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Formulation and Evaluation of Pantoprazole Sodium Floating Tablets

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ABSTRACT

The purpose of the present study was to develop an optimized gastric floating drug delivery system (GFDDS) containing Pantoprazole sodium as a model drug using different concentrations of polymers like HPMC, Guar gum. The design of the delivery system was based on controlled release formulation with floating and swelling features in order to prolong the gastric retention time of the drug delivery systems. All the formulations were evaluated for hardness, friability, swelling index, dissolution time, buoyancy lag time, duration of buoyancy, drug content & *in vitro* drug release. Based on the *in vitro* dissolution studies, it was concluded that the formulation, F6 containing Guar gum is the best formulation and it can be used to increase the GRT of the dissolution fluid in the stomach to deliver the drug in a controlled manner.

INTRODUCTION

The oral route is the most preferable route of drug delivery due to ease of administration, patient compliance, and flexibility in the formulations.[1] Gastro retentive drug delivery systems are designed to be retained in the stomach for a prolonged period of time and release their active ingredients and thereby enable sustained and prolonged input of the drug to the upper part of the GI tract.[2] Prolonged gastric retention time improves bioavailability, reduces drug wastage, and improves solubility of drugs that are less soluble in a high pH environment.[3]

GRDF will also greatly improve the pharmacotherapy of the stomach itself through local drug release leading to high drug concentrations at the gastric mucosa, which isis sustained over a long period of time.[4]

Gastro retention helps to provide better availability of new products with new therapeutic possibilities and substantial benefits for patients.[5, 6, 7, 8] This technology has generated enormous attention over the last few decades owing to its potential application to improving the oral delivery of some important drugs for which the prolonged retention in the upper GIT can greatly improve their oral bioavailability.[9]

Pantoprazole is a protein pump inhibitor used for the treatment of acute duodenal ulcer, acute benign gastric ulcer, gastroesophageal reflux disease and prophylactic use in duodenal ulcer. The recommended oral dosage is generally 20 mg for an acute duodenal ulcer, acute benign gastric ulcer and is prescribed for a duration of 8-12 weeks. The drug has a short biological half-life (1-2 hr) and local action in the stomach which makes it suitable to formulate as a floating drug delivery system.[10]

MATERIALS & METHODS:

MATERIALS:

Pantoprazole sodium was used as an active ingredient. HPMC & Guar gum were used as polymers. Sodium bicarbonate was used as an effervescent agent. The other ingredients used were PVP, microcrystalline cellulose, Magnesium stearate, talc. All the materials used in the experimental works were obtained from MLR Institute of Pharmacy, Hyderabad, Telangana. All the reagents used were of analytical grade.

METHODS:

Formulation of Pantoprazole floating tablets:

The floating tablets of Pantoprazole were developed by direct compression method. Pantoprazole sodium and all other ingredients were passed through sieve no. 60. All the ingredients were mixed thoroughly for 15 min by triturating. The powder mixture was lubricated with magnesium stearate. The tablets were prepared according to the formulation table 1.

Table 1: Composition of different formulations of floating tablets

Ingredients (mg)	F1	F2	F3	F4	F5	F6
Pantoprazole sodium	150	150	150	150	150	150
HPMC	50	75	100	----	----	----
Guar gum	----	----	----	50	75	100
Talc	2	2	2	2	2	2
PVP	7	7	7	7	7	7
Sodium bicarbonate	35	35	35	35	35	35
MCC	184	159	134	184	159	134

Evaluation of pre-compression parameters of drug and polymeric blend

Excipients, polymers, and drug were characterized for their physical properties such as angle of repose, bulk density, tapped density, compressibility, Hausner's ratio

Evaluation of floating tablets:

Thickness:

The crown thickness of individual tablets was measured by Vernier caliper. The crown thickness of individual tablet is also determined for the purpose of determining the density of tablet compacts.[11]

Hardness:

The hardness of the tablet is determined by Monsanto hardness tester. The tablet to be tested is placed between the spindle and anvil and pressure is applied by turning the knurled knob just sufficient to hold the tablet in position. The reading of pointer on the scale is then adjusted to zero. The pressure is now increased as uniformly as possible until tablet breaks. The pointer now reads the pressure required to break the tablet.

Friability:

Twenty tablets were accurately weighed and placed inside the friability chamber. The apparatus was operated for 100 revolutions. After rotations, the tablets were reweighed and the loss in weight was determined. The loss in weight should not be more than 1%.

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

Weight variation test:

Twenty tablets of each formulation were weighed individually using electronic balance. From that average weight was calculated. The % deviation was calculated by comparing individual tablet weight with average weight.[12]

Floating behavior:

The *in vitro* buoyancy was determined by floating lag time and floating time. The tablets were placed in the dissolution vessel containing 900 ml of 0.1 N HCl. The time required for the tablet to rise to the surface and float was determined as floating lag time. The duration for which the tablet remains afloat on the surface of the solution is known as floating time.[13]

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Buoyancy time:

The time during which tablets remained buoyant was measured.[14]

Swelling index:

The swelling behavior of a dosage unit was measured by studying its weight gain. The swelling index of tablets was determined by placing the tablets in the basket of dissolution apparatus using dissolution medium as 0.1 N HCl at 37±0.5˚C. After 0, 2, 4, 6 hr each

dissolution basket containing tablet was withdrawn, blotted with tissue paper to remove excess water and weighed on an analytical balance. [15-16] The experiment was performed in triplicate for each time point.

Swelling index was calculated using the following formula:

$$\text{Swelling index} = \frac{\text{Wet weight of tablet - dry weight of the tablet}}{\text{The dry weight of the tablet}}$$

Uniformity of drug content:

10 tablets were weighed from each batch. Tablets were triturated in mortar and quantity of powder equivalent to 10mg of Pantoprazole was transferred to the 100ml volumetric flask. Sufficient quantity of 0.1N HCl was added with shaking and volume was made up to the mark. Further dilutions were made and the absorbance was recorded at 291nm against 0.1N HCl as a blank.[17]

***In vitro* dissolution studies:**

USP Dissolution test apparatus (Type I) was used to determine the *in-vitro* release of Pantoprazole floating tablet. 900 ml of 0.1N HCl was used as a dissolution buffer. The temperature was maintained at

37 ± 0.5˚C and stirred at 50 rpm. At predetermined time intervals, 5ml of the sample was withdrawn and replaced with an equal amount of 0.1 N HCl. The collected samples were filtered and suitably diluted with 0.1N HCl and analyzed spectrophotometrically at 291nm to determine the amount of drug release in the dissolution medium [18]

RESULTS AND DISCUSSION:

Pre-compression parameters:

The bulk density and tapped density obtained for all the formulations are in the range of 0.33-0.52gm/ml and 0.41-0.61gm/ml. the Carr's index and Hausner's ratio were found to be in the range of 16.25% -9.65% and 1.85%-1.0% respectively. The angle of repose of all formulations of the powder blend was found to be in the range of 23.32˚-36.17˚ which

indicates good flow property. Hence the experimental values are in the good agreement with the official values. Results obtained are shown below.

Table 2: Pre compression parameters of powder blend:

Formulation code	Angle of repose (°) ± SD	Bulk density (gm/ml) ± SD	Tapped density (gm/ml) ± SD	Carr's index (%) ± SD	Hausner's ratio ± SD
F1	23.32± 0.011	0.33± 0.013	0.41± 0.016	16.25± 0.12	1.85± 0.21
F2	25.55± 0.075	0.37 ±0.062	0.45± 0.058	14.33± 0.10	1.52 ±0.01
F3	26.18± 0.012	0.41 ±0.010	0.49± 0.026	14.21± 0.22	1.32± 0.52
F4	29.27 ±0.010	0.45 ±0.122	0.52± 0.098	11.85± 0.11	1.09± 0.65
F5	33.10± 0.282	0.48 ±0.062	0.58± 0.122	10.24 ±0.25	1.05± 0.98
F6	36.17 ±0.182	0.52 ±0.007	0.61± 0.511	9.65 ±0.85	1.0± 0.29

EVALUATION OF FLOATING TABLETS:

Table 3: Evaluation of physicochemical properties of the tablet:

Formulation code	Thickness (mm)	Weight variation (%)	Hardness (kg/cm^2)	Friability (%)	Drug content (%)
F1	2.90±0.02	1.87±0.20	5.18±0.11	0.59±0.09	100.06±1.07
F2	2.93±0.03	1.96±0.26	5.36±0.19	0.56±0.03	98.76±0.732
F3	3.01±0.03	2.31±0.35	5.40±0.28	0.52±0.08	99.58±0.689
F4	2.96±0.01	1.90±0.42	5.47±0.26	0.61±0.02	100.26±0.276
F5	3.05±0.04	2.05±0.53	5.32±0.32	0.68±0.06	100.73±1.118
F6	3.07±0.02	2.11±0.61	5.51±0.39	0.65±0.03	100.21±1.847
Standard	----------	<5%	4 -6	<1%	98.5-101

The tablets were observed visually and did not show any defect such as capping, chipping & lamination. The % deviation from average tablet weight for all the tablets are found to be within the specified limits and hence all formulations complied with the test for weight variation. The thickness of the tablets was found to be between 2.90 to 3.074mm. The hardness of tablets was found be in the range of 5.18 to 5.51 kg/cm^2. Hardness values are satisfactory and indicated the good mechanical strength of tablets. Drug content of all tablets was found between 98.76% to 100.95% which is within limits of pharmacopeial specifications. The friability was below 1% indicating the good mechanical resistance of the tablet.

Swelling behavior:

Table 4: Swelling index of Pantoprazole sodium floating tablets

Time (hr)	Swelling index ratio					
	F1	**F2**	**F3**	**F4**	**F5**	**F6**
0	0	0	0	0	0	0
2	32	35	42	46	50	55
4	46	48	50	51	58	60
6	52	55	58	65	67	72
8	59	61	66	70	74	80

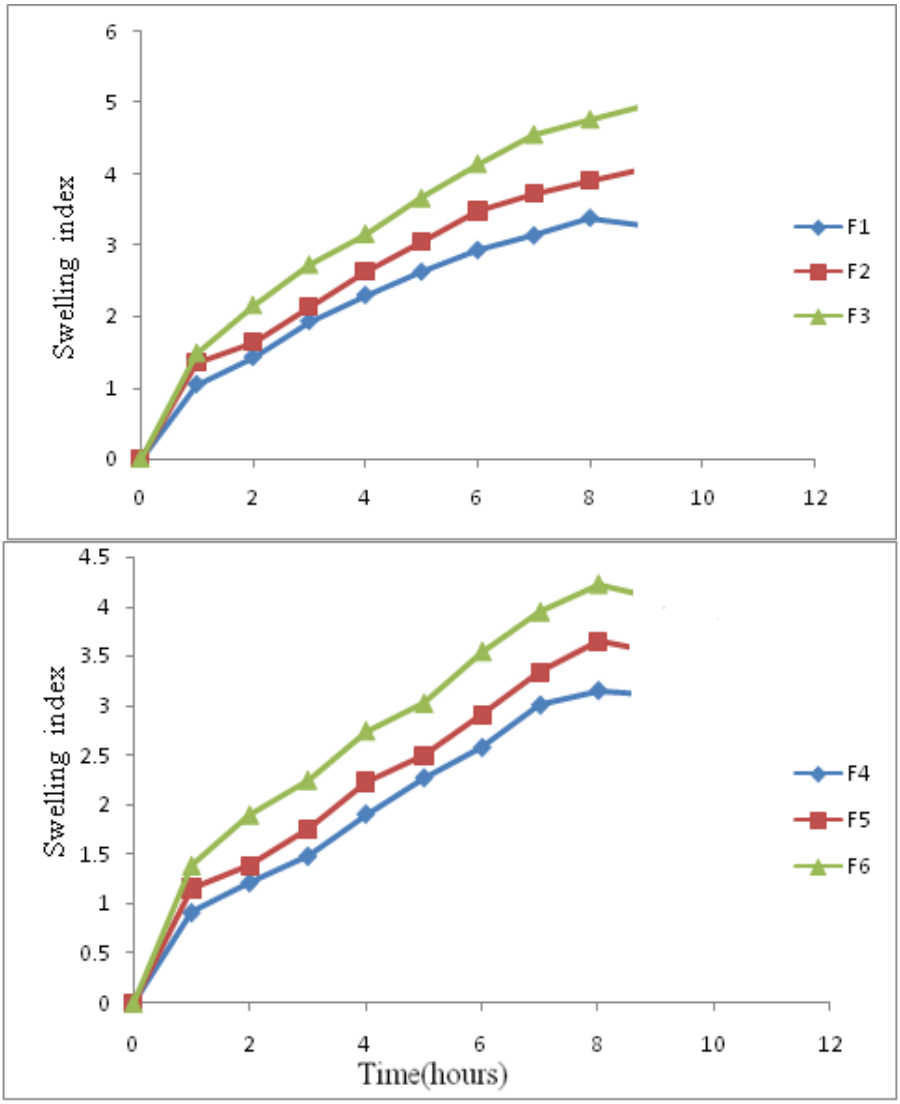

Figure 1 and 2: Swelling index of Pantoprazole sodium floating tablets F1-F6

Swelling studies were performed on all the batches (F1 to F6) for 8hours. From the results, it was concluded that swelling increases as the number of polymer increases. The swelling of the tablet increases up to 6 to 8 hours depending upon polymer concentration because the

polymer gradually absorbs the water due to its hydrophilicity. After the specified period, the swelling of the tablet slightly decreased. It was also concluded that the tablet with natural polymers exhibited a greater degree of swelling compared to semi-synthetic polymers.

***In vitro* buoyancy studies of Pantoprazole sodium:**

Table 5: *In vitro* buoyancy studies of Pantoprazole sodium floating tablets

Formulation code	Floating lag time (sec)	Floating time (hr)
F1	63	>12
F2	75	>12
F3	82	>12
F4	89	>12
F5	93	>12
F6	98	>12

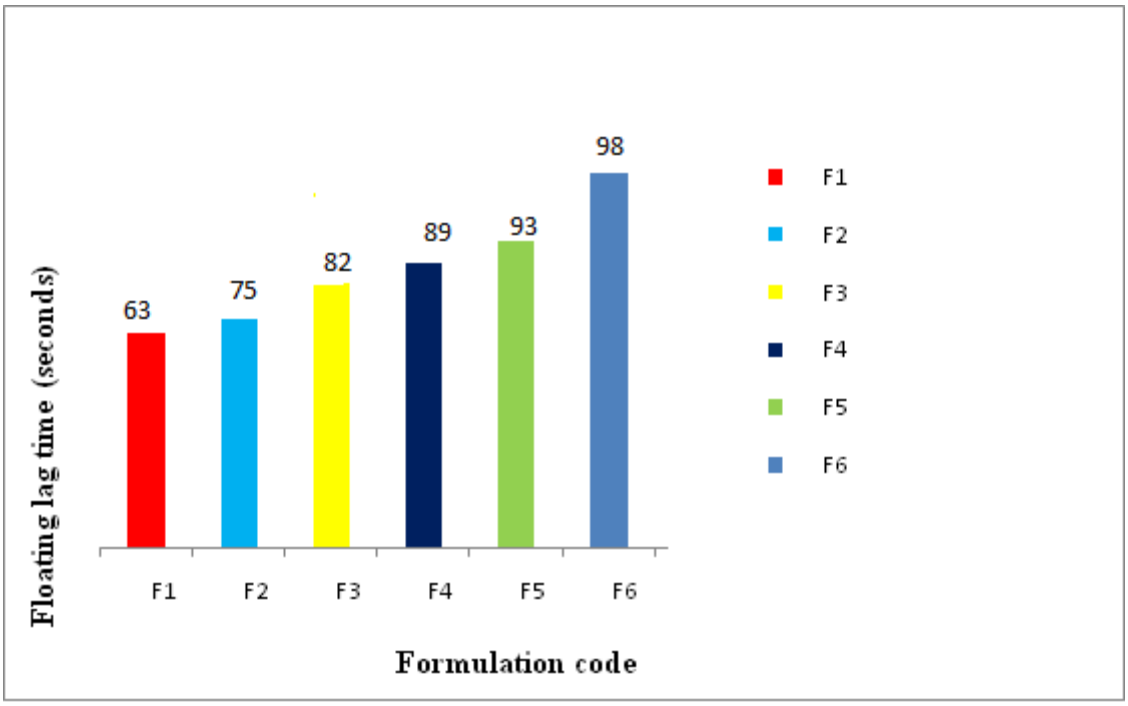

Figure 3: Floating lag time of F1-F6

The floating lag time and total floating time for all the formulations was tested in a dissolution vessel containing 900 ml of 0.1N HCl solution. All the tablets showed floating lag time between 63 to 98 seconds & the total floating time of more than 12 hours. The buoyancy lag-time of tablets depends on the amount of sodium bicarbonate involved in co_2 formation.

For a floating system, the ideal matrix material should be highly permeable to dissolution media in order to initiate rapid generation of co_2 and allow the release of co_2 to promote floating. The floating time of all formulations was found to be increasing with the increasing amount of polymer concentration and as the concentration of the gas generating agent ($NaHco_3$) increases the floating lag time is decreases.

***In vitro* Dissolution Profile of Tablets:**

Table 6: Cumulative percentage drug release from F1-F6

Time(hrs)	F1	F2	F3	F4	F5	F6
1	9.42	11.45	15.22	17.39	19.78	20.57
2	17.31	18.11	22.39	24.44	27.97	28.84
3	25.12	27.26	33.28	36.63	38.32	40.78
4	33.76	34.62	37.48	39.28	40.56	42.30
5	52.66	53.41	56.52	60.56	62.02	67.08
6	65.95	69.29	71.67	73.43	76.33	79.96
7	70.99	72.30	75.95	79.65	82.81	85.35
8	79.45	84.87	88.73	90.48	94.23	98.48

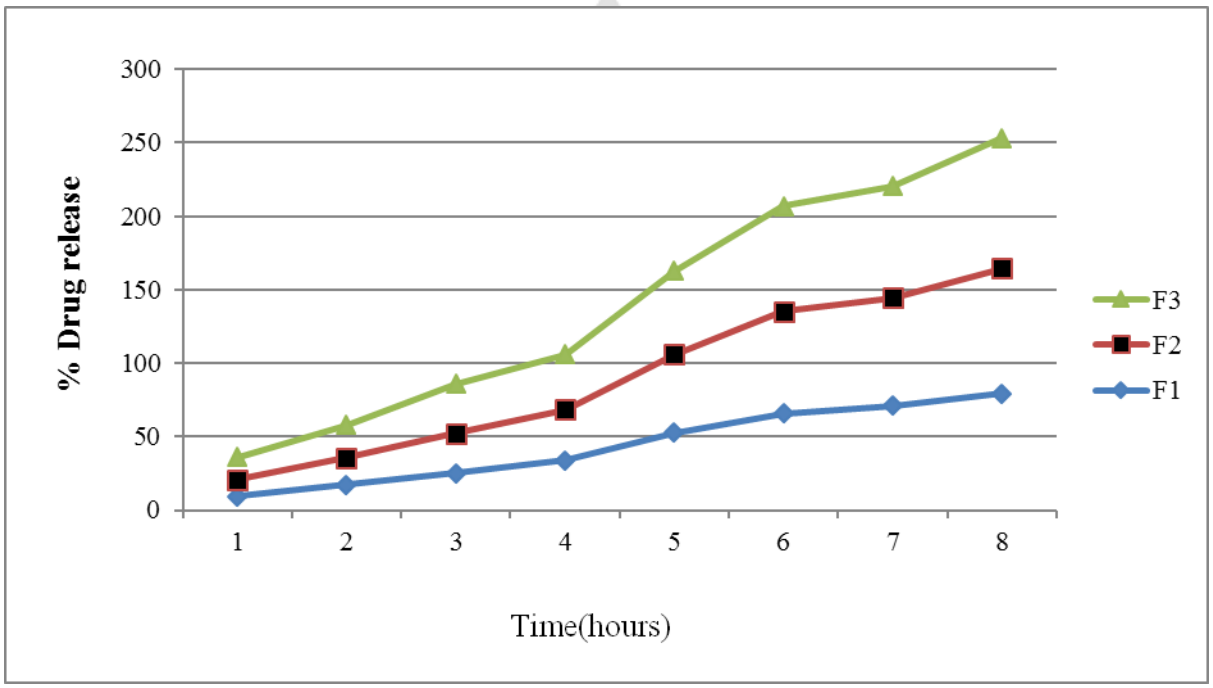

Figure 4: Percentage drug release of Pantoprazole sodium F1-F3

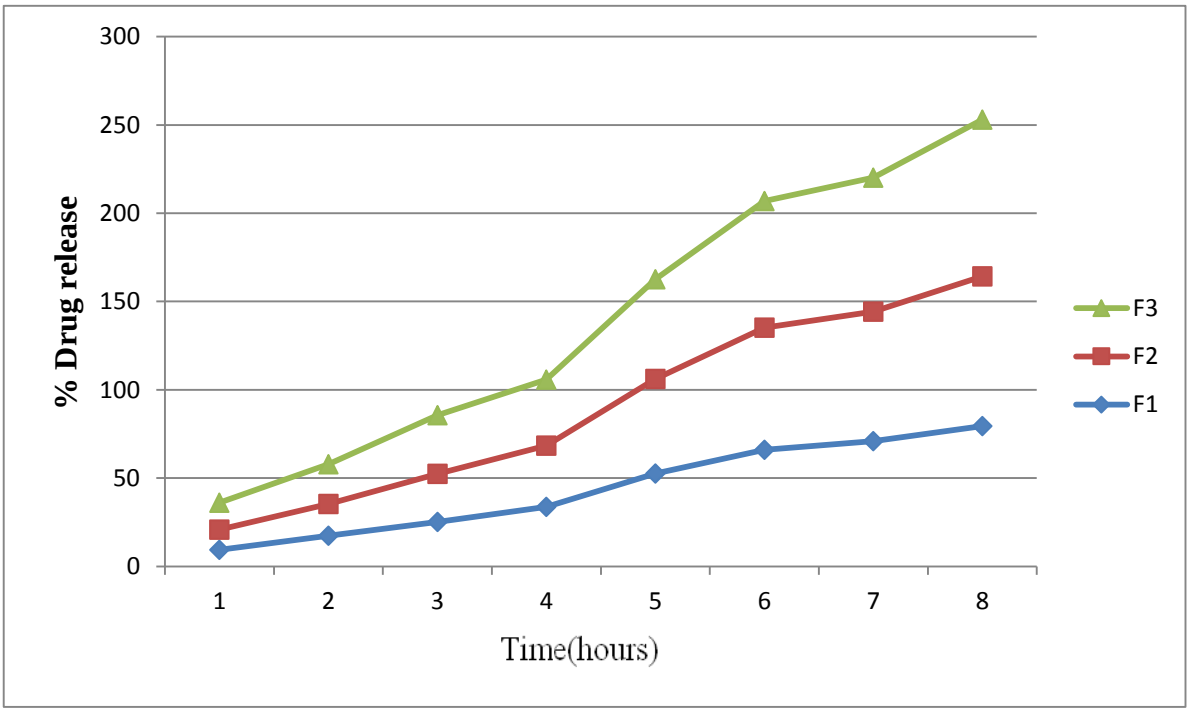

Figure 5: Percentage drug release of Pantoprazole sodium F4-F6

In vitro dissolution studies were performed in 0.1N HCl and the results are tabulated in table 6 and graphs were depicted in figure 18 and 19.Formulations F1, F2, F3, F4, F5 and F6 show drug release of 79.45%, 84.87%, 88.73%, 90.48%, 94.23 and 98.48 respectively at the end of 8 hours. Among all the formulations, formulation F6 was found to be the most promising formulation as it has shown the most consistent drug release (98.48%) up to 8 hours as compared to other formulations.

CONCLUSION

Gastro retentive dosage form using Guar gum was prepared to develop a floating tablet of Pantoprazole sodium that could retain in the stomach for longer periods of time delivering the drug to the site of action, i.e., stomach. The pre-compression parameters of all formulations showed good flow properties and these can be used for tablet manufacture.

The post-compression parameters of all formulations were determined and the values were found to be satisfactory. From the drug content and in-vitro dissolution studies of the formulations, it was concluded that the formulation F6 i.e. the formulation containing Guar gum, PVP, Sodium bicarbonate, microcrystalline cellulose and Magnesium stearate is the best formulation. As a result of this study, it may be concluded that the floating tablets using

a guar gum in optimized concentration can be used to increase the GRT of the dissolution fluid in the stomach to deliver the drug in a controlled manner. The concept of formulating floating tablets of Pantoprazole sodium offers a suitable and practical approach in serving the desired objectives of gastro retentive floating tablets.

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