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Original Research Article

Formulation and evaluation of herbal gel for management of mouth ulcers

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ABSTRACT

Background: Aphthous stomatitis or mouth ulcers is the most common condition that we encounter. Clinically the lesions are single or multiple superficial and deep sealed and are associated with microbial invasions.

Aim: This study was conducted with the aim of evaluating the effectiveness of herbal drugs for treatment of Aphthous stomatitis.

Materials and Methods: In the research work, mouth ulcer gels were formulated incorporating the ethanolic extracts of as *Aloe barbedensis*, *Ocimum tenuiflorum* and *Azadirachta indica* using carbopol 934 as the gelling agent. Seven batches were formulated by varying the concentration of the herbal ingredients (F1 to F7) The prepared formulations were evaluated for various parameters like physical appearance, pH, Spreadability, Homogeneity and antimicrobial activity against fungi and bacteria. The antimicrobial activity was also compared with a marketed gel formulation.

Results and Discussion: All the prepared formulation using different concentration of plant extract showed the pH values in between 6.1 ± 0.2 to 7.0 ± 0.1 . The spreadability values ranged between the 5.0 to 8.0 cm. Out of all the formulations, formulation F7 containing all the three herbal extracts showed a good spreadability and very promising antimicrobial activity comparable with a marketed gel.

Conclusion: Thus stable, effective gels containing herbal ingredients for management of mouth ulcers can be developed.

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1. Introduction

Aphthous stomatitis or mouth ulcer is an ulcerative condition that is related to the oral mucosa and is characterised by repeating ulcers in the throat and oral cavity.¹ Mouth ulcers are usually generated by a number of causes, such as biting the inner layer of cheek, food allergies, hard teeth brushing, hormonal changes, vitamin deficiencies, bacterial infection and diseases.² Treatment of mouth ulcers may include soothing/ antiseptic mouthwashes, such as chlorhexidine mouthwash or povidone iodine mouthwash or use of antibiotic or anaesthetic gel formulations³

Semi-solid formulations include gel having a liquid phase which are then thickened by other components. Topical gels are intended for the application on skin or to certain mucosal surfaces for local action or percutaneous penetration of medicament preparations.⁴ A large number of Indian medicinal plants are attributed with various pharmacological activities as they contain diversified classes of phytochemicals. As the conventional synthetic drugs suffer from a numerous side effects, these herbal ingredients provide a good alternative.⁵

Leaves of *Aloe barbedensis* commonly called as aloe vera, belonging to family Asphodelaceae, are very commonly used in skin care products. They are rich in phytoconstituents such as aminoacids, anthraquinones,

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Fig. 1: Aphthous stomatitis

enzymes, hormones, lignin, minerals, salicylic acid, saponins, sterols, sugars, vitamins. The mechanism involved in production of antiulcer activity of the plant is due to its antioxidant, anti-inflammatory, mucus secreting, cytoprotective or healing activities. Reported pharmacological activities of the plant are hypoglycemic, hypolipidemic, woundhealing, immunomodulatory, antifungal and hepatoprotective. It is traditionally used for mouth ulcer treatment.⁶ Leaves of *Azadirachta indica*, commonly called as neem, belonging to family Meliaceae, are rich in several phytoconstituents such as nimbin, nimbidin, nimbolide, and limonoids, quercetin and sitosterols. They have very strong antibacterial, antifungal and anti-inflammatory activity⁷ and are quite commonly used for oral and dental treatments. Leaves of *Ocimum tenuiflorum*, called as tulsi, belonging to family Lamiaceae, is a common herb known for its wide variety of pharmacological activities such as antimicrobial, anti-oxidant, anti-inflammatory, analgesic, antipyretic, immunomodulatory, hepatoprotective and neuroprotective effects. Pharmacological activities of *Ocimum tenuiflorum* could be attributed due to the presence of the phytoconstituents such as eugenol, methyl eugenol, carvacrol, sesquiterpine, apigenin, luteolin, and ursolic acid.⁸ Thus in the present research work, the ethanolic extracts of these plants have been incorporated in gel formulations which could be used for the management of mouth ulcers, a condition that is associated with microbial invasion.

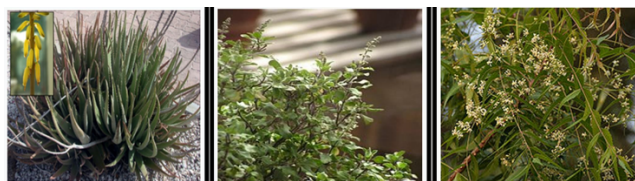


Fig. 2: Leaves of aloe barbadensis, ocimum tenuiflorum and azadirachta indica

2. Materials and Methods

2.1. Collection of materials

The leaves of *Azadirachta indica*, *Ocimum tenuiflorum*, *Aloe barbadensis* were collected from the medicinal garden and authenticated from Department of Botany, RTMNU, Nagpur. Carbopol 934 was procured from Colorcon, Asia. All the other solvents were of analytical grade.

2.2. Preparation of extracts

The juice of Aloe leaves was macerated with ethanol 95% for 3 days and separated by centrifugation at 3000 rpm to obtain the ethanolic extract of aloe (EEA). The leaves of *Azadirachta indica* and *Ocimum tenuiflorum* were dried to retain the phytoconstituents and macerated separately with ethanol and separated by centrifugation to obtain ethanolic extract of *Ocimum tenuiflorum* (EEO) and ethanolic extract of *Azadirachta indica* (EEZ) respectively. All the extracts were stored at room temperature.

2.3. Phytochemical screening

All the above prepared extracts were subjected to preliminary phytochemical screening tests^{9,10} to identify the presence of various components, by using different tests and reagents.

2.4. Formulation of gel

A sufficient amount of Carbopol 934 was soaked in distilled water overnight, and then mixed with distilled water with continuous stirring using a mechanical stirrer.¹¹ Another solution containing varying concentrations of EEA, EEO and EEZ and the required quantity of methyl paraben and propyl paraben were added with continuous stirring. Propylene glycol was also added to the solution. This prepared solution was further mixed with Carbopol 934 solution thoroughly with continuous stirring, volume was made up to 30ml with water and the pH was adjusted by addition of triethanolamine to obtain gel of required consistency. Seven formulations (F1 to F7) of the herbal gel were prepared.

3. Evaluation of Gel¹¹⁻¹⁴

3.1. Visual appearance

The prepared gels were tested for color, clarity, texture, transparency and presence of any gritty particles.

3.2. Measurement of pH

The pH of herbal gel formulations were determined by using digital pH meter. 1 gm of gel was taken and dispersed in 10 ml of distilled water and kept 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.

3.3. 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 agglomerates.

3.4. Spreadability

Spreadability is expressed in terms of time in seconds taken by two slides to slip off from gel that is placed in between the slides under the direction of certain load. If the time taken for separation of two slides is less then better the spreadability. Spreadability is calculated by using the formula:

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

Where M = weight tied to upper slide

L = length of glass slides

T = time taken to separate the slides

Spreadability of gel formulations were reported in Table 3.

3.5. Viscosity

The viscosity of all the prepared formulations were analysed by the Brookfields viscometer LVDVE with helipath , using spindle number 96 at 10 rpm. The results are shown in Table 3.

3.6. Antimicrobial activity

The antimicrobial activity of all seven gel formulations and a marketed moth ulcer gel (Hiora gel) was carried out by well diffusion method.¹⁵ Two microbial cultures *Candida Albicans* (fungi) and *E-coli* (bacteria) were used.

The antibacterial activity of the prepared gel formulations was performed by agar well diffusion method. The plates of the nutrient agar media were prepared. Each plate was inoculated with an aliquot (0.1 ml) of the bacterial suspension which was spread evenly on the surface of the medium of the plate. After 15 min, wells with 6 mm diameter were made with the help of a sterile cork borer in the solid medium and filled with 0.5g of gel. All the plates were incubated at 37 °C for 24 h. The antibacterial activity was assessed by measuring the diameter of the zone of inhibition (ZOI) in mm. Triplicates were carried out for each extract against each of the test organism. For the antifungal activity, the plates of the sabouraud dextrose agar media were prepared. Each plate was inoculated with an aliquot (0.1 ml) of the fungal suspension which was spread evenly on the solid media. After 15 min, the wells with 6 mm diameter were made by using sterile cork borer and filled with 0.5g of gel formulations. All the plates were incubated at 27 °C for 5-7 d and then the diameter of the

zone of inhibition was recorded. Triplicates were carried out for each extract against each of the test organism

4. Result and Discussion

4.1. Collection and authentication of plant

The collected leaves of *Azadirachta indica*, *Ocimum tenuiflorum*, *Aloe barbadensis* were identified and authenticated by Dr N.M. Dongarwar Department of Botany, authentication number 10330,10332and 10333 respectively.

4.2. Phytochemical screening

The preliminary quantitative phytochemical investigations of plant extracts are as shown in Table 1

Thus, the three extracts contain varied types of phytoconstituents which might be responsible for their antimicrobial activity.

4.3. Formulation of herbal gel

Seven formulations of herbal gels were formulated by varying the herbal ingredients in each of the formulation as shown in Table 2

4.4. Evaluation of gel

All the prepared gel formulations were evaluated for parameters such as physical appearance, pH, homogeneity, spread ability and viscosity.

The observation reveals that the gels were having smooth texture and were elegant in appearance. The pH of all prepared gels was found to be in range of 6.5-7.0. All the gels showed good spreadability. Also from the above data it was observed that increase the concentration of plant extract increases the spreadability. All the prepared gels showed good homogeneity with absence of lumps. The developed preparations were much clear and transparent. The viscosity of all the developed gels was found to be excellent and with in the range. The results are shown in Table 3.

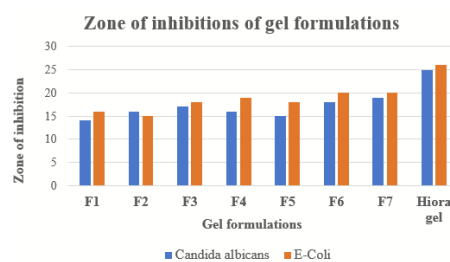


Fig. 3: Antimicrobial activity of gel formulations

Table 1: Phytochemical Investigation of extracts.

S.no	Phytochemical constituents	Aloe barbadensis (EEA)	Azadirachta indica (EEZ)	Ocimum tenuiflorum (EEO)
1.	Carbohydrates	-	-	-
2.	Proteins	+	-	-
3.	Amino acids	+	-	-
4.	Glycosides	-	-	+
5.	Flavonoids	-	+	+
6.	Alkaloids	-	+	+
7.	Tannins	-	+	+
8.	Saponins	+	+	+
9.	Phenolic compounds	+	+	+
10.	Steroids	+	+	+

+ Present - absent

Table 2: Formulation of herbal gels

S.No	Ingredients	F1	F2	F3	F4	F5	F6	F7
1.	EEA(ml)	4	-	-	4	4	-	4
2.	EEZ (ml)	-	3	-	3	-	3	3
3.	EEO (ml)	-	-	3	-	3	3	3
4.	Carbopol 934 (g)	20	20	20	20	20	20	20
5.	Methyl paraben (g)	0.2	0.2	0.2	0.2	0.2	0.2	0.2
6.	Propyl paraben (g)	0.1	0.1	0.1	0.1	0.1	0.1	0.1
7.	Propylene glycol (ml)	2	2	2	2	2	2	2
8.	Water (ml) upto	30	30	30	30	30	30	30

Table 3: Various parameters of prepared gel formulations

Formulation	Physical appearance			pH	Homogeneity	Spreadability (g.cm/sec)	Viscosity (cps)
	Colour	Texture	Clarity				
F1	Green	Smooth	Clear	6.20±0.04	Homogenous	6.35±1.96	135000±2.00
F2	Greenish brown	Smooth	Clear	6.84±0.08	Homogenous	6.95±2.31	128900 ±1.96
F3	Slightly yellow	Smooth	Clear	6.80 ±0.05	Homogenous	7.12±1.87	195400 ±2.31
F4	Greenish brown	Smooth	Clear	7.00 ±0.09	Homogenous	7.21±1.45	185400±1.65
F5	Green	Smooth	Clear	6.87±1.10	Homogenous	7.53±1.79	205000±1.85
F6	Green	Smooth	Clear	6.72 ±0.02	Homogenous	7.97±2.32	198500±1.78
F7	Greenish brown	Smooth	Clear	6.77±0.03	Homogenous	8.17±2.38	195500±1.23

Data represented± S.D (n=3)

4.5. Antimicrobial activity

The antimicrobial activity was studied using the well diffusion method. Out of all the formulations, F7 gel containing the all the three ethanolic extracts showed the highest zone of inhibition and it was comparable with the marketed Hiora gel formulation, both against *C. albicans* and *E. coli*. The result is shown in Figure 3.

5. Conclusions

Nowadays there is a lot of demand for herbal formulations in the market due to their cost effectivity and absence of

any side effects. From the above experimental data it is clear that a gel formulation with herbal ingredients such as aloe, neem and tulsi has good characteristics, viscosity and also possesses a good antimicrobial activity which is necessary in the management of mouth ulcers.

6. Source of Funding

None.

7. Conflict of interest

None.

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