



Research Article

Flash Dissolving Film of Domperidone for Motion Sickness using *Ocimum Basilicum* GumYOGESH S. THORAT^{1*}, VIPUL L. PULLI¹, AVINASH H. HOSMANI², VIVEKANAND G. KHYAMGONDE¹¹Department of Pharmaceutics, D.S.T.S. Mandal's College of Pharmacy, Solapur University, Solapur, Maharashtra, India 413004²Department of Pharmaceutics, Government College of Pharmacy, Ratnagiri, Maharashtra.**ARTICLE DETAILS***Article history:*

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ABSTRACT

The oral route is most popular route for the administration of therapeutic agents because of the low cost of therapy and ease of administration lead to high levels of patient compliance. In some cases such as motion sickness, sudden episode of allergic attack, fear of choking and an unavailability of water, the swallowing of tablet or capsules may become difficult. To overcome these difficulties, several fast-dissolving drug delivery systems have been developed. Oral fast dissolving film (FDF) rapidly dissolves on tongue releasing the medication readily available for absorption. Domperidone is widely used as antiemetic drug It is also effective in gastro paresis, pediatric gastro esophageal reflux (infant vomiting). In the current work, *Ocimum basilicum* Gum was employed as a superdisintegrant to assist the flash dissolution of the film. The film was formulated on Film Forming machine by solvent casting method. HPMC was also incorporated in the film for enhancing the properties of the film. The prepared film was evaluated for different parameters. All the formulations of FDF displayed optimum folding endurance above 100 folds. The results were found to be promising ensuring safe and effective dosage form. From the result obtained, it was concluded that the formulation of fast dissolving film has better physical chemical properties with good dissolution property.

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INTRODUCTION

In present time, various problems of pediatrics and geriatrics patients demand different benefits from dosage form. Similarly different diseases also need to be treated with some diverse formulation strategy to achieve enhanced therapeutic benefit as well as better patient compliance. The oral routes are most preferred route for drug delivery because of ease of handling versatility, ease of administration and invasive method. Motion sickness is one of the diseases making the patient very uncomfortable during travel. This would be the time in which patient will experience various difficulties to administer the conventional dosage form. Hence fast dissolving film can impart few advantages like ease of administration and possibility of administration without water^[1].

Buccal mucosa and sublingual region is highly vascularised which gives rapid absorption of drugs than oral route. Drugs that are absorbed through the buccal mucosa and sublingual route directly enter the systemic circulation bypassing the first-pass metabolism in the liver. The buccal mucosa provides a readily accessible route for transmucosal delivery. The film is prepared by using polymer and dissolves in the mouth within a few minutes. It was developed in the late in 1970 as an alternative to capsules, tablets and syrups for the patients who have difficulties in swallowing and chewing ^[2].

Domperidone is widely used as antiemetic drug acting by an inhibition of the dopaminergic receptor. Domperidone does not cross blood brain barrier. Domperidone is also effective in gastro paresis, pediatric gastro esophageal reflux (infant vomiting). It undergoes extensive gastric and hepatic first pass metabolism after oral dosing resulting in low bioavailability (15%) which therefore, may not minimize the rate of vomiting^[3, 4].

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O.basillicum is a readily available and economical material. *O.basillicum* readily dissolves in presence of a small quantity of water without any bad taste. Thus use of the gum can be done for fast disintegration of the film in saliva.

The objective of the present work was to formulate the flash dissolving film of Domperidone for effective treatment of motion sickness. An attempt of use of *O.basillicum* as a superdisintegrant was done in this study to explore the applicability of this naturally obtained and economical ingredient in the pharmaceutical field.

MATERIALS AND METHODS

Materials

Domperidone was kindly gifted by Vamsi Labs Ltd. MIDC, Solapur. HPMC K 100M was kindly gifted by Wockhart Pharmaceuticals, Aurangabad (India). Citric acid, Mannitol, Methanol, Propylene Glycol and other chemicals were of analytical reagent grade. Ocimum basilicum seeds were procured from local market.

Extraction of Mucilage from Ocimum basilicum seeds

Basil seeds were rinsed with water to remove foreign particles. Seeds were soaked in 50 parts of water for 30 minutes. The swollen seeds were subjected to high pressure using syringe to remove the mucilage. The same procedure was carried out for 4-5 times for complete extraction. The separated gel layer was collected and passed through a muslin cloth to remove unwanted particles. It was poured in Petri plates for complete drying. The dried powder was collected by scraping Petri plate with spatula or glass rod and stored in air-tight containers [1,2].

Preparation of Oral fast dissolving films:

The Fast dissolving Films were prepared by solvent casting technique^{5,6}. In the formulation of FDP, HPMC K100M was used as gelling agent along with basil gum as superdisintegrant. The formulation design also includes mannitol as sweetening agent and citric acid as saliva stimulating agent to aid the flash dissolution of the film. FDF was prepared by dissolving film forming HPMC K100M in the distilled water, then solution was continuously stirred up to an hour to above solution drug solution was added and kept for an hour to remove all the air bubbles entrapped. The formulation was casted on a suitable platform by using film forming machine

and dried to form a film. Then the film was carefully removed and cut into suitable size.

Table 1: Composition of Flash dissolving film

Sr. no	Ingredients	A	B	C
1	Domperidone	40 mg	40 mg	40 mg
2	Methanol	2 ml	2 ml	2 ml
3	HPMC K 100 M	100 mg	100 mg	200 mg
4	Propylene Glycol	0.5 ml	1 ml	2 ml
5	Mannitol	50 mg	50 mg	50 mg
6	Citric Acid	50 mg	50 mg	50 mg
7	Ocimum Basilicum Powder	40 mg	40 mg	40 mg
8	Distilled Water q.s.	20 ml	20 ml	20 ml

Evaluation of *O. basilicum* gum powder

O. basilicum gum powder was passed through standard sieve # 80 to measure bulk density, tapped density, Angle of Repose, Carr's Index (% Compressibility) and Hausner's Ratio by conventional methods [7,8]. Loss on drying of powder was also measured by observing the percent weight difference in initial and final weight of the sample occurred after the heating of sample to constant weight.

Evaluation of Flash dissolving film of Domperidone

a) Weight of Films [5-6,8-10]

It is desirable that films should have nearly constant weight. It is useful to ensure that a film contains the proper amount of excipients and API. Weights of 3 individual film diameters were taken. Oral fast dissolving films were weighed and average weight was determined for each film.

Thicknesses of Films

The thickness of the film was measured by digital micrometer screw gauge at five different places; an average of three values was calculated. This is essential to ascertain uniformity in the thickness of the film this is directly related to the accuracy of dose in the film.

pH value

The pH value was determined by dissolving film in 10 ml distilled water and the pH of the obtained solution was measured.

Folding Endurance

Folding endurance of the film is an essential parameter to ensure the elasticity of the film

during storage and handling. The folding endurance of the films was determined by repeatedly folding one film at the same place till it break. This is considered to reveal good film properties. A film (3 X 3 cm) was cut evenly and repeatedly folded at the same place till it breaks.

Percent moisture content

Films of various sizes were cut out and weighed accurately and kept in desiccators containing fused anhydrous Calcium chloride. After 24 h the film was removed and weighed.

Percent Elongation

Percent elongation was mainly based on tensile strength of films. The nature of polymers affects tensile strength and % elongation. Percent elongation was calculated by measuring the increase in length of film after tensile strength.

Drug Content

Drug content was determined by dissolving the film containing 2 mg of drug in 100 ml water to get 20 µg/ml solutions. An aliquot of 2ml sample was withdrawn and diluted to 10 ml with water. Then solution was filtered through Whatman filter paper and analyzed by UV-spectrophotometer at λ max of drug. Content uniformity studies were carried out in triplicates for each batch of the film.

RESULTS & DISCUSSION

Drug Authentication

Melting Point

Melting point of Domperidone was found to be 243-245°C. The result was in good agreement with the literature.

Determination of Drug Excipients Compatibility Study

FTIR spectrum of drug was correlated with FTIR spectra of drug given in IP. No change in peak of FTIR was found. Hence according to IP specifications drug used was found to pure.

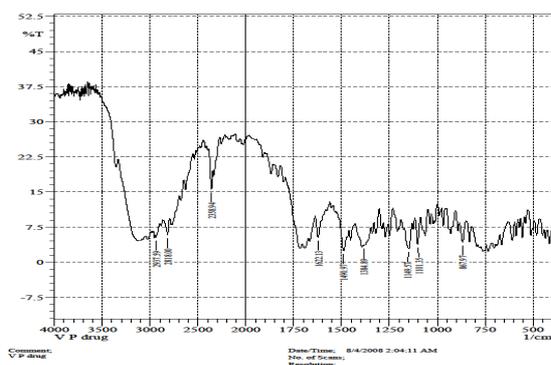


Figure 1: IR spectra of Domperidone

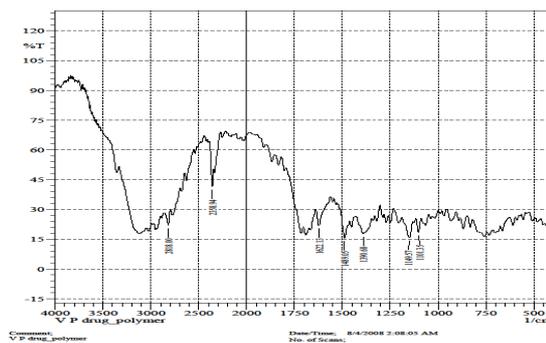


Figure 2: IR spectra of API + Polymer

Evaluation of powder characteristics:

Domperidone was evaluated for preformulation parameters such as angle of repose, bulk Density, tapped density, Carr's Index, Hauser's ratio and flow rate. The results are depicted in following Table. It was observed that the drug shows good flow characteristics while basil gum powder demonstrates poor flow. This may be due to the natural and raw nature of basil gum powder as well as irregular particle morphology.

Evaluation of Flash Dissolving Oral Film

The FDF formulations were subjected to various evaluation parameters. The results are tabulated in table. As the results indicate the FDF show uniform weight and film thickness as well as good folding endurance to withstand the mechanical events encountered during shipping and use. The drug content is found to be acceptable range. The films readily dissolve in the artificial saliva to ensure the fulfillment of the objective.

Formulation C disintegrated in 70 seconds and released 86% of drug within 3 minutes and was considered as the best formulation. As the concentration of film forming polymers gets increased it also increases the film forming capacity of the films.

CONCLUSION

The objective of the work was to formulate flash dissolving film of Domperidone by solvent casting technique using film forming machine. The formulation containing HPMC K 100 M combine with propylene glycol as plasticizer has shown excellent *in vitro* disintegration time and folding endurance, compared to other formulations.

The films prepared of various diameters using HPMC K100 M as film forming polymer, propylene glycol as plasticizer, Citric acid as saliva stimulating agent, Mannitol as sweetener.

Table 2: Preformulation parameters

Sample	Flow rate gm/sec	Bulk density (gm/cm ³)	Tapped density (gm/cm ³)	Carr's index (%)	Hausner's Ratio	Angle of Repose (Deg)
Domperidone	5.52±0.5	0.55±0.04	0.62±0.04	28±0.2	1.08±0.05	34.52±0.07
OB Powder	8.2±0.2	0.65±0.01	0.77±0.02	11±0.3	1.12±0.03	26.65±0.06

Table 3: Evaluation of Flash dissolving film

Batch	Weight of film (mg)	Film thickness (mm)	pH value	Folding Endurance	Drug content (%)	Percent Elongation (%)	Percent Moisture content (%)
A	16±2	0.37±0.03	6.60±0.02	40±3.51	96.72±0.89	18.15±0.85	6.88±0.50
B	18±2.5	0.35±0.05	6.60±0.04	52±4	93.61±0.65	17.20±0.44	5.58±0.76
C	20±2.8	0.33±0.06	6.60±0.07	60±7	99.07±0.34	16.66±0.70	4.54±0.66

All the values represent mean ± Standard Deviations were n=3

Table 4: Comparative study

Sr.No	Parameters	Innovators Product	Optimized Batch (3x3)
1	Weight of film	22±1.8	20±2.8
2	Film thickness	0.37±0.03	0.33±0.06
3	pH value	6.52±0.02	6.65±0.07
4	Folding endurance	54±4	60±7
5	Content of Uniformity	85.22±0.55	89.07±0.34
6	% Elongation	15.73±0.30	16.66±0.70
7	% Moisture content	3.23±0.20	4.54±0.66

The work explores the possibility of use of *Ocimum basilicum* mucilage dry powder as superdisintegrant.

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