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FORMULATION AND EVALUATION OF GASTORETENSIVE FLOATING MATRIX TABLETS OF DOMPERIDONE

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ABSTRACT
Domperidone is widely used in the management of gastric disorders, particularly gastro esophageal reflux disorder and peptic ulcer. But the short half-life of domperidone leads to poor patient compliance and adverse reactions. Hence matrix floating tablets of domperidone were needed to achieve better therapeutic efficacy and to improve patient compliance. The purpose of the present study was to develop an optimized gastoretentive floating matrix tablets of domperidone. Formulations were prepared using different polymers like chitosan, ethyl cellulose, HPMC K 100, HPMC K 15, HPMC K 4 and carbopol 934 by dry granulation method. Prepared tablets were evaluated for weight variation, hardness, friability, drug content, in-vitro buoyancy studies and in vitro dissolution studies. It was concluded that the formulation F2 is the best formulation as the extent of drug release was found to be 98.77 %.This batch also showed immediate floatation and total floating time of 12 hours.

Keywords *Domperidone, gastoretensive, floating tablets, HPMC, carbopol 934*

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INTRODUCTION

The oral route is the most frequently used route for drug administration. Oral dosage forms are intended for systemic effects resulting from drug absorption through gastro intestinal tract .Rapid gastrointestinal transit could result in incomplete drug release from the device above the absorption zone leading to diminished efficacy of the administered dose [1]. Therefore, different approaches have been proposed to retain the dosage form in the stomach. These include floating systems, bioadhesive systems, swelling, expanding systems, delayed gastric emptying systems and low density super porous systems [2]-[8]. Oral delivery of drugs is by far the most preferable route of drug delivery due to the ease of administration, patient compliance, non-evasive in nature and flexibility in formulation. From immediate release to site specific delivery, oral dosage forms have really progressed. A gastric

floating drug delivery system (GFDDS) can overcome at least some of these problems and is particularly useful for drugs that are primarily absorbed in the duodenum and upper jejunum segments. The GFDDS is able to prolong the retention time of a dosage form in the stomach, thereby improving the oral bioavailability of the drug [9], [10].

Domperidone is a synthetic benzimidazole compound that acts as a dopamine D2 receptor antagonist. Its localization outside the blood-brain barrier and antiemetic properties has made it a useful adjunct in therapy for Parkinson's disease. Domperidone is also used as a prokinetic agent for treatment of upper gastrointestinal motility disorders [11]. It is rapidly absorbed from the stomach and the upper part of the gastrointestinal tract after the oral administration and few side effects have been reported [11], [12].

The major objective of the present investigation was to develop a gastroretentive drug delivery system containing domperidone using different polymers.

MATERIALS AND METHODS

Materials

Domperidone was received as a gift sample from Ronak Pharmaceuticals pvt Ltd., Patan. Chitosan was purchased from Rajesh chemical Co., Mumbai. Ethyl cellulose (EC), Hydroxy propyl methyl cellulose (HPMC) K 100, HPMC K 15, HPMC K 4, carbopol 934, citric acid, sodium bi carbonate, magnesium stearate, talc, micro crystalline cellulose (MCC) were purchased from Central Drug House (P) Ltd., New Delhi.

Method [4], [7], [14], [15]

Ingredients were weighed accurately and mixed thoroughly. All the composition mix together (except magnesium state and talc) and punched the composition in tablet punching machine. Reduction of slugs is done in order to obtain granules for compression and passed granules through the 20 mm sieves. After that magnesium stearate and talc were added in the granules and compressed to form tablet by using a 10 station rotary tablet machine. These fabricated tablets were evaluated. The tablets were white round and flat, the details of composition are given in Table 1.

Table: 1 Composition of floating matrix tablets of Domperidone.

BATCH CORD	INGREDIANT (mg)												
	Domperodone	EC	HPMC K 100	HPMC K 15	HPMC K 4	Chitosan	Carbopol 934	Citric acid	Sodium bi carbonate	Lactose	MMC	Magnesium stearate	Talc
F1	20	95	-	-	-	-	-	6	14	35	26	2	2
F2	20	-	95	-	-	-	-	6	14	35	26	2	2
F3	20	-	-	95	-	-	-	6	14	35	26	2	2
F4	20	-	-	-	95	-	-	6	14	35	26	2	2
F5	20	-	-	-	-	95	-	6	14	35	26	2	2
F6	20	-	-	-	-	-	95	6	14	35	26	2	2

EVALUATION

1. **Weight variation test:** [2], [6], [13]
   20 tablets were selected at random, individually weighed and the average weight was calculated. None of the tablets deviated from the average weight by more than ±7.5%.
2. **Hardness test:** [5], [8]
   Tablets require a certain amount of strength or hardness and resistance to friability to with stand mechanical shocks. The hardness of tablet was measured by Monsanto hardness tester.
3. **Friability:** [2], [8], [11]
   Twenty tablets were weighed and placed in a Roche friabilator and the equipment was rotated at 25 rpm for 4 min. The tablets were taken out, dedusted, and reweighed. The percentage friability of the tablets was calculated by:

$$\% \text{ Friability} = \frac{\text{initiat weight} - \text{final weight}}{\text{initial weight}} \times 100$$

4. **Drug content:** [14], [15], [16]
   Twenty tablets were selected randomly and transferred to a suitable tare container and weighed, and then average weight per tablet was calculated, the tablets were powdered with the help of mortar and pestle. Domperidone solution was prepared by dissolving the required amount of powder in a suitable solvent. Absorbances of the resultant solutions were measured after suitable dilutions at 284 nm by using UV/Visible spectrophotometer.
5. **In-vitro buoyancy studies:** [17]
   The in-vitro buoyancy was determined by floating lag time and total floating time. The tablets were placed in a 100 ml glass beaker containing simulated 0.1N Hydrochloric acid, as per USP. The time required for the tablet to rise to the surface and float was determined as the floating lag time. Total floating time was also determined.
6. **In-vitro dissolution studies:** [7], [17]
   In vitro dissolution studies were performed using type II (paddle) dissolution apparatus at 50 rpm and 900 ml of 0.1 N Hydrochloric acid (pH 1.2) was used as a dissolution medium. Temperature of dissolution medium was maintained at 37±0.5°C. Five milliliters aliquot of the dissolution medium was withdrawn at specific time intervals. Absorbance of filtered solution was measured by UV–visible spectrophotometer at 285 nm, and the percent of drug released was determined using standard curve. Dissolution rate was studied for the prepared formulations.

RESULTS

Formulations were prepared by dry granulation techniques using different polymers. Parameters like weight variation, hardness, friability, drug content, in-vitro buoyancy studies and in-vitro dissolution studies were performed and results are described in Table 2, Table 3 and Table 4. All formulations evaluated for variation in weight and results indicated that for all formulations exhibit very low weight variation which lies within the pharmacopoeia limits i.e., average weight ± 7.5%. The hardness of the tablets was found to be in the range of 4.7 to 5.3 kg/cm^2. The percentage friability was less than 1% for all formulation ensuring mechanical stability of the formulated tablets. Content uniformity in all the formulations were found in the range of 97.32 ± 0.76 to 99.32 ± 0.57 indicating the compliance with the pharmacopoeia limits.

Floating lag time from all the prepared formulation was found to be in following order: F1<F4<F3<F5<F2<F6. F1 formulation was floated in very short time.

% Cumulative drug release from all the prepared formulation was found to be in following order: F2>F4>F3>F5>F1>F6. % Cumulative drug release from F2 was found to be for 12 hours, from F5 and f6 for 10 hours, from F3 and F4 for 9 hours and from F1 for 8 hours. Formulation F2 shows high % Cumulative drug release.

Table: 2 Evaluation of floating matrix tablets of Domperidone.

TESTS	BATCH CORD					
	F1	F2	F3	F4	F5	F6
Weight variation (mg)	Pass	Pass	Pass	Pass	Pass	Pass
Hardness kg/cm^2	4.7	5.3	4.9	4.8	5.1	5.2
% Friability	0.58	0.44	0.49	0.54	0.66	0.42
% Content uniformity	97.55 ± 0.43	99.32 ± 0.57	97.32 ± 0.76	98.45 ± 0.47	97.43 ± 0.23	98.76 ± 0.49

Table: 3 In-vitro Buoyancy study of formulations

Batch	Floating lag time (second)	Total floating time (hour)
F1	44	8 hour
F2	65	12 hour
F3	51	9 hour
F4	45	9 hour
F5	56	10 hour
F6	98	10 hour

Table: 4 In-vitro dissolution studies of floating matrix tablets of Diazepam

Time (hour)	% Cumulative drug release					
	F1	F2	F3	F4	F5	F6
1	20.34 ± 0.87	08.48 ± 0.65	14.76 ± 0.76	22.64 ± 0.66	23.33 ± 0.74	18.27 ± 0.40
2	35.76 ± 0.46	17.75 ± 0.86	31.39 ± 0.39	35.73 ± 0.73	34.87 ± 0.63	29.87 ± 0.56
3	48.65 ± 0.29	30.39 ± 0.48	45.58 ± 0.42	49.84 ± 0.26	39.64 ± 0.77	38.54 ± 0.34
4	55.96 ± 0.84	47.57 ± 0.51	54.84 ± 0.63	58.33 ± 0.64	46.84 ± 0.45	47.76 ± 0.54
5	68.87 ± 0.35	59.91 ± 0.23	62.76 ± 0.76	63.72 ± 0.54	57.99 ± 0.76	55.87 ± 0.31
6	75.43 ± 0.54	65.87 ± 0.45	72.66 ± 0.44	77.53 ± 0.43	63.87 ± 0.54	65.09 ± 0.69
7	82.24 ± 0.39	72.43 ± 0.49	88.99 ± 0.73	89.66 ± 0.53	69.66 ± 0.73	71.77 ± 0.39
8	91.43 ± 0.87	82.43 ± 0.35	94.33 ± 0.65	93.39 ± 0.76	80.38 ± 0.63	85.54 ± 0.84
9	-	91.46 ± 0.39	95.43 ± 0.63	97.48 ± 0.89	88.76 ± 0.88	89.55 ± 0.66
10	-	94.34 ± 0.62	-	-	92.46 ± 0.76	90.33 ± 0.28
11	-	97.49 ± 0.73	-	-	-	-
12	-	98.77 ± 0.66	-	-	-	-

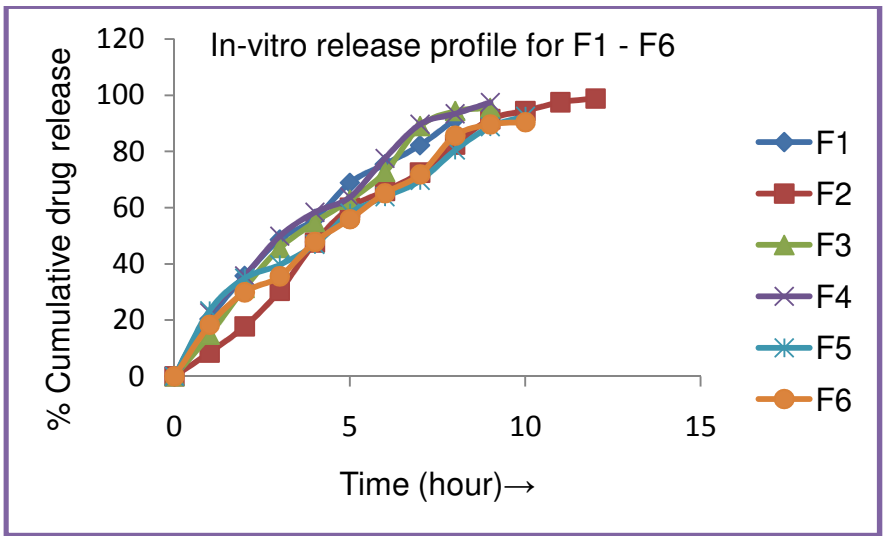

Figure: 1 In-vitro release profile for F1-F6

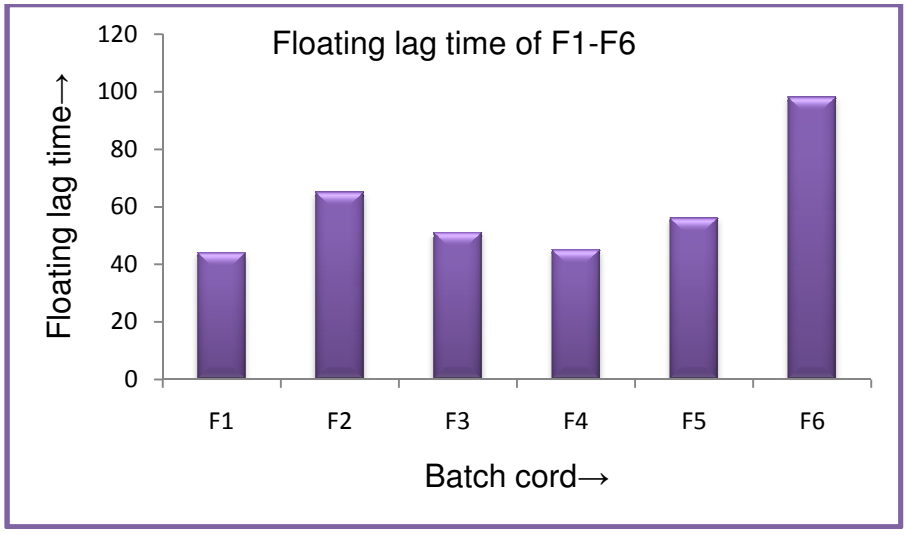

Figure: 2 Floating lag time of F1-F4

DISCUSSION

Different formulations were prepared using different polymers like chitosan, ethyl cellulose, HPMC K 100, HPMC K 15, HPMC K 4 and carbopol 934. The tablets prepared by dry granulation technique were found to have adequate hardness, friability, content uniformity, floating lag time and total floating time. In 3 different HPMC grade, there was an increase in the floating lag time which could be attributed to the fact that tablets containing low viscosity grade HPMC swell rapidly than tablets with high viscosity grade HPMC. Also higher floatation time of these tablets could be explained by a slower carbon dioxide formation because of the presence of the effervescent agents within the HPMC matrix. Medium can penetrate these tablets easily and react with Sodium bicarbonate to liberate carbon dioxide. Tablets of all batches remained floatable throughout the study. It was concluded that the formulation F2 is the best formulations as the extent of drug release was found to be 98.77 % within 12 hours and total floating time was 12 hour. Based on the results we can certainly say that floating type gastroretentive drug delivery system holds a lot of potential for drug having stability problem in alkaline pH or which mainly absorb in acidic pH. This route of drug delivery can certainly be explored for improved bioavailability and increased stability those drugs which degrades in intestinal pH for many existing drugs.

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