Research Article

Formulation and Evaluation of Floating Beads of Pantoprazole Sodium for Peptic Ulcer

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ABSTRACT

Background: Oral route of administration gets the highest priority for the delivery of drug as well as better patient compliance. Floating bead is selected for achieving a prolonged and predictable drug delivery profile in the gastrointestinal tract to control the gastric residence time using a gastro-retentive dosage forms that will provide as with new and important therapeutic options.

Objectives: The present study was aimed to prepare a floating bead drug delivery system to design a controlled release oral dosage form of Pantoprazole sodium. This helps to overcome the demerit of limited residence time of the drug in the gastrointestinal tract and hence to increase the duration of release.

Methods: The floating beads delivery system of Pantoprazole sodium by emulsion gelation method with Sodium alginate was prepared and evaluated for different parameters such as beads size measurements, buoyancy lag time, floating time, swelling index, drug entrapment efficiency, invitro drug release studies and anti-ulcer activity studies.

Result: These considerations have leads to the development of oral controlled gastro-retentive dosage forms possessing gastric retention capabilities. Pantoprazole floating beads are used to treat and prevent peptic ulcer in the stomach.

Keywords: Pantoprazole sodium, Floating beads, Sodium alginate, Sodium bicarbonate.

INTRODUCTION

There has been a notable rise in interest in innovative medication delivery systems and modified drug delivery systems over the past two to three decades. It combines modern technology with innovative dosage forms that are vastly superior to traditional dosage forms and medical equipment. It increases medication potency, regulates drug release to have a prolonged therapeutic impact, offers higher safety, and particularly targets a medicine to a desired area.

The term "modified release" refers to both delayed and extended-release systems for oral administration as well as other delivery systems designed specifically to modify the release of drugs. Modified-release dosage forms are those that alter the timing or rate of release of drug substances. For example, oral drug products having delayed release, (sustained release, controlled release) gastro-retentive drug delivery systems (floating system, mucoadhesive systems, high density systems etc.), transdermal drug delivery systems (patches, sonophoresis), ophthalmic drug delivery systems (in-situ gel, implants, particulate drug delivery systems etc.).[1]

A substituted benzimidazole derivative called pantoprazole is a protein pump inhibitor (PPI) that reduces the amount of acid that the stomach parietal cells secrete. More than 80 nations throughout the world currently have access to IV pantoprazole, which is intended for the treatment of Zollinger-Ellison syndrome, gastric and duodenal ulcers, and gastroesophageal reflux disease (GERD). In numerous nations, IV pantoprazole is now recommended for the prophylaxis of acute bleeding stress ulcers as well as the treatment of bleeding peptic ulcers and the prevention of rebleeding. In this study, the evidence for the use of IV pantoprazole in the treatment of PUB, prophylaxis against acute bleeding stress ulcers, and prevention of re-bleeding is rigorously analysed.[2]

GRDDSs are the systems that retain drugs for a long time in the stomach and continuously release them. It can improve bioavailability by the controlled delivery of drugs that have an absorption window by continuously releasing the drug for a prolonged period of time before it reaches its absorption site. The various reasons that required a GRDDS are an unpredictable gastric emptying rate that varies from person to person, a brief GIT transit time (8-12h), and the existence of an absorption window in the upper small intestine and low solubility and stability at intestinal pH for several medicines.[3, 4]

Ulcer can be developed inside the inner lining of the stomach (gastric ulcer) or the small intestine (duodenal ulcer). Both the ulcers are also cumulatively referred to as peptic ulcers. It affects nearly 10% of the world population.[5]

The two most common types of peptic ulcer are gastric ulcer, duodenal ulcer. They form when the digestive juices damage the walls of your stomach or intestine. Duodenal ulcer develops in the lining of the beginning of the small intestine. Today, research shows that most ulcers (85% of gastric ulcers & 95% of duodenal ulcers) develop as a result

of infection with a bacterium called H. pylori infection, which is generally affecting more than a billion people worldwide. Ulcers also come about as a result of excess secretion of acid than required, and this may take place when due to inequality among the digestive juices utilized by the stomach to break down food and the various factors that protect the lining of the stomach and duodenum.[6]

MATERIALS AND METHODS

Materials

Sodium alginate was obtained from Loba Chemical, Pvt. Ltd., India, xanthan gum was obtained from Herbal Medical Store, Calcium chloride from Ranbaxy Fine Chemicals Ltd. New Delhi. Acetic acid and Sodium bicarbonate from Sarabhai M Chemicals, Baroda.

Preparation of Floating Beads

The final beads were prepared in two steps. The first step includes the preparation of Sodium-alginate aqueous solution for core, and in the next step the chitosan/xanthan gum (C/X) solution was prepared for coating of the beads. First Sodium-alginate was dissolved in 10 ml deionized water and 200 mg NaHCO3 was then added into the solution, and stirred at 500 rpm for 1 h. For coating of the beads, the C/X solution was prepared by mixing chitosan solution and xanthan gum solution. The chitosan solution was fabricated by dissolving chitosan powders in 1% v/v acetic acid aqueous solution, and xanthan gum solution was prepared by dissolving xanthan gum in DI water. Chitosan and xanthan gum solutions were mixed with different C/X ratios of 4:1, 4: 2, 4:3, 1:1 and 1:4, 3:4, 2:4 where calcium chloride ($CaCl_2$) was also added as the concentration of 1% w/v. The sodium-alginate solution was extruded through a 26-gauge needle into the continuously stirred C/X solution containing calcium chloride. The C/X shell layer was then formed outside the alginate core, and the solution with floating beads was stabilized after continuously stirred for 15 min. After the beads were collected and washed with DI water, they were vacuum dried for 48 h and then stored in 4 °C until used and results shown in table 1.

Table 1: Formulation table containing core-shell composition of pantoprazole floating beads

Batch No.	Water (ml)	Drug (mg)	Core Polymer (mg)	Gas Generating Agent ($NaHCO_3$ mg)	Coating solution					
		Pure	Na Alginate		Water (ml)	$CaCl_2$ (%w/v)	Acetic acid (%v/v)	Chitosan (mg)	Xanthan (mg)	C/X ratio
F1	10	50	200	200	100	1	1	50	12.5	4/1
F2	10	50	200	200	100	1	1	50	25	4/2
F3	10	50	200	200	100	1	1	50	37.5	4/3
F4	10	50	200	200	100	1	1	50	50	4/4
F5	10	50	200	200	100	1	1	12.5	50	1/4
F6	10	50	200	200	100	1	1	37.5	50	3/4
F7	10	50	200	200	100	1	1	25	50	2/4

EVALUATIONS OF BEADS

Beads size measurements

The particle size distribution of the beads was evaluated by sieve analysis. **One hundred grams** of the beads were weighed and sieved through a set of sieves No: (12, 16, 18, 22, and 25) on a vibratory sieve shaker (PritecAC-99, M.B. Instruments, Delhi-7, India.) for 20 minutes, and the weight distribution was determined.

Buoyancy lag time

To determine the buoyancy lag time of the beads, was determined using 0.1N HCl as media in USP dissolution apparatus II. The initial time taken by the beads to float to the surface was noted as lag time; the total number of beads floating was noted as % floating efficiency; and the total time of floating up to 12 hours was also observed.

Floating Time

The duration for which beads float constantly on the surface of the simulated gastric fluid (0.1 N HCl- pH 1.2) at temperature 37 ± 0.5°C subjected to paddle rotation of 50 rpm was measured using stopwatch.

Swelling index

The swelling properties of floating beads were determined by placing them in dissolution test apparatus in 900 ml of 0.1N HCl, (pH 1.2) at 37 ± 0.5°C for 12 hr. Swollen beads were removed periodically from the dissolution medium, and excess water was removed by means of a soft paper and weighed. Swelling characteristics were expressed in terms of percentage swelling index.

Drug entrapment efficiency

Dried beads (100 mg) were powdered and placed in 100 mL of distilled water. The beads were stirred for 2 hours with occasional shaking with a vortex mixer, and the resulting solution was filtered. The filtrate was analysed for drug content after suitable dilution by a UV spectrophotometer at 323 nm. The drug entrapment efficiency was calculated by using the following formula:

% Entrapment efficiency = Theoretical content/ Practical content × 100

In vitro drug release

The drug release studies were carried out at 37 ^{0}C at 100 rpm using 900mL of 0.1N HCl as the dissolution medium by using USP dissolution apparatus type II. At predetermined intervals, the samples were withdrawn and suitably diluted and the absorbance was noted down. Estimate the cumulative amount of drug release by using the absorbance. Following each withdrawal, the media was replaced with fresh medium to maintain the sink condition.

ANTI-ULCER ACTIVITY

Experimental Animals

Wistar Albino rats (200-250g) of either gender will be obtained from Animal House of HIPER-Lucknow. Animal will allow to acclimatize for 1 week and housed in standard polypropylene cages and access to commercial standard pellet diet. Animal will be maintained under controlled room temperature (23 ± 2^{0}C) and relative humidity (60+5%) with 12 h light/12 h dark cycle. The care of the animals was carried out as per the guidelines of the Committee for the Purpose of Control and Supervision of Experiments on Animals (CPCSEA), Ministry of Environment and Forest, Government of India.

Ethanol induced ulcer model

Grouping and dosing of animals will be done as per table no.1 & 2. All the treatments will be given for 14 days. At the end of the dosing schedule i.e., 14th day, animals fasted for 12 hr with free access to water only. The animals will be sacrificed by high dose of Phenobarbitone (300mg/kg i.p.). All the rats in the study groups, their stomachs were immediately removed and opened along the greater curvature and their contents were drained into centrifuge tubes. Finally, the stomachs were gently washed with cold normal saline (0.9%) and examined on a wax plate and results shown in table 2.

Table 2: Grouping of Animals: Ethanol induced ulcer model

S. No.	Group	Treatment	Route	No. of Animals
1	Normal control (NC)	Normal saline (1ml/kg)	Oral	5
2	Negative control group (NCG)	Ethanol (1mg/kg)	Oral	5
3	Test control (low dose) (TC)	Ethanol (1mg/kg) + Test drug (20mg/kg)	Oral	5
4	Standard control (SC)	Ethanol (1mg/kg) + Pantoprazole sodium (20mg/kg)	Oral	5
		Total		**20**

Histopathological Studies

For histopathological examination, the rodents will be sacrificed and stomach will be isolated samples, washed and fixed in 10% neutral buffered formalin. The tissue samples will be section at 5 µm thick, slides will be prepared and stained with Haematoxylin & Eosin.

Collection and Measurement of gastric juice

The stomachs were excised carefully by keeping the oesophagus closed and opened along the greater curvature, luminal contents were removed. The gastric contents were collected and centrifuged at 100 rpm for 10 min. the centrifuged samples were decanted and volume of gastric juice was noted.[7]

Determination of pH of Gastric juice

1 ml of the supernatant liquid was diluted to 10 ml using distilled water. The pH of the solution was recorded by digital pH meter.[7]

Estimation of Free and Total Acidities

The above solution was titrated against 0.01 N NaOH using Topfer's reagent as indicator. When the solution turned orange in colour, volume of NaOH was noted that corresponds to free acidity. Further, the titration was continued till the solution regained pink colour. The total volume of NaOH was noted, that corresponds the total acidity.[7]

Assessment of Ulcer index

Mean ulcer score for each animal is expressed as ulcer index. The stomachs were washed in running water to detect ulcers in the glandular portion of the stomach. The number of ulcers per stomach was noted and severity scoring was done microscopically with the help of hand lens (10X) and scoring was done.[7]

0 = Normal colour stomach

0.5 = red coloration

1 = spot ulcers

1.5 = haemorrhagic streaks

2 = Deep ulcer

Calculation of Percentage Protection

The percentage protection was calculated by the following formula:

Percentage protection = CMUI – TMUI / CMUI X 100

CMUI = Control mean ulcer index, TMUI = test mean ulcer index

Calculation of Triable acidity

The volume of NaOH record was noted and was taken as corresponding to the total acidity.

Acidity was expressed as-

Acidity = volume of NaOH X Normality X 100 mEq/lt/0.1.[7]

Statistical Analysis:

Values are given as mean ± SEM. The significance of difference between means was evaluated using one way analysis of variance (ANOVA) followed by Dunnett's multiple comparison test. $P < 0.05$ was considered significant.

RESULTS AND DISCUSSION

PRE-FORMULATION STUDY

Identification of Drug

Pre-formulation studies are the means to generate information useful in developing stable and Bioavailable dosage forms. Various pre-formulation Characteristics were shown in Table 3. Appearance of the drug was found to be white to off-white crystalline powder. Melting point of pantoprazole drug was determined by using melting point apparatus and found to be in the range of 138-141°C. Pantoprazole drug was found to be soluble in 0.1 N HCl, slightly soluble in water and insoluble in n-Hexane.

Solubility of Pantoprazole sodium

The solubility of pantoprazole was freely soluble in 0.1N HCl, slightly soluble in Ethanol and distilled water and insoluble in n-Hexane which are shown in table 3.

Table 3: Organoleptic properties and Solubility data of drug in different solvents of pantoprazole sodium (PS)

S. No.	Organoleptic properties		Solubility data		
	Characteristics	Results	Solvents	Concentration (mg/ml)	Results
1	Appearance	White to off-white crystalline powder	Distilled water	5	Slightly soluble
2	Melting point	138-141^0 C	0.1 N HCl	5	Free soluble
3	Solubility	Freely soluble in 0.1 N HCl solution, very slightly soluble in water.	Ethanol	5	Slightly soluble

Melting point

The melting point of pantoprazole sodium was found to be 138-141^0 C.

FTIR spectroscopy of pantoprazole sodium

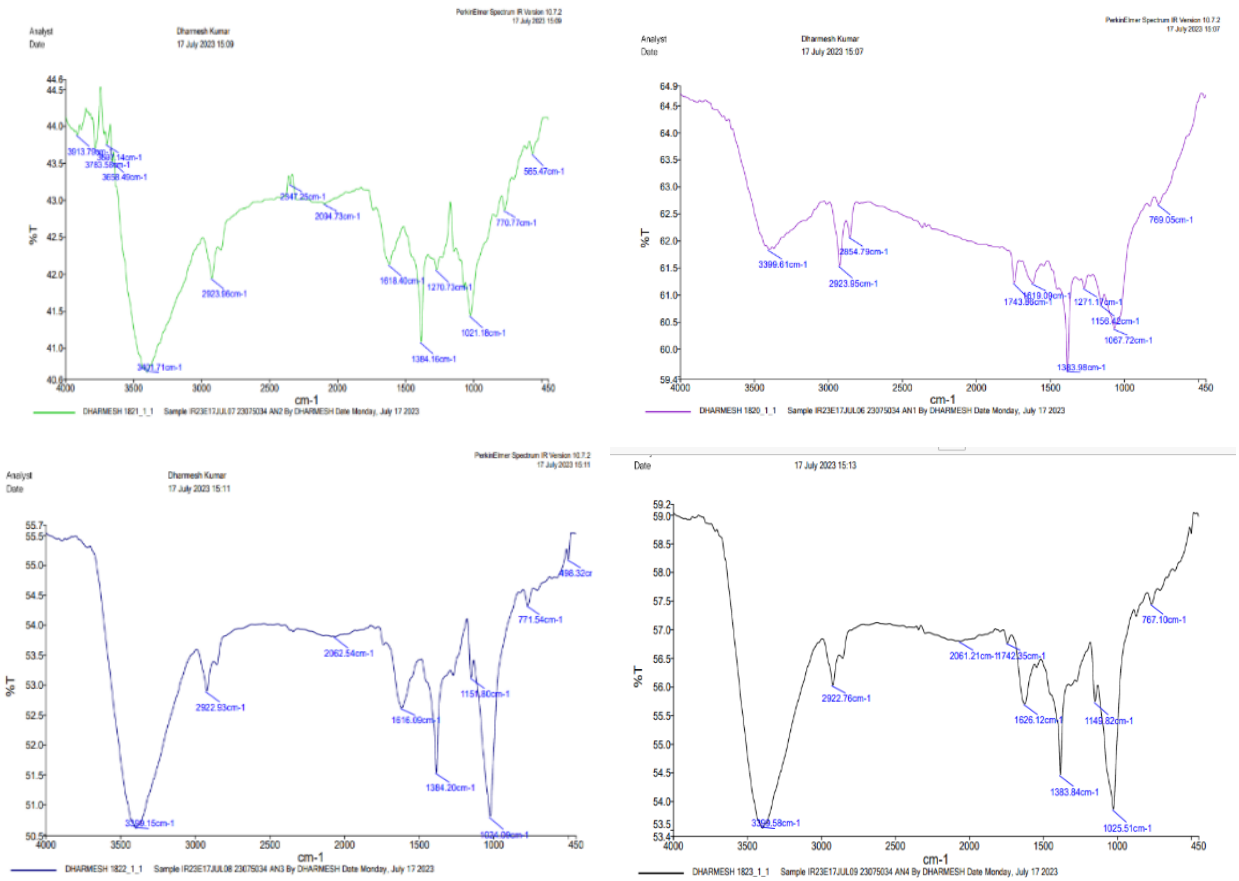


Figure 1: FTIR spectroscopy of pantoprazole sodium

Drug Excipients compatibility studies

The FTIR studies for drug with each excipient were performed and spectral peaks recorded between the wavelengths from 4000 cm-1 to 450 cm-1. Obtained graphs depicted that there was no interaction between the drug and excipients.

EVALUATION OF FORMULATION

Swelling Index:

The swelling properties of floating beads were determined by placing them in dissolution test apparatus and the maximum swelling index was found to be 208.33 % which are shown in table 4 and figure 2.

FLOATING TIME

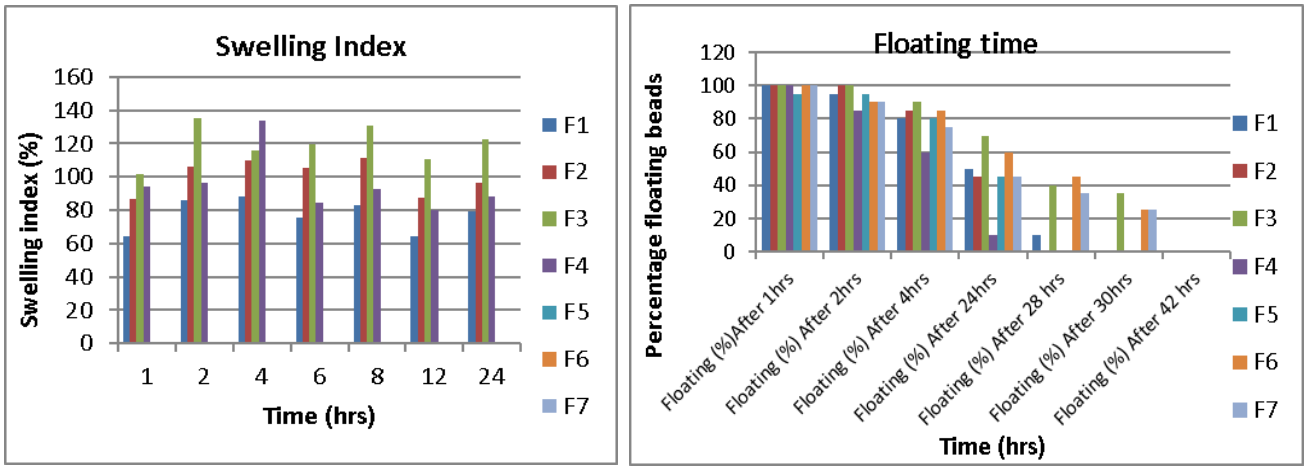
The duration for which beads float constantly on the surface of the simulated gastric fluid are tabulated in Table 5 and figure 2.

Beads size measurement

The particle size is determined by the sieve technique, using standard sieves (mesh) on an electrically equipped shaker for 15 minutes. The settled fractions were collected after weighing them individually, the particle size was found to be range 0.890 to 1.132 mm as shown in Table no. 6.

Table 4: Swelling index

Formulation Code	Weights of beads (mg)	No. of beads	Swelling Index (%)						
			Time in Hours						
			1	2	4	6	8	12	24
F1	13.4	20	64.17	86.56	101.49	94.02	134.72	188.88	208.33
F2	10.2	20	86.27	105.88	135.29	96.07	112.87	115.84	123.76
F3	50	20	88	110	116	134	46.47	61.97	77.46
F4	11.4	20	75.43	105.45	119.29	84.21	58.82	70.58	88.23
F5	10.4	20	82.69	111.53	130.76	92.3	61.64	73.97	117.8
F6	12.8	20	64.06	87.5	110.93	79.68	73.33	85.33	96
F7	11.7	20	79.48	96.58	122.22	88.03	37.5	45.83	55.55



(a) **(b)**

Figure 2: (a) Swelling index of formulation (F1 – F7), (b) Floating time of formulations (F1- F7)

Table 5: Floating time

Formulation Code	Percentage Floating				Floating lag time (min)
	Floating time (h)				
	4 hrs	6 hrs	8 hrs	12 hrs	
F1	60	45	35	0	1
F2	50	30	20	0	2
F3	80	60	30	0	1
F4	55	45	40	0	1
F5	50	40	20	0	3
F6	70	50	20	0	2
F7	55	35	25	0	1

Drug entrapment efficiency

The percentage of drug entrapment efficiency was found to be 66.94% to 89.45% as shown in Table 6.

Table 6: Beads size and drug entrapment efficiency of formulations (F1 – F7)

Formulation code	Beads size (mm)	Drug entrapment efficiency
F1	0.890	67.61 ± 1.23
F2	0.971	61.45 ± 2.43
F3	1.132	79.87 ± 1.29
F4	0.911	83.92 ± 2.76
F5	1.102	66.94 ± 2.41
F6	0.891	89.45 ± 2.03
F7	1.092	69.87 1.02

***In-vitro* Drug Release**

Table 7: *In vitro* drug release

Time (hrs)	F1	F2	F3	F4	F5	F6	F7
0.50	31.92	32.87	33.21	34.87	33.75	33.21	30.87
1.00	39.21	38.72	39.78	40.53	37.74	40.67	37.98
1.50	44.73	45.89	46.89	47.45	46.56	47.73	48.45
2.00	51.87	52.74	53.9	54.67	58.94	53.67	54.39
3.00	59.42	63.32	60.56	61.23	63.54	62.34	59.76
4.00	66.72	69.64	70.64	68.95	71.32	69.89	63.43
5.00	73.82	75.62	76.89	75.78	79.67	74.35	70.76
6.00	82.64	83.54	85.46	86.84	83.43	79.76	81.23

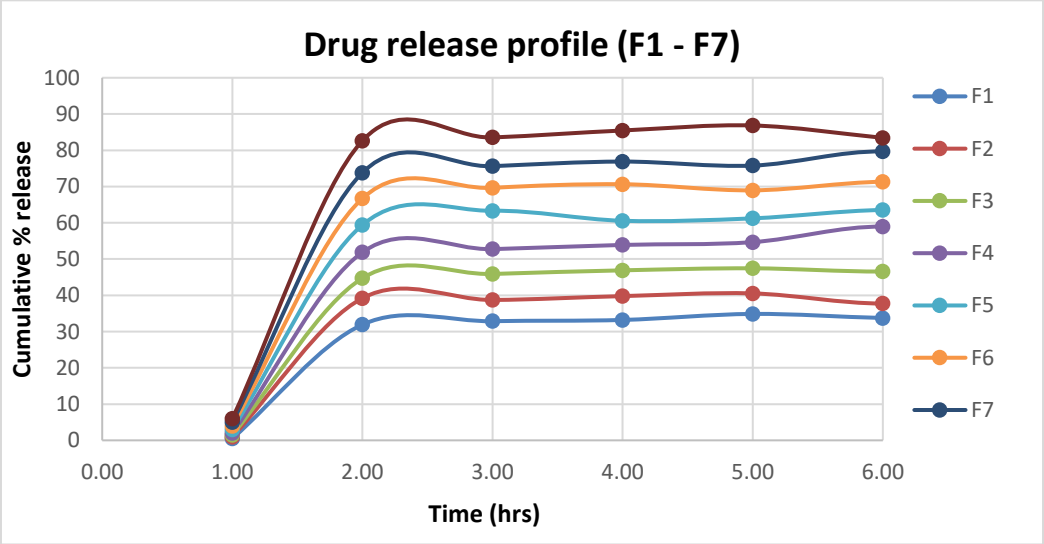


Figure 3: Drug release profile (F1 – F7)

Table 8: Estimation of Free and Total Acidities, pH determination and Ulcer index

S.No.	Group	Free acidity	Total acidity	pH detection	Ulcer Index
1	Disease control	37.80±0.67	83.40±0.86	4.16±0.19	23.19±0.009
2	Standard control	18.60±0.38	38.60±1.12	2.63±0.14	9.65±0.16
3	Test	13.80±0.61	27.60±0.56	3.71±0.42	4.23±0.06

Significance level denoted by * significant at P<0.05n=6, readings are in Mean± SEM

Anti-ulcer Activity

In this technique, ulcer index and percentage inhibition of pantoprazole beds was determined. In the same context, Group 1 was treated with distilled water, Group 2 administered Ethanol (1mg/kg) while Group 3 administered pantoprazole beds in the dose 20mg/kg and Group 4 treated with standard drug pantoprazole sodium in the dose of 20mg/kg.

Group 1 exhibited UI score of 1.68±0.07 but PI was observed Nil. Whereas, group 2 (pantoprazole sodium 20mg/kg) demonstrated UI as 23.19±0.009 and PI as 9.65±0.16 that is highly significant as it serves at standard drug. So, UI was achieved minimum after pantoprazole sodium administration and PI was noted optimum in terms of ulceration inhibition. Group3 (n=5) given pantoprazole beds (20mg/kg) that reduced the ulcer index by up 9.65±0.16 and PI was observed in ascending manner as 4.23±0.06.

Whereas, group 4 which was treated with pantoprazole beds (20mg/kg) was demonstrated the ulcer index as 4.23±0.06 and percentage inhibition was recorded as 9.65±0.16 which is near to standard drug treatment.

So, in this model the result indicates that bark extract of Test drug in higher dose is much effective which is comparable to standard anti-secretary drug pantoprazole sodium.

The following table confers the UI and PI effect of bark extract of Test drug in ethanol-induced ulcer model and results are shown in table 8.

pH DETECTION

In evaluation of anti-ulcer potential, ulcer index and percentage inhibition of bark extract of test drug was determined. In the same context, Group 1 administered ethanol (1mg/kg) while Group 2 administered pantoprazole sodium in the dose 20mg/kg and Group 3 treated with pantoprazole beds in the dose of 20mg/kg.

Group 1 given omeprazole in the dose of 30mg/kg showed optimum and increased pH in the range of 4.16±0.19. Group 2 administered standard drugs for 15 days of continuous exposure, the pH was recorded as 2.63±0.14 whereas Group3 given pantoprazole beds once a day for 15 days and showed pH as 3.71±0.42. Therefore, the maximum pH increasing effect was seen in higher dose when compared to standard drug pantoprazole sodium (20mg/kg) which is shown in table 8.

Volume of gastric content

In evaluation of anti-ulcer potential, ulcer index and percentage inhibition of bark extract of test drug was determined. In the same context, Group 1 was treated with distilled water, Group 2 administered ethanol (1mg/kg) while Group 3 administered bark extract of pantoprazole sodium in the dose 20mg/kg and Group 4 treated with pantoprazole beds in the dose of 20mg/kg.

Group 1 administered with ethanol in the dose of 1 mg/kg recorded for volume of gastric content as 5.63±0.24**ml. The volume of gastric content (ml) for Group 2 treated with standard drug was observed as 7.97±0.14**ml whereas group 3 exhibited and decreased level of secreted volume of gastric content as 6.11±0.18**ml which is much significant and comparable to standard group which is shown in table 9.

Free acidity

In screening of anti-ulcer potential, ulcer index and percentage inhibition of pantoprazole beds was determined. In the same context, Group 1 administered ethanol (1mg/kg) while Group 2 administered Standard drug pantoprazole sodium (20mg/kg) and Group 3 treated with pantoprazole beads (20mg/kg) in the dose and results shown in table 9.

Group 1 treated with ethanol in the dose of (1mg/kg), all the animals exhibited mean value of free acidity as 24.48±2.20** mEq/l. Animals treated with test drug- bark extract of Standard drug pantoprazole sodium (20mg/kg) produced free acidity in the range of 35.68±1.27*** mEq/l whereas group 3 treated with same in the dose of pantoprazole beds (20mg/kg) showed 29.52±1.26*** mEq/l free acidity which is near to standard drug ranitidine.

The following table depicts the response of pantoprazole beds (20mg/kg) on free acidity.

Total acidity

In reference to anti-ulcer potential determination, ulcer index and percentage inhibition of bark extract of Test (20mg/kg) was evaluated. In the same context, Group 1 administered Ethanol (1mg/kg) while Group 2 administered Standard drug pantoprazole sodium in the dose (20mg/kg) and Group 3 treated with pantoprazole beds (20mg/kg).

Group 1 treated with Ethanol in the dose of (1mg/kg) exhibited total acidity as 46.35±2.69**mEq/l. Whereas, group 2 showed total acidity as65.16±1.42**mEq/l that was administered bark extract of Standard drug pantoprazole sodium in the dose of (20mg/kg) for persistently 15 days. At last, group 3 given pantoprazole beds (20mg/kg) were evaluated for total acidity as observed as56.26±1.24*** mEq/l. The following table 9 shows the response of pantoprazole beds on total acidity.

MICROSCOPIC STUDIES

The microscopic examination of isolated stomach was done using 100X magnification power compound microscope. Firstly, the stomach was dissected washed thoroughly with saline solution to make it fat and gastric content free. After, it kept in saline solution until examination was completed by using high magnification power compound microscope which is shown in figure 4.

Effect of gastric ulcer index

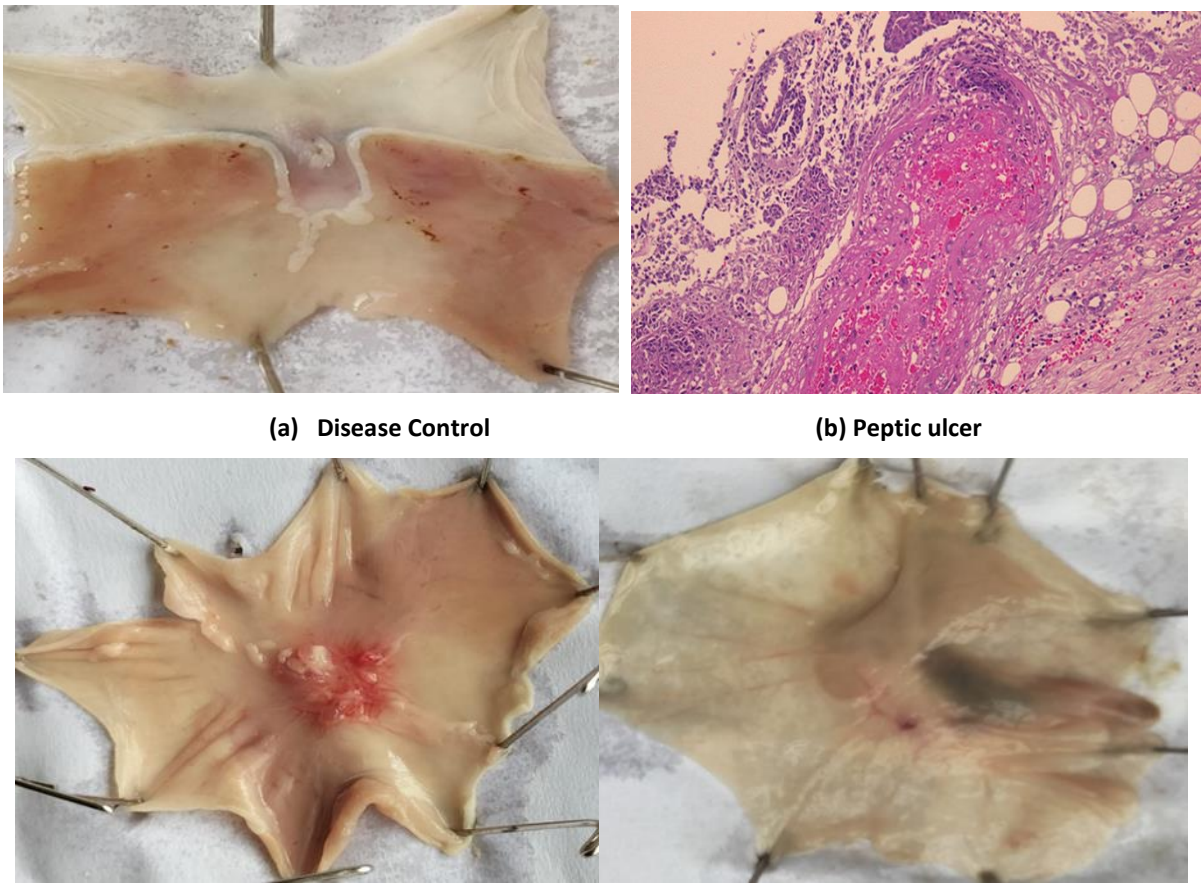
Table 4 shown that oral administration of ethanol 1mg/kg dose, inhibited gastric ulcer formation induced by ethanol in a dose dependent manner. The gastric ulcer decreasing (anti-ulcerogenic effect) was highly significantly higher with the 20mg/kg dose.

Table 9: Response of pantoprazole beds (20mg/kg) on Volume of gastric content (ml), free acidity (mEq/l), Total acidity(mEq/l)

Sl. No.	Groups	Treatment	Volume of gastric content (ml)	Free acidity (mEq/l)	Total acidity (mEq/l)
1	Normal control (NC)	Ethanol (1mg/kg)	5.63±0.24**	24.48±2.20**	46.35±2.69**
2	Negative control group (NCG)	Ethanol (1mg/kg) +Standard drug pantoprazole sodium (20mg/kg)	7.97±0.14**	35.68±1.27***	65.16±1.42**
3	Test control (low dose) (TC)	Ethanol (1mg/kg) + pantoprazole beds (20mg/kg)	6.11±0.18**	29.52±1.26***	56.26±1.24***

Significance level denoted by * significant at P<0.05n=6, readings are in Mean ± SEM

Histopathological Studies



(a) Disease Control **(b) Peptic ulcer**

(c) Standard **(d) Test**

Figure 4: Histopathology: (a) Disease control, (b) Peptic ulcer, (c) Test, (d) Test

The following figure demonstrates the streaking and mucosal oedema. It confirms the level of oedema in Group 3.

All the rats were treated for continuously 15 days as per once-a-day schedule.

- In all the microscopical studies it showed that minimal mucosal edema, leukocyte infiltration was recorded in group 4 that was administered of Ethanol (1mg/kg) + pantoprazole beds in the dose of (20mg/kg).
- So, the response observed in the dose dependent manner. Less anti-ulcer was seen in the group 3 treated with bark extract of standard drug pantoprazole sodium in the dose of (20mg/kg).

DISCUSSION

The following table depicts the ulceration in the standard group which is minimal-

- The pH was determined as low as compared to compared and standard group. As hyperacidity is the first factor behind its anti-ulcerogenic potential so decreasing the pH is much supported treatment in ulcer as anti-ulcer agent. It makes act due to its neutralizing potential of acidity or increase release of some alkaline bicarbonate ion and others to raise the pH (alkaline). The highest pH decrease was recorded in the group 2and group 4 treated with Ethanol (1mg/kg) and pantoprazole beds (20mg/kg), respectively.
- Volume of gastric content was found less when compared to control group. However, the group 4 demonstrated a well and efficient role in lowering the volume of gastric content might be due to blocking property at Histamine receptors located in gastric wall. In turn, it decreases the release the gastrin and thus gastric juice. It was much comparable in the dose of pantoprazole beads (20mg/kg) to standard group.
- The free acidity was found decreased after the exposure to pantoprazole beads (20mg/kg) for continuously 15 days. It might give action to neutralize the free acid and thus to modulate the high and severe action of free acid to develop ulcer and perforation in gastric wall. It might be so due to long term exposure of plant extract to accommodate and produce pharmacological action.
- Total acidity when observed was also found less after treatment among different group of animals. It demonstrated that total acidity was also gets reduced in the group 2, 3 and 4. The mechanism behind this pharmacological activity is not known as such.
- In all the protocols, pantoprazole beads showed a significant anti-ulcerogenic activity when compared to reference group. The response was observed as dose-dependent, in ascending order.
- When we compared the results obtained in pylorus ligation, it was found that the anti-ulcer potential was recorded and studied by microscopically.
- Standard group of animals treated with Ethanol (1mg/kg) showed highest anti-ulcerogenic potential being the reference and well proved anti-ulcer as it decreases the release of gastrin in turn gastric juice (hydrochloric acid). Mucosal damage, infiltration of leucocytes was observed as negligible in test groups.
- Standard drug pantoprazole sodium in the dose of (20mg/kg) is also effective when compared with the control group of animals that were treated with distilled water in the same dose. Whereas, higher dose demonstrated a highly efficient anti-ulcerogenic activity when compared to standard drug administered group of rats.

CONCLUSION

The findings of this study indicated that natural polymers and gas-forming agents may be effectively used in the design of a sodium alginate multiple unit floating medication delivery system. For the duration of the experimental study of the formulation's effectiveness, it was discovered to be stable and compatible. All the metrics fell within the permissible range, and by appropriately adjusting the ratio of sodium alginate to xanthan gum and sodium bicarbonate as a gas-forming agent, the drug release was maintained. Thus, by using certain natural and synthetic polymers in combination with an appropriate concentration of gas producing agent to induce the necessary buoyancy and so lengthen the stomach emptying period, the sustained administration of several drug categories might be accomplished.

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