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Original Research Article

FORMULATION & EVALUATION OF THE HERBAL ORAL DISSOLVING FILM FOR TREATMENT OF RECURRENT APHTHOUS STOMATITIS

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ABSTRACT:
In this present study herbal oral dissolving film prepared for mouth ulcer treatment. Use of herbal drugs minimizes the side effect which is caused due to synthetic drugs as they absorb from oral mucosa and directly enter in blood circulation. Formulated herbal oral dissolving films contain herbal plants extract and powders of Ocimum tenuiflorum (tulasi), Azadiracta indica (neem), Syzygium aromaticum (lavanga), Boerhaavia diffusa (punarnava), Glycyrrhiza glabra (yastimadhu), Jasminum grandiflorum (jasmine), (triphala). These plants possess antiulcer, astringent, antimicrobial and anti-inflammatory activity. HPMC and ethyl cellulose for the formulation of the films suitable polymers and plasticizers are selected. The films were subjected to physical investigations such as uniformity of thickness, weight, drug content, folding endurance, tensile strength, surface pH. Also evaluation of the films is done by using parameter like disintegration time, % moisture absorption, % moisture loss, surface pH, swelling index etc. The obtained results for prepared herbal films indicate that was higher for those formulations containing higher percentage of HPMC. these films are economic, convenient and dose not show any side effects.
Keywords: Herbal oral dissolving film, Mouth Ulcer, Ulcer Treatment

INTRODUCTION

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. [1]

A side effect is basically an unintended occurrence that results from taking a drug. All drugs that come in the market cause side effects, where many are minor and few are serious (Table No. 1).

The main objective of the present study is to formulate herbal mouth dissolving filmss, by preparing this herbal filmss; side effects can be minimized.

Ocimum basilicum (Tulasi) Studies indicate Ocimum basilicum to possess analgesic, anti inflammatory, antimicrobial, antioxidant, anti ulcerogenic.[3] Chewing of Tulsi leaves also cures ulcers and infections of mouth.[4]

Azadirachta indica (Neem) having Anti-inflammatory, Antifungal and Antibacterial, which helps heal mouth ulcers. [5]

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Table No. 1. Pharmacotherapies used in Aphthous Stomatitis[2]

Drug type	Intended action	Example(s)
Topical covering agents / barriers	Reduce pain	Orabase (often combined with triamcinolone).
Topical analgesics /anesthetics / anti-inflammatory agents	Reduce pain	Benzydamine hydrochloride mouthwash or spray, Amlexanox paste, viscous lidocaine, diclofenac in hyaluronan.
Topical antiseptics	Hasten healing (prevent secondary infection)	Doxycycline, tetracycline, minocycline, chlorhexidine gluconate, triclosan.
Topical mild potencycorticosteroids	Reduce inflammation	Hydrocortisone sodium succinate.
Topical moderate potencycorticosteroids	Reduce inflammation	Beclomethasone dipropionate aerosol, fluocinonide, clobetasol, betamethasone sodium phosphate, dexamethasone.
Orally administered drugs	Various, mostly modulating immune response	Prednisolone, colchicine, pentoxifylline, azathioprine, thalidomide,[dapsone, mycophenolate mofetil, adalimumab, vitamin B12, Clofazimine, Levamisole, Montelukast, Sulodexide, levamisole

Glycyrrhiza glabra (Yastimadhu) constituents are having effect on both the oral microbial pathogens and the host immune response involved in common ora-dental diseases (dental caries, periodontitis, candidiasis, and recurrent aphthous ulcers). [6]

Pharmacological studies have demonstrated that *Boerhaavia diffusa* (Punarnava) possesses punarnavoside, which exhibits a wide range of properties – diuretic; anti-inflammatory and antibacterial activity. [7, 8]

Syzygium aromaticum (Lavanga) in addition to its antimicrobial, antioxidant, antifungal and antiviral activity, clove essential oil possesses antiinflammatory, cytotoxic, insect repellent and anaesthetic properties. [9, 10]

An Indian ayurvedic herbal formulation, Triphala at both the dose levels produced excellent analgesic and antipyretic effect, with the absence of gastric damage. [11].

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The methanolic extract of *J. grandiflorum* leaf (jati) improves the rate of wound healing by enhancing the rate of collagen synthesis and also by improving the antioxidant status in the newly synthesised healing wound tissue.[12]

Oral Dissolving Film is a very thin oral strip, to be placed on the tongue or any part of oral mucosal membrane; the film rapidly hydrates by saliva and adheres onto the site of application. Mouth dissolving films rapidly disintegrates and dissolves to release the medication for oromucosal and intragastric absorption. [13]

MATERIAL & EQUIPMENTS:

Ethyl cellulose, Hydroxylpropylmethyl cellulose, Propylene glycol, Dichloromethane, Carbopol 934 and Cross carmellose sodium were obtained from Research lab fine chem. Industries,Mumbai. All other chemicals were of pharmacopoeial grade. Double distilled water was used whenever required. *Ocimum basilicum* (Tulasi), *Azadirachta indica* (Neem), *Glycyrrhiza glabra* (Yastimadhu), *Boerhaavia diffusa* (Punarnava), *Syzygium aromaticum* (Lavanga), Triphla and *Jasminum grandiflorum* (jati) powder were obtained from Himalaya Pure Harbs.

EXPERIMENTAL:

Formulation of Herbal Films:

Powders of herbal drugs were weighted (Table No. 2) and mixed in mortar. Films were prepared by the solvent casting method using EC and HPMC in the ratios of 1:0.5, 1:1 and 0.5: 1. Higher levels of EC gave films which could not be removed from the Petri dish. Propylene glycol was used as the plasticizer. Herbal plant extracts as herbal drug was dissolved in 10 ml of ethanol. EC was then added to this solution and stirred till dissolved. To this solution, 8 ml of dichloromethane was added, followed by the HPMC. The mixture was constantly stirred on a magnetic stirrer until the polymers had completely gone into solution and a clear gel was obtained. Propylene glycol was mixed and the volume was adjusted to 20 ml with alcohol. The vessel was closed and kept aside for a few hours until all the entrapped air had escaped. The solution was then cast into a glass Petri dish of 9 cm diameter and allowed to dry overnight at room temperature. The films were removed carefully and circular films of 15mm diameter were punched out so that each films contained 10 mg of the herbal drug(Table No.2). The samples were packed in aluminium foil and stored in a glass container maintained at room temperature. This condition maintained the integrity and elasticity of the films [14].

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Table No.2: Content of 0.36 gm herbal drug[15]

Sr. No.	Name of plant extract	Weight(gm)
1.	*Ocimum basilicum* (Tulasi)	0.041
2.	*Azadirachta indica* (Neem)	0.030
3.	*Glycyrrhiza glabra* (Yastimadhu)	0.057
4.	*Boerhaavia diffusa* (Punarnava)	0.0432
5.	*Syzygium aromaticum* (Lavanga)	0.036
6.	Triphla	0.0432
7.	*Jasminum grandiflorum* (jati)	0.14

By taking various concentrations of polymers following film formulations are made and F1, F2 , F3, F4 ,F5, F6 numbers are given which are shown in Table No. 3

Table No.3: composition of films

Ingredients	F1	F2	F3	F4	F5	F6
Herbal drug	o.36gm	0.36gm	0.36gm	0.36gm	0.36gm	0.36gm
Ethyl cellulose	0.5 gm	0.75gm	-	o.25gm	0.25gm	-
Hydroxypropylmethylcellulose	0.25gm	0.25gm	0.75gm	0.75gm	o.5gm	0.75gm
Carbopol934	-		0.25gm	-	-	0.25gm
Dicloromethane	8 ml	8 ml	8 ml	8 ml	8 ml	8 ml
Propyleneglycol	1 ml	1ml	1ml	1ml	1ml	1ml
Ethanol	20ml	20ml	20ml	20ml	20ml	20ml
Cross carmulose	-	-	-	0.0072gm	-	0.0072gm

Evaluation Herbal Films [16, 17]:

1. Weight of film:

Herbal Films were weighed on analytical balance and average weight can be determined for each film. It is desirable that films should have nearly constant weight.

2. Thickness:

It can be measured by micrometer screw gauge at different strategic locations.

3. Folding endurance:

Folding endurance is determined by repeated folding of the strip at the same place till the strip breaks. The number of times the film is folded without breaking is computed as the folding endurance value.

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4. Surface pH of film:

Surface pH of the films is determined by placing the film on the surface of 1.5% w/v agar gel followed by placing pH paper (pH range 1-11) on films. The change in the colour of pH paper is observed and reported.

5. In vitro disintegration studies:

The film as per the dimensions (3 × 2 cm) required for dose delivery was placed on a stainless steel wire mesh placed in a petridish containing 10 ml phosphate buffer pH 6.8. Time required for the film to break was noted as in vitrodisintegration time.

6. Percent moisture absorption:

The PMA test was carried out to check the physical stability of the mouth dissolving film at high humid conditions. Three films were taken, weighed accurately and placed in a desiccator containing saturated solution of aluminumchloride, keeping the humidity inside the desiccators at 79.5 %. After 72 hours the films were removed, weighed and percentage moisture absorption was calculated by using the following formula: PMA = (Final weight – Initial weight) x 100

7. Percent moistire loss:

Percentage moisture loss was calculated to check the integrity of films at dry condition. Three 1cm square films was cut out and weighed accurately and kept in desiccators containing fused anhydrous calcium chloride. After 72 hours the films were removed and weighed. The percentage moisture loss was calculated by using formula :

PML= (Initial weight – Final weight) x100

8. Swelling Percentage (% S):

A drug loaded film was placed in a beaker and 50 ml of phosphate buffer (pH 6.8) was poured into the beaker .An increase in the weight of the film was noted after every 15 minutes for 60 minutes[18]. The swelling percentage was calculated by using the following formula :

$$\% S = (Xt - X0) \times 100$$

Where, % S - swelling percentage, Xt –the weight of swollen film after time t, X0 - weight of film at zero time .

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RESULT & DISCUSSION

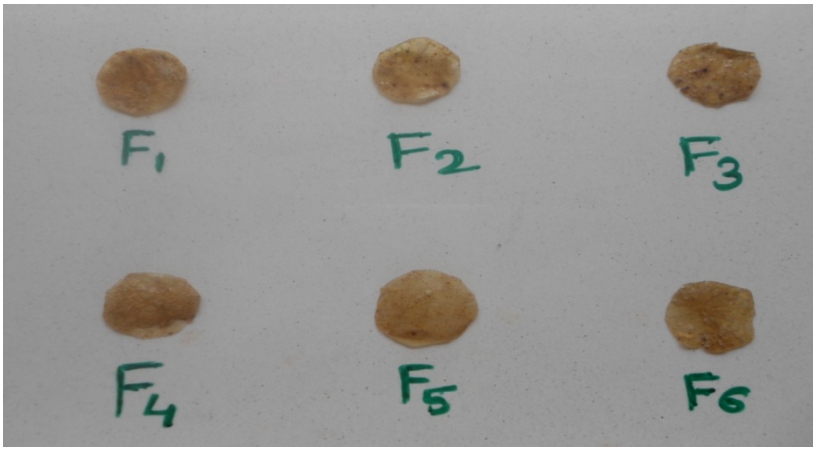

Fig No.1: Formulated films

Table No. 4: weight, Thikness, Folding endurance, Surface pH of the films

Patch no.	Weight(gm)	Thickness(mm)	Folding endurance	Surface pH
F 1	0.0400	0.31	>300	6.5 ± 0.14
F2	0.0450	0.32	>300	6.5 ± o.15
F3	0.0704	0.32	>300	6.6 ± 0.21
F4	0.0578	0.6	>300	6.3 ± 0.18
F5	0.063	0.28	>300	6.2 ± 0.22
F6	0.0663	0.43	>300	6.4 ± 0.13

As the thickness of Herbal Films is directly concerned with drug content uniformity so it is necessary to ascertain uniformity in the thickness of the film.

Films F1, F2 with higher percentage of EC could not be prepared since they could not be removed easily from the Petri dish in which they were cast and tended to fragment.

From the results of the tests for physical characterization conducted, it is observed that the weight and thickness of all film samples was uniform within each formulation. Films formulated from EC were smooth. All film formulations exhibited good folding endurance exceeding 300, indicating that they are tough and flexible.

If Surface pH is acidic or alkaline pH of administered dosage forms can irritate the buccal mucosa. The measured surface pH was found to be close to neutral in all the formulations which means that they have less potential to irritate the buccal mucosa and therefore they should be fairly comfortable

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Table No.5: Swelling Percentage (% S), Disintegration time, %, moisture absorption, % moisture loss

Patch no	Swelling index	Disintegration time (min)	% moisture absorption	% moisture loss
F1	4	18	0.03	1.87
F2	8.9	20.3	0.5	1.42
F3	32	13.25	0.78	0.54
F4	20.62	5.47	0.93	1.06
F5	8.18	8.15	1.02	1.62
F6	26	7.70	0.66	2.97

The measurement of Swelling Index (Table No.5)indicates that maximum swelling takes place in the formulations containing higher proportions of HPMC namely F3, F4 and F6 and the least in those containing higher proportions of ethyl cellulose which is water insoluble and less hydrophilic and therefore subject to lesser swelling upon hydration.

It was also observed that films containing the hydrophilic polymers disintegrated very fast. The presence of the hydrophilic polymer, HPMC seems to increase the surface wettability and swelling of the films. Time required for films containing high amount of HPMC polymer & *croscarmellose* sodium is around 5.47minutes where as time for films containing EC polymer is more than 7.70 minutes.

9. CONCLUSION:

The result of the present study indicates that the herbal films can be formulated by using polymers like HPMC,EC, Carbopol 934 in ratio used in patch F3, F4, F6. We can use cross carmelose as superdisintegrant. By evaluation study we can conclude that these three films having disintegration time within 15 minutes. So they can adhere to mucosa and shows effects. Side effects of synthetic drugs are avoided by use of herbal drugs. As film contain herbal drugs, gives no side effects of drug even after absorption from mucosal membrane.

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