed world. The human being exploited to alleviate his suffering from injuries of deceases utilizing plant growing around him. The plant kingdom still hold many species of plant containing substance of medicinal value which have yet to be discovered and the large no. of plant are constantly being screened for their possible pharmacological value in addition to already exploited plants.

Mouth ulcers

Mouth ulcers are small, painful sores on the inside lining of the mouth. They usually develop on the inside of the lips and cheeks and on the underneath and edge of the tongue. Medicines from a pharmacist can reduce the pain and help mouth ulcers to heal. Mouth ulcers include lesions, sores, laceration, abrasions, or any open break in the mucosa of the mouth, lips or tongue. Mouth ulcers may also be called Recurrent aphthous stomatitis and are a symptom of a variety of mild to serious diseases, disorders and conditions. Mouth ulcers can result from vitamin deficiencies, infection, inflammation, trauma, malignancy and other diseases and abnormal processes.^[7]



Recurrent aphthous stomatitis: (RAS; aphthae; canker sores)^[8,9,10]

Recurrent aphthous stomatitis (RAS) is the most frequent form of oral ulceration, characterised by recurrent oral mucosal ulceration in an otherwise healthy individual. It affects 1 in 5 persons and usually begins in adolescent and teenage years. During an episode, there may be 1-5 painful ulcers that last 5-14 days. These ulcers are located on the inner cheeks, inner lips, underside of the tongue, or soft palate. Idiopathic aphthae are the most frequently occurring inflammatory lesions of the oral mucous membrane.

Causes of mouth ulcer

In many cases the underlying cause of mouth ulcers is not known, but they may be associated with stress or tissue injury. Causes of mouth ulcers include:

- Biting or chewing the inside of the cheek
- Damage to the inside of the mouth from very hot food or drinks

- Damage to the inside of the mouth from some foods (e.g., caffeine, chocolate, acidic)
- Brushing the teeth and gums too hard
- Some toothpastes and mouth rinses

Sign & Symptoms

Some people feel a tingling or burning on the inside of the lips or cheeks, 1 -2 days before an ulcer appears. Mouth ulcers are:

- Round or oval shaped, shallow sores, usually less than 1cm across

- Yellow to grey-white in colour with a raised red rim; there may be redness and swelling around them.
- Usually very painful.

2. MATERIALS AND METHODS

2.1. Collection

The Fresh Plant Leaves of Guava, Neem, Tulasi were collected from a medicinal garden of our college. Other Polymers and chemicals used in present study were of analytical grade.

| Sr.No | Chemicals | Name and address |
|-------|------------------|---|
| 1 | Carbopol 940 | Reasearch fine chem. Industries , India |
| 2 | Guargum | Inr Chem , india |
| 3 | Glycerin | Finar Chemicals limited, india |
| 4 | Propylene glycol | Qualikems fine chem. Pvt ltd, india |
| 5 | Methyl paraben | Oxford laboratory , india |
| 6 | Propyl paraben | Oxford laboratory , india |
| 7 | Triethanolamine | Finar Chemicals limited, india |

2.2. EXTRACTION

Preparation of Pharmaceutical Aqueous Extract^[39]

The Fresh Plant Leaves of Guava, Neem, Tulasi were carefully selected washed to remove impurities and dried kept in hot air oven for drying purpose at 45 °C and grinded into small pieces. By using blender were crushed to make powder. The fine powder was passed through

sieve no.43 and stored in an airtight container for further use. Desired quantities of herbal drug were weighed and each herb macerated with water in conical flask. Dried herbs were allow to mix with water by moderate shaking of conical flask for 3 days. After 3 days content were filtered out by using simple filtration method and filtrates were collected in separately vessel.

Composition of extract

| S.No | Name of ingredients | Quantity |
|------|---------------------|----------|
| 1 | Extract of Guava | 0.500 mg |
| 2 | Extract of neem | 0.250 mg |
| 3 | Extract of tulasi | 0.250 mg |

2.3. Filtration

Filtration of extract was done by using simple filter paper and funnel for two times.

2.4. Evaporation

Evaporation was done by using electronic water bath. Filtrates were allowed to evaporate in evaporating pan at 60 °C temperature until the desired concentration of the extract was obtained.

2.5. FORMULATION OF HERBAL GEL

2.5.1. PREFORMULATION STUDY

Preformulation studies are needed to ensure the development of a stable as well as effective and safe dosage form. It is a stage of development during which the pharmacist characterizes the physico –chemical properties of the drug substances and its interaction with various formulation components. Goals of Preformulation study: To determine the necessary physico- chemical parameter of a new drug substance.

2.5.2. Experimental design

During formulation two gelling agents used at different concentrations, resulting in six different batches of gels for herbal leaves extract, total six batches prepared. In

this case Carbopol 940, Guar gum .these two types of gelling agents were taken. Two gelling agents were used as follows:

- Carbopol 940 (at concentration 0.5%,1% and1.5%)
- Guargum (at concentration 0.5%,1% and1.5%)

2.5.3. Preparation of Gel^[11]

i) Preparation of gel with Carbopol 940

Accurately weighed Carbopol 940 was taken in a beaker and dispersed in 50 ml of distilled water. Kept the beaker aside to swell the Carbopol 940 for half an hour and then stirring should be done using mechanical/lab stirrer at 1200 rpm for 30 min. Take 2 ml of Propylene glycol and Glycerin required quantity of Extract. And add weighed quantity of methyl paraben and propyl paraben to it and stirred properly. After all Carbopol 940 dispersed,1 gm Extract and preservatives solutions were added with constant stirring. Finally volume made up to 100 ml by adding remaining distilled water and Triethanolamine was added drop wise to the formulations for adjustment of required pH (6.8-7) (Das 2010).And to obtain the gel at required consistency.

i) Preparation of gel with Guar gum

Accurately weighed Guar gum was taken in a beaker and dispersed in 50 ml of distilled water. Kept the beaker aside to swell the Guar gum for half an hour and then stirring should be done using mechanical/lab stirrer at 1200 rpm for 30 min. Take 5 ml of propylene glycol and required quantity of Extract. Take 2 ml of Propylene glycol and Glycerin required quantity of Extract. And

add weighed quantity of methyl paraben and propyl paraben to it and stirred properly. After all Guar gum dispersed, 1gm Extract and preservatives solutions were added with constant stirring. Finally volume made up to 100 ml by adding remaining distilled water and Triethanolamine was added drop wise to the formulations for adjustment of required pH (6.8-7) (Das 2010). And to obtain the gel at required consistency.

Quantitative composition of leaves extract gel formulation

| INGREDIENTS | F1 | F2 | F3 | F4 | F5 | F6 |
|----------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|
| Leaves extract(g) | 1 | 1 | 1 | 1 | 1 | 1 |
| Carbopol 940(g) | 0.5 | 1 | 1.5 | - | - | - |
| Guar gum(g) | - | - | - | 0.5 | 1 | 1.5 |
| Glycerin(ml) | 2 | 2 | 2 | 2 | 2 | 2 |
| Propylene glycol(ml) | 2 | 2 | 2 | 2 | 2 | 2 |
| Methyl paraben(g) | 0.2 | 0.2 | 0.2 | 0.2 | 0.2 | 0.2 |
| Propyl paraben(g) | 0.1 | 0.1 | 0.1 | 0.1 | 0.1 | 0.1 |
| Triethanolamine(ml) | q.s+pH 6.5 - 7 | q.s+pH 6.5 - 7 | q.s+pH 6.5 - 7 | q.s+pH 6.5 - 7 | q.s+pH 6.5 - 7 | q.s+pH 6.5 - 7 |
| Distilled water(ml) | 100 | 100 | 100 | 100 | 100 | 100 |

3. Physicochemical evaluations^[12]

A) Appearance/clarity

The topical gel formulations were observed carefully by naked eye for appearance/clarity, colour, odour and presence of suspended particulate matter if any. It was further assessed by observing them against a dark and white background.

B) Determination of pH

The pH of various gel formulations was determined by using previously calibrated digital pH meter. 1 gram of gel was dissolved in 10 ml distilled water. The values were recorded immediately after preparation and after storage for 24hrs. at room temperature.

c) Determination of Viscosity

The measurement of viscosity of the prepared gel was measure by using Brookfield Viscometer. The gels were rotated at 100 rotations per minute and the viscosity values were noted.

Test conditions

- Type of equipment-Brookfield RVDV-II +Pro
- Spindle- T-bar
- Spindle code -S 96
- Sample volume- 10.0ml
- Rpm -100

D) Spreadability

It gives spreading capacity of formulated gel when it applied on the skin or affected area of skin. It is expressed as time in seconds taken by two slides to slip off from gel. Spreading value is important for knowing the therapeutic potency of a topical formulation. 1gm gel was placed in between the two slides under the direction of certain load. The time taken by the slide to separate was observed and noted.

It was calculated using the following formula:

$$S = M \times L/T$$

Where, S – Spreadability

M – Weight in the pan

L – Length moved by the glass slide

T – Time (in sec.) taken to separate slides completely.

E) Bioadhesive strength

For this, Individual samples of gel formulation were applied to the base of inverted glass vial using double sided adhesive tape to secure the gel in position. The distance between two vials was adjusted in such a way that the gel sample remain adhere to mucosal membrane. Sufficient pressure was applied on both side of the vial for 10 sec to allow proper adhesion of the gel to mucosa. A constant weight was added to the pan connected to the other arm of modified balance which pulls the vial away from the other vial. The weight required for detaching the two vials was noted.

Bioadhesive strength (dynes/cm²) = Mg /A

Where, M= weight required for detachment in gram, g = acceleration due to gravity (980 cm/s²), A = area of mucosa exposed

F) Extrudability

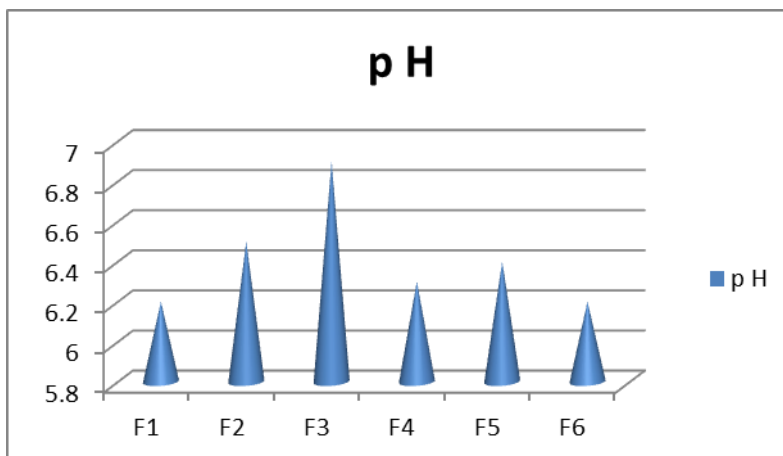
It was used for determination extrudability of gel. A collapsible tube filled with a gel, then pressed firmly at the crime end. When the cap was removed, gel extrudes until pressure dissipated. Weight in grams required to 0.5cm ribbon of gel was determined in 10 sec. Average extrudation pressure in gram observed.

4. RESULTS AND DISCUSSION

The present work aimed to increase anti ulcer activity of gel formulation with using various gelling agents. The prepared formulations were characterized for Physical appearance, pH, Spreadability, Viscosity, Homogeneity, Extrudability.

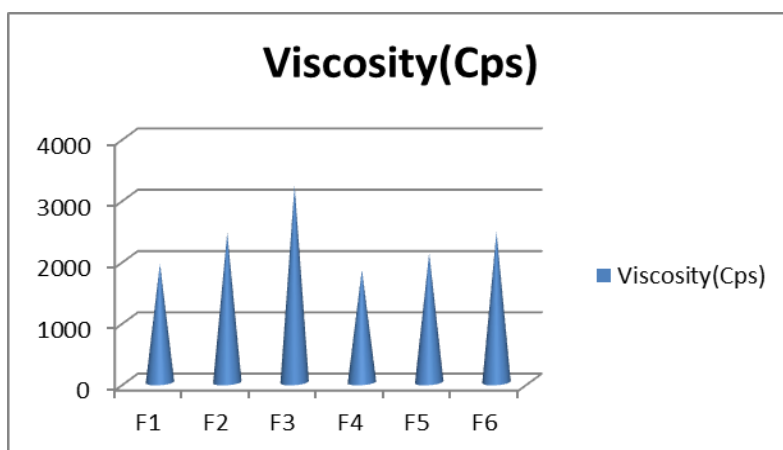
4.1. Evaluation of p H and Appearance

| Formulations | Physical Appearance | p H |
|--------------|---------------------|-----|
| F1 | Greenish | 6.2 |
| F2 | Greenish | 6.5 |
| F3 | Greenish | 6.9 |
| F4 | yellowish green | 6.3 |
| F5 | yellowish green | 6.4 |
| F6 | yellowish green | 6.2 |



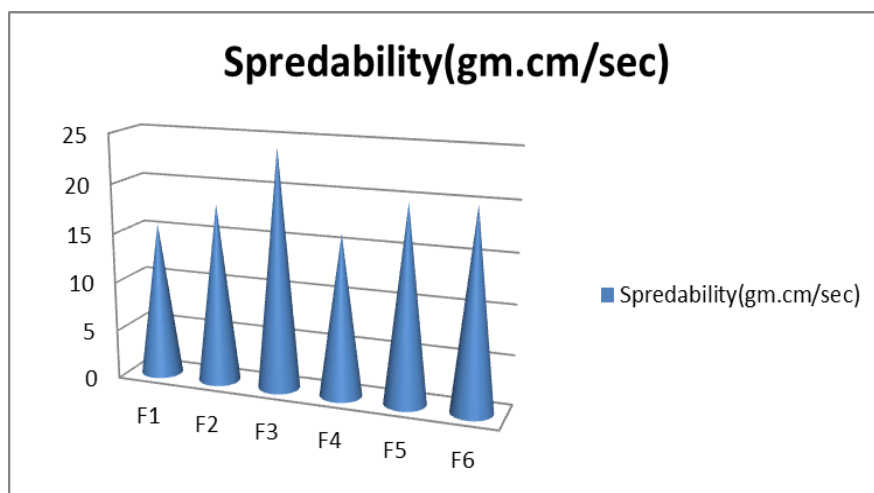
4.2. RHEOLOGICAL STUDY

| Formulations | Viscosity(Cps) |
|--------------|----------------|
| F1 | 1935 |
| F2 | 2435 |
| F3 | 3214 |
| F4 | 1833 |
| F5 | 2100 |
| F6 | 2452 |



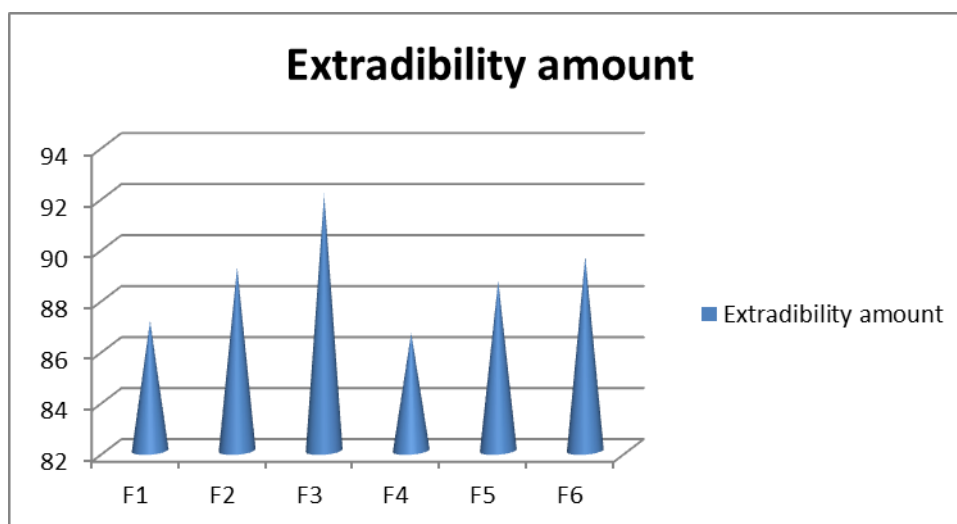
4.3. SPREADABILITY OF ALL FORMULATIONS

| Formulations | Spredability(gm.cm/sec) |
|--------------|-------------------------|
| F1 | 15.65 |
| F2 | 18.12 |
| F3 | 24.14 |
| F4 | 16.22 |
| F5 | 19.75 |
| F6 | 20.02 |



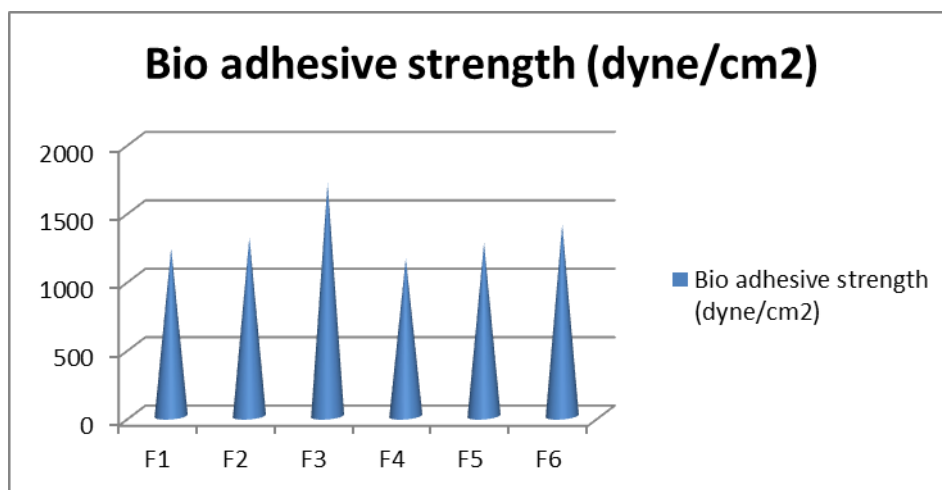
4.4. EXTRUDABILITY OF ALL FORMULATIONS

| Formulations | Wt of the formulation | Wt of the grams extruded | Extradibility amount |
|--------------|-----------------------|--------------------------|----------------------|
| F1 | 16.65 | 14.50 | 87.08 |
| F2 | 17.05 | 15.21 | 89.20 |
| F3 | 17.65 | 16.25 | 92.06 |
| F4 | 17.56 | 15.21 | 86.61 |
| F5 | 17.82 | 15.80 | 88.66 |
| F6 | 16.85 | 15.10 | 89.61 |



4.5. IN VITRO EVALUATION PARAMETERS

| Formulations | Bio adhesive strength (dyne/cm ²) |
|--------------|---|
| F1 | 1225 |
| F2 | 1306 |
| F3 | 1704 |
| F4 | 1152 |
| F5 | 1264 |
| F6 | 1400 |



5. SUMMARY AND CONCLUSION

- Herbal formulations have growing demand in the world market as natural products are more acceptable in the belief that they are safer than synthetic one. It is very good attempt to establish the herbal gel containing aqueous extracts of Guava, Neem, Tulasi leaves. The plants have been reported in literature having good anti-ulcers, antibacterial, anti-inflammatory, anti oxidant activity.
- The physical compatibility studies suggest that polymers selected i.e. Carbopol 940, Guar gum were found to be compatible with drug extract.
- All the formulations were evaluated by determining various parameters like Physical appearance, pH, Rheological studies, Spreadability, Extrudability etc.
- However, the Carbopol 940 based F3 Herbal gel proved to be the formula of choice, since it showed the highest percentage of good spreadability, extrudability, and rheological properties. Formulation F3 with 1 % leaves extract herbal gel showed the best formulation. The prepared F3 Herbal gel having good appearance, good effective in nature.

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