Internationale Pharmaceutica Sciencia

Available Online: https://ipharmsciencia.edwiserinternational.com/home.php

Development and Evaluation of Ranitidine Floating Tablet for Ulcer Healing and Soothing

Nitish Nirala[1,*], Ram Kumar Choudhary[1], Debankini Dasgupta[2] and Archana[2]

[1]Department of Pharmaceutics, Government Pharmacy Institute, Patna, Bihar-800007, India
[2]Department of Pharmacy, MGM College of Pharmacy, Patna, Bihar-801105, India

ARTICLE INFO

Received: 16 August 2023
Revised: 01 September 2023
Available Online: 10 Sep 2023

*Corresponding author: Nitish Nirala, Department of Pharmaceutics, Government Pharmacy Institute, Patna, Bihar-800007, India

ABSTRACT

In this current work floating tablets of ranitidine and aloe vera was prepared. The objective behind the work was to develop a formulation of H2 antagonist in collaboration with aloe vera to produce an ulcer soothing and ulcer protective effect. Ranitidine is a histamine H2-receptor antagonist. It is widely prescribed in active duodenal ulcers, gastric ulcers, Zollinger-Ellison syndrome, gastroesophageal reflux disease, and erosive esophagitis. The effective treatment of erosive esophagitis requires administration of 150 mg of Ranitidine, four times a day. A conventional dose of 150 mg can inhibit gastric acid whereas aloe vera will produce ulcer soothing affect and laxative effect too. In- vitro buoyancy studies were performed for all the ten formulations as per the method described by Rosa et al. The randomly selected tablets from each formulation were kept in a 100ml beaker containing simulated gastric fluid, pH 1.2 as per USP. The time taken for the tablet to rise to the surface and float was taken as floating lag time (FLT).

Keywords: *Floating tablets; GERD; Ranitidine; Aloe vera; Gastro-retentive drug delivery system.*

Introduction

Tablets are the most widely used dosage forms because of their convenience in self-administration, compactness, and ease of manufacturing. However, oral administration has limited use for important drugs from various pharmacological categories with poor oral bioavailability due to incomplete absorption or degradation in the gastrointestinal (GI) tract. A narrow absorption window at the upper part of the gastrointestinal tract characterizes some of these drugs [1]. Rapid and unpredictable gastrointestinal transit could result in incomplete drug release from the device above the absorption zone, leading to diminished efficacy of the administered dose! Gastro Retentive Drug Delivery Systems (GRDDS) can be developed to increase the gastric retention time of drugs. These systems remain in the gastric region for several hours and can, therefore, significantly prolong the gastric residence time of the drugs. Prolonged gastric retention improves bioavailability, reduces drug waste, and improves the solubility of less soluble drugs in the small intestine's high pH environment. It is quite difficult to achieve extensive retention of the GRDF, as the natural activity of the stomach is to evacuate its contents into the intestine. The main approaches that have been examined are low-density GRDDS that remains buoyant above the gastric fluid; high density, which retains the dosage form in the body of the stomach; concomitant administration of drugs or excipients, which slows the motility of the gastrointestinal tract; and bioadhesive or mucoadhesive dosage forms. As most absorption windows are located in the proximal small intestine

(duodenum), the most effective strategy to improve drug absorption will be to retain the formulation in the stomach [2]. Ranitidine hydrochloride is a histamine H2-receptor antagonist. It is widely prescribed for active duodenal ulcers, gastric ulcers, Zollinger-Ellison syndrome, gastroesophageal reflux disease, and erosive esophagitis [3]. The effective treatment of erosive esophagitis requires the administration of 150 mg of Ranitidine four times a day. A conventional dose of 150 mg can inhibit gastric acid secretion for up to five hours but not up to 10 hours. An alternative dose of 300 mg leads to plasma fluctuations; thus, a sustained-release dosage form of Ranitidine hydrochloride is desirable. The short biological half-life of the drug (-2.5-3 hours) also favors the development of a sustained release formulation; Ranitidine is absorbed only in the initial part of the small intestine and has 50% absolute bioavailability. Moreover, the colonic metabolism of Ranitidine is partly responsible for the poor bioavailability of ranitidine from the colon [4].

The gastro retentive drug delivery systems can be retained in the stomach and assist in improving the sustained oral delivery of drugs with an absorption window in a particular region of the gastrointestinal tract. These systems help continuously release the drug before it reaches the absorption window, thus ensuring optimal bioavailability. The gastro retentive drug delivery systems can be retained in the stomach and assist in improving the sustained oral delivery of drugs with an absorption window in a particular region of the gastrointestinal tract. These systems help continuously release the drug before it reaches the absorption window, thus ensuring optimal bioavailability [5].

Aloe Vera was added to the formulation to provide laxative effect Anthraquinones present in latex are a potent laxative. It increases intestinal water content, stimulates mucus secretion, and increases intestinal peristalsis. It will also provide a soothing effect on the ulcer as Mucopolysaccharides help bind moisture into the skin [6].

Materials and Methods

Materials

Ranitidine hydrochloride was received as gift sample from East India Pharmaceuticals, West Bengal and Hydroxy propyl Methyl Cellulose (HPMC), polyvinyl pyrrolidone (PVP), sodium bicarbonate and colloidal silicon dioxide (Aerosil) were obtained as gift samples from Strides Arcolab's and Zydus Recon, Bangalore. Gum Tragacanth and dicalcium phosphate were obtained as gift samples from Jagath Pharma, Bangalore. Magnesium stearate and talc were received as gift samples from Eros Pvt. Ltd., Bangalore. BHA was obtained as gift sample from Merk Specialities Private Limited, Mumbai.

Methodology

Tablet was made by wet granulation technique. Chemicals used were sodium bicarbonate, dicalcium phosphate, Aloe Vera powder, Ranitidine hydrochloride (400 mg for each batch) and binders used were PVP, gum tragacanth, hydroxy propyl methyl cellulose (HPMC). Drug and chemicals were accurately weighed and mixed. In other beaker water was made lukewarm in water bath gum tragacanth, PVP, HPMC was added and made mucilage with the help of glass rod. Drops of binder were taken then dried at 40ºC [7]. Then granules were compressed as tablet (Table 1).

Weight Variation Test

If the drug forms greater part of the tablet, any variation in the tablet weight obviously indicates a variation in the active ingredient this test resembles weight uniformity test. 20 tablets were selected at random and average weights were determined. Then individual tablets weighed, and the individual weight was compared with the average.

Average weight of tablets = Total weight of tablets/Number of tablets

Thickness of Tablets

The thickness uniformity studies were carried out by using Vernier Callipers. Six tablets were used for thickness uniformity studies and denoted in millimetre. The data obtained was used to calculate mean and standard deviation.

Friability

The friability of the tablet was determined using Roche Friabilator. It is expressed in percentage (%). 20 tablets were initially weighed and transferred into the friabilator. The friabilator was operated at 25 rpm per min for 4 min (100 revolutions). The tablets were weighed again (W final). The % friability was then calculated by:

$$F = \{(W\ initial) - (W\ final)/(W\ initial)\} \times 100.$$

Citation: *Nirala N, Choudhary RK, Dasgupta D, et al Development and Evaluation of Ranitidine Floating Tablet for Ulcer Healing and Soothing. Int Pharm Sci 2023; 16(1):127. doi: 10.31531/2231-5896.1000127*

Formulation Table

Table 1: Development of different formulations containing varying proportions of polymers.

Ingredients → Trial ↓	Ranitidine HCL (mg)	Aloe Vera Powder (mg)	Dicalcium Phosphate (mg)	Sodium bicarbonate (mg)	BHA (mg)	HPMC (mg)	PVP (mg)	Gum Tragacanth (mg)	Magnesium Stearate (mg)	Talc (mg)	Aerosil (mg)
Trial-I	40	q.s	q.s	50	5	70	40	60	15	10	10
Trial-II	40	q.s	q.s	60	5	60	50	60	15	10	10
Trial-III	40	q.s	q.s	80	5	100	70	-	12	10	10
Trial-IV	40	q.s	q.s	70	5	60	60	60	12	10	10
Trial-V	40	q.s	q.s	60	5	80	50	50	15	10	10

Hardness

The hardness of prepared formulation was measured by using Monsanto Hardness tester. Six floating tablets were used for hardness uniformity studies. The hardness data used to calculate mean and standard deviation.

In vitro Buoyancy / Floating Study

In vitro buoyancy studies were performed for all the formulations. The randomly selected tablets from each formulation were kept in a 100 ml beaker containing simulated gastric fluid, pH1.2 as per USP. The time taken for the tablet to rise to the surface and float was taken as Floating Lag Time (FLT). The duration of time the dosage form constantly remained on the surface of medium was determined as the Total Floating Time (TFT).

Disintegration

Disintegration time of a tablet was determined by using disintegration test apparatus as per IP specifications. Place each tablet in each 6 tubes of the disintegration apparatus a then add a disc to each tube containing 6.8 pH phosphate buffer. The temperature of the buffer should maintain at 37°C and run the apparatus raised and lowered for 30 cycles per minute [8].

Results

The results of different evaluation study are tabulated in Table 2.

Weight variation test

Selection of 10 tablets from each batch should be done and note down the weight of the tablet individually and check for any variation in its weight. According to US Pharmacopeias' small variations in the weight is negligible and can be accepted. The weight ranged from 401 mg to 443.6 mg.

Thickness of Tablets

The thickness of tablets is measured by Vernier callipers average thickness ranged 6 mm-7 mm.

Friability

"Roche friabilator" is the equipment which is used for the determination of friability. It is expressed in percentage. Have to note down the initial weight of the tablets individually (W initial). Tablets are placed in a circular polyethylene chamber which revolves at 25 rpm, and they are subjected to fall from a height of 6 inches in the friabilator for about 100 revolutions. Then measure the weight of the tablet (Wfinal) and observe any weight difference before tablet and after the friabilator processing. The results were between 0% to 0.6%.

Citation: *Nirala N, Choudhary RK, Dasgupta D, et al Development and Evaluation of Ranitidine Floating Tablet for Ulcer Healing and Soothing. Int Pharm Sci 2023; 16(1):127. doi: 10.31531/2231-5896.1000127*

Table 2: Data of weight variation, thickness, friability, hardness, disintegration, floating lag time and floating time of developed formulation.

Batch No.	Weight variation(mg)	Thickness (mm)	Friability (%)	Hardness (kg/cm^2)	Disintegration (hrs)	Floating Lag Time(secs)	Floating Time
B-1	401	6.5	0.18	4.9	5 hrs	87	>24
B-2	421.4	7	0	4.5		65	>24
B-3	410.7	6.8	0.67	4.3		45	>24
B-4	412.5	6.3	0.21	4.5		52	>24
B-5	443.6	6	0.5	5		72	>24

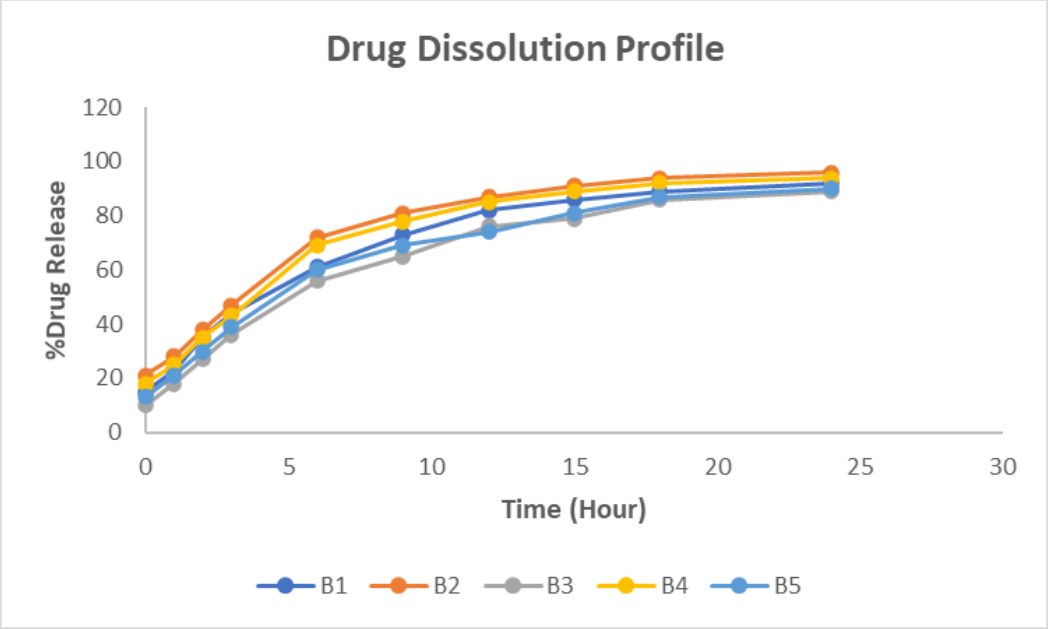

Figure 1: Comparative in-vitro % drug release profiles for all the prepared formulations.

Hardness

The ability of a tablet to withstand for mechanical shocks is known as hardness. Pfizer hardness tester and Monsanto hardness tester are the instrument which is used to determine the hardness of tablet. It is expressed in kg/cm2. Take three tablets from each batch and hardness should be determined and the selection of tabled should be done randomly. Result varied between 4.3 kg/cm^2 to 5 kg/cm^2.

Floating time

With an increase in the concentration of the hydrophilic polymer total floating time was found to be decreased due to increase in the solubility.

Disintegration

Disintegration time of a tablet was determined by using disintegration test apparatus as per IP specifications. Place each tablet in each 6 tubes of the disintegration apparatus a then add a disc to each tube containing 6.8 pH phosphate buffer. The temperature of the buffer should maintain at 37°C and run the apparatus raised and lowered for 30 cycles per minute. The time taken for the complete disintegration of the tablet was found to be 5 hrs (Figure 1).

Conclusion

In this study the researchers have prepared 5 different formulations of Ranitidine floating tablets. HPMC and PVP showed good batch to batch reproduce ability with respect to weight variation, thickness, friability, hardness, floating lag time and floating time. These results indicate that the floating tablets have potential

to deliver Ranitidine following GI administration. Overall study suggested that drug entrapped floating tablet can be a good choice to achieve instant as well as prolong affect. In this way need not to take frequent drug dose, as well as we can increase biological half-life and shelf life of drug.

Funding

No financial assistance was provided for this project.

Conflict of Interest

None declared.

References

1. Iannuccelli V, Coppi G, Bernabei MT, Cameroni R. Air compartment multiple-unit system for prolonged gastric residence- Part I. Formulation study. Int J Pharm 1998;174:47-54.
2. Hoffman A, Stepensky D, Lavy E, Eyal S, Klausner E, Friedman M. Pharmacokinetic and pharmacodynamic aspects of gastroretentive dosage forms. Int J Pharm 2004;277:141-53
3. Physician's Desk reference. Description and clinical pharmacology of Zantac® Tablets (Ranitidine Hydrochloride USP). 56th ed: Medical economic company; 2002.
4. Abdul WB, Larry FL. Colonic metabolism of ranitidine, implications for its delivery and absorption. Int J Pharm 2001;227:157-65.
5. Chithra P, Sajithlal G, Chandrakasan G. Influence of aloe vera on the glycosaminoglycans in the matrix of healing dermal wounds in rats. J Ethnopharmacol. 1998;59:179–86.
6. Marshall JM. Aloe vera gel: What is the evidence? Pharma Jr. 1990;24:3602
7. Chithra R Sajithlal GB, Chandrakasan G. Influence of aloe vera on collagen characteristics in healing dermal wounds in rats. Mol Cell Biochem. 1998;181:71–6.
8. Heggers J, Kucukcelebi A, Listengarten D, Stabenau J, Ko F, Broemeling LD, et al. Beneficial effect of aloe on wound healing in an excisional wound model. J Altern Complement Med. 1996;2:271–7.