Journal of Pharmaceutical Research International

Volume 35, Issue 35, Page 1-12, 2023; Article no.JPRI.111561
ISSN: 2456-9119
(Past name: British Journal of Pharmaceutical Research, Past ISSN: 2231-2919, NLM ID: 101631759)

Formulation and *in vitro* Evaluation of a Novel Gastroretentive Gas-Generating Floating Matrix Tablets of Domperidone

Muhammad Abid Mustafa [a*], Seerat Shahzad [b], Zuha Tariq [a++], Obeda Asghar [a++], Umar Ali [a++], Rabia Zaka [a++], Muhammad Suffyan [a++], Muhammad Junaid Yaqoob [a++], Rimsha Riaz [a++], Kaif Ali [a++], Umair Ahmed [a++], Aneeza Safdar [b], Muhammad Aamir [b] and Muhammad Zahid Iqbal [b]

[a] Department of Pharmaceutics, Faculty of Pharmaceutical Sciences, Lahore University of Biological and Applied Sciences, Lahore, Pakistan.
[b] Department of Pharmacy Practice, Faculty of Pharmaceutical Sciences, Lahore University of Biological and Applied Sciences, Lahore, Pakistan.

Authors' contributions

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

Article Information

DOI: 10.9734/JPRI/2023/v35i357482

Open Peer Review History:
This journal follows the Advanced Open Peer Review policy. Identity of the Reviewers, Editor(s) and additional Reviewers, peer review comments, different versions of the manuscript, comments of the editors, etc are available here: https://www.sdiarticle5.com/review-history/111561

Original Research Article

Received: 19/10/2023
Accepted: 24/12/2023
Published: 26/12/2023

ABSTRACT

Aim and Objective: Domperidone floating matrix tablets were developed to increase the drug's bioavailability by prolonging its stomach residence time. These systems aim to provide controlled release, enhanced bioavailability, and improved patient compliance compared to conventional systems, especially for drugs with prolonged gastric residence.

[++] Research Student;
**Corresponding author: E-mail: abidbhatti222@gmail.com;*

Methodology: The wet granulation method was employed in formulating the tablets, utilizing polymers such as carboxymethylcellulose and carbopol. Various physical attributes of the tablets, including hardness, thickness, friability, weight variation, FTIR, XRD, drug content, and floating properties, were evaluated. Furthermore, the 12-hour in vitro drug release properties of the tablets were examined.
Results: As the tablets floated in the dissolving medium, they exhibited extended and sustained drug release characteristics. It was established that the drug release mechanism from these tablets followed Fickian diffusion, highlighting the crucial roles played by polymer rearrangement and water diffusion in the process of drug release. The choice of the optimal formulation (F3) was based on its in vitro characteristics.
Conclusion: The investigations conducted affirmed that the tablets are poised to deliver the intended therapeutic effects while maintaining an optimal residence time in the stomach, coupled with prolonged drug release.

Keywords: Floating time; gastric emptying time; CMC; anti-emetic; and prolong release.

1. INTRODUCTION

Oral administration is a popular and convenient method for both conventional and novel drug delivery systems. Tablets are popular due to patient acceptance, ease of administration, and flexibility. However, conventional formulations require multiple doses, leading to disadvantages in long-term therapy. Oral administration also results in low systemic bioavailability, shorter therapeutic activity duration, and the formation of inactive or toxic metabolites [1].

The normal gastric emptying period is two to three hours. This can result in diminished efficacy and inadequate medication release. Intimate contact with the absorbing membrane can increase absorption, which led to the creation of gastric retention-capable oral-controlled gastro-retentive dose forms. Floating, swelling, expanding, and high-density devices are examples of current methods [2].

Low bulk density, hydrodynamically balanced floating drug delivery systems, or FDDS, enable long-term, controlled drug release in the stomach's acidic environment.

Oral-controlled drug delivery systems aim to maximize and maintain consistent bioavailability; however, they face physiological problems such as the inability to precisely control and localize administration within the gastrointestinal tract. Drugs with a gastric retentive portion can be best absorbed locally, absorbed mostly in the stomach, poorly soluble, have a limited window of absorption, and are broken down in the colon [3]. Domperidone is a chemical compound with the molecular formula $C_{22}H_{24}C_1N_5O$. Its melting point is between 244°C and 246°C, and its molecular weight is 425.911 g/mol [4].

Domperidone has a poor bioavailability of 15% and a short biological half-life of 7 hours. Domperidone has fewer adverse effects and is quickly absorbed from the stomach and upper portion of the GIT after oral intake. It is a weak basic that dissolves well in acidic pH environments but much less readily in alkaline ones. Thus, the upper gastrointestinal system might be the focus of oral controlled-release dose formulations. The aim of the study is to develop gas-generating gastro-retentive drug delivery systems that offer advantages in terms of controlled release, improved bioavailability, and patient compliance compared to conventional drug delivery systems, especially for drugs that benefit from extended gastric residence [5].

1.1 Aim and Objectives

Aim and objectives of designing floating tablet of Domperidone was

- To improve patient compliance by sustain release.
- To lessen the drug adverse effect and reduce dose frequency.
- To enhances the bioavailability and retain it on site of absorption.
- To prolong its effect up to 12 hrs.

2. MATERIALS AND METHODS

2.1 Materials

Domperidone (99.98% purity) was provided as a gift sample by local pharmaceuticals in Lahore. The excipients, including carboxymethylcellulose

(K4M), carbopol, sodium bicarbonate, lactose, isopropyl alcohol, talc, and magnesium stearate, were sourced from Sigma-Aldrich Germany. All the polymers and excipients received were of pharmaceutical grade and were utilized as they were received. Additionally, other materials and solvents used in the study were of analytical grade.

2.2 Preformulation Studies

2.2.1 Organoleptic properties

As per the physical observation through the senses, the physical appearance is powder, the colour is white, the taste is bitter, and the odour is characteristic.

2.2.2 Salt formation

Domperidone are formed as domperidone succinate salt [4].

2.2.3 Solubility studies

Solvents such as methanol, alcohol, water and dimethylformamide are used for the solubility studies. The sample of 100 mg of domperidone is very slightly soluble in water and sparingly soluble in ethanol, methanol, and dimethylformamide. Domperidone's solubility studies show that it is a member of BCS-II. These findings suggest that in order to formulate an extended-release layer, a high-viscosity hydrophilic polymer is required to delay the release of the drugs, in this example, domperidone [4].

2.2.4 Solubilization

According to a study, domperidone is a water-insoluble drug with a poor dissolution pattern. Domperidone exhibits gastroprokinetic properties and is an antiemetic. It exhibits poor solubility in alkaline pH and is a weak base. Various techniques are being utilized to improve the solubility of domperidone, regardless of its solubility being dependent on pH. The current protocol aims to improve the solubility of domperidone by designing solid dispersions based on polyethylene glycol (PEG). The fusion method was used to create PEG 8000-based solid dispersions with the drug in various mass ratios, such as 1:1, 1:3, 1:5, and 1:7 [4].

2.2.5 pKa determination

A study showed domperidone have pka value 7.9. The sample was measured by 96-Capillary Array CE using aqueous buffers and have pka value of 4.25 [6].

2.2.6 Angle of Repose

Granules' angle of repose was measured using the free-standing cone and fixed funnel methods. The finely measured grains were placed in a funnel. The funnel's height was adjusted so that the tip of the funnel just touched the top of the granule pile. Granules were free to pour onto the surface through the funnel [7].

The diameter of the powder cone measured and angle of repose was calculated using the following formulae:

$$tan\theta = \frac{h}{r}$$

Where h is the height of the heep and r is the radius of the heep

2.3 Determination of Bulk Density and Tapped Density

The graduated cylinder was carefully filled with a precisely weighed quantity of grains or powder (W), and the volume (V0) was measured. Next, the graduated cylinder was put inside the tap density tester (USP) and sealed with a lid. The density apparatus was then set for powder, and the volume (Vf) was measured. This process was repeated until the two successive readings were equal [7].

The bulk density and the tapped density were calculated using the following formulae respectively:

Bulk density = (Weight of granules before tapping (Wi)) / (Volume of granules before tapping (VO))

Tapped density = (Weight of granules after tapping (Wf)) / (Volume of granules after tapping (Vf))

2.4 Carr's Compressibility Index

We looked at Carr's indirect approach to measuring powder flow from bulk densities. A powder's potential strength and stability as an arch or bridge could be determined directly by looking at its % compressibility [7].

Carr‘s index of each formulation was calculated according to equation given below:

Carr's compressibility Index (%) = [(TD-BD) × 100] / TD

Where TD is the tapped density and BD is the bulk density

2.5 Hausner’s Ratio

Hausener’s Ratio is calculated with the following formulae:

$$Hausner'sRatio = \frac{Tapped\ density\ (TD)}{Bulk\ density\ (BD)}$$

Domperidone Hausner's ratio was determined to be 1.51. The organoleptic properties Domperidone meet IP and USP monograph requirements, respectively. With the exception of the fact that the Hausner ratio value of domperidone implies very poor flow, the flow properties, poured density, tapped density, compressibility index, and Hausner ratio also meet the specifications, showing that the former exhibits poor flow and the latter exhibits very poor flow. Table 1 illustrates the powder's flow characteristics [7].

2.6 Melting Point

Melting point of the drug was determined by using capillary tube method.

2.7 Result

Melting point of domperidone was found 242.5 °C [8].

2.8 Stability Studies

To conduct stability studies, two solutions of domperidone (10 ml) each are prepared: one with 15 µg/ml of 1N HCl added and left to stand at room temperature for 24 hours; the other solution is made with 15 µg/ml of 1N NaOH added and left to stand at room temperature for 24 hours. A 50 mg dose of the drug was maintained at 60ºC for eight hours. Next, the mixture was ready to attain a domperidone concentration of 15 µg/ml. A dosage of about 50 mg was exposed to direct sunlight for a duration of 12 hours. Next, the mixture was ready to achieve a domperidone concentration of 15 µg/ml. The sample displays 11.5% photolytic degradation, 100% thermal degradation, 36.06% basic degradation, and zero acid degradation [9].

2.9 Method of Preparation

The wet granulation method was used to develop the formulation. By using a spatula, combine the needed amount of polymer (CMC K4M, carbopol 934P, or SA), lactose, and sodium bicarbonate in a mortar for five minutes. Drop by drop, isopropyl alcohol is added until a mass that is appropriate for granulation is reached. Sieve number 40 is used to granulate the moist substance. After an hour of drying at room temperature (35°), the granules are combined with talc and magnesium stearate and squeezed in a single punch machine using an 8-mm standard flat-face die punch set. Three formulations were prepared by using different polymer concentrations, as shown in Table 2. The weight variation, hardness, friability, and assay comply with a limit as per the specification. The tablets were floated and released the domperidone about 12 hours [10].

2.10 Characterization

2.10.1 Physical characterization

Twenty tablets were tested for weight variation, six tablets for hardness using a Monsanto hardness tester, twenty tablets for thickness using a screw-gauge micrometer, and twenty tablets for percentage friability using a Roche friabilator [11].

2.10.2 Content uniformity

Twenty tablets were taken, and each tablet's drug content was measured. After the tablets were crushed in a mortar, 100 mg of the drug's powder was added to a 100 ml standard flask. To get the final volume with an acceptable (0.1N HCl) solution, the powder was dissolved in an appropriate solvent. After the sample was mixed, it was filtered using a 0.45µ membrane filter. Using 0.1N HCl solution as a blank, the filtered solution was suitably diluted before being subjected to a UV spectrophotometer analysis at 240.2 nm to determine the drug content [11].

2.10.3 Diameter and thickness

When it comes to tablet packaging, the thickness of the tablet matters. Extra thick tablets have an impact on how well they fit into plastic containers or blisters. The diameter of the die, the volume of

Table 1. Flow properties of powder

	Flow properties	Reference	Measured	Flowability
1	Angle of repose	30.63 ± 0.7	38.66± 0.52	Excellent
2	Bulk density, tapped density	0.521± 0.01g/cc	0.521± 0.01g/cc	Excellent
3	Carr's compressibility Index	5.97	6.45	Excellent
4	Hausner's Ratio	1.12	1.06	Excellent

Table 2. Concentration of different material in formulations

Ingredients	F1	F2	F3
Domperidone	30mg	30mg	30mg
CMC	93mg	_	46mg
Carbapol	_	90mg	47mg
Lactose	30mg	33mg	30mg
Sodium bicarbonate	20mg	20mg	20mg
Magnesium stearate	3.4mg	3.4mg	3.4mg
Talc	3.6mg	3.6mg	3.6mg

fill that can fit inside the die, and the force or pressure used during compression all affect the thickness of the tablet. One can measure the tablet's thickness manually or with automated machinery. The Vernier Caliper was used to measure the tablets' diameter and thickness. It is stated in millimeters [11].

2.10.4 Thickness Uniformity studies

Vernier callipers were used to conduct the thickness uniformity studies. For the purpose of studying thickness uniformity, six tablets with millimeter markings were used. The mean and standard deviation were computed using the collected data [11].

2.10.5 Hardness uniformity studies

A Monsanto Hardness tester was used to measure the hardness of the prepared formulation. Hardness uniformity studies were conducted using six floating tablets. The mean and standard deviation were computed using the hardness data [11].

2.10.6 Friability

The Roche Friabilator was used to assess the tablet's friability. The unit of expression is percentage (%). Weighing twenty tablets at first, they were put into the friabilator. For four minutes, or 100 revolutions, the friabilator was run at 25 revolutions per minute. Once more, the tablets were weighed (W final). The % friability was then calculated by: [11]

Friability = 100 × (1 – Final Weight (Wf) / Initial Weight (W0))

2.10.7 Weight uniformity test

This test is similar to the weight uniformity test in that, if the drug makes up a larger portion of the tablet, any variation in the tablet weight clearly indicates a variation in the active ingredient.

The average weights of 20 tablets were calculated after they were chosen at random. Next, each tablet was weighed individually, and the results were compared to the average.

Determine the average tablet weight by dividing the total tablet weight by the total number of tablets [11].

The average tablet weight (X) is equal to (X1+X2+X3+...+X20) / 20.

2.11 Assay of Tablets

Dissolution Testing Apparatus 2 (paddle method) was used to measure the domperidone release rate from floating tablets (n=3) in accordance with British Pharmacopoeia (BP). 900 cc of 0.1N HCl, temperature of 37±0.5°C, and 50 rpm rotation were used for the dissolution test. For a full day, a 5-milliliter sample of the solution was taken out of the dissolving equipment every hour, and the sample was replaced with brand-new dissolving media. Following a 0.45 µ membrane filter, 0.1N HCl was used to dilute the samples to an appropriate concentration. A Shimadzu UV-1700 UV/Vis double-beam spectrophotometer (Kyoto, Japan) was used to measure the absorbance of these solutions at 284 nm. The amount of time the pill remained suspended in

the dissolving solvent was recorded as the total floating time [12].

2.12 Floating Capacity

In a 100 ml beaker filled with 0.1 N HCl, the pills were added. The floating lag time was calculated as the amount of time needed for the tablet to rise to the surface and float. Three copies of the experiments were carried out. Throughout in vitro dissolving investigations, total floating times were recorded [13,12].

2.13 *In-vitro* Buoyancy Studies

A 100-mL beaker of 0.1N HCl was filled with the pills. We called this floating lag time, the amount of time it took for the tablet to rise to the surface and float.

2.14 FTIR Analysis

FT-IR spectroscopy was used to investigate drug-polymer interactions utilising the Shimadzu, Japan, FTIR-8400S device.The spectra were obtained for the drug domperidone in its pure form as well as for the drug and polymer combination formulation in matrix tablets. The samples were prepared in KBr discs (2 mg of sample in 200 mg of KBr) and subjected to a hydrostatic press for three minutes at a force of 5.2 N/m2. The resolution was 4 cm-1, and the scanning range was 400–4000 cm-1 [14].

2.15 XRD

To examine the physical state of domperidone in the formulations, X-ray diffraction analysis was performed on the formulations using a Philips PW 170 system (Philips USA) with Cu-Kα radiation (400 kV, 30 mA, and scan speed 1^/min) [14].

2.16 *In vitro* Dissolution Studies

The release rate of domperidone from floating tablets (n=3) was determined in accordance with British Pharmacopoeia (BP) using Dissolution Testing Apparatus 2 (paddle technique). For the dissolving test, 900 millilitres of 0.1N HCl were employed, and the experiment was carried out at 37±0.5° and 50 rpm. A sample (5 ml) of the solution was removed from the dissolving apparatus every hour for the duration of the day, and fresh dissolving medium was added in its place. Following their passage through a 0.45 µ membrane filter, the samples were diluted to the proper concentration using 0.1N HCl. These solutions' absorbance at 284 nm was measured using a Shimadzu UV-1700 UV/Vis double-beam spectrophotometer (Kyoto, Japan) [12].

2.17 Kinetic Modeling of Drug Release

The kinetic modelling of drug release was determined by fitting the dissolution profiles of all formulations into zero order, first order, and Korsmeyer-Peppas models.

3. RESULTS AND DISCUSSION

3.1 Evaluation of the Prepared Tablets

Physical characteristics such as hardness, thickness, weight variation, and friability were tested for each formulation, and the results showed that they were all within pharmacopeial bounds. The test results were totaled up. All of the formulations' drug contents were assessed and found to be within the allowable limit as described by the US Pharmacopeia. According to this study, every prepared formulation was excellent. The pre-compression studies were described in Table 3.

Table 3. Pre compression Parameter

Parameters	F1	F2	F3
Angle of repose	27°55	29°39	28°81
Bulk density	0.63	0.55	0.47
Tapped density	0.66	0.63	0.52
% Compressibility	4.76	14.54	10.63
Hausner’s ratio	1.047	1.14	1.10

3.2 Post Compression Parameter

3.2.1 Shape of the tablet

Each formulation batch's tablet revealed a round shape without cracks upon physical inspection. We looked inside the crushed tablet shape using a magnifying glass. The same shape of the tablets was observed by Anand Patel et. al. (2009) during the development and in vivo floating behaviour of Verapamil HCl Intragastric Floating Tablets [1].

3.2.2 Hardness test

The hardness was assessed using a manual hardness tester known as the Monsanto hardness tester. Six tablets from each batch were employed for hardness measurements, and the resulting data were used to calculate the average hardness.

The hardness measurements for tablets in each batch fell within the range of 4 to 10 kg/cm², indicating favorable handling properties for all formulations. A similar range of 4–10 kg/cm2 was observed by Laila Saddam C Shaikh et. al. during the formulation and evaluation of ibuprofen gastro-retentive floating tablets [15].

3.2.3 Friability test

After weighing ten tablets, they were put in a friabilator (roche, switzerland). For four minutes, friabilator was circulated at 25 rpm. after eliminate the ground powder, the tablets were weighed once more. using the given equation friability was determined,

$$F = 100 \times (1 - Wf / W0)$$

All formulations had a friability percentage of less than 1%, which guaranteed the tablets' mechanical stability. A similar friability trend of less than 1% was observed by Saša Baumgartner, et al. during the optimization of floating matrix tablets and evaluation of their gastric residence time [16].

3.2.4 Weight variation test

For the calculation of average weight 20 tablets were weighed individually. Then both individual weight and average weight of tablets were used to calculate the percentage deviation using formula.

Percentage deviation= (Average weight – Individual weight) / (Average weight)

Every tablet successfully met the weight variation test, as the percentage weight variation remained within the Pharmacopeial limit of 5% of the weight. The tablets displayed uniform weight characteristics, supported by low standard deviation values. A similar weight variation range was observed by Navjot Kanwar et. al. during the preparation and evaluation of floating tablets of pregabalin [17].

All post-compression analyses were shown in Table 4.

3.2.5 Floating time

One tablet was placed in a 200 mL glass beaker that was 37˚C and contained 0.1 N HCl. The time it took for the tablet to reach the surface was quantified as the floating lag time, and the amount of time it floated in 0.1 N HCl was measured visually, duration time of floating. F3 shows maximum duration of floating of more than 24hrs.Mixture of sodium bicarbonate act as effervescent agent. The floating lag time and floating duration of different formulations were shown in Table 5 [18].

3.3 Buoyancy Study

When placed in a 0.1N HCl solution at pH 1.2 and a temperature of 37°C, the tablets exhibited buoyancy, remaining afloat without disintegrating. The buoyancy study results lead to the conclusion that Formulation F3, which includes both CMC and Carbopol polymers, demonstrated superior buoyancy lag time (BLT) and total floating time (TFT) compared to Formulation F1, consisting of CMC alone, and Formulation F2, which contained Carbopol separately. *In vitro* buoyancy of formulation was shown in Fig. 1 [19].

3.4 FTIR Analysis

The FT-IR of the pure drug showed the following features: N-H deformation at 1693.38 cm- Fig. 1. *In vitro* buoyancy of formulation.

Table 4. Post Compression parameters

Formulation	Weight Variation (mg)	Friability (%)	Thickness(mm)	Diameter(mm)
F1	180± 0.5	0.69±0.04	3.5	8.05
F2	181± 0.5	0.64±0.06	3.5	8.05
F3	179± 0.5	0.54±0.03	3.5	8.05

Table 5. Floating time

Formulation	Floating lag time (sec)	Duration of floating time (hrs)
F1	60	=12
F2	53	>10
F3	62	>12

Fig. 1. *In-vitro* Buoyancy of tablet

1, aromatic C-H stretching at 3024.18 cm-1, C = C at 1622.02 cm-1, asymmetrical C-H stretching at 2937.38 cm-1, symmetric C-H stretches at 2817.81 cm-1, and N-H stretching at 3122 cm-1, meaning that the drug was free of the -CONH group, as demonstrating that formulation contain 100% domperidone as Keyur S. Patel et al. (2021) reported similar results [20]. It was inferred from the foregoing interpretation that there had not been a significant change in the bands of functional groupings. No indications of incompatibility were seen since the band peak and peak intensity did not significantly vary with the excipients. The FT-IR spectra of the pure drug and formulation mixture was shown in Fig. 2.

3.5 XRD

The domperidone XRD was seen in Fig. 3, showed sharp and strong, and less dispersed peaks, suggesting that the drug is crystalline. The diffractogram of tablets with floating matrix display a comparable pattern with a little reduction in peak intensity, indicating that the drug was able to diffuse nearly evenly throughout the tablet. This finding validates a partial transition of domperidone from a crystalline to an amorphous solid form. Mohamed et al. (2022) produced a comparable finding with a comparable explanation [21].

3.6 *In-vitro* Dissolution Study

The percentage of drug release was determined during a 12-hour period, as shown in Table 6. In the kinetic study, the drug release percentage vs. time graph plot was used to ascertain the release sequence for every formulation. In most of the formulations tested in dissolving tests, 85% of the drug was released after 10 hours. At time zero, no drug is released. The drug's first release was relatively slow. The drug's first release was relatively slow. In the case of F3, more than half of the drug was released early; after 6 hours, F3 released the maximum amount of drug, 99.7%, after 12 hours, as shown in Fig. 4 [22].

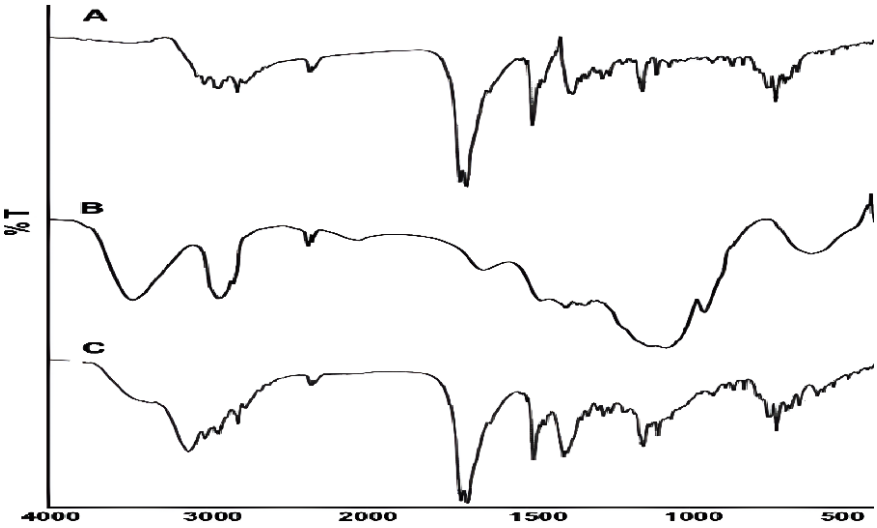

Fig. 2. FTIR spectra of (A) Domperidone, (B) Carbopol, and (C) physical mixture of tablet

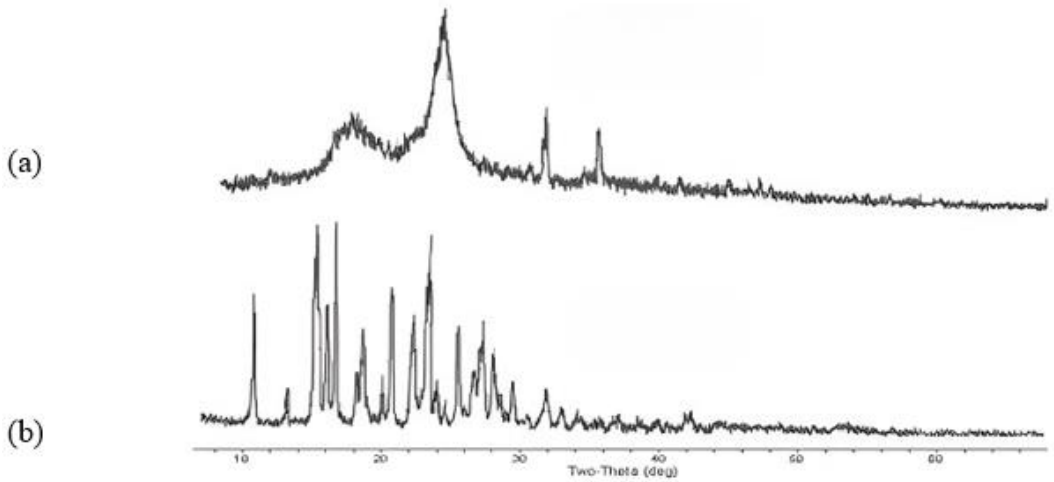

Fig. 3. XRD diffractogram of (a) physical mixture of tablets, and (b) domperidone

Table 6. *In vitro* dissolution study

Time (hours)	Percentage drug release		
	F1	F2	F3
0	0	0	0
1	8.67	7.36	14.67
2	16.91	15.92	36.91
4	42.67	39.36	54.67
6	78.91	74.92	86.91
10	96.24	98.92	97.24
12	98.10	99.21	99.7

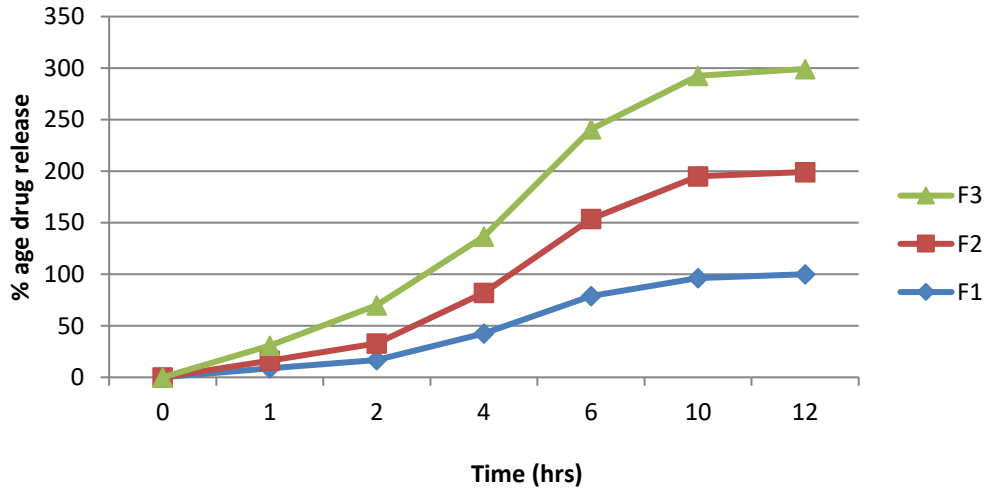

Fig. 4. *In vitro* drug dissolution studies

3.7 Release Kinetic Studies

The drug release data for famotidine were fitted to models representing Higuchi's, zero-order, first-order, and Korsmeyer's equation kinetics to know the release mechanisms. The data were processed for regression analysis using the MS Excel DD Solver add-in statistical function. The results are shown in Table 7. The kinetic data (Table 5) showed that the release of drugs

Table 7. Release Kinetic Studies

Formulation	Zero Order		First Order		Korsmeyer	
	K_0	R(Square)	K_1	R(Square)	kKP	n
F1	3.409	0.9327	0.074	0.9703	10.36	0.39
F2	3.781	0.9185	0.054	0.9915	9.873	0.31
F3	3.111	0.9603	0.068	0.9981	1.247	0.26

followed formulations. Diffusion is related to the transport of drugs from the dosage form into the in vitro fluid, depending on the concentration. As the gradient varies, the drug is released, and the distance for diffusion increases. In the present study, in vitro release profiles could be best expressed by first order, as the optimised formulation (F3) showed good linearity (R2: 0.9981), indicating that diffusion is the dominant mechanism of drug release with these formulations. In Korsmeyer and Peppa's release kinetics model, the n value describes the formulation's defined drug release using Fick's law of diffusion. In this situation, a Fickian transport mechanism corresponds to a n value less than 0.45. A similar trend was observed by Ravi Kumar et. al. (2009) during the formulation and evaluation of an effervescent floating tablet of famotidine [23].

3.8 Limitation of Study

The system for drug delivery in the stomach requires high fluid levels and is not suitable for drugs with solubility or stability issues in the gastric tract (GIT). It may not be suitable for drugs well-absorbed along the entire GIT and undergo first pass metabolism. Additionally, drugs irritated by the gastric mucosa and unstable in the stomach's acidic environment are not suitable. Dosage should be administered with a full glass of water.

4. CONCLUSION

The goal of this study is to develop floating Domperidone tablets. Because domperidone has a lower stomach residence time, an attempt was made in this study to extend its GI residence time by encapsulating it in floating tablets. We successfully designed and prepared a floating tablet of domperidone. These tablets provide excellent floating times and swellibility. Among all F3 formulations, the maximum floating time was more than 12 hours. The swelling index of the formulation showed that CMC showed good swellibility. The gas-generating agent allowed the tablet to release gas and come up to the service for floating. Release kinetics of all the formulations followed the first-order model of kinetics. The design can be used in the future for better formulation of floating tablets.

CONSENT AND ETHICAL APPROVAL

It is not applicable.

ACKNOWLEDGEMENT

We would like to express our sincere gratitude to the Deanship Faculty of Pharmaceutical Sciences, Lahore University of Biological and Applied Sciences (UBAS), for providing the necessary resources and support that made this research possible. Their commitment to fostering academic excellence has been invaluable.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

REFERENCES

1. Patel A, et al, Development and in vivo floating behavior of verapamil HCl intragastric floating tablets. Aaps Pharmscitech. 2009;10(1):310-315. Available:https://doi.org/10.1208/s12249-009-9210-9
2. Streubel,A, Siepmann J, Bodmeier R. Gastroretentive drug delivery systems. Expert opinion on drug delivery. 2006;3 (2):217-233. Available:https://doi.org/10.1517/17425247.3.2.217.
3. Sadozai SK, et al. Formulation development and evaluation of domperidone sustained release matrix tablets by two different methods using guar gum as a sustaining agent. World Applied Sciences Journal. 2013;25(12): 1704-1712. DOI:10.5829/idosi.wasj.2013.25.12.76174.
4. Bruni G, et al, Structure and properties of domperidone and its succinate salt. Acta

Crystallographica Section B: Structural Science, Crystal Engineering and Materials. 2013; 69(4):362-370
DOI: org/10.1107/S2052519213016989

5. Patil HG, et al, Formulation and development of orodispersible sustained release tablet of domperidone. Drug development and industrial pharmacy, 2016;42(6):906-915
Available:https://doi.org/10.3109/03639045.2015.1088864
6. Guimarães CR, et al, Use of 3D properties to characterize beyond rule-of-5 property space for passive permeation. Journal of chemical information and modeling. 2012; 52(4):882-890.
DOI: https://doi.org/10.1021/ci300010y
7. Ganesan V, Formulation and Evaluation of Mucoadhesive Microspheres-of Venlafaxine HCL Using Three Factors at Two Level Full Factorial DesignSwamy Vivekanandha College of Pharmacy, Tiruchengode; 2009.
8. Zheng M, et al. Solubility modelling and solvent effect for domperidone in twelve green solvents. Journal of Molecular Liquids. 2018;261:50-56.
9. Sunil S, et al. Analysis of population genetic structure of Indian Anopheles culicifacies species A using microsatellite markers. Parasites & vectors. 2013;6:1-8.
Available:https://doi.org/10.1186/1756-3305-6-166
10. Prajapati S, Patel L, Patel D, *S*tudies on formulation and in vitro evaluation of floating matrix tablets of domperidone. Indian journal of pharmaceutical sciences, 2009;71(1):19.
DOI: 10.4103/0250-474X.51944
11. Rahamathulla M, et al. Design and evaluation of losartan potassium effervescent floating matrix tablets: In vivo x-ray imaging and pharmacokinetic studies in Albino Rabbits. Polymers. 2021;13 (20):3476.
12. Prajapati ST, Patel LD, Patel DM. Studies on formulation and in vitro evaluation of floating matrix tablets of domperidone. Indian J Pharm Sci. 2009;71(1):19-23
DOI: 10.4103/0250-474x.51944.
13. Prajapati ST, Patel LD, Patel DM, Gastric floating matrix tablets: Design and optimization using combination of polymers. Acta Pharm 2008;58(2):221-9
DOI: 10.2478/v10007-008-0006-3
14. Jelvehgari M, et al. Effect of formulation and processing variables on the characteristics of tolmetin microspheres prepared by double emulsion solvent diffusion method. Indian Journal of Pharmaceutical Sciences. 2010;72(1):72
DOI: 10.4103/0250-474X.62251
15. Shaikh SC, et al, Formulation and evaluation of Ibuprofen gastro-retentive floating tablets. Universal Journal of Pharmaceutical Research. 2018;3(4):19-23
DOI:
https://doi.org/10.22270/ujpr.v3i4.178.
16. El Nabarawi MA, et al. Formulation, release characteristics, and bioavailability study of gastroretentive floating matrix tablet and floating raft system of Mebeverine HCl. Drug design, development and therapy. 2017:1081-1093.
17. Rahamathulla M, Saisivam S, Gangadharappa H. Development of valsartan floating matrix tablets using low density polypropylene foam powder: In vitro and in vivo evaluation. AAPS PharmSciTech. 2019;20:1-10.
18. Senjoti FG, et al. Design and In-vitro Evaluation of Sustained Release Floating Tablets of Metformin HCl Based on Effervescence and Swelling. Iran J Pharm Res. 2016;15(1):53-70.
PMID: 27610147; PMCID: PMC4986121.
19. Bhambar KV, Pande SD, Bhambar RS, Formulation and evaluation of floating matrix tablets of drotaverine hydrochloride. Journal of Drug Delivery and Therapeutics. 2019;9(3):200-206.
20. Patel KS, et al. Formulation and Evaluation of Gastroretentive Floating Tablets of Quetiapine Fumarate. Journal of Drug Delivery and Therapeutics. 2021;11(3-S):65-73
Available:https://doi.org/10.22270/jddt.v11i3-S.4833
21. Mohamed JMM, et al. Ameliorated stomach specific floating microspheres for emerging health pathologies using polymeric konjac glucomannan-based domperidone. BioMed Research International; 2022.
Available:https://doi.org/10.1155/2022/3670946
22. Zayed GM, et al. *In vitro* and *in vivo* characterization of domperidone-loaded fast dissolving buccal films. Saudi

Pharmaceutical Journal. 2020;28(3):266-273
Available://doi.org/10.1016/j.jsps.2020.01.005

23. Puri V, et al. synthesis and characterization of thiolated gum ghatti as a novel excipient: Development of compression-coated mucoadhesive tablets of domperidone. ACS omega. 2021;6(24): 15844-15854.
Available:https://doi.org/10.1021/acsomega.1c01328.

Peer-review history:
The peer review history for this paper can be accessed here:
https://www.sdiarticle5.com/review-history/111561