ISSN : 2320 4850

BI MONTHLY

Asian Journal of Pharmaceutical Research And Development

(An International Peer Reviewed Journal of Pharmaceutical Research and Development)

AJPRD

Volume - 03 Issue - 04 JUL-AUG 2015

website: www.ajprd.com

editor@ajprd.com

Asian Journal of Pharmaceutical Research and Development
(An International Peer-Reviewed Journal of Pharmaceutical Research and Development)
www.ajprd.com
ISSN 2320-4850

Research Article

FORMULATION AND EVALUATION OF RANITIDINE FLOATING TABLETS

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Received: April 2015 ***Revised and Accepted: May 2015***

ABSTRACT:

The gastroretentive drug delivery systems can be retained in the stomach and assist improving the oral sustained delivery of drugs that have an absorption window in a particular region of the gastrointestinal tract. These systems help in continuously releasing the drug before it reaches the absorption window, thus ensuring optimal bioavailability. This research article describes the preparation and in vitro evaluation of floating tablet of ranitidine hydrochloride by direct compression technique using different concentrations of different grades of polymers (HPMC K4 M and HPMC K100 M) with sodium bicarbonate and citric acid, magnesium stearate and talc Sodium bicarbonate and citric acid were incorporated as gas generating agents. Tablets were prepared by direct compression technique. The tablets were characterized by lag time, floating time, weight variation, and drug content. The results indicated that combination of polymers of both synthetic and natural polymers shows the best result.

Keywords:
In vitro buoyancy, HPMC K4M, HPMC K100M, ranitidine hydrochloride, Xanthan gum,

INTRODUCTION:

Ranitidine hydrochloride is a histamine H2-receptor antagonist that inhibits stomach production. Its chemical name is N'-[2-[[5-(Dimethylaminomethyl)-2-furyl]methylsulfanyl]ethyl]-N-methyl-2-nitro-ethene-1,1-diamine [1]. It is commonly used in treatment of peptic ulcer disease (PUD) and gastro esophageal reflux disease (GERD). Ranitidine is also used alongside fexofenadine and other antihistamines for the treatment of skin conditions such as hives. Ranitidine HCl, the model drug for this study, 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 recommended adult oral dosage of ranitidine is 150 mg twice daily or 300 mg once daily. The effective treatment of erosive esophagitis requires administration of 150 mg of ranitidine 4 times a day [2]. A conventional dose of 150 mg can inhibit gastric acid secretion up to 5 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 HCl is desirable [3]. The short biological half-life of the drug (~2.5-3 hours) also favors development of a sustained-release formulation. A traditional oral sustained-release formulation releases most of the drug at the colon; thus, the drug should have an absorption window either in the colon or throughout the gastrointestinal tract. Ranitidine is absorbed in only the initial part of the small intestine and has 50% absolute

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bioavailability [4,5]. Moreover, colonic metabolism of ranitidine is partly responsible for the poor bioavailability of ranitidine from the colon [6].

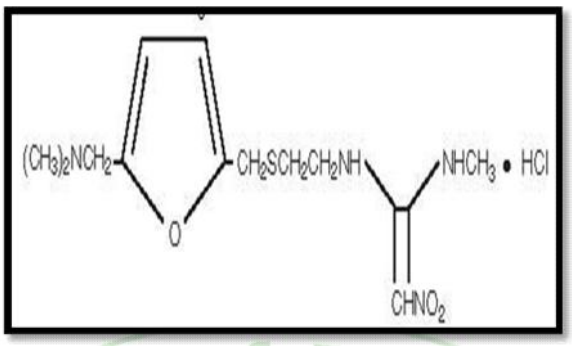

Figure 1: Structure of Ranitidine Hydrochloride

The volume of distribution of the drug is about 1.4L/Kg having serum protein binding is 15%. It has hepatic metabolism. It is metabolized to the N –oxide (4%), S-oxide (1%) and N-dimethyl metabolites (1%) of the dose. The principal route of excretion is the urine (active tubular excretion, renal clearance 410 ml/min) with approximately 30 % or the orally administrated dose collected in the urine as unchanged drug in 24 hrs urinary excretion of unchanged drug I.V is 70-80%. It has 29 ml/min in clinically significant renal function impairment and 3ml/min/kg in neonatel patients. The low bioavailability (40-45%), short biological half life (2.5-4.0 hours) and associated adverse effects like diarrhoea, dizziness, headache and anorexia etc, which may also exhibits toxic effect in prolong use. This approach also reduces the unwanted side effects of the drug, the tablet remain buoyant for a long period on the gastric contents, exhibiting a prolonged gastric residence time, resulting in sustained drug release and consistent blood levels of drug.[**7]**

MATERIALS AND METHODS

Ranitidine was obtained as gift sample other chemical and polymers such as Hydroxyl Propyl Methylcellulose (HPMC K4M, K100M) was obtained as gift sample. All other reagents and chemicals used were of analytical grade.

EVALUATION STUDIES:

Angle of Repose

The angle of repose of powder blend was determined by the funnel method. The accurately weight powder blend were taken in the funnel. The height of the funnel was adjusted in such a way the tip of the funnel just touched the apex of the powder blend. The powder blend was allowed to flow through the funnel freely on to the surface. The diameter of the powder cone was measured and angle of repose was calculated using the following equation. Tan Θ= h/r Where, h and r are the height and radius of the powder cone. [8]

Table 1: Effect of Angle of Repose (Θ) on Flow Property

Angle of repose (Θ)	Type of flow
<20	Excellent
20-30	Good
30-34	Passable
>35	Very poor

Bulk Density and Tapped Density

Both loose bulk density (LBD) and tapped bulk density (TBD) was determined. A quantity 2gm of powder blend from each formula, previously shaken to break any agglomerates formed, was introduced in to 10 ml measuring cylinder. After that the initial volume was noted and the cylinder was allowed to fall under its own weight on to a

hard surface from the height of 2.5 cm at second intervals. Tapping was continued until no further change in volume was noted. [9]
Bulk density = weight of powder / bulk volume

Compressibility Index

The Compressibility Index of the powder blend was determined by Carr's compressibility index. It is a simple test to evaluate the LBD and TBD of a powder and the rate at which it packed down. The formula for Carr's Index is as below [8]
Carr's index (%) = [(TD-BD) X100}/TD

Hausner's Ratio

It is the ratio of bulk volume to tapped volume or tapped density to bulk density. Hausner's ratio is an important character to determine the flow property of powder and granules. This can be calculation by the following formula.[10]
Hausner's ratio = Tapped density / Bulk Density

Weight Variation Test

To study weight variation twenty tablets of the formulation were weighed using a Sartorius electronic balance and the test was performed according to the official method.

Table no 2: Percentage deviation in weight variation

Average weight of a tablet	Percentage deviation
130 mg or less	10
>130 mg and <324 mg	7.5
324 mg or more	5

Drug Content

Five tablets were weighed individually, and the drug was extracted in 0.1 N HCl, and the solution was filter through 0.45 membrane. The absorbance was measured at 315 nm after suitable dilution using a Shimadzu UV-1601 UV/Vis double beam spectrophotometer [11]

Hardness

The hardness of five tablets was determined using the Pfizer hardness tester and the average values were calculated.[9]

Friability

Friability is the measure of tablet strength. Roche friabilator was used for testing the friability using the following procedure. Twenty tablets were weighed accurately and placed in
the tumbling apparatus that revolves at 25 rpm dropping the tablets through a distance of six inches with each revolution. After 4 min., the tablets were weighed and the percentage loss in tablet weight was determined. [12]

Floating Lag Time

The lag time was carried out in beaker containing 100 ml of 0.1 N HCl as a testing medium maintained at 37 °C. The time required for the tablet to rise to the surface and float was determined as floating lag time. [13]

Floating Time

Floating time was the time, during which the tablet floats in 0.1 N HCL dissolution medium (including floating lag time)
On immersion in 0.1N HCl solution pH (1.2) at 37 0 C, the tablets floated, and remained buoyant
without disintegration. Formulation containing HPMC K4M, HPMC K100M and Xanthan gum
(FM-7) showed good FLT of 48 sec.

Swelling index study

Swelling index study was performed on all the batches (FM-1 to FM-10). The results of swelling index were shown in (Figure No.2). In the present study, the higher swelling index was found for tablets of batch FM-9 containing combination of HPMC K4M, HPMC K100M and Xanthan gum and guar

gum. Thus, the viscosity of the polymer had major influence on swelling process, matrix integrity, as well as floating capability, hence from the above results it can be concluded that linear relationship exists between swelling processes.

In vitro Drug Release Study

The release rate of Ranitidine HCl from floating tablets was determined using USP Dissolution Testing Apparatus II (Paddle type). The dissolution test was performed using 900 ml of 0.1 N HCl, at 37 ± 0.5°C and 50 rpm. Aliquot volume was withdrawn from the dissolution apparatus hourly for 8 hr, and the samples were replaced with fresh dissolution medium. After filtration and suitable dilution the amount of drug release was determined from the calibration curve. [14, 15, 16]

Table 3: Pre compression parameters of granules

Formulation	Bulk density (gm/cm^3)	Tapped density (gm/cm^3)	Angle of repose (Θ)	Hausner's ratio (Hg)	Carr's index
F1	0.468	0.681	24.35	0.148	25.09
F2	0.466	0.61	31.91	0.125	28.67
F3	0.522	0.621	30.99	0.091	24.9
F4	0.56	0.63	29.688	0.098	20.43
F5	0.457	0.589	24.51	0.149	19.78
F6	0.438	0.601	30.68	0.178	28.12
F7	0.461	0.643	26.59	0.066	25.88
F8	0.418	0.587	28.13	0.15	18.56
F9	0.514	0.618	24.58	0.112	22.3
F10	0.45	0.599	25.6	1.136	26.52

Table no 4: Swelling index of tablet prepared by natural polymer

Time	Swelling index (%)									
	F1	F2	F3	F4	F5	F6	F7	F8	F9	F10
1 hrs	20.18	13.25	17.33	19.55	27	16.99	13.00	15.72	16.88	15.51
2 hrs	30.22	30.66	24.43	29.44	35.00	36.45	30.01	26.01	35.76	24.84
3 hrs	57.14	46.93	41.85	56.68	60.98	62.74	44.99	94.96	62.57	45.88
4 hrs	74.56	52.66	60.18	73.70	72.54	79.12	97.90	63.09	85.43	61.81
5 hrs	90.20	65.30	72.65	94.52	96.97	91.67	96.90	71.94	94.57	72.00

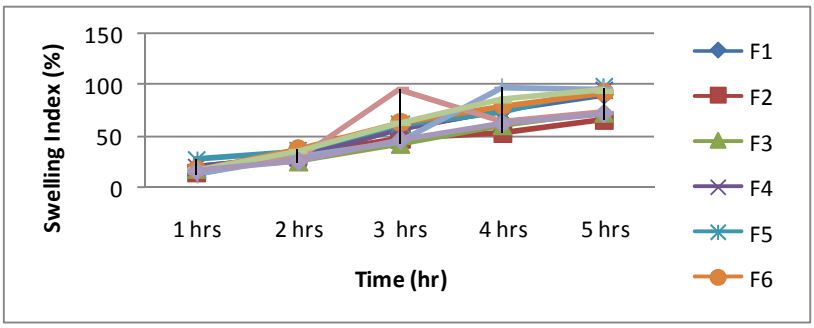

Figure 2: Swelling index of Formulation F1 to F10

Table 5: In vitro floating studies of floating tablets

Formulation code	Floating lag time (sec)	Floating time (hr)
F1	86	8
F2	101	8
F3	97	8
F4	74	8
F5	46	8
F6	78	8
F7	110	8
F8	109	8
F9	125	8
F10	94	8

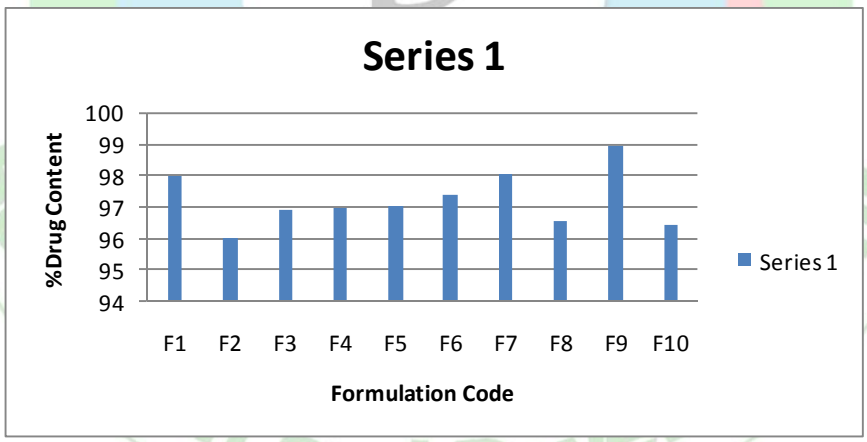

Figure 3: % Drug Content of Formulation F1 to F10

RESULT AND DISCUSSION:

This study discusses the preparation of floating tablets of Ranitidine. The effervescent-based floating drug delivery was a approach to achieve *in vitro* buoyancy. The addition of gel-forming polymer HPMC K4 M, HPMC K15 M, carbopol 934P xanthan gum and guar gum and gas-generating agent sodium bicarbonate was essential to achieve *in vitro* buoyancy. Addition of citric acid, to achieve buoyancy under the elevated pH of the stomach, caused an enhancement in drug release. The type of polymer affects the drug release rate and the mechanism. Polymer swelling is crucial in determining the drug release rate and is also important for flotation. A prolonged floating duration could be achieved by varying the amount of effervescent and using different polymer combinations. The *in vitro* drug release profiles obtained for tablets (F9) made with

combinations of HPMC K4 M, HPMC K100M, and carbopol 934P a prolonged floating duration.

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