Research Article

IN VITRO AND IN VIVO EVALUATION OF THE GASTRORETENTIVE FLOATING DOSAGE FORM

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Article Received on: 31/07/14 Revised on: 20/08/14 Approved for publication: 12/09/14

DOI: 10.7897/2230-8407.0509142

ABSTRACT

The aim of the present investigation was to develop and optimize gastro retentive floating system of Pantoprazole for the efficient treatment of acid related disorders and *H. Pylori* infections. Floating tablets were developed using central composite design (CCD), and optimization was done by employing response surface methodology. The floating tablets were prepared with HPMC K₄M/Ethyl cellulose and natural seed polymer of *Delonix regia* by wet granulation technique. Buoyancy was achieved by adding an effervescent mixture of sodium bicarbonate and anhydrous citric acid. The Optimized formulation (BS₃) showed no significant change in physical appearance, drug content, total buoyancy time, or *in vitro* dissolution pattern after storage at 40°C/75 % relative humidity for 1 month. The best formulation was selected based on *in vitro* characteristics and was used for the *in vivo* radiographic studies by incorporating BaSO₄. Evaluation of Gastric retention using x-Ray imaging studies were performed on rabbit to justify the increased gastric residence time of the dosage form in the stomach, based on the floating principle. Further the floating tablets were evaluated for its antiulcer activity in Male wistar rats by ethanol induced ulcer in comparison with standard. The floating formulation shows excellent buoyancy and better gastric cytoprotection when compared with standard drug.

Keywords: *In vivo* buoyancy; anti ulcer activity; floating dosage forms, ethanol induced ulcer, X-ray imaging studies.

INTRODUCTION

Helicobacter pylori is one of the most common pathogenic bacterial infections, colonizing an estimated half of all humans¹. It is associated with the development of serious gastro duodenal disease – including peptic ulcers, NSAID-induced ulcer, Zollinger-Ellison syndrome and Barrett's esophagus, gastric lymphoma and acute chronic gastritis². Approximately 500000 new cases and 4 million recurrences of peptic ulcer are reported each year worldwide. *H. pylori* reside mainly in the gastric mucosa or at the interface between the mucous layer and the epithelial cells of the antral region of the stomach³. In the present study Pantoprazole was selected as the payload model drug. Pantoprazole is a proton pump inhibitor used as an antiulcer drug in the treatment of *Helicobacter pylori* infections with a bioavailability of 77 % or more and protein binding of 98 %^{4,5}. Its half life is 1hr with poor absorption may be because of degradation and poor solubility. The objective of the present investigation was the design and *in vitro/in vivo* evaluation of Pantoprazole floating tablets based on: (i) release-retarding gel-forming polymers like hydroxyl propyl methyl cellulose (HPMC K₄M100) and Natural seed polymer of *Delonix regia* and (ii) a gas-former like sodium bicarbonate (NaHCO₃). The optimum formula that combined excellent floating and swelling behavior, sustained drug release characteristics which showed good physical stability after storage at 40 °C/75 % RH for 3 months. This optimized formula was chosen for further study (i) to investigate the potential gastric protective effects of floating tablet of Pantoprazole to evaluate anti-ulcerogenic properties of Ethanol in rats. Ethanol-induced gastric mucosal lesions in rats were used as an animal model and (ii) to undertake *in vivo* investigations in six healthy male rabbits to determine the *in vivo* floating behavior of tablets.^{6,7}

MATERIALS AND METHODS

Pantoprazole was provided as a gift sample from Fourt's India Company Pvt. Ltd., Chennai, India and hydroxy propyl methyl cellulose K₄M and were obtained as a gift sample from Vapi Care Pharma Pvt Ltd. Vapi. Other excipients and chemicals were of analytical grade and purchased from Pure Chem. Laboratories, Pune, India.

Formulation Design

Preparation of Pantoprazole Floating Tablets

Tablets containing 20 mg of Pantoprazole were manufactured with the aim of achieving a SR product for 24 h release period. Drug and filler premixes were mixed thoroughly in a double cone blender (Jyothi Scientific Industries, India, Model no.1240) with various proportions of HPMC K₄M 100 and EC polymers and then mixed powder was granulated with PVPK -30 (5 % w/w in premix powder) solution in IPA. The wet mass was passed through 12 mesh screen and dried in conventional hot air oven. The dried granules were passed through the 18 mesh screen. The granules were blended with lubricant/glidant mixture (2 % magnesium stearate and 1 % Talc) and compressed into tablets on a 10 station tablet punching machine (Cadmach, Ahmedabad, India) using round, standard concave tools that target to produce tablet of ~ 150 mg. Tablets of 8 different formulations (AF1- 1AF8) were prepared with different proportion of polymers and diluents as the compositions mentioned in Table 1. Further optimization studies were carried out and the formulation BS₃ mentioned in Table 2 was found to be the best, based on the evaluation studies performed⁸⁻¹¹.

In vitro Buoyancy Studies

The time taken for tablet to emerge on surface of medium is called the floating lag time (FLT) and duration of time the dosage form to constantly remain on surface of medium is called the total floating time (TFT). The *in vitro* buoyancy was determined by floating lag time, per the method

described by Rosa *et al* as shown in Figure 1. The tablets were placed in a 250-mL beaker containing 0.1N HCl. The time required for the tablet to rise to the surface and float was determined as floating lag time^{12,13}.

In vitro Dissolution Studies

The release rate of pantoprazole from floating tablets was determined using United States Pharmacopeia (USP) Dissolution Testing Apparatus 2 (paddle method). The dissolution test was performed using 900 ml of 0.1N hydrochloric acid, at $37 \pm 0.5^\circ\text{C}$ and 50 rpm. A sample (10 ml) of the solution was withdrawn from the dissolution apparatus hourly and the samples were replaced with fresh dissolution medium. Absorbance of these solutions was measured at 285 nm using a UV/Visible spectrophotometer. The percentage drug release was plotted against time to determine the release profile¹⁴.

Stability Study

In view of the potential utility of optimized formulation BS₃ for delivering pantoprazole for long term use, the accelerated stability studies were performed for this batch at $40 \pm 2^\circ\text{C}/75\% \pm 5\% \text{ RH}$ 6 months (climatic zone IV conditions for accelerating testing) to assess their stability in the stability chamber (Thermo labs, India). After storage, optimized formulation BS₃ was studied for physical appearance, drug content and *in vitro* drug release characteristics.¹⁵

Animals Used

Studies were carried out using Healthy wistar albino rats of either sex weighing between (150-200 g). These animals were kept in polypropylene cages in a room maintained under controlled atmospheric conditions. The animals were stabilized for a week. They were maintained in a standard condition at room temperature and relative humidity at $60 \pm 5\%$ for 12 hours light dark cycle. There were given standard pellet diet and water *ad-libitum* throughout the course of study. Food were withheld overnight prior to experiment. The experimental protocol was approved by Institutional Animal Ethics Committee (IAEC) of Annamalai University, Chidambaram, India vide Reg. number 160/1999/CPCSEA, Proposal No.895 dated 29.05.2010^{16,17}.

In vivo antiulcer study

Ethanol induced ulcer model

The gastric ulcer was induced in rats by administering Ethanol (EtOH, 100 %, 2 ml/100 g, 1 hour). Ethyl alcohol was administered on the day of the experiment. All the animals were fasted for 24 h before administration of ethanol. The standard drug and single unit tablet administered orally two hours before the administration of ethanol. After two hours of ethanol administration, under ketamine HCL (100 mg/kg, i.m.) and xylazine HCL (16 mg/kg, i.m.) anesthesia. The animals were slaughtered by cervical dislocation and stomach was incised along with greater curvature and examined for ulcers. The ulcer index was scored, based upon the product of length and width of the ulcer present in the glandular portion of the stomach millimeter square/rat (mm^2/rat). The results are given Table 5.¹⁶

Antiulcer and Cytoprotective Studies

The animals were divided into six groups, each consisting of six rats.

Group I – Normal control (0.1 % sodium CMC suspension)

Group II – Toxic control (Ulcer induced rats)

Group III – Pure Pantoprazole as standard drug in sodium CMC suspension at the dose of 4 mg/kg body weight, Group IV, V and VI – Pantoprazole floating tablet of optimized formulation BS₃ in sodium CMC suspension at the dose equivalent of 4 mg/kg body weight.¹⁶

Histopathological evaluation

The gastric tissues samples were fixed in neutral buffered formalin for 24 h. Sections of tissues from stomach were examined histopathologically to study the ulcerogenic and / or anti-ulcerogenic activity of pure Pantoprazole and floating tablets. The tissues were fixed in 10 % formalin and were processed using a tissues processor. The slides were stained with hematoxylin and eosin using routine procedures. The slides were examined microscopically for pathomorphological changes such as congestion, hemorrhage, oedema and erosions using an arbitrary scale for the assessment of severity of these changes¹⁷.

Evaluation of gastric retention using X-Ray imaging

X-ray technique was used to determine the gastric residence time of the floating tablet. The *in vivo* floating study was carried out by administering floating tablet to rabbits and monitoring them by a radiological method. To make the floating tablet radiopaque, barium sulphate was incorporated into polymeric solution and radiopaque floating tablet (the same formulation composition BS₃) were prepared using a similar procedure to that mentioned in the preparation of floating tablet. Six healthy one year old male albino rabbits, weighing 2-2.5 kg were used to assess *in vivo* floating behavior. The animals were housed in individual cages, and the experiment was conducted in a sanitized room at a temperature maintained at around 24°C . The animals were fasted for 12 h. The first x-ray photograph was taken to ensure absence of radiopaque material in the stomach. During the experiment, rabbits were not allowed to eat but water was provided *ad libitum*. Floating tablet was administered through oral gastric tube with 15 ml water in fasted state. Afterwards, the animals were not allowed to eat throughout the study (Up to 6 h). At every hour interval, 10 ml of water was administered to animals throughout the study. Before taking X-ray photographs, the animals were placed in upright posture. The position of the floating tablet in the rabbit's stomach was monitored by X-ray photographs of the gastric region at different time intervals (at 0, 2, 4 and 6 h). The experimental protocol was approved by Institutional Animal Ethics Committee (IAEC) of Annamalai University, Chidambaram, India vide approval number 160/1999/CPCSEA dated 29.05.2012^{18,19}.

RESULTS AND DISCUSSION

All the parameters for the evaluation of blend were found within characteristics range. Results indicated the formulation BF₇ is the best option for further optimization of composition for Central composite design. BF₇ showed drug release $95.56 \pm 1.38\%$ and sustained release for 18 hours. Among the optimized formulation, BS₃ was found to be the best formulation based on the physico-chemical properties such as *in vitro* buoyancy studies and dissolution studies as shown in Table 3 and Table 4. The stability data on the floating tablets are presented in Table 4. The result showed that the content and release rate of Pantoprazole from the tablet did not change over the six months accelerated stability test period as shown in Figure 2. This indicated that the floating tablet were stable at accelerated storage condition. However real time

stability studies for a period of 2 years are required to establish the stability of developed formulation

***In vivo* Antiulcer Study**

Ethanol induced ulcer model

The present *in vivo* investigations demonstrated that there was a marked difference in the reduction of ulcer index in case of floating tablets. The Pathological evaluation of rat stomach showed that there was no degeneration when blank tablets were given, with an average ulceration index equal to zero. The number of ulcerogenic lesions was found to be less in case of administration of Pantoprazole floating tablets compared to that obtained after administration of free drug with average. The ulcer index after 8 h of treatment was found to be $1 \pm 0.9345^*$ in case of pure Pantoprazole, while ulcer index was significantly reduced to 0.5 ± 0.4163 in case of floating tablets of Pantoprazole. So it was considered that floating tablet has significantly decreased the number of ulcers as shown in Table 5 and Figure 3. The calculated percent protection was 52.63 %. Analysis of variance for the calculated parameters indicated the significant high extent of protection

Histopathological Evaluation

Microscopic observations of gastric lesions in rats treated with oral administration of Pantoprazole showed mild damage to the gastric mucosa and edema and leucocytes infiltration of the sub mucosal layer (Figure 4C). Rats that were treated with floating tablets of Pantoprazole each had comparatively better protection of the gastric mucosa as seen by the reduction in ulcer area, showed regeneration and prevents the formation of haemorrhage and oedema and absence of leucocytes infiltration (Figure 4D)

Statistical Analysis

It was done by one-way ANOVA followed by Dunnett's multiple comparison tests Significant at $*P < 0.05$ as compared to control. Values are expressed in mean $\pm$ SD for six observations.

***In vivo* Floating Behavior**

To examine whether the prepared optimized oral floating dosage system could be floated in the stomach, evaluation using an X-ray apparatus was conducted in 6 albino rabbits. The behavior of floating tablet was studied in using radiographic imaging technique. Images were taken at different time points to find the location of the floating tablet. *In vivo* evaluation was carried out in fed state. The X-ray photographs results of *in vivo* floating efficacy of floating tablet at different time intervals in rabbit's stomach are shown in Figure 5 A-D. Figure 5A shows X-ray taken 0 h. after administration of floating tablet. Floating tablet can be seen in the stomach. Next image, Figure 5B, taken at 2 h shows change in position of floating tablet; this shows that floating tablet did not adhere to gastric mucous. Next image, Figure 5C and D, taken at 4 h and 6 h after administration of floating tablet showed that floating tablet was still found to be buoyant on gastric content, respectively. The amount of barium sulphate was sufficient to ensure visibility by X-ray and at the same time was low enough to enable floating tablet to float. The results clearly indicated that the prepared floating tablet of Pantoprazole remained buoyant for at least 6 hours in rabbit's stomach and that they had good floatability *in vivo*.

Table 1: Composition of different floating tablet formulation of Pantoprazole

Ingredients	Formulation Code (Quantities in mg)							
	BF ₁	BF ₂	BF ₃	BF ₄	BF ₅	BF ₆	BF ₇	BF ₈
Pantoprazole	20	20	20	20	20	20	20	20
HPMC K ₄ M100	10	15	20	25	10	15	20	25
Ethyl cellulose	10	15	20	25	-	-	-	-
Delonix regia seed polymer	-	-	-	-	10	15	20	25
PVP K 30	6	6	6	6	6	6	6	6
Isopropyl alcohol	QS	QS	QS	QS	QS	QS	QS	QS
NaHCO ₃	7.5	7.5	7.5	7.5	7.5	7.5	7.5	7.5
Citric Acid	1.5	1.5	1.5	1.5	1.5	1.5	1.5	1.5
Mg Stearate	3	3	3	3	3	3	3	3
Talc	1.5	1.5	1.5	1.5	1.5	1.5	1.5	1.5
Lactose	89	79	69	59	89	79	69	59
PVA	1.5	1.5	1.5	1.5	1.5	1.5	1.5	1.5

Table 2: Composition (%) of final optimized formulation BS₃ of Pantoprazole floating tablet

Name of components	Quantities in mg
Pantaprazole	20.00
DRSP	20.46
HPMC K ₄ M100	25.00
PVP K 30	6
Isopropyl alcohol	QS
NaHCO ₃	7.5
Citric Acid	1.5
Mg. Stearate	3
Talc	1.5
Lactose	63.54
PVA	1.5

Table 3: *In vitro* release of optimized formulation BS₃ of Pantoprazole floating tablet

Time (hours)	0.00	1	2	4	6	8	10	12	14	16	18
Release	0.00	5.76 ± 0.87	14.31 ± 1.10	26.40 ± 0.78	34.14 ± 1.00	44.23 ± 0.98	50.12 ± 1.60	64.12 ± 1.07	75.32 ± 0.56	87.34 ± 1.34	95.13 ± 1.76

Table 4: Stability study (40 C / 75 % RH) of Optimized Formulation (BS₃)

Parameters	Initial Month	1 st Month	3 rd Month	6 th Month
Physical appearance	Off white flat smooth faced	Off white flat smooth faced	Off white flat smooth faced	Off white flat smooth faced
Weight Variation (mg)	148 ± 0.012	148 ± 0.012	148 ± 0.012	148 ± 0.122
Hardness (Kg/cm ²)	4.83 ± 0.14	4.94 ± 0.12	4.90 ± 0.21	5.02 ± 0.10
Drug Content (%)	99.69 ± 0.08	99.34 ± 0.23	98.72 ± 0.15	98.02 ± 0.27
Friability (%)	0.57 ± 0.08	0.54 ± 0.02	0.52 ± 0.06	0.50 ± 0.08
Buoyancy Lag Time (s)	90.56 ± 0.34	91.21 ± 0.45	94.56 ± 0.24	99.50 ± 0.36
Total floating time in hours	18	18	18	18
Buoyancy on disturbing	Float	Float	Float	Float
In vitro release (%)	95.61 ± 1.13	95.01 ± 1.52	94.86 ± 0.93	94.05 ± 1.32

Table 5: Effect of Pantoprazole floating tablets on ulcer index of ulceration in rat stomach

Parameter	Normal control (n = 6)	Toxic control (n = 6)	Standard Pantoprazole free drug	Pantoprazole floating tablet
Average ulcer index	5 ± 0.2140	7 ± 0.632	1 ± 0.9345*	0.5 ± 0.4163*

Figure 1: Photographs of BS₃ optimized formulation at different time intervals (a), (b) and (c) within one minute (d) after 1 h (e) after 5 h and (f) after 12 h Figure 2: Comparative dissolution study of optimized formulation BS₃ initial and after 1, 3 and 6 months

FIG.3. Effects of Anti - Ulcer activity of Pantoprazole floating tablets on rats.

Fig.4. Biopsy of Rat stomach induced with ulcer.

- Section of Stomach from Normal control rat shows normal architecture.
- Section of stomach from diseases control rat shows severely damaged cells.
- Section of stomach from Pantoprazole treated rat shows mild damaged cells.
- Section of stomach Pantoprazole formulation treated rat shows mild damaged cells.

Fig.5. x-ray Photographs of floating tablet of Pantoprazole in the gastric region of rabbit, after dosing of formulations.

- 0 hr after dosing
- 1 hr after dosing
- 4 hrs after dosing
- 6 hrs after dosing.

Figure 3: Effects of Anti Ulcer activity of Pantoprazole floating tablets on rats

CONCLUSION

Peptic ulcers are caused when the natural balances between the aggressive factors of acid, pepsin, defensive mechanisms of mucus, bicarbonate, mucosal turnover and blood supply (mucosal barrier) are disturbed^{20,21} suggested it is reported that acid and pepsin are relatively less important as causative agents and that a defect in the defensive mechanism of gastric mucosa is the first step toward ulcer formation²². Optimized formulation BS₃ in Pantoprazole had shown good *in vitro* buoyancy and controlled release behavior and hence was finally selected for *In vivo* study. In stability study, optimized formulation was selected as a promising formulation and was found stable at $40 \pm 2^\circ\text{C}$ /75 % for 6 months. It is known that gastric lesions produced by ethanol administration appeared as multiple hemorrhagic red bands of different sizes along the glandular stomach. Studies suggest that the ethanol damage to the gastrointestinal mucosa starts with microvascular injury, namely disruption of the vascular endothelium resulting in increased vascular permeability and edema formation. Ethanol produces necrotic lesions in the gastric mucosa by its direct toxic effect, reducing the secretion of bicarbonates and production of mucus.²² Exposure to ethanol increases the extension of cellular damage in a dose-dependent way. *In vivo* antiulcer study, there was a marked difference in the reduction of ulcer index in the case of floating tablets. The calculated percent protection was 52.63 %. *In vivo* X-ray study conducted to determine the gastric retention time and to assess the gastrointestinal transit of this floating controlled drug delivery system. X-ray studies revealed the location of floating tablets in six healthy rabbits. The optimized floating formulation BS₃ showed excellent *in vivo* buoyancy and remain floating upto 6 hours.

ACKNOWLEDGEMENTS

Authors are heartily thankful to Annamalai University, Chidambaram, India PRIST University, Puducherry and Thanjavur campus for providing facilities to carry out this research work and I specially thank Fourt's India Company Pvt. Ltd. Chennai, India for providing gift sample of Pantoprazole.

REFERENCES

- Patel SS, Ray S, Thakur RS. Formulation and evaluation of floating drug delivery system containing clarithromycin for *Helicobacter pylori*. Acta Pol Pharmacy 2006; 63: 53-61.
- Nayak AK, Maji R, Das B. Gastro retentive drug delivery systems: a review. Asian Journal of Pharmaceutical and Clinical Research 2010; 3: 2-10.
- Khan FN, Dehghan MHG. Gastro retentive drug delivery systems: a patent perspective. International Journal of Health Research 2009; 2: 23-44.
- Singh BN, Kim KH. Floating drug delivery systems: an approach to oral controlled drug delivery via gastric retention. Journal of Controlled Release 2000; 63: 235-259. [http://dx.doi.org/10.1016/S0168-3659\(99\)00204-7](http://dx.doi.org/10.1016/S0168-3659(99)00204-7)
- Garg R, Gupta GD. Progress in controlled gastro retentive delivery systems. Tropical Journal of Pharmaceutical Research 2008; 7: 1055-1066. <http://dx.doi.org/10.4314/tjpr.v7i3.14691>
- Prabhu P, Nayari HM, Ahmed GM, Yadav B, Charyulu NR, et al. Formulation and *in vitro* evaluation of gastric oral floating tablets of glipizide. Indian Journal of Pharmaceutical Education Research 2008; 42: 174-183.
- Jamzad S, Fassihi R. Development of a controlled release low dose class II drug-Glipizide. International Journal of Pharmacy 2006; 312: 24-32. <http://dx.doi.org/10.1016/j.ijpharm.2005.12.037>
- Monica RP Rao, Girish S Sonar, Rachana R Mandasaurwale, Swapnila D Vanshiv. Evaluation of effervescent floating matrix tablet formulations of salbutamol sulfate using full factorial design, Asian Journal of Pharmaceutics 2009; 3(1): 43-49. <http://dx.doi.org/10.4103/0973-8398.49174>
- ST Prajapati, LD Patel, DM Patel. Studies on Formulation and *In Vitro* Evaluation of Floating Matrix Tablets of Domperidone, Indian Journal of Pharmaceutical Science 2009; 71(1): 19-23. <http://dx.doi.org/10.4103/0250-474X.51944>
- Anilkumar J Shinde, Manojkumar S Patil, Harinath N More. Formulation and Evaluation of an Oral Floating Tablet of Cephalixin,

- Indian Journal of Pharmaceutical Education and Research 2010; 44(3): 243-252.
11. Havaladar VD, Kulkarni AS, Dias RJ, Aloorkar NH, Mali KK. Floating matrix tablets of atenolol: Formulation and *in vitro* evaluation. Asian Journal of Pharmacy 2009; 3: 286-291. <http://dx.doi.org/10.4103/0973-8398.59952>
12. Nama M, Gonugunta CS, Reddy Veerareddy P. Formulation and evaluation of gastro retentive dosage forms of Clarithromycin. AAPS Pharm Science Tech 2008; 9: 231-237. <http://dx.doi.org/10.1208/s12249-008-9038-8>
13. Patel A, Modasiya M, Shah D, Patel V. Development and *in vivo* floating behavior of verapamil HCl intra gastric floating tablets. AAPS Pharm Science Tech 2009; 10: 310-315. <http://dx.doi.org/10.1208/s12249-009-9210-9>
14. Gambhire MN, Ambade KW, Kurmi SD, Kadam VJ, Jadhav KR. Development and *in vitro* evaluation of an oral floating matrix tablet formulation of Diltiazem hydrochloride. AAPS Pharm Science Tech 2007; 8: E73. <http://dx.doi.org/10.1208/pt0803073>
15. Natalie Mc Clure. Stability studies in overview of ICH guidelines for drug products. Matrix Pharmaceutical Inc; 1997.
16. Ligumsky M, Sestieri M, Okon E, Ginsberg I. Antioxidants inhibit ethanol-induced gastric injury in the rat. Scandinavian Journal of Gastroenterology 1995; 30: 854-60. <http://dx.doi.org/10.3109/00365529509101591>
17. Lam SK, Cho CH, Chen BW, Lai KC, Chin CK, Ho CS, Li YN. Gastric cytoprotection by amoxycillin in rat. Journal of Gastroenterology 1994; 9: 514-8.
18. Baumgartner S, Kristl J, Vrečer F, Vodopivec P, Zorko B. Optimization of floating matrix tablets and evaluation of their gastric residence time. International Journal of Pharmacy 2000; 195: 125-135. [http://dx.doi.org/10.1016/S0378-5173\(99\)00378-6](http://dx.doi.org/10.1016/S0378-5173(99)00378-6)
19. Ali J, Arora S, Ahuja A, Babbar AK, Sharma RK, et al. Formulation and development of hydrodynamically balanced system for metformin: *in vitro* and *in vivo* evaluation. European Journal of Pharmacy and Biopharmaceutics 2007; 67: 196-201. <http://dx.doi.org/10.1016/j.ejpb.2006.12.015>
20. Baron TH, Langman MTS, Wastell C. Stomach and duodenum. In: I.A.D/ Bouchier (Ed.), Recent Advances in Gastroenterology. Churchill Livingstone, London; 1980. p. 23-29.
21. Marhuenda E, Martin MJ, Alarcon De La Lastra C. Anti ulcerogenic activity of aescine in different experimental models. Phytotherapy Research 1993; 7: 13-16. <http://dx.doi.org/10.1002/ptr.2650070105>
22. Ligumsky M, Sestieri M, Okon F, Ginsburg I. Antioxidants inhibit ethanol-induced gastric injury in the rat. Role of manganese, glycine and carotene. Scandinavian Journal of Gastroenterology 1995; 30: 854-860. <http://dx.doi.org/10.3109/00365529509101591>

Cite this article as:

Sarojini Sarangapani, Jayanthi Bangaru, Manavalan Rajappan. In vitro and In vivo evaluation of the gastroretentive floating dosage form. Int. Res. J. Pharm. 2014; 5(9):695-700 <http://dx.doi.org/10.7897/2230-8407.0509142>

Source of support: Nil, Conflict of interest: None Declared