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DEVELOPMENT AND EVALUATION OF ORAL FILM OF HERBAL EXTRACTS OF *PIPER BETEL* AND *FOENICULUM OFFICINALIS*

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ABSTRACT

Oral dissolving drug delivery system offers a solution for those patients having difficulty in swallowing tablets/capsules, etc. This work investigates the possibility of developing *Piper betel* and *Foeniculum officinalis* oral dissolving films allowing fast, reproducible dissolution in oral cavity; thus bypassing first pass metabolism. The oral dissolving films were prepared by solvent-casting method. HPMC for the formulation of the films is suitable polymer and plasticizers are selected. The films were subjected to physical investigations such as uniformity of weight, folding endurance, surface pH. Also evaluation of the films is done by using parameter like thickness, weight uniformity, folding endurance, percentage of moisture content, drug content analysis, disintegration time and *in-vitro* dissolution studies. The obtained results for prepared herbal films disintegrate within 1 minute. The formulation F-3 resulted into excellent palatability along with least disintegrating time and found to be stable when compared with other formulations. So, it was concluded that formulation F-3 is the best film forming as well as stable polymer with respect to *Piper betel* and *Foeniculum officinalis* oral dissolving film.

Keywords: Film-forming polymers, Oral thin films, Solvent-casting method, *Piper betel*, *Foeniculum officinalis.*

INTRODUCTION

Development of herbal medicines in novel drug delivery systems is the need of hour. This approach is an interesting blend of therapeutic effectiveness of herbal medicines and advantages of novel drug delivery systems. This increases the patient compliance for the useful herbal drugs, which generally are free from side effects. From past one decade, there has been an enhanced demand for more patient-friendly and compliant dosage forms. As a result, the demand for developing new technologies has been increased greatly. Oral dissolving films (ODF) are the latest development in this field. ODFs are the ultrathin films of postage stamp size with an active agent or active pharmaceutical ingredient and other excipients.[1] These dosage forms can rapidly disintegrate and/ or dissolve to release the medicament as soon as they come in contact with saliva thus obviating the need for water during administration, an attribute that makes them highly attractive for pediatric and geriatric patients.[2] ODFs provide accurate

dosing in safe and efficacious format, without the need of measuring devices as is the case with liquid oral dosage forms.

Piper betel commonly known as 'Paan' or 'Nagvalli' (family-Piperaceae) is an evergreen and perennial creeper [3] Significance of leaves has been explained in relationship to every sphere of human life including social, culture, religious and is very much relevant even in modern days. [4] *Foeniculum vulgare* Mill is a medicinal plant belonging to the Umbelliferae (Apiaceae) family, known and used by humans since antiquity, due to its flavor. [5] It was cultivated in almost every country. [6] It is universally known as Fennel and is known by more than 100 names. It is a traditional and popular herb with a long history of use as a medicine.

There are no ODF of *Piper betel* and *Foeniculum officinalis* in the market. Hence, there is a need to develop the same. The aim of present invention is to formulate and develop ODFs of *Piper betel* and *Foeniculum officinalis*. The ODFs were formulated using film-forming agents hydroxypropyl methylcellulose (HPMC). HPMC is known for its good film-forming properties and has excellent acceptability.

Materials and methods

Plant material collection

The plants *Piper betel* Linn and *Foeniculum officinalis* were collected from local area of Bhopal (M.P.) in the month of Oct, 2017.

Storage

Drying of fresh plant parts was carried out in sun but under the shade. Dried *Piper betel* Linn and *Foeniculum officinalis* were preserved in plastic bags and closed tightly and powdered as per the requirements.

Defatting and extraction of plant material

Piper betel Linn and *Foeniculum officinalis* were shade dried at room temperature. The shade dried plant material was coarsely powdered and subjected to extraction with petroleum ether by maceration. The extraction was continued till the defatting of the material had taken place. Dried powdered *Piper betel* Linn and *Foeniculum officinalis* has been extracted with hydroalcoholic solvent using maceration process for 48 hrs, filtered and dried using vaccum evaporator at 40 ºC.

Formulation development of fast dissolving oral film of *Piper betel* and *Foeniculum officinalis*

Casting process of fast disintegrating oral film

Various methods are available for casting of oral films (OF). On the laboratory scale solvent casting technique was adopted though so far has cast the fast denigrating oral films.[7-9]

Solvent casting technique

The OF is preferably formulated using the solvent casting method, where by the water-soluble ingredients are dissolved to form a clear viscous solution. The API and other agents are dissolved in smaller amounts of the solution and combined with the bulk. This mixture is then added to the aqueous viscous solution. The entrapped air is removed by vacuum. The resulting solution is cast as a film and allowed to dry, which is then cut into pieces of the desired size. [10]

Selection and optimization of film forming agents

Two film forming agents and one co-film forming were selected for this research work. The concentration of film forming was important to form a proper thickness for appropriate packaging and handling of oral films. Concentration of film forming agent is optimized on the basis of thickness and appearance of film.

Table 1: Selection and optimization of formulation

Name of ingredients	F1	F2	F3	F4	F5	F6	F7	F8	F9
Piper betel	50	50	50	50	50	50	50	50	50
Foeniculum officinalis	50	50	50	50	50	50	50	50	50
HPMC	200	200	200	200	200	200	200	200	200
SSG	50	60	70						
CS	-	-	-	50	60	70	-	-	-
CP	-	-	-	-	-	-	50	60	70
Citric acid	10	10	10	10	10	10	10	10	10
Glycerin	qs	qs	qs	qs	qs	qs	qs	qs	qs
PEG-600	qs	qs	qs	qs	qs	qs	qs	qs	qs
DM water qs to	20	20	20	20	20	20	20	20	20

Selection and optimization of plasticizer

Two film plasticizer and one co- plasticizer were selected for this research work. The concentration of plasticizer was important to tensile strength percentage elongation and folding endurance of film. Concentration of plasticizer optimized on the basis of tensile strength percentage elongation and folding endurance of film.

Optimized formulation

Table 2: Optimized formulation

Name of Ingredients	Composition
Piper betel	50
Foeniculum officinalis	50
HPMC	200
PEG-400	0.5
SSG	70
Citric Acid	10
DM Water qs to	20 ml

Thickness

The thickness of patches was measured at three different places using an absolute outside micrometer.

Weight uniformity

For each formulation, three randomly selected patches were used. For weight variation test, 3 films from each batch were weighed individually by digital electronic balance and the average weight was calculated.

The tensile testing gives an indication of the strength and elasticity of the film, reflected by the parameters- tensile strength, elastic modulus, % strain, and load at yield.

Folding endurance

This was determined by repeatedly folding one film at the same place until it broke. The number of times the film could be folded at the same place without breaking / cracking gave the value of folding endurance. [11]

Percentage of moisture content

The films were weighed individually and kept in desiccators containing activated silica at room temperature for 24 hrs. Individual films were weighed repeatedly until they showed a constant weight.

The percentage of moisture content was calculated as the difference between initial and final weight with respect to final weight.

Drug content analysis

The patches (n = 3) of specified area were taken into a 10 ml volumetric flask and dissolved I in methanol and volume was made up with 10 ml methanol. Subsequent dilutions were made and analyzed by UV spectrophotometer.

Disintegrating time

The most important criteria of present work are to that dosage form should be dissolved within few seconds. The incorporation of super disintegrating agent to minimizes the disintegrating time. Three super disintegrating agent were selected for this work. [12-15]

Results and discussion

Determination of visual appearance thickness and weight of all the formulations are shown in Table 3. Visual appearance of all films was found to be translucent and free of air bubbles, which is necessary for aesthetic appeal.

Table 3: Formulation development

Formulation code	General Appearance	Thickness in µm	Weight mg
F1	TL	36.21	41.25
F2	TL	38.21	41.50
F3	TL	38.51	41.60
F4	TL	38.61	41.80
F5	TL	38.95	41.95
F6	TL	40.12	42.00
F7	TL	40.53	42.15
F8	TL	40.73	42.45
F9	TL	40.90	42.56

*TP – Transparent, TL - Translucent

The difference in the thickness of these formulations might be due to the different concentration of the polymers which were used to formulate the films. Batch F3 seems to produce desired thickness and weight to produce about 120 mg of prochlorperazine maleate film. The batch was found transparent too. Disintegration time of this batch also suitable fast disintegration oral film aimed about 25 sec.

Table 4: Result of folding endurance, tensile strength & percentage elongation

Formulation code	Folding endurance	Tensile strength in Kg/cm^2Kg	Disintegrating time (sec.)
F1	150±35	0.589	62
F2	165±32	0.519	55
F3	175±22	0.592	45
F4	181±56	0.574	49
F5	158±14	0.582	62
F6	165±22	0.567	65
F7	168±12	0.592	58
F8	156±23	0.569	52
F9	180.54	0.595	62

The mechanical properties of the film give idea about to what extent the film can withstand the force or stress during processing, packaging, transport and handling. The desirable characteristics of film are moderate tensile strength, low elastic modulus, high% strain and high load at yield. From the above table, the polymer should give soft but tough film.

Hence batch no F3 were optimized with selection of PEG-400 due to better tensile strengths high flexibility (folding endurance)

The most important criteria of present work are to that dosage form should be dissolved within few seconds. The incorporation of super disintegrating agent to minimizes the disintegrating time. Three super disintegrating agent were selected for this work.

Table 6: Results of optimized formulation

F. code	Dis. Time	General appearance	Thickness in µm	Weight in mg	Folding endurance	Tensile strength in Kg/cm^{2}Kg	Drug Content
F3	4.5	Transparent	38.51	41.60	175±22	1.056	99.6±0.8

Herbal products may contain a single herb or combination of several different herbs believed to have complimentary or synergistic effects. Herbal products are sold either as raw plants or extracts of the portions of the plants. Fast disintegrating drug delivery is rapidly accepting new technology for quick dissolving or disintegrating the drug molecule/extract within few minutes. OFD are not well defined in the literature but, no doubt a revolutionary and an innovative drug delivery system for all the population groups, specifically geriatric, pediatric patients and patients with swallowing difficulties. OFD are also having great potential of delivering the medicinal agent systemically as well locally and have several advantages over many dosage forms even over the fast disintegrating formulations.

Conclusion

The mouth dissolving strips of herbal drugs was prepared by solvent casting method show acceptable mechanical proportional and satisfactory drug release within one minute. The result of the present studies indicate that herbal film can be formulated by using polymer like HPMC we can use SSG as super disintegrant. By evaluation studies we can conclude that the film having disintegration time within one minute they can adhere to mucosa and show therapeutic effect. 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. Among the prepared formulations, formulation F3 was found to have transparent visual appearance, best film forming capacity, least disintegration time and also found to be stable at accelerated stability studies.

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