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Mouth Dissolving Film of Domperidone: An approach towards Formulation and its Evaluation

Khanderao Jadhav[1*], Shivraj Jadhav[1], Deepak Sonawane[1], Deepak Somvanshi[1], Hina Shah[1] and Hitesh Khairnar[2]

[1]Department of Pharmaceutics, Shreeshakti Shaikshanik Sanstha's Divine College of Pharmacy, Satana, 423301, Maharashtra, India.
[2]H R Patel College of Pharmacy, Shirpur, Dhule, 425 405, Maharashtra, India.

Authors' contributions

This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.

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ABSTRACT

The objective of the current work is to formulate and evaluate the mouth dissolving film of domperidone. It is ideally suitable for the treatment of emesis. The mouth dissolving film of domperidone is useful in the vomiting through the journey. Mouth dissolving films were formulated by the solvent casting technique and its *in-vitro* as well as *the in-vivo* evaluation was done by the usual pharmacopoeial and unofficial tests and by using human volunteers. The main benefit of the preparation technique includes fewer operation units, better content consistency. The mouth dissolving film formed was found to be disintegrated in 1 minute. The ratio of components in the aqueous phase affected the thickness, drug content, tensile strength, percentage elongation, folding endurance, and release profile of mouth dissolving film and the best results were obtained for the HPMC E15 and polyethyleneglycol. The compatibility between domperidone and excipients was confirmed by FTIR and DSC studies. The developed mouth dissolving film of domperidone demonstrated usefulness for fast release of drug in mouth, for better drug utilization, and improved patient compliance. The optimized formulation, due to low HPMC E15 content, has optimum tensile strength and thickness. Formulation F8 containing HPMC E15 and PG showed a cumulative % drug release of 95.10 at the end of 12 minutes. HPMC E15 films showed higher cumulative % drug release than films of other HPMC E grades at different concentrations. It was found to be stable

**Corresponding author: E-mail: krjadhav25@gmail.com;*

during the accelerated stability study. The effect of different concentrations of polymers and plasticizers on *in-vitro* evaluation parameters was evaluated. Hence, data showed that formulation F8 was the most suitable for the development of fast dissolving oral films of domperidone.

Keywords: Fast dissolving oral films; solvent casting method; HPMC E15; PG; β-cyclodextrin.

1. INTRODUCTION

The oral route is the maximum favored route for the delivery of drugs to date as it allows various advantages over the other routes of drug administration, but oral drug delivery systems still need some advancements because of some problems associated with a particular class of patients which include geriatric, pediatric and dysphasic patients related with various medical conditions as they have trouble in swallowing or chewing solid dosage forms. So, fast-dissolving drug delivery systems came into presence in the late 1970s as a substitute for tablets, capsules, and syrups for pediatric and geriatric patients. These systems contain solid dosage forms that disintegrate and dissolve quickly in the oral cavity without the administration of water.

Research and development in the oral drug delivery segment have led to the evolution of dosage forms from simple orthodox tablets or capsules to modified-release tablets or capsules to oral disintegrating tablets to wafer to the current development of oral fast dissolving films. Oral strip technology is gaining much attention [1].

Orally fast dissolving film is a new drug delivery system for the oral delivery of drugs. It was developed based on the technology of the transdermal patch. It then quickly disintegrates and dissolves to release the medication for oromucosal absorption or with formula modifications, will maintain the quick-dissolving aspects allow for gastrointestinal absorption to be achieved when swallowed [2].

Mouth dissolving film is a very thin oral strip, which is merely placed on the patients tongue or any oral mucosal tissue, promptly wet by saliva, the film rapidly hydrates and adheres onto the site of application [3].

Numerous excipients used in the formulation of mouth dissolving film are film formers, plasticizers, sweetening agents, saliva stimulating agents, flavoring agents, coloring agents, etc. Solvent casting, semi-solid casting, hot-melt extrusion, solid dispersion extrusion, rolling, are some approaches applied for the formulation of fast dissolving films [4].

Domperidone is a dopamine antagonist it acts as a gastrointestinal emptying (delayed) adjunct and peristaltic stimulant. The gastroprokinetic properties of domperidone are connected to its peripheral dopamine receptor blocking properties. Domperidone enables gastric emptying and decreases small bowel transfer time by increasing oesophageal and gastric peristalsis and by lowering oesophageal sphincter pressure. The antiemetic properties of domperidone are related to its dopamine receptor blocking activity at both the chemoreceptor trigger zone and at the gastric level. It has strong affinities for the D2 and D3 dopamine receptors, which are found in the chemoreceptor trigger zone, located just outside the blood-brain barrier, which - among others - regulates nausea and vomiting [5].

2. MATERIALS AND METHODS

Domperidone was obtained as a gift sample from Glenmark Pharmaceuticals, Nashik. Other excipients such as HPMC E-15 were obtained from Vital care, Pvt. Ltd., Nashik, Propylene glycol was obtained from Fine Chem Industries, Mumbai, Citric acid from Lobe Chemie, Mumbai and Sucralose and potassium dihydrogen phosphate from Modern science, Nashik. The obtained chemicals were used without further purification.

2.1 Preformulation Studies

Preformulation studies are designed to ensure the development of a stable, safe, and therapeutically effective dosage form. Preformulation testing is designed to assess the influence of physicochemical properties of drugs and excipients on formulation properties of dosage form, method of manufacturer, pharmacokinetic and biopharmaceutical properties of the resulting product. A thorough understanding of physicochemical properties may ultimately confirm that no significant barriers are present for the formulation development.

Organoleptic properties such as colour, odour and appearance, solubility and melting point, UV analysis, FTIR, DSC, and compatibility study were carried out.

2.2 Ultraviolet Spectrum

The Domperidone was subjected to UV spectroscopic analysis (Shimadzu; UV 2450, Calibrated) to find out the wavelength (λ_{max}) at which it shows maximum absorbance. The drug was accurately weighed and dissolved in water to obtain a stock solution of 1000 µg/ml. This solution was then suitably diluted with the same solvent to get a solution of concentration 100 µg/ml and further diluted to 10 µg/ml. Then the UV spectrum of this concentration was recorded over the wavelength range 200-400 nm. The UV spectrum of the drug was also taken insolvent 6.8 pH phosphate buffer.

2.3 Fourier Transfer Infrared Spectrum

The drug was subjected to FT-IR studies (Shimadzu; 8400S) for characterization. IR technique is one the most powerful technique of chemical identification. The drug was mixed with potassium bromide in 1:99 proportion and the spectrum was obtained in the range of 400-4000 cm^{-1}. Potassium bromide was used as a blank while running spectrum.

2.4 Differential Scanning Calorimetry

A small amount of Domperidone (4 mg) was accurately balanced in an aluminium pan, hermetically sealed, and analysed. The sample was heated from ambient temperature 30 ℃ to 300 ℃, with a heating rate of 100 ℃/min. The inert atmosphere was provided by purging nitrogen gas flowing at 100 ml/min.

2.5 Compatibility Study

A compatibility study for domperidone was carried out with potential formulation excipients to determine the possibility of any drug-excipient interaction. Excipients studied included citric acid, sucralose, PG, HPMC E-15. Drug + polymer mixtures were subjected to compatibility studies and stored for 90 days at elevated temperature and humidity conditions of 40 ± 20 ℃ / 75 ± 5 % RH, one without moisture and the other is with moisture.

2.6 Formulation and Development of Mouth Dissolving Film

2.6.1 Screening of film formers

Some of the water-soluble polymers used as film former are HPMC E3, E5, E6 and E15, Pectin, Gelatin, Sodium Alginate, Polyvinyl alcohol, etc. Various film formers are weighed in 10 mg and poured in a different beaker containing 20 ml distilled water each. After the addition of propylene glycol, the mixture is kept on a magnetic stirrer for proper mixing. After that, the mixture is poured into Petri plates and kept in the oven for 7-8 hours at 45 ℃. Once the film is formed, it was removed from the Petri plate and observed physically for appearance, transparency, and disintegration time [6].

2.6.2 Taste Masking Procedure of drug (Complexation method)

The calculation for the amount of drug and amount of β-cyclodextrin required to form a complex are as follows,

Molecular weight of β-cyclodextrin = 1134.98

Molecular weight of drug = 425.91

Dose of drug = 10 mg

1135 mg (β-cyclodextrin) = 426 mg (Drug)

x = 10 mg (drug)

x= 1135 * 10/426

x= 26.64 mg (β -cyclodextrin should be weighed for 10 mg drug)

After adding 10 mg drug complex will be 36.64 mg.

Accurately 10 mg of drug and 26.64 mg of β-cyclodextrin were weighed. Poured them into clean and dry glass mortar pestle and triturated in the same direction for proper mixing. After proper mixing complexation is done.

2.6.3 Calculation of drug quantity for one film

A glass Petri plate of 9 cm diameter was used as a casting surface. So total amount of complex required was calculated as follows,
Formula:

The total surface area of casting surface,

$A = \pi r^2$……1

r = Radius of glass Petri plate (4.5 cm)

$A = 3.14 \times (4.5)^2$
$= 63.585\ cm^2$

Desired quantity of domperidone was 10 mg (dose of the drug) per 3 cm^2 films. Therefore, the

quantity required for 20 ml solution to be poured on 63.585 cm^2 area was calculated as follows;

36.64 mg = 3.0 cm^2

? mg = 63.585 cm^2
? mg = (36.64 × 63.585) / 3.0
= 776.58 mg

As per the above calculation amount of complex required for the formation of the film is 776.58 mg.

2.6.4 Preparation of mouth dissolving films

Optimization study in brief: The 2^3 full factorial design was applied for optimization. The two factors were concentrations of HPMC E15 and PG. The three levels of each factor were three different concentrations of HPMC E15 and PG as indicated in Table 1. So, nine formulations, as shown in Table 2 were formulated and were evaluated for evaluation parameters, and an optimized formulation was selected.

Various formulations were developed by taking the different quantities of polymers as shown in Table 2. Weighed a quantity of HPMC E-15 (film former) and transferred it to a small beaker containing 10 ml of distilled water. Kept it soaking for 24 hours. A weighed amount of drug and B-cyclodextrin complex (776.58 mg) was taken and transferred into a beaker containing 10 ml Distilled water. Then by using a magnetic stirrer beaker A (HPMC E-15) was placed at 40 rpm/min and the solution of beaker B (Drug Complex) was added dropwise in the rate as one drop/sec. Polyethylene Glycol (Plasticizer) was then added to the mixture. The resulting solution is poured into a neat and clean Petri plate having a 9 cm diameter. The Petri plate was then placed in the oven for 7-8 hours at 45 ℃. After proper drying, the film is cut into pieces of 3 by 3 cm.

2.7 Evaluation of mouth dissolving films

2.7.1 Physical appearance

Films of each formulation were casually chosen and inspected visually as well as by feel or touch for texture.

2.7.2 Thickness [7,8]

Five films of each formulation were taken and the film thickness was determined by using a micrometer screw gauge at different strategic locations (5 locations). Mean thickness and standard deviation were calculated.

2.7.3 Weight variation test [7,8]

For the weight variation test, 10 films of every formulation were casually selected and weighed separately to determine the average weight and standard deviation was calculated.

2.7.4 Percent moisture loss [9]

Three films of each formulation were taken. Primarily, these selected films were weighed accurately and kept in a desiccator comprising fused anhydrous calcium chloride. After 3 days, films were removed, weighed and percentage moisture loss was calculated. Mean percentage moisture loss and standard deviation were calculated. The percentage moisture loss was calculated using the following formula

$$\% \text{ of moisture loss} = \frac{Initial\ weight - Final\ weight}{Initial\ weight} * 100 \quad \ldots\ldots 2$$

2.7.5 Surface pH of films [9,10]

The surface pH of films was determined to examine the probable side effect because of change in pH *in-vivo*, since an acidic or alkaline pH may irritate oral mucosa. The film to be tested was placed in a test tube and was moistened with 1 ml of distilled water and kept for 30 seconds. The pH was noted subsequently bringing the electrode of the pH meter in contact with the surface of the formulation and permitting equilibrating for 1 minute. The average of three determinations for each of the formulations was taken.

2.7.6 Drug content uniformity[10]

Content uniformity is determined by estimating the API content in the individual strip. Three films from individual formulations were taken and individually dissolved in 50 ml of 6.8 pH phosphate buffer to produce solutions of 10 µg/ml concentration. These solutions were filtered and the absorbance of each solution was recorded at 271 nm (λ_{max} of Domperidone) using the placebo patch (patch without drug) solution as a blank. The percentage of drug content was determined. Mean of the percentage drug content and standard deviations were calculated.

2.7.7 Disintegration time[10]

The disintegration time limit of 30 seconds or less for orally disintegrating tablets designated in CDER guidelines can be applied to fast

dissolving oral strips. Although no official guidelines are available for oral fast disintegrating films, this may be used as a qualitative guideline for quality control tests or at the development stage. This test is carried out using the disintegration apparatus. Three films from each formulation were taken and performed disintegration test by placing the films in the cylindrical glass tube of disintegration apparatus containing 6.8 pH phosphate buffer. The time at which the film disintegrated is noted. Mean and standard deviation was calculated. Normally disintegration time for fast dissolving oral films is 5-30 seconds.

2.7.8 Folding endurance [7,11]

Three films of each formulation of 4 cm^2 (2×2 cm) were cut by using a sharp blade. Folding endurance was determined by continually folding a small strip of film at the same place till it breakdowns. The number of times, the film could be folded at a similar place without breaking gave the value of folding endurance. The mean value of three readings was calculated.

2.7.9 Percent elongation [12,13]

When stress is applied, a strip stretches referred to as a strain. Strain is the distortion of a strip divided by the original dimension of the sample.

$$\% \text{ of elongation} = \frac{Final\ Length - Initial\ Length}{Initial\ Length} * 100 \quad \ldots\ldots 3$$

2.7.10 Dissolution test [2,13]

The dissolution test is performed in pH 6.8 phosphate buffer using the standard basket apparatus at 36 ± 0.5 °C and 50 rpm. A single film was placed in 500 ml dissolution media. 5 ml of samples were withdrawn at suitable time intervals and replaced with a new dissolution medium. Then samples were determined using a UV visible spectrophotometer at 271 nm and cumulative drug release was calculated.

2.7.11 Stability Study

A stability study was carried out for the optimized formulation. The formulation was wrapped in aluminium foil and then placed in an amber-coloured bottle. It was stored at 40 °C, 75% relative humidity for 3 months. The stored films were evaluated for drug content and *in-vitro* drug release after three months. The obtained data were compared with the drug content and *in-vitro* dissolution obtained before the stability study. The formulations were evaluated mainly for their physical characteristics at predetermined intervals like appearance/clarity, pH, viscosity, and drug content. Test conditions for stability study are shown in Table 3.

Table 1. Independent variables

Name	units	Minimum -1	Medium 0	Maximum +1
HPMC E15	Mg	400	600	800
PG	Ml	0.5	1	1.5

Table 2. Composition of mouth dissolving films of Domperidone

Name of Excipient	Different batches of mouth dissolving films of Domperidone								
	F1	F2	F3	F4	F5	F6	F7	F8	F9
Physical mixture of Drug + β-cyclodexrin (mg)	776.58	776.58	776.58	776.58	776.58	776.58	776.58	776.58	776.58
HPMC-E15 (mg)	400	400	400	600	600	600	800	800	800
PG (ml)	0.5	0.5	1.0	0.5	1.5	1.0	1.5	1.5	1.0
Sucralose (mg)	2.5	2.5	2.5	2.5	2.5	2.5	2.5	2.5	2.5
Citric Acid (mg)	2.2	2.2	2.2	2.2	2.2	2.2	2.2	2.2	2.2
Flavour (vanilla)	Q. S.	Q. S.	Q. S.	Q. S.	Q. S.	Q. S.	Q. S.	Q. S.	Q. S.

2.7.12 *In-Vivo* Studies: Taste masking Studies [14]

Domperidone + BCD Complex was prepared by the complexation method. The Taste masking study of the above complex is performed on the panel of 9 healthy human volunteers in the age group of 18-30 years of both sexes from whom written consent has been obtained as per guidelines provided in Declaration of Helsinki. Here, firstly physical mixture & complex having high % drug release (10 mg) is placed on the tongue of each volunteer separately for 30 seconds, and taste is evaluated for resident time & reported. Volunteers were asked to gargle immediately after each evaluation. The bitterness is recorded immediately according to a scale ranging from 0 to 5 as follows;

0- No bitter 1- Threshold bitter
2- Slight bitter 3- moderate bitter
4- Bitter 5- Strong bitter

3. RESULTS AND DISCUSSION

3.1 Preformulation Study of the Drug

The sample of drug received was studied for its organoleptic characters such as colour, odour, appearance. The colour is yellow, odourless and its appearance is like a fine powder.

3.2 Solubility

Domperidone was found to be soluble in water and phosphate buffer pH 6.8. In water 0.090 mg/ml solubility is observed while in phosphate buffer 6.8, 0.112 mg/ml solubility is observed.

3.3 Melting Point

The melting point of Domperidone observed was 244 to 246 ℃. The standard melting point of domperidone is 240 to 245 ℃ [15].

3.4 UV Spectrophotometric analysis of Domperidone

The UV spectrum was recorded in the range of 200 to 400 nm. The wavelength of maximum absorption (λ_{max}) was determined from the scan. The λ_{max} of Domperidone was found to be 271 nm and the absorbance of each solution was measured at 271 nm.

3.5 Differential Scanning Calorimetry (DSC)

One of the most classic applications of DSC analysis is the determination of the possible interactions between a drug entity and the excipients in its formulation. Fig. 1 illustrates DSC profiles of pure domperidone and physical mixture. The DSC thermogram of the drug depicts a sharp exothermic peak followed by an endothermic peak at 243.96 °C. DSC of domperidone showed a sharp peak at 243.95 °C. So, the melting point of Domperidone was confirmed. Hence, the identity of domperidone was confirmed. DSC of domperidone + HPMC E15 + BCD showed sharp peak at 230.37 °C. No shifting of the peak was observed. So, no interaction was detected between domperidone, HPMC E15, BCD. Hence, domperidone was found to be compatible with HPMC E15 and BCD. Both DSC spectra are indicated in Fig. 1.

3.6 Fourier Transforms Infrared Spectroscopic (FTIR) Studies

FTIR spectrum of domperidone was recorded and analysed for the functional groups corresponding to the functional groups present in the structure of domperidone. FTIR spectrum of domperidone is shown in Fig. 2.

Spectra of Domperidone + HPMC E15 + BCD showed that characteristic peaks were not found to be shifted from their characteristic wavenumber. So, no interaction was detected between Domperidone and excipients. Hence, domperidone was found to be compatible with HPMC E15, PG.

3.7 Compatibility Study

Pure drug along with selected excipients was placed in an environmental chamber for compatibility study. Samples were observed for changes in physical parameters like colour change, change in physical state, and formation of odour. No significant physical change was observed after 90 days which suggests compatibility between drug and other excipients.

3.8 Screening of Film Formers

By using different film formers, films were prepared and observed physically for appearance, transparency, and disintegration time. The results are shown in Table 4.

From the above result, it was found that HPMC E15 has shown a good film property with desired disintegration time. The combination formed more transparent, flexible films than other polymers. Hence it is used further for the development of films.

3.9 Preparation of Mouth Dissolving Films

2^3 factorial design was used for the optimization of formulation by taking into consideration 3 levels of two factors which are HPMC E15 and propylene glycol. A total of 9 formulations were developed. These 9 formulations were evaluated for physical appearance, thickness, weight variation, percent moisture loss, surface pH, drug content uniformity, disintegration time, folding endurance, percent elongation dissolution study, and results are indicated in Tables 5 and 6.

From the above results batch, F8 was having high folding endurance and low disintegration time (25.4 seconds). Also, batch F8 showed about 95.10 % drug release in 12 minutes and drug content uniformity is also 94.3 %. Hence batch F8 is considered optimized. Fig. 3 indicates the film of batch F8. This batch is further utilized for stability study purposes.

3.10 Stability Study

Batch F8 was subjected to stability study as per ICH protocol. Optimized batch is tested for weight, thickness, folding endurance, surface pH, drug content uniformity, and disintegration time after 15, 30, 60, and 90 days intervals. Results are indicated in Table 7.

The batch F8 showed good stability after 90 days on all evaluation parameters. Drug content uniformity was slightly decreased after 90 days.

3.11 *In-vivo* Studies

In-vivo studies were performed for the study of taste masking of the drug by using β-cyclodextrin. The results obtained by this study are shown in Table 8.

From an *in-vivo* study, it was evident that formulation without complexation showed more bitterness in taste while formulation with complex showed less bitterness. This suggests that complexation with BCD causes taste masking.

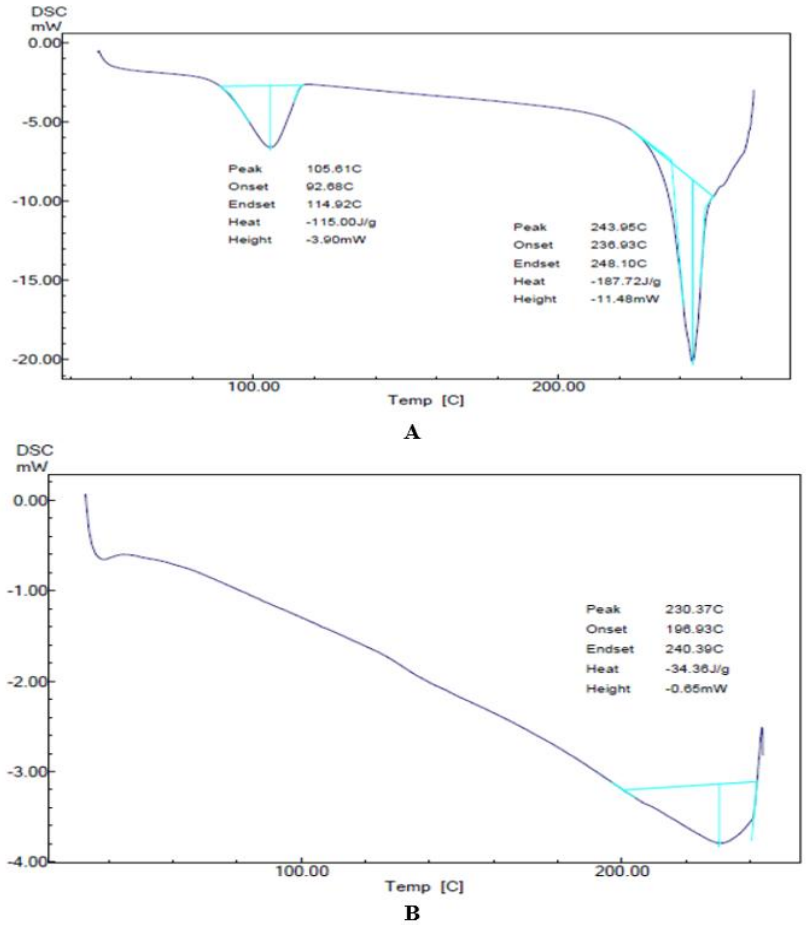

Fig. 1. DSC spectra of Domperidone (A) and Domperidone + Excipients (B)

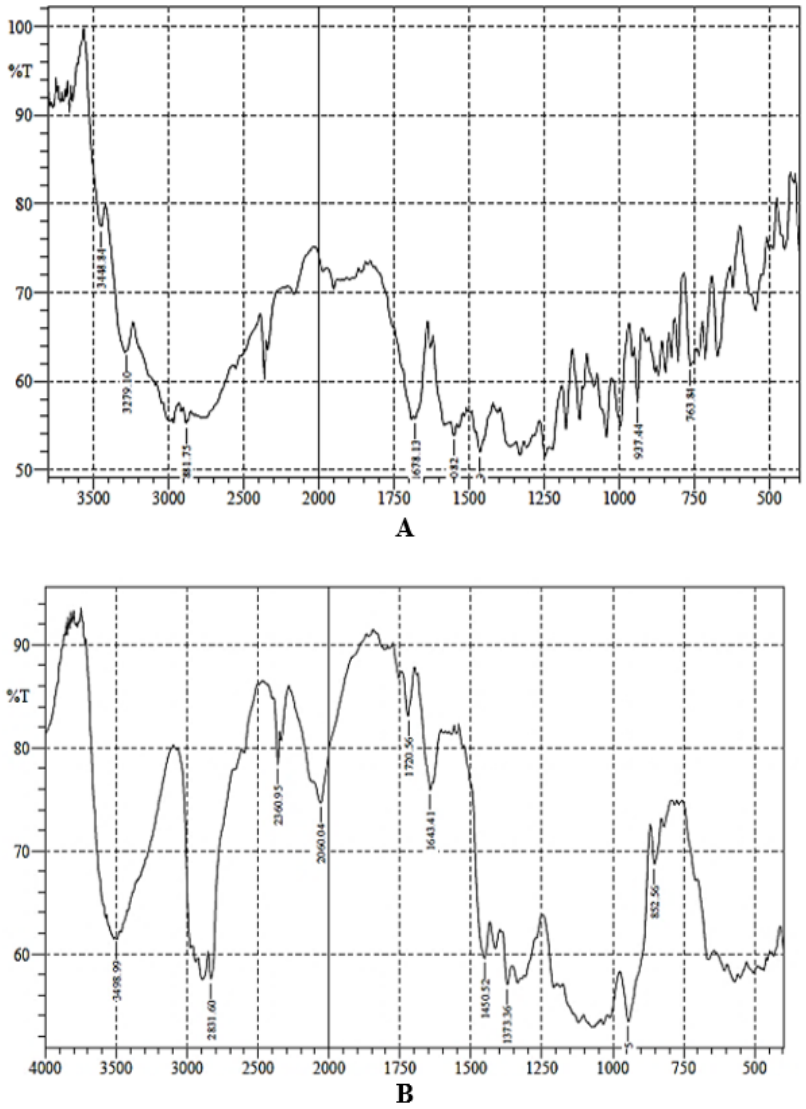

Fig. 2. FTIR spectra of pure domperidone (A) and FTIR spectrum of Domperidone + BCD + HPMC (B)

Table 3. Test conditions for the stability study

Duration of study	3 months
Temperature condition	40 ℃ ± 2℃
Relative humidity	75 ± 5 %
Time frame	0-3 month

Table 4. Screening of film formers

Polymers Used	Film appearance	Appearance	Disintegration time
HPMC E3	Poor	Transparent	30 seconds
HPMC E5	Poor	Transparent	33 seconds
HPMC E6	Poor	Transparent	35 seconds
HPMC E15	Good	Transparent	30 seconds
PVP	Good	Transparent	35 seconds
PVA	Average	Transparent	48 seconds
Sodium Alginate	Poor	Translucent	50 seconds
Gelatin	Poor	Translucent	45 seconds

Table 5. Evaluation of batches for optimization

Batch	Weight† (mg)	Thickness† (mm)	Folding Endurance†	Surface pH †	Drug Content uniformity (%)†	Disintegration time (seconds)†
F1	48.95±0.25	0.62 ±0.01	280±0.2	6.3±0.1	91.3±0.7	58.6 ± 0.51
F2	52.32±0.03	0.73 ±0.03	290±0.2	6.3±0.2	91.2±0.1	52.4 ± 0.28
F3	56.31±0.49	0.78 ±0.012	285±0.5	6.4±0.5	92.3±0.2	49.8 ± 0.26
F4	58.23±0.21	0.81 ±0.04	290±0.6	6.4±0.6	90.5±0.2	41.2 ± 0.36
F5	61.84±0.41	0.85 ±0.02	284±0.2	6.2±0.8	89.6±0.1	38.4 ± 0.26
F6	65.24±0.31	0.95 ±0.02	286±0.2	6.6±0.4	91.6±0.1	36.4 ± 0.22
F7	63.44±0.21	0.65 ±0.02	281±0.2	6.1±0.9	88.6±0.1	31.2 ± 0.12
F8	71.84±0.21	0.71 ±0.01	291±0.2	6.7±0.3	94.3±0.1	25.4 ± 0.15
F9	68.24±0.31	0.79 ±0.02	283±0.2	6.6±0.8	90.6±0.1	38.4 ± 0.12

† All values are mean ± SD, (n=9)

Table 6. Dissolution data of batches for optimization

Time (Min)	Cumulative % Drug Release								
	F1	F2	F3	F4	F5	F6	F7	F8	F9
2	41.23 ± 0.12	41.11±0.14	38.24±0.02	36.52±0.03	35.23±0.06	35.20±0.03	38.20±0.02	42.23±0.06	35.20±0.03
4	55.32±0.23	53.26± 0.03	56.24±0.32	55.23±0.05	53.41±0.10	54.10±0.01	55.23±0.01	55.32±0.05	45.10±0.02
6	68.35 ±0.56	68.25± 0.02	65.43±0.01	68.23±0.06	66.27±0.02	68.35 ±0.04	63.25±0.02	68.32±0.05	55.20±0.03
8	81.94±0.14	78.39± 0.03	75.82±0.01	74.32±2.04	72.85±0.17	75.40±0.13	81.24±0.04	73.27±0.04	61.20±0.03
10	92.13 ±0.10	90.54± 2.24	89.63± 1.2	86.36±0.01	80.45±0.03	88.30±0.02	91.20±0.10	85.36±0.10	75.10±0.03
12	96.10±0.16	95.32± 0.20	90.47±0.15	88.91±0.13	86.22±0.15	95.20±0.03	87.35±0.12	95.10±0.03	85.10±0.03

Table 7. Physical evaluation parameters of formulation F8 during stability study

Interval	Weight (mg)	Thickness (mm)	Folding Endura-nce	Surface pH	Drug Content uniformity (%)	Disintegration time (Seconds)
Initial	53.91±0.49	0.78±0.01	280-300	6.4±0.2	94.3±0.2	39±0.5
15 days	53.05±0.12	0.76±0.03	280-300	6.5±0.2	93.8±0.2	39±0.12
30 days	53.62±0.15	0.76±0.04	280-300	6.5±0.1	93.5±0.1	39±0.04
60 days	53.20±0.11	0.76±0.04	270-300	6.5±0.2	92.8±0.1	38±0.02
90 Days	53.20±0.11	0.76±0.04	260-300	6.5±0.2	91.3±0.1	36±0.01

Table 8. Evaluation sheet of *in-vivo* studies

Volunteer code	Formulation (Without complexation)	Taste (Grading)	Formulation (With complexation)	Taste (Grading)
A	3 x 3 cm^2 film	4	3 x 3 cm^2 film	0
B	3 x 3 cm^2 film	3	3 x 3 cm^2 film	1
C	3 x 3 cm^2 film	4	3 x 3 cm^2 film	0
D	3 x 3 cm^2 film	4	3 x 3 cm2 film	2
E	3 x 3 cm^2 film	3	3 x 3 cm^2 film	2
F	3 x 3 cm^2 film	4	3 x 3 cm^2 film	0
G	3 x 3 cm^2 film	4	3 x 3 cm^2 film	1
H	3 x 3 cm^2 film	3	3 x 3 cm^2 film	0
I	3 x 3 cm^2 film	3	3 x 3 cm^2 film	0

Fig. 3. Film of batch F8

4. CONCLUSION

The inclusion complex of Domperidone with β-cyclodextrin was prepared by kneading method and the mouth dissolving film was prepared by using the prepared complex of Domperidone. The solvent-casting method was used for the formulation using a hydrophilic film-forming polymer HPMC E-15 and PG as a plasticizer. Films prepared were smooth and elegant and showed no visible cracks; were uniform in thickness, weight, and drug content. Optimization of mouth dissolving film was carried out using 2^3 factorial designs, with independent variables as the concentration of HPMC (X1) and concentration of PG (X2). This design was employed to study the effect of independent variables on various dependent variables such as *in-vitro* drug release for 12 minutes, disintegration time, thickness, and folding endurance. The nine formulations prepared were subjected to physical evaluation parameters like physical appearance, thickness, weight uniformity, moisture content loss, surface pH measurement, drug content uniformity, and folding endurance. The result of the *in-vivo* test showed satisfactory taste-masking properties of the formulation.

DISCLAIMER

The products used for this research are commonly and predominantly use products in our area of research and country. There is absolutely no conflict of interest between the authors and producers of the products because we do not intend to use these products as an avenue for any litigation but for the advancement of knowledge. Also, the research was not funded by the producing company rather it was funded by personal efforts of the authors.

CONSENT

It is not applicable.

ETHICAL APPROVAL

It is not applicable.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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