International Journal of Current Pharmaceutical Research

ISSN- 0975-7066 Vol 15, Issue 2, 2023

Original Article

FABRICATION AND EVALUATION OF MOUTH-DISSOLVING FILMS OF DOMPERIDONE

SARFARAZ MD*, SUSHIL KUMAR, H. DODDAYYA

Department of Pharmaceutics, NET Pharmacy College, Raichur 584103, Karnataka, India
Email: sarfindia@gmail.com

Received: 07 Jan 2023, Revised and Accepted: 18 Feb 2023

ABSTRACT

Objective: The objective of present research work was to fabricate and evaluate mouth-dissolving films of domperidone by solvent casting method using hydroxypropyl methyl cellulose as polymer for rapid release of drug.

Methods: Domperidone (DMP) is specific blocker of dopamine receptors (D2 and D3) and is widely used to treat emesis. Since domperidone solubility is less, domperidone solid dispersion (DMP SD's) were prepared with β-cyclodextrine inclusion complexes in different ratio (1:1, 1:2, 1:3 and 1:4) by kneading method to increase the solubility. The DMP mouth dissolving films (MDF) were developed using DMP SD's by solvent casting method. Hydroxypropyl methyl cellulose (HPMC) was used as film forming agent and glycerine was used as plasticizer. Nine formulations were fabricated and were evaluated for their various physico-mechanical properties, *in vitro* disintegration time and *in vitro* dissolution characteristics.

Results: The solid dispersion SD3 increased the solubility of drug compared to pure drug. FTIR studies revealed the integrity of the drug in its pure form in both drug-βcyclodextrine complex and finished MDF. The thickness uniformity, weight uniformity, folding endurance, surface pH and drug content of mouth dissolving films were uniform and reproducible. Formulation F1 released highest percentage of drug i.e., 100% of drug in 16 min compared to other formulations in *in vitro* release studies and disintegrated within 2.5 min and hence was considered as optimized formulation. The mechanism of drug release of prepared mouth dissolving films was Non-Fickian diffusion controlled kinetics.

Conclusion: Complexation by Kneading technique was found satisfactory for solid dispersion of domperidone. Solvent casting method was successfully used to obtain uniform mouth dissolving films containing drug-β cyclodextrine solid dispersion. Mouth dissolving films containing domperidone could be successfully developed and optimised.

Keywords: Mouth dissolving film, Domperidone, β cyclodextrin, Solvent casting method, HPMC

DOI: https://dx.doi.org/10.22159/ijcpr.2023v15i2.2088 Journal homepage: https://innovareacademics.in/journals/index.php/ijcpr

INTRODUCTION

The buccal delivery of drugs has recently emerged as an effective and safe alternative over other conventional routes of drug administration. Buccal administration easily releases the loaded drug into the buccal cavity for either local or systemic effects. This route of administration is especially suitable in pediatric and geriatric, where patients often struggle to ingest traditional oral solid dosage forms. Moreover, the buccal route is very convenient for drugs that are inactivated in the gastric environment, drugs that irritate the gastrointestinal tract, and during nausea and vomiting episodes [1-7]. Various buccal dosage forms are now commercially available, including muco-adhesive films and tablets, oral disintegrating tablets, hydrogels, and fast dissolving films.

Mouth dissolving films is the most advanced form of oral solid dosage form due to more comfort and flexibility [8]. Mouth dissolving films gives instant bioavailability and quick absorption of drugs due to permeability of oral mucosa. Mouth dissolving films are useful in geriatrics, emetic patients, pediatric, diarrhea etc. it is also mainly useful as local anesthetic for oral ulcers, toothaches or cold sores. Mouth dissolving films started gaining popularity and acceptance as new drug delivery system due to better patient compliance. These oral films have predominance over major drawbacks of rapid disintegrating tablets related to fear of friability, choking and can be utilized for schizophrenic and dysphasic patients [9]. Different polymers, such as hydroxypropyl methylcellulose (HPMC), methylcellulose, polyethylene glycol (PEG), pullulan, polyvinylpyrrolidone (PVP), gelatin, and maltodextrin, have been successfully used in the preparation of mouth dissolving films [1, 10, 11]. Domperidone (DMP) is an anti-emetic drug which is poorly soluble in water (1 mg/ml) and its oral bioavailability is in the range of 15–17% of the administered dose. Such a low oral bioavailability stems from its low aqueous solubility, extensive first pass effect, and efflux mediated by transporters in the small intestine [12, 13]. Therefore to increase the solubility of drug Solid dispersion (SD) technique was used which is common method to enhance solubility of drugs and thereby improve the dissolution rate. Buccal delivery of DMP might be used as an alternative route to overcome the disadvantages of its oral administration. Therefore objective of present work was to fabricate and evaluate MDF of domperidone by solvent casting method to improve its solubility and makeit suitable forthe treatment of nauseous and vomiting patients.

MATERIALS AND METHODS

Domperidone was obtained as gift sample from Hetero labs, Hyderabad, India**.** Bcyclodextrine was gifted from Ajanta Pharmaceuticals, Mumbai. Hydroxy propyl methylcellulose 5cps andPotassium dihydrogen orthophosphate was procured from SD Fine chemicals Pvt. Ltd., Mumbai. Sodium hydroxide was purchased from Rankem Fine chemicals Pvt Ltd., Thane. Sucrose, citric acid. Sodium lauryl sulphate and glycerine were purchased from SD Fine chemicals Pvt Ltd., Mumbai. All other chemicals utilised were of analytical grade.

Preparation of domperidone solid dispersion (DMP SDs)

Domperidone solid dispersion was prepared with β-cyclodextrine inclusion complexes in different ratio (1:1, 1:2, 1:3 and 1:4) by kneading method. In this method required amount of drug and β-cyclodextrine was taken and transferred into a china dish. The mixture was size reduced gently by stirring with pestle. Distilled water was added in required quantity to the above physical mixture and continuously stirred until the slurry mass was formed. Slurry mass was collected and dried at room temperature. The resultant mass was passed through sieve no.60 and stored in a desiccator (table 1).

Table 1: Composition of domperidone-β cyclodextrin solid dispersion

Solid dispersion	Ratio	Drug	β cyclodextrin
SD1*	1:1	80 mg	80 mg
SD2	1:2	80 mg	160 mg
SD3	1:3	80 mg	240 mg
SD4	1:4	80 mg	320 mg

*SD1-drug β Cyclodextrin solid dispersion

Characterisation of domperidone-βcyclodextrin solid dispersion [14]

Determination of percent yield

The percent yield of DMP SDs was determined using the following formula:

$$\text{Percent yield} = \frac{\text{Weight of prepared solid dispersion}}{\text{Weight of drug + carriers}} \times 100$$

Drug content

Amount of SD equivalent to 10 mg of DMP was weighed accurately and dissolved in 25 ml of ethanol. The volume was made up to the mark with ethanol. The solution was suitably diluted with ethanol and spectrophotometrically assayed for drug content at 284 nm using the following formula:

$$\text{Percent drug content} = \frac{\text{Concentration of drug released in medium}}{\text{Labeled claim}} \times 100$$

The test was done in triplicate.

Saturation solubility

Solubility studies of domperidone were determined using DMP and DMP SDs equivalent to 10 mg of drug in phosphate buffer pH 6.8 stirring for 24 h at 37±0.5 °C, which was then assayed by UV spectrophotometry at 284 nm. The solubility studies were assessed in triplicate and data were the average values.

Fourier transform infrared spectroscopy studies (FTIR)

The Pure drug, selected DMP SDs was subjected for FTIR analysis to check the compatibility/interaction between the drug and carrier. The samples were prepared on KBr-press (Agilent Technologies Hyderabad, INDIA). The samples were scanned over a range of 4000-600 cm^{-1} using Fourier transformer infrared spectrophotometer (8600, Shimadzu Corporation, Japan). Spectra were analysed for drug carrier interactions.

Fabrication of mouth dissolving films

Procedure [15]

Domperidone-loaded mouth dissolving films were prepared using the solvent casting method. Briefly, selected DMP SDs, HPMC and other excipients were accurately weighed; HPMC was weighed and dispersed in ethanol (5 ml) with the help of stirrer to form solution. The selected DMP SDs was added to polymeric solution with continuous stirring to get homogenous clear solution. In another beaker 3 ml of ethanol is taken and weighed quantity of citric acid, SLS and sucrose are added and mixed. To it glycerine is added as plasticizer (30% w/w of polymer). The plasticiser solution is transferred to polymeric solution and mixed with stirring. The film solution is sonicated to remove any bubbles formed. The film solution is then poured in a clean glass bangle (an area of 4.41 cm^2) which is placed in a petri-plate and dried at room temperature for 48 h. The film after drying is removed and cut in desired size of 2 X 2 cm^2 each and preserved in a butter paper and in a desiccator. The composition of mouth dissolving films is given in table 2.

Calculation of amount of drug per batch of film (Dose calculation)

Oral Dose of Domperidone is 10 mg

Each film contains 10 mg of Domperidone

Radius of petri plate: 4.7 cm

Area of each film: 2 cm × 2 cm = 4 cm^2

Area of petri plate: πr^2 = 3.14 × $(4.7)^2$ = 69.36 cm^2

4 cm^2 area of film contains 10 mg of Domperidone

69.36 cm^2 area of film contains = 69.36×10/4 = 173.4 mg

400 mg SD contains 80 mg drug

173.4 mg drug is present in 867 mg of SD

Hence 867 mg domperidone SD was taken for whole petri plate area

Number of patches = area of petri plate/area of film = 69.36/4 = 17.34

Hence for single patch measuring 2 × 2 cm^2 51 mg domperidone SD is needed.

Fig. 1: Domperidone mouth dissolving film-F1

Table 2: Composition of mouth dissolving films of domperidone

Ingredients (mg)	Formulation code								
	F1	F2	F3	F4	F5	F6	F7	F8	F9
Domperidone SD*	51	51	51	51	51	51	51	51	51
HPMC	250	300	350	400	450	500	550	600	650
Glycerine in ml (30% w/w of polymer)	0.067	0.067	0.067	0.067	0.067	0.067	0.067	0.067	0.067
Citric acid	60	60	60	60	60	60	60	60	60
Sodium lauryl sulphate	30	30	30	30	30	30	30	30	30
Sucrose	60	60	60	60	60	60	60	60	60
Ethanol	10	10	10	10	10	10	10	10	10

*51 mg of DMP SD contains 10 mg of pure domperidone drug for each film of 2×2 cm^2

Evaluation of Mouth dissolving films of domperidone

The Mouth dissolving films of domperidone prepared were evaluated for the following parameters:

Physical appearance

All the prepared films were visually inspected for color, clarity, flexibility and smoothness.

Film thickness uniformity

As the thickness of a film is directly concerned with drug content uniformity, it is necessary to ascertain uniformity in the thickness of the film. The thickness of the formulated film was measured at 3 different points using a micrometer screw gauge at different strategic locations and average of three reading was taken.

Film weight variation

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

Folding endurance

Folding endurance is another procedure to estimate the mechanical properties of a film. It is measured by repeatedly folding a film at the same point until it breaks. Folding endurance value is number of times the film is folded without breaking. Higher folding endurance value depicts the more mechanical strength of a film. A direct relation exists between mechanical strength and folding endurance of films. As mechanical strength is governed by plasticizer concentration so it is clearly evident that plasticizer concentration also indirectly affects folding endurance value.

The folding endurance was measured manually for the prepared films. A strip of film (2 x 2 cm) was cut and repeatedly folded at the same place till it broke. The number of times the film could be folded at the same place without breaking/cracking gave the value of folding endurance.

Surface pH

The pH value of a film is usually determined by putting the prepared film in petri dish and subsequently film is made wet by using distilled water and noting pH by touching the film surface with a pH meter electrode. Determination of surface pH is vital as acidic or basic pH is liable to cause oral mucosal irritation.

Drug content uniformity

Film (size of 2 × 2 cm^2) was taken from different areas of the film and placed in a 10 ml volumetric flask; 10 ml of phosphate buffer pH 6.8 was added and kept aside till the film dissolves completely; from this solution, 1 ml was pipetted out and diluted to 10 ml with phosphate buffer pH 6.8. The solution was analyzed by UV–Visible spectrophotometer at 284 nm. The experiments were carried out in triplicate for the strips of all formulations and average values were recorded.

Disintegration time

Normally, the disintegration time is the function of composition of film as it varies with the formulation. There are no official guidelines available for determining disintegration time of orally fast disintegrating films. The following method was used for determining disintegration time of film:

Petri dish method

A film is placed onto 2 ml distilled water taken in petri dish. Time taken by the film to disintegrate completely is considered as the disintegrating time [15, 16].

***In vitro* dissolution studies**

In vitro dissolution study for all the formulations was performed for in USP type I basket apparatus. Test was performed by placing the oral strip (2 × 2cm^2) in the basket securely. The dissolution medium consisted of 500 ml of phosphate buffer pH 6.8 was kept at 37 ± 0.5 °C and baskets were rotated at 50 rpm. A 5 ml of sample was taken at time intervals from 1 to 30 min and the same volume was replenished with fresh buffer solution maintained at 37 °C. The samples were filtered and analyzed at 284 nm using double beam UV/Visible spectrophotometer (Shimadzu 1700, Mumbai, India); the content of drug was calculated using equation generated from standard calibration curve of domperidone [17-19]. The *in vitro* release profile of optimized formulation was compared with that of a marketed product.

Kinetic study [20, 21]

For analyzing the mechanism of drug release kinetics of the mouth dissolving films, the dissolution data obtained was fitted to various kinetic equations of zero order, first order, Higuchi model and Korsmeyer-Peppas model. The regression coefficient was calculated. Graphs of kinetic models were plotted with suitable data and the n value was used to characterize different release mechanisms.

Fourier transformer infrared spectroscopy (FTIR) study

The compatibility between drug, polymer and other excipients was detected by FTIR spectra (Bruker, Canada). The pellets were prepared on KBr-press (Spectra lab, India). The spectra were recorded over the wave number range of 4000 to 500 cm^{-1}.

Stability Studies [22]

The selected mouth dissolving film were wrapped with aluminum foil and stability studies were carried out according to ICH guidelines at 25°±2 °C/60%±5%RH and 40°±2 °C/75±5%RH for three months by storing the samples in stability chamber.

RESULTS AND DISCUSSION

Table 3: Characterisation of domperidone-β cyclodextrin solid dispersion

Drug: cyclodextrine SD	Percent yield	Percentage drug content*	Saturation solubility*
Pure drug	-	-	
SD1	85.6	90	4.8
SD2	84.4	86	6.65
SD3	80.3	89	7.56
SD4	78.4	85	6.00

*Average of three determination.

Characterisation of domperidone-β cyclodextrin solid dispersion

Percent yield

Various DMP SD using β cyclodextrin, at different ratios (1:1, 1:2, 1:3, 1:4) were prepared. The percent yield of various DMP SD was found to be within the range of 78.4 to 85.6% [table 3]. The yield was less as the SD prepared were sticky and resulted in loss of SD while collecting.

Drug content

The percentage drug content of prepared DPM SD's ranged from 85.0 to 90%, as reported in table 3. The values indicated that DMP was uniformly distributed in all of the prepared SD formulations.

Solubility studies

The saturation solubility of DMP and various prepared DMP-SD were measured in phosphate buffer pH 6.8 for 24 h at 37±0.5 °C. DOM-

SD's showed higher saturation solubility than pure drug (table 3). Solubility of drug in the SD was found to be 0.960, 1.330, 1.512 and 1.200 mg/ml respectively for SD1, SD2, SD3 and SD4 which was more than pure drug (0.0850 mg/ml). This enhancement in solubility might be an indicative reason for an improvement of wetting of drug particles and localized solubilization by the water-soluble carrier. However it was observed that SD3 (1:3) gave better solubility than SD4 (1:4). This may be due to increasing the β cyclodextrin concentration beyond certain percentage decreases the thermodynamic potential of the drug [23].

Fourier transform infrared spectroscopy studies

The FTIR spectrum of the pure drug domperidone and selected drug β cyclodextrine complex SD3 showed the characteristic absorption bands in the IR region. It is observed from the IR spectra of pure drug domperidone, polymer, solid dispersion that the values of significant peaks in the respective compounds have resolved in their respective expected regions, indicating that all the above compounds used are in pure state. Hence it is evident that there is no interaction of the drug with the carrier β cyclodextrine. The results are shown in fig. 2, 3, and 4.

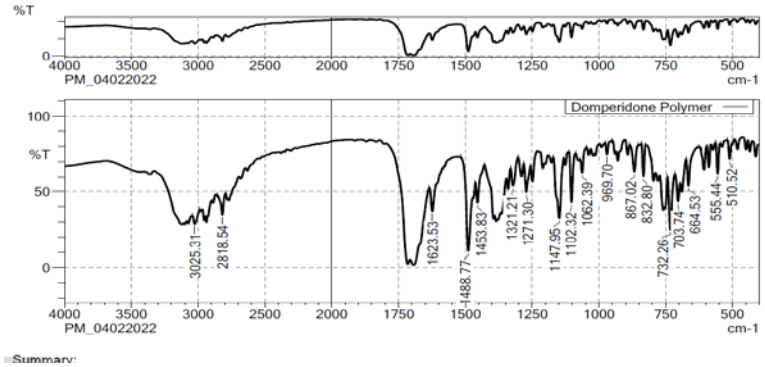

Fig. 2: FTIR spectra of pure drug domperidone

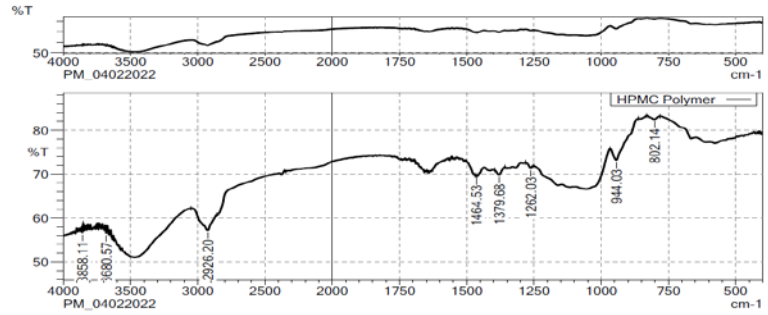

Fig. 3: FTIR spectra of polymer HPMC

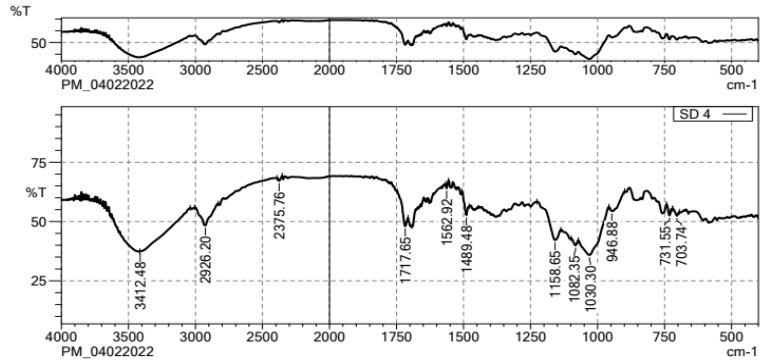

Fig. 4: FTIR spectra of domperidone solid dispersion SD3

Evaluation of Mouth dissolving films of domperidone

The Mouth dissolving films of domperidone prepared were evaluated for the following parameters:

Physical appearance

Visual inspection of a prepared domperidone mouth dissolving films showed that films were white in color, homogenous, nontransparent, flexible and smooth. HPMC showed good film forming capacity.

Film thickness uniformity

All the formulations contained varied amount of polymer and hence thickness of each film was varied between the ranges of 0.14 mm-0.32 mm. When the concentration of HPMC was increased from 54-75%, thickness of the film also increased (table 4).

Film weight variation

Weight of the films was found to be in the range of 58.2 mg to 93 mg. As the proportion of the polymer increased, correspondingly the weight of film also increased. The results were depicted in table 4.

Folding endurance

Folding endurance is dependent on polymer and plasticizer concentration. The folding endurance was measured manually for the prepared films. The folding endurance for all the formulation was found to be in the range of 98-180 which revealed good strength and elasticity that can be attributed to the use of the plasticizer. The result is shown in shown in table 4. Folding endurance indicates packaging conditions of the product. This allows the product to be safely transported without breakage. Folding endurance was found to increase with increase in the concentration of film forming polymer HPMC.

Surface pH

The surface pH of domperidone mouth dissolving films was determined in order to investigate the possibility of any side effects *in vivo*. As an acidic or alkaline pH may cause irritation to the oral mucosa, it was determined to keep the surface pH as close to neutral as possible. A combined pH electrode was used for this purpose. Domperidone mouth dissolving films showed surfaces pH ranging from 6.9 to 7.0, hence the films will not cause any irritation to oral mucosa (table 4).

Drug content uniformity

The drug content results of all individual formulation are mentioned in table 5. The average values of content uniformity were found to be in the range of 9.30–9.84 mg. The result indicated that the process employed to prepare mouth dissolving films was capable of producing films with uniform drug content.

Disintegration time

The disintegration time of the mouth dissolving films was done by Petri dish method and was found to be in the range of 2.5–6.8 min (table 5). It was observed that as the concentration of polymer in the films increased, the disintegration time also increased. This might be due to increased level of polymer, results in the formation of high viscosity gel layer caused by more intimate contact between the particles of polymer. Due to intimate contact the mobility of drug particles in swollen matrices is decreased, which leads increase in disintegration time.

Table 4: Evaluation parameters of domperidone mouth dissolving films

Formulation code	Film thickness* (mm)	Weight (mg)*	Folding endurance	Surface pH
F1	0.14	58.2	98	6.9
F2	0.15	60.6	106	6.9
F3	0.16	64.8	117	6.9
F4	0.17	69.5	128	6.9
F5	0.19	81.3	132	7.0
F6	0.22	82.7	141	6.9
F7	0.23	85.8	156	7.0
F8	0.30	91.4	167	6.9
F9	0.32	93.0	180	6.9

*Average of 3 determinations

Table 5: Evaluation parameters of domperidone mouth dissolving films

Formulation code	Drug content (mg)*	Disintegration time (min)*
F1	9.50	2.5
F2	9.42	3.0
F3	9.49	3.5
F4	9.62	3.8
F5	9.53	4.0
F6	9.48	4.5
F7	9.30	5.0
F8	9.84	6.3
F9	9.62	6.8

*Average of 3 determinations

***In vitro* dissolution studies**

The *in vitro* dissolution of domperidone mouth dissolving films was studied in pH 6.8 phosphate buffer using USP XXIV dissolution test apparatus by basket method. The cumulative percentage release for different formulations is shown in fig. 5. DMP MDF'S showed maximum drug release of 98.266% (F8) to 100% (F1) at the end of dissolution. All formulations released the drug completely at different intervals of time. The formulation F1 released 100% drug in 16 min, F2 released 98.85% in 24 min, F3 released 99.74% in 28 min, F4 released 99.80% in 28 min, F5 released 100.4% in 32 min, F6 released 98.913% in 32 min, F7 released 99.313% in 36 min, F8 released 98.266% in 44 min and F9 released 99.73% drug in 48 min respectively. It was observed that polymer concentration was affecting the release of the drug; as the polymer concentration increased the films took more time to dissolve and release the drug in the medium. The thickness of films also increased with an increase in polymer concentration thereby controlling the release of drug for longer period of time. F1 was selected as optimised based on percentage release of drug and disintegration time.

The *in vitro* release profile of optimised mouth dissolving film F1 was compared with a marketed product i.e., VOMISTOP-10 a tablet. The marketed tablet released 99.53% of drug in 44 min and whereas the formulation F1 released 100% in 16 min (fig. 6). Thus prepared mouth dissolving film F1 releases the drug faster compared to the marketed product.

Kinetic study

To investigate the mechanism of drug release from the domperidone mouth dissolving films various kinetics models like zero order, first order, Higuchi's and Korsmeyer-Peppas equations were applied to the *in vitro* release data. The values of correlation-coefficient (r^2) for all the selected formulations were high enough to evaluate the drug release behavior. The kinetic results revealed that the selected formulations followed zero order, as correlation-coefficient (r^2) values (0.9235-0.9951) of zero order are higher than that of first order values (0.6659–0.951). When the data was plotted as per Higuchi kinetics, fairly linear plots were obtained with correlation coefficient values ranging from 0.8824-0.9874 for all the

formulations. The drug release was proportional to square root of time indicating that the drug release from domperidone mouth dissolving films was diffusion controlled. The release data obtained were also put in Korsemayer-Peppas model in order to find out n values, which describe the drug release mechanism. The n values of domperidone mouth dissolving films were found in the range of 0.8978-1.703 indicating the mechanism of drug release was non-Fickian diffusion super case II type which is indicative of drug release mechanism involving combination of diffusion and chain relaxation mechanism. The above observations led us to conclude that, all the domperidone mouth dissolving films followed diffusion controlled first order kinetics.

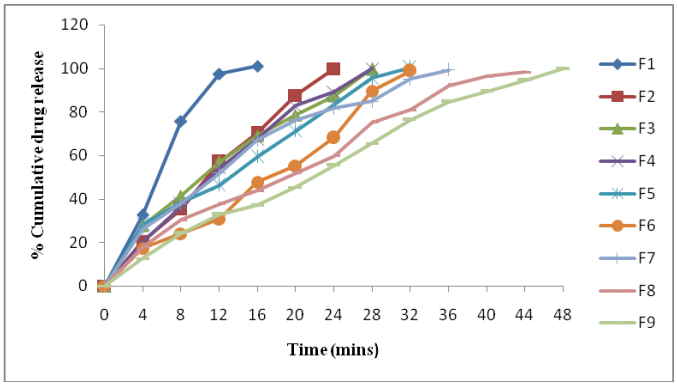

Fig. 5: *In vitro* release data of domperidone mouth dissolving film F1-F9

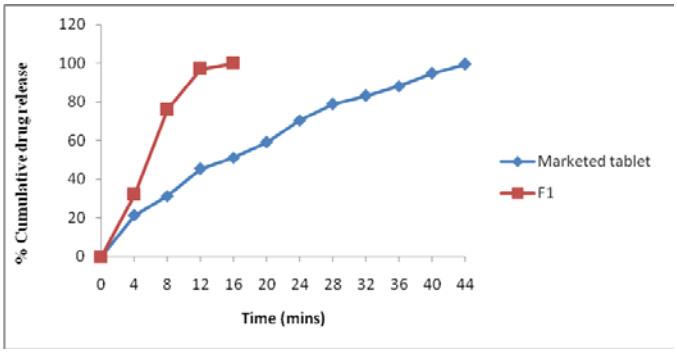

Fig. 6: Comparison of *in vitro* release profiles of marketed tablet-VOMISTOP and optimized mouth dissolving film F1

Fourier transformer infrared spectroscopy (FTIR) study

It was observed from IR spectra of the domperidone mouth dissolving film (F1) that all the peaks of the pure drug, beta cyclodextrin and the polymer have resolved properly even though few peaks of both drug and polymer overlap. After the formulation of the film the drug and the polymer have not changed and they retained their structural identity, indicating that the drug has not interacted with the polymer and other excipients (fig. 7).

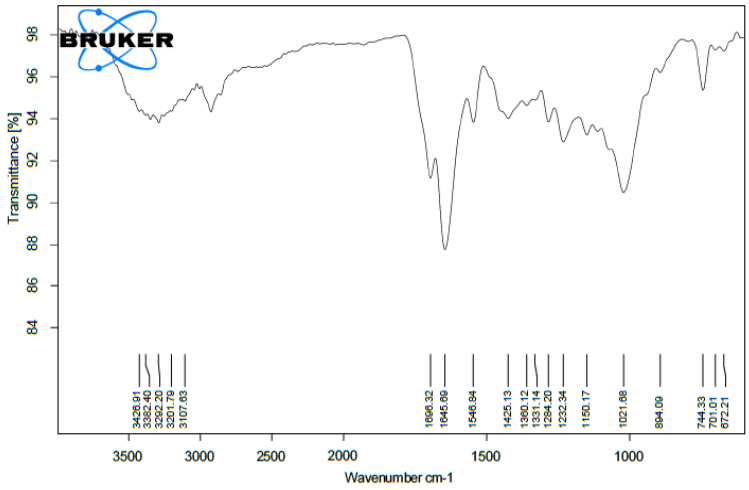

Fig. 7: FTIR spectra of optimiseddomperidone mouth dissolving film F1

Stability studies

The stability studies were carried out for the optimized formulation (F1) at25±2 °C/60±5% RH and 40±2 °C/75±5% RH as per ICH guidelines for a period of three months. No significant changes in the appearance, weight of the domperidone mouth dissolving films was observed during the stability study. The *in vitro* release data of F1 after stability period showed that F1 released 97.0% at 25 °C and 94% at 40 °C (fig. 8). As observed from the above results, the domperidone mouth dissolving films remained fairly stable during stability period.

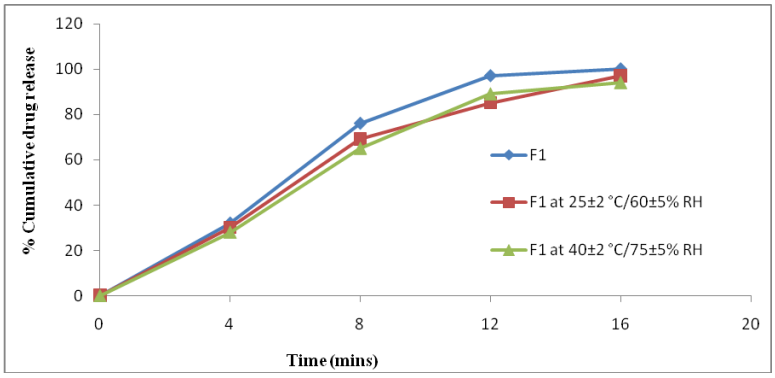

Fig. 8: *In vitro* release profile of Optimised domperidone mouth dissolving film F1 after a period of three months

CONCLUSION

Complexation by Kneading technique was found satisfactory for solid dispersion of domperidone. The domperidone solid dispersion SD3 increased the solubility of drug compared to pure drug. Solvent casting method was successfully used to obtain uniform mouth dissolving films containing drug-β cyclodextrine solid dispersion. The adopted method yielded uniform and reproducible mouth dissolving films with the method and polymer used. Glycerine acted as a model plasticizer at 30% w/w of polymer used. HPMC proved to be good drug reservoir polymer for domperidone mouth dissolving films. The drug release was found to be inversely proportional to the polymer concentration. Disintegration and dissolution data of mouth dissolving film were directly proportional to the polymer concentration. The mechanism of drug release of prepared mouth dissolving films was Non-Fickian diffusion controlled kinetics. Mouth dissolving films containing domperidone could be successfully developed and optimised. The films showed promising results and there exists a scope for further *in vivo* evaluation using suitable models.

ACKNOWLEDGEMENT

Authors are thankful to Mr. Suryanarayana Ch. Hetero labs ltd., Hyderabad, Dr. R. H. Udupi, Dr. Sunil Kumar B, NET Pharmacy College, Raichur for providing help to carry out this research.

FUNDING

Nil

AUTHORS CONTRIBUTIONS

All the authors have contributed equally.

CONFLICT OF INTERESTS

Declared none

REFERENCES

1. Arya A, Chandra A, Sharma V, Pathak K. Fast dissolving oral films: an innovative drug delivery system and dosage form. Int J ChemTech Res. 2010 Jan;2(1):576-83.
2. Rao NR, Shravani B, Reddy MS. Overview on buccal drug delivery systems. J Pharm Sci Res. 2013 Apr 1;5(4):80-8.
3. Reddy RJ, Anjum M, Hussain MA. A comprehensive review on buccal drug delivery system. Am J Advan Drug Deliv. 2013;1:300-12.
4. Almeida NMG, Lima R, Alves TFR, Rebelo MdA, Severino P, Chaud MV. A novel dosage form for buccal administration of bupropion. Braz J Pharm Sci. 2015 Jan;51(1):91-100. doi: 10.1590/S1984-82502015000100010.
5. Aboutaleb AE, Abdel Rahman SI, Ahmed MO, Younis MA. Design and evaluation of domperidone sublingual tablets. Int J Pharm Pharm Sci. 2016;8(6):195-201.
6. Mandeep K, Rana A, Nimrata S. Fast dissolving films: an innovative drug delivery system. Int J of Pharm Res and All Sci. 2013;2(1):14-24.
7. Junmahasathien T, Panraksa P, Protiarn P, Hormdee D, Noisombut R, Kantrong N. Preparation and evaluation of metronidazole-loaded pectin films for potentially targeting a microbial infection associated with periodontal disease. Polymers. 2018 Sep 13;10(9):1021-33. doi: 10.3390/polym10091021, PMID 30960947.
8. Siddiqui MN, Garg G, Sharma PK. A novel approach in oral fast dissolving drug delivery system and their patents. Adv Biol Res. 2011;5(6):291-303.
9. Bhura N, Sanghvi K, Patel U, Parmar B, Patel D. A review on fast dissolving film. IJPRBS. 2012;1(3):66-89.
10. Pathare YS, Hastak VS, Bajaj AN. Polymers used for fast disintegrating oral films: a review. Int J Pharm Sci Res. 2013 Jul;21(1):169-78.
11. Teodorescu M, Poly BM (vinylpyrrolidone)–a versatile polymer for biomedical and beyond medical applications. Polym Plast Technol Eng. 2015 Jun 23;54(9):923-43.
12. Helmy SA, El Bedaiwy HM. Pharmacokinetics and comparative bioavailability of domperidone suspension and tablet formulations in healthy adult subjects. Clin Pharmacol Drug Dev. 2014 Mar;3(2):126-31. doi: 10.1002/cpdd.43, PMID 27128456.
13. Athukuri BL, Neerati P. Enhanced oral bioavailability of domperidone with piperine in male Wistar rats: involvement of CYP3A1 and P-gp inhibition. J Pharm Pharm Sci. 2017 Jan 24;20:28-37. doi: 10.18433/J3MK72, PMID 28459658.
14. Chaturvedi S. Solubility and dissolution enhancement of domperidone using 2-hydroxypropyl-β-cyclodextrin by kneading method. Asian J Pharm. 2017 Sep 9;11(03):168-75.
15. Joshi P, Patel H, Patel V, Panchal R. Formulation development and evaluation of mouth dissolving film of domperidone. J Pharm Bioallied Sci. 2012;4(Suppl 1):S108-9. doi: 10.4103/0975-7406.94159, PMID 23066181.
16. Thorat KV, Khade P, Kakade S, Bhosale A. Formulation and evaluation of fast dissolving mouth film of domperdone. World J Pharm Res. 2021;10(12):2104-21.
17. Zayed GM, Rasoul SA, Ibrahim MA, Saddik MS, Alshora DH. *In vitro* and *in vivo* characterization of domperidone-loaded fast dissolving buccal films. Saudi Pharm J. 2020 Mar 1;28(3):266-73. doi: 10.1016/j.jsps.2020.01.005, PMID 32194327.
18. Bala R, Khanna S, Pawar P. Design optimization and *in vitro-in vivo* evaluation of orally dissolving strips of clobazam. J Drug

Deliv. 2014;2014:392783. doi: 10.1155/2014/392783, PMID 25328709.

19. Abdelbary A, Bendas ER, Ramadan AA, Mostafa DA. Pharmaceutical and pharmacokinetic evaluation of a novel fast dissolving film formulation of flupentixol dihydrochloride. AAPS PharmSciTech. 2014 Dec;15(6):1603-10. doi: 10.1208/s12249-014-0186-8, PMID 25142820.
20. Higuchi T. Mechanism of sustained-action medication. Theoretical analysis of rate of release of solid drugs dispersed in solid matrices. J Pharm Sci. 1963 Dec;52:1145-9. doi: 10.1002/jps.2600521210, PMID 14088963.
21. Reza MS, Quadir MA, Haider SS. Comparative evaluation of plastic, hydrophobic and hydrophilic polymers as matrices for controlled-release drug delivery. J Pharm Pharm Sci. 2003 May 1;6(2):282-91. PMID 12935440.
22. http://www.ich.org/FileAdmin/Public_Web_Site/ICH_Products/Guidelines/Quality/Q1A_R2/Step4/Q1A_R2__Guideline.pdf [Last accessed on 21 Aug 2022].
23. Saokham P, Muankaew C, Jansook P, Loftsson T. Solubility of cyclodextrins and drug/cyclodextrin complexes. Molecules. 2018 May 11;23(5):1161. doi: 10.3390/molecules23051161, PMID 29751694.