RESEARCH ARTICLE

Formulation and Evaluation of Floating Matrix Tablet of Ranitidine HCl

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ABSTRACT

Ranitidine HCl is used for the H2 receptor antagonist. It is an absorption window limited drug, whose solubility decreases with increase in the pH and has a short half life of 2-3 h. Therefore the present investigation is concerned with the development of the floating matrix tablets, which after oral administration were designed to prolong the gastric residence time and thus to increase the bioavailability of the drug and its half life. Ranitidine HCl showed maximum absorption at wavelength 324 nm in 0.1N HCl. Drug-polymer compatibility studies by DSC give conformation about their purity and showed no interaction between drug and selected polymers. Various formulations were developed by using release rate controlling and gel forming polymers like HPMC K4 M, and Polyethylene oxide WSR 303 in single by direct compression method with the incorporation of sodium bicarbonate as gas generating agent. All the formulations had floating lag time below 4 minutes and constantly floated on dissolution medium for more than 12 h. Swelling studies indicated significant water uptake and contributed in drug release. From all the developed formulations, batch F5 and F6 prolonged the drug release for longer period of time, they were nominated as best formulations. The best formulations followed power law kinetics while the drug release mechanism was found to be diffusion through and polymer relaxation. The best formulations were found to be stable during stability studies for one month. Thus, best formulations satisfied physico-chemical parameters, floating time, swelling index and in vitro drug release profile requirements for a floating drug delivery system.

KEYWORDS

Ranitidine HCl, Floating Drug Delivery System, Floating Matrix tablet.

INTRODUCTION

The real challenge in the development of an oral controlled-release drug delivery system is not just to sustain the drug release but also to prolong the presence of the dosage form within the gastrointestinal tract (GIT) until all the drug is completely released at the desired period of time. Indeed, gastric drug retention has received significant interest in the past few decades. Most of the conventional oral delivery systems have shown some limitations related to fast gastric-emptying time .[1,2]

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Classified the gastroretentive dosage forms into four main classes: (i) floating systems, (ii) expandable systems, (iii) bioadhesive systems and (iv) high density systems. Floating systems are of two types: (A) effervescent systems, depending on the generation of carbon dioxide gas upon contact with gastric fluids, and non-effervescent systems. The latter systems can be further divided into four sub-types, including hydrodynamically balanced systems; microporous compartment systems, alginate bead and hollow microspheres/microballons. In addition, super-porous hydrogels and magnetic systems were described.[2,3,4] As suggested by Singh and Kim, floating drug delivery is of particular interest for drugs which: (a) act locally in the stomach; (b) are primarily

absorbed in the stomach; (c) are poorly soluble at an alkaline pH; (d) have a narrow window of absorption; and (e) are unstable in the intestinal or colonic environment.

A traditional oral sustained release formulation releases most of the drug at the colon, thus the drug should have absorption window either in the colon or throughout the gastrointestinal tract. Ranitidine is absorbed only in the initial part of the small intestine and has 50% absolute bioavailability. Moreover, colonic metabolism of ranitidine is partly responsible for the poor bioavailability of ranitidine from the colon. These properties of ranitidine hydrochloride do not favor the traditional approach to sustained release delivery. Hence, clinically acceptable sustained release dosage forms of ranitidine hydrochloride prepared with conventional technology may not be successful.[3, 4]

The gastroretentive drug delivery systems can be retained in the stomach and assist in 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.[3,4]

It is also reported that oral treatment of gastric disorders with an H$_2$-receptor antagonist like ranitidine or famotidine used in combination with antacids promotes local delivery of these drugs to the receptor of the parietal cell wall. Local delivery also increases the stomach wall receptor site bioavailability and increases the efficacy of drugs to reduce acid secretion. This principle may be applied for improving systemic as well as local delivery of ranitidine hydrochloride, which would efficiently reduce gastric acid secretion.

Several approaches are currently used to prolong gastric retention time. These include floating drug delivery systems, also known as hydrodynamically balanced systems, swelling and expanding systems, polymeric bioadhesive systems, modified-shape systems, high-density systems and other delayed gastric emptying devices. The principle of buoyant preparation

offers a simple and practical approach to achieve increased gastric residence time for the dosage form and sustained drug release.[4,5]

Ranitidine hydrochloride 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. A conventional dose of 150 mg can inhibit gastric acid secretion up to 5 h but not up to 10 h. 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 drug (~2.5-3 h) also favors development of a sustained release formulation.

In context of the above principles, a strong need was recognized for the development of a dosage form to deliver ranitidine hydrochloride in the stomach and to increase the efficiency of the drug, providing sustained action. The present investigation applied a systematic approach to the development of gastroretentive ranitidine hydrochloride dosage forms.[3,5,6]

MATERIALS AND METHODS

MATERIALS

Poly Ethylene Oxide WSR 300 was obtained from Torrent Pharmaceutical Ltd. HPMC K 4 M was obtained from Torrent Pharmaceutical Ltd. Gift sample of Ranitidine HCl was kindly provided by Torrent Pharmaceutical Ltd Ahmedabad. Sodium Bicarbonate, Microcrystaline cellulose, Talc and Mg stearate supplied from Seva fine chemicals, Ahmedabad.

METHOD[7, 8, 9]

Different tablets formulations were prepared by direct compression technique. All the powders were passed through 80 mesh sieve. Required quantity of drug, matrix polymer and low density powder were mixed thoroughly. Talc and magnesium stearate were finally added as

glidant and lubricant respectively. The blend was compressed (9.5 mm diameter, punches) using multipunch tablet compression machine. Each tablet contained 150 mg of ranitidine hydrochloride and other pharmaceutical ingredients as listed in tables in each section. Different polymers natural and synthetic were selected as matrix forming polymer for formulating a sustained release matrix floating drug delivery system.

Table 1: Composition of Tablet

Ingredient	F1 (mg)	F2 (mg)	F3 (mg)	F4 (mg)	F5 (mg)	F6 (mg)
Drug	150	150	150	150	150	150
PEO WSR 303	60	65	70	75	80	85
NaHCO$_3$	50	50	50	50	50	50
MCC	80	75	70	65	60	55
Talc	5	5	5	5	5	5
Mg stearate	5	5	5	5	5	5
Total wt	350	350	350	350	350	350

Determination of UV Absorbance Maxima of Ranitidine HCl[5, 6]

A solution of ranitidine hydrochloride was prepared in 0.1 N HCl and UV Spectrum was taken using Shimadzu UV-1601 UV/Vis double beam spectrophotometer. The UV maximum of ranitidine hydrochloride was found to be 323 nm in 0.1 N HCl.

Preparation of Standard Calibration Curve of Ranitidine Hydrochloride[5, 6]

Ranitidine Hydrochloride (10 mg) was dissolved in 0.1 N HCl and volume was made up to 100 ml in 100 ml volumetric flask. This solution (100 mcg/ml) was further diluted with 0.1 N HCl to obtain solution of 10 to 100 mcg/ml. Absorbance of each solution was measured at 323.8 nm using UV double beam spectrophometer.

Identification of Drug by FTIR[5, 6, 7]

Fourier-transform infrared (FT-IR) spectra were obtained using an FT-IR spectrometer (Shimadzu 8400S, Japan). The pure Ranitidine HCl was mixed thoroughly with potassium bromide, an infrared transparent matrix, at 1:5 (Sample: KBr) ratio, respectively. The KBr discs were prepared by compressing the powders at a pressure of 5 tons for 5 min in a hydraulic press. Forty scans were obtained at a resolution of 4 cm^{-1}, from 4000 to 400 cm^{-1}.

Identification of Drug by DSC[6, 7]

The Differential Scanning Calorimetry study was carried out using DSC-60 (Shimadzu, Tokyo, Japan). The instrument comprises of calorimeter, flow controller, thermal analyzer and operating software. The drug were heated in sealed aluminum pans under air flow (30 ml/min) at a scanning rate of 20°C/min from 50 to 300°C. Empty aluminum pan was used as a reference. The heat flow as a function of temperature was measured for the samples.

Micromeritic Properties of Powder Blend

Angle of Repose[9, 10]

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.

$$\tan \theta = h/r$$

Where, h and r are the height and radius of the powder cone.

Bulk Density and Tapped Density [11]

Both loose bulk density (LBD) and tapped bulk density (TBD) was determined. A quantity of 2

gm 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. LBD and TDB were calculated using the following equations.

LBD= Weight of the powder blend/Untapped Volume of the packing

TBD=Weight of the powder blend/Tapped Volume of the packing

Compressibility Index [9]

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:

Carr's Index (%)=[(TBD-LBD) x100]/TBD

Table 2: Scale of flow ability by Compressibility index

C.I.	Category
<10	Excellent
11 – 15	Good
16 – 20	Fair
21 – 25	Passable
26 – 31	poor
32 – 37	Very poor
>38	Very very poor

Total Porosity [11]

Total porosity was determined by measuring the volume occupied by a selected weight of a powder (V_{bulk}) and the true volume of the powder blend (The space occupied by the powder exclusive of spaces greater than the intermolecular spaces, V)

Porosity (%) = V_{bulk}-V/V_{bulk} x 100

Drug Content [8,9,10]

An accurately weight amount of ranitidine hydrochloride powder blend (100 mg) was extracted with 0.1 N HCl and the solution was filter through 0.45µ membrane. The absorbance was measured at 323 nm after suitable dilution using a Shimadzu UV-1601 UV/Vis double beam spectrophotometer.

Hausner's Ratio[12]

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-

Hausner's ratio = Tapped density / Bulk density

Value < 1.25 indicate good flow (=20% Carr's index)

While > 1.50 indicate poor flow (=35% Carr's index)

Table 3: Standard value of Hausner's Ratio

Flow Character	Hausner's Ratio
Excellent	1.00–1.11
Good	1.12–1.18
Fair	1.19–1.25
Passable	1.26–1.34
Poor	1.35–1.45
Very poor	>1.46–1.59

Between 1.25 and 1.5, adding glidant will improve flow. The index of carr is a one point determination and does not reflect the ease or speed with which consolidation occur. Indeed some materials have high index suggesting poor flow but may consolidate rapidly, which is

essential for uniform filling on tablet machines when the power flows at nearly equal to bulk density in to the die and consolidates to approaching tapped density prior to compression.

EVALUATION OF TABLETS [14, 13, 12, 11, 5]

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.

Drug Content

Five tablets were weighed individually, and the drug was extracted in 0.1 N HCl, and the solution was filter through 0.45µ membrane. The absorbance was measured at 315 nm after suitable dilution using a Shimadzu UV-1601 UV/Vis double beam spectrophotometer[5]

Hardness

The hardness of five tablets was determined using the fizer hardness tester and the average values were calculated.[12,13]

Thickness

The thickness of the tables was determined by using vernier calipers. Five tablets were used, and average values were calculated.[11,12]

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.[13, 11]

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.[15,13,12]

Floating Time

Floating time was the time, during which the tablet floats in 0.1 N HCL dissolution medium (including floating lag time).[15, 13, 12]

Swelling Characteristics[16, 14]

The swelling properties of matrix tablet containing drug were determined by placing the tablet matrices in the USP Dissolution Testing Apparatus II, in 900 ml of 0.1 N HCl at 37 ± 0.5 °C, rotated at 50 rpm. The tablets were removed periodically from dissolution medium, blotted to remove excess water and weighed. Swelling characteristics were expressed in terms of percentage water uptake (WU %) according to the equation.

$$WU \% = \frac{\text{Wt. of swollen tablet} - \text{Initial wt. of the tablet}}{\text{Initial wt. of the table}} \times 100$$

In vitro Drug Release Study[17,18,19]

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.

Details of Dissolution Test:

1. Apparatus : USP Type II
2. Volume of medium : 900 ml
3. Temperature : 37 °C
4. Paddle Speed : 50 rpm
5. Dissolution medium used : 0.1 N HCl
6. Aliquot taken at each time interval: 10 ml

Application of Kinetic Models[20,9,7]

The dissolution data of all controlled-release microparticles and control formulation was fitted to kinetics models i.e., Zero order, First order, Higuchi, and Korsmeyer–Peppas to find out drug release pattern and mechanism.

To analyze the mechanism of the drug release rate kinetics of the dosage form, the data obtained were graphed as:

1) Cumulative percentage drug released Vs Time (*In-Vitro* drug release plots)

2) Cumulative percentage drug released Vs Square root of time (Higuchi's plots)

3) Log cumulative percentage drug remaining Vs Time (First order plots)

4) Log percentage drug released Vs Log time (Peppas plots)

A. Zero order release rate kinetics:

The equation for zero order treatment is represented as;

$$Q_t = K_0 t$$

Where Q_t = amount of drug released in time (t)

K_0 = zero order release constant

When the data is plotted as cumulative percent drug release versus time, if the plot is linear then the data obeys zero-order release kinetics, with a slope equal to K_0.

B. First Order Kinetics

The equation for first order treatment is represented as

$$Log\ Q = Log\ Qo - \frac{K_1 t}{2.303}$$

Where Q = amount of drug remaining unreleased at time t

Q_0 = initial amount of drug in solution

K_1 = first order rate constant

When the data is plotted as cumulative percent drug remaining versus time yields a straight line, it indicates that the release follows First-order kinetics. The constant 'K_1' can be obtained by multiplying 2.303 with slope values.

C. Higuchi Release Model

The simplified Higuchi equation is represented as

$$Q_t = K_H t_{1/2}$$

Where; Q_t = amount of drug released in time t

K_H = Higuchi's constant

A linear relationship between amount of drug released (Q) versus square root of time ($t_{1/2}$) is observed if the drug release from the matrix is diffusion controlled.

D. Hixson-Crowell Model

The simplified equations is represented as

$$Q_0^{1/3} - Q_t^{1/3} = K_{HC}.t$$

Where Q_t = amount of drug released in time (t)

Q_0 = initial amount of drug in solution

K_{HC} = cube–root constant

A graphic representation of cubic root of unreleased fraction of drug versus time will be linear if geometric shape of the formulation diminishes proportionally over time.

E. Korsmeyer and Peppas release model

The Korsmeyer-Peppas model relates drug release exponentially to time. It is described by the following equation;

$$\frac{M_t}{M_\infty} = Kt^n$$

Where, M_t / M_∞ = fractional release of drug

K = constant depending on structural and geometric characteristics of the drug dosage form

n = release exponent

The value of n indicates the drug release mechanism. For a slab the value **n=0.5** indicates **Fickian** diffusion and values of n between **0.5** and **1.0** or **n=1.0** indicate **non-Fickian** mechanism. In case of a cylinder **n=0.45** instead of **0.5**, and **0.89** instead of **1.0**.

This model is used to analyze the release of drug from polymeric dosage forms, when the release mechanism is not understood or when there is a possibility of more than one type of release mechanisms are involved.

Table 4: Interpretation of diffusional release mechanism from polymeric membrane

Release exponent (n)	Drug transport mechanism
0.5	Fickian diffusion
0.5 < n < 1.0	Anomalous transport
1.0	Case-II
> 1.0	Super case-II transport

Stability Studies of the Standardized Formulation[7, 6]

Stability testing of drug products begins as a part of drug discovery and ends with the demise of the compound or commercial product. To assess the drug and formulation stability, stability studies were done according to ICH guidelines Q1C.

The stability studies were carried out on the most satisfactory formulations as per ICH guidelines Q1C. The most satisfactory formulation sealed in aluminum packaging and kept in humidity chamber maintained at $35 \pm 2°C$ / 60 ± 5 %RH and 40 ± 2 °C / 75 ± 5 %RH for 2 months. At the end of studies, samples were analyzed for the drug content, in vitro dissolution, floating behavior and other physicochemical parameters.

RESULTS AND DISCUSSION

UV Absorbance Maxima of Ranitidine HCl

A solution of ranitidine hydrochloride was prepared in 0.1 N HCl and UV Spectrum was taken using Shimadzu UV-1601 UV/Vis double beam spectrophotometer. The UV maxima of ranitidine hydrochloride were found to be 323 nm in 0.1 N HCl.

At the outset, method for the estimation for the drug was developed. Ranitidine HCl showed maximum absorption at wavelength 324 nm in 0.1N HCl. Standard calibration curve obeyed Beer's law at given concentration range of 5 µg/ml to 25 µg /ml and when subjected to regression analysis, the value of regression co-efficient was found to be 0.999, which showed linear relationship between concentration and absorbance.

Standard Calibration Curve of Ranitidine HCl

y = 0.034x + 0.005
R^2 = 0.999
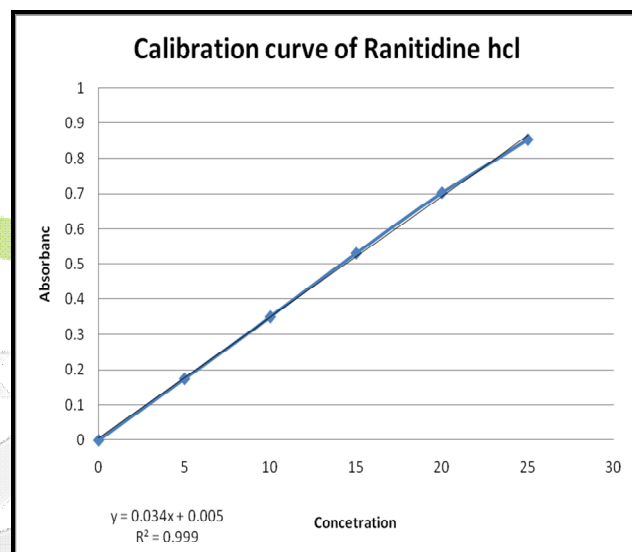
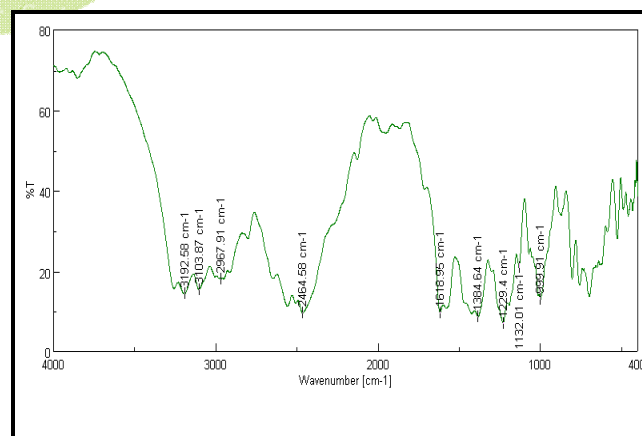**Identification of Drug by FTIR**

Figure 1: FTIR spectra of Ranitidine HCl

Identification study was performed using FTIR spectrophotometer. The IR spectrum of pure drug of drug was studied by making a KBr disc. The characteristic absorption peaks of Ranitidine HCl were obtained at different wave

numbers. The peaks obtained in the spectra of pure drug correlates with the peaks of official spectrum of British Pharmacopeia which confirms the purity of drug.

Identification of Drug by DSC Spectra

The DSC thermogram of Ranitidine HCl analyses was conducted to explore the melting activities of drug. DSC analysis showed a sharp endothermic peak at 147.8^{o}C which is an indication of melting point of Ranitidine HCl.

Micromeritic Properties of Powder Blend

The micromeritic properties of the powder blend of the best batch formulation were checked, wherein the angle of repose was found to be around 29.11^{0}, which shows good flowing property of the blend. The LBD and TBD were found to be 0.119 g/ml and 0.142 g/ml respectively. The compressibility index and total porosity was observed to be 16.20 % and 16.25 % which is good. The drug content was in the range of 98.92–99.92%, which passes official requirement.

Table 5: Micromeritics properties

Powder blend	Angle of Repose (^{0})	Loose Bulk Density (g/ml)	Tapped Bulk Density (g/ml)	Compressibility Index (%)	Total Porosity (%)	Drug Content (%)
F3	22.25	0.135	0.154	17.48	16.72	97.8±0.80
F4	29.45	0.112	0.157	16.25	17.56	98.68±0.91
F5	28.97	0.110	0.147	16.27	16.25	99.45±0.95
F6	29.11	0.119	0.142	16.20	16.18	99.92±0.93

Performed melting pointing capillary method got corresponded to the melting point of the pure drug (146-149$^{°}$C). So, it was found to be very close to authentic range of official standards. The identity of a compound was also confirmed by verification of the presence of functional groups in Ranitidine HCl by IR spectra.
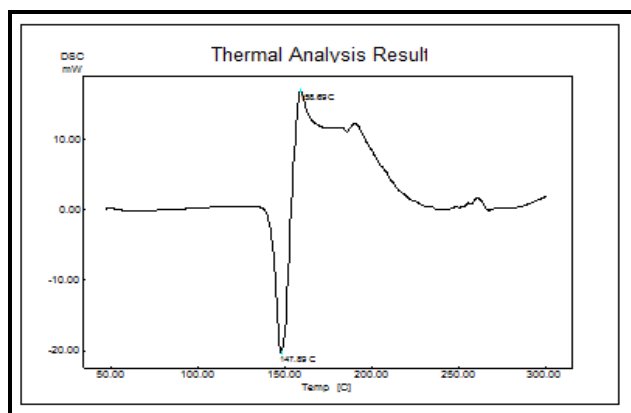

Figure 2: DSC spectra of Drug

The drug content in all the batches of ranitidine hydrochloride floating tablets was in the range of 98 to 100 % (i.e., a variation of ± 2%). This ensured the uniformity of the drug content in the tablets.

Evaluation of Physico-Chemical Parameters of Developed Tablet

Weight variation

Weight variation data of the prepared tablets indicated no significant difference in the weight of individual tablet from the average value.

Hardness

Hardness of the prepared tablets was observed within the range of 4.9 ± 0.16 kg/cm^{2}.

Thickness

Thickness of all the tablets was found in the range of 2.7 ± 0.2 mm.

Table 6: Physico-chemical parameters

Formulation Code	Hardness (kg/cm^2)	Friability (%)	Weight variation (%)	Thikness of tablet (mm)	Floating lag time (sec)	Floating Time (hr)
F 18	4.16 ± 0.16	0.29	349±1.5	2.76 ± 0.015	23	> 12
F 19	4.33 ± 0.16	0.14	353±3.5	2.65 ± 0.015	21	> 12
F 20	4.5 ± 0.28	0.26	346±2.7	2.54 ± 0.015	17	> 12
F 21	4.9 ± 0.16	0.39	349±2.1	2.43 ± 0.005	13	> 12

Friability

Friability of the developed formulations varied from 0.12% to 0.58 % which was less than less than 1% as per official requirement of IP.

Floating lag time

The buoyancy lag time of tablets depend upon the type and amount of polymer used. For floating system, the ideal matrix forming polymer should be highly permeable to dissolution media in order to initiate rapid generation of CO_2 and should be permeable for CO_2 to promote floating. In the present study, based on the preliminary studies, an ideal quantity of sodium bicarbonate was fixed at 50 mg in all the developed formulations. All the developed formulations showed buoyancy lag time, which varied from 13 ± 1.0 seconds to 23± 6.50 seconds.

Formulations, F5 and F6 showed the lowest floating lag time, which varied from 6 to 13 seconds. It has been concluded that the selection of high molecular weight and less hydrophilic grades of polymers like PEO WSR 303 improved floating characteristics. As the PEO WSR 303 concentration increased in formulation as seen with formulations F1 to F6 the floating lag time decreased.

Sodium bicarbonate is used widely as gas generating agent in the formulation to make the tablets float. In the present study, sodium bicarbonate serves two purposes like, along with making the tablet float, it also acted as buffering agent as the solubility of Ranitidine HCl decreases with increase in the pH in the GIT.
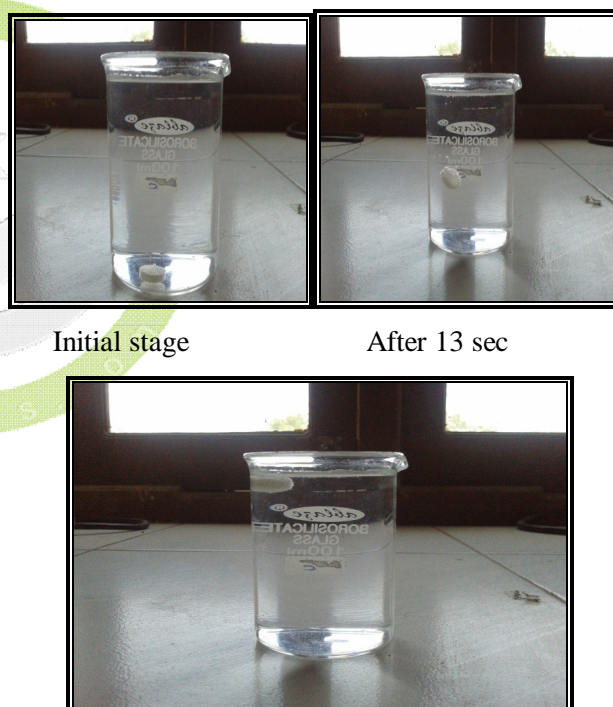

Initial stage   After 13 sec

Figure 3: Floating Lag Time Study

Floating Time

Floating time was found to depend on types of polymers & their concentration. In batch no F1 to F6 all observed total floating time more than 12 hr. F5 and F6 had the lowest floating time.

Swelling index

The swelling index of tablets was determined n 0.1 N HCl (pH 1.2) at room temperature. The swollen weight of the tablets was determined at predefined time intervals. The swelling index was calculated by the following equation:

$$\text{Swelling index} = \frac{W_t - W_o}{W_o}$$

W_0 = initial weight of tablet, and W_t = weight of the tablet at time t.

The percentage water uptake of the formulations F3 to F6 varied from 41.32 % to 130.64 %. The percentage water uptake was found to improve by increasing the concentration of PEO WSR 303 in formulations. Formulation F6 had maximum swelling index of 98.32 %. The highest degree of hydration was achieved by PEO WSR 303, i.e. F3 to F6, indicating that the ionic interaction between the cellulose ether increased the water uptake capacity to a greater extent.

Table 7: Swelling characteristic

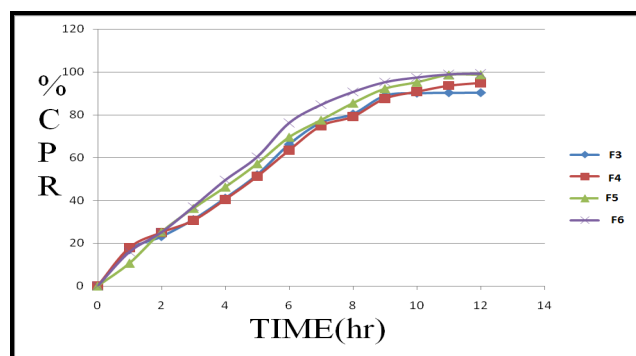| Batch (%)	1 hr	4 hr	8 hr	12 hr
F3	41.23	60.54	96.58	110.25
F4	64.36	80.26	96.47	98.23
F5	60.17	85.36	92.56	98.12
F6	62.24	84.75	91.23	98.32

In vitro Drug Release Study

Figure 4: Effect of PEO WSR 303 on the release profile of floating

The effect of PEO WSR 303 on drug release profile was checked out on formulations containing the drug release in the first hour for all the four batches F3 to F6 was approx. near to 11 % to 15% and that after 8 hours was more than to 90 % (> 90%). During the in vitro buoyancy test, a significant change was observed in the floating lag time of the formulation with increased amount of PEO WSR 303. The FLT for formulation batch F6 was just 13 seconds. Evaluating all these parameters, batch F6 was selected as the optimized batch since it had the minimum concentration of low density copolymer required to float the tablets (FLT: approximately 13 seconds).

Drug Release Kinetics of Batch F4 to F6 of Floating Matrix Tablet of Ranitidine HCl

The drug release data were fitted to models representing zero order (cumulative amount of drug released vs. time), first order (log percentage of drug unreleased vs. time), Higuchi's (cumulative percentage of drug released vs. square root of time), and Korsmeyer's equation (log cumulative percentage of drug released vs. time) kinetics to know the release mechanisms. The results are summarized in table 8. The formulations F5 and F6 were best fitted with Higuchi model, in which drug release is characterised by diffusion. F19 follow zero order release pattern.

Stability Study

Stability studies were carried out on the most satisfactory formulations F4 to F6 at 30 ± 2 °C/65±5%RH and 40±2 °C/75±5%RH for 1 month to assess their long term stability as per ICH guidelines Q1C. At various time intervals of 15 days and 30 days end, samples were evaluated. There was no major change in the various physico-chemical parameters evaluated like hardness, drug content and floating properties, in vitro dissolution pattern at the various sampling points. There was no significant difference was observed between stability study batch and F6 optimized batch.

Table 8: Drug release kinetics of batch F4 to F6

Batch Code	Regression			
	Zero Order Kinetic	Higuchi Kinetic	Korsmeyer Peppas	First Order Kinetic
F4	0.962	0.959	0.719	0.612
F5	0.953	0.991	0.779	0.632
F6	0.934	0.958	0.737	0.605

CONCLUSION

Ranitidine HCl is one of the drugs, which is used for the peptic ulcer. It is an absorption window limited drug, whose solubility decreases with increase in the pH in the GIT and has a short half life of 2-3hr. Therefore the present investigation is concerned with the development of the floating matrix tablets, which after oral administration were designed to prolong the gastric residence time and thus to increase the bioavailability of the drug and its half life. Various formulations were developed by using release rate controlling and gel forming polymers like HPMC, and Poly ethylene oxide WSR 303 in single by direct compression method with the incorporation of sodium bicarbonate as gas generating agent. Developed floating tablets possessed the required physico-chemical parameter such as like hardness, friability, weight variation, drug content, swelling index and floating properties. All the developed matrix tablets floated up to 12 h. Swelling studies indicated significant water uptake and contributed in drug release and gastroretention. The higher viscosity polymer had been seen to inhibit the initial burst release of Ranitidine HCl from the FDDS. From among all the developed formulations, since formulation F6 prolonged the drug release for longer period of time of beyond 12 h, they were selected as the best formulations. The most satisfactory formulations had showed no significant change in physicochemical properties, drug content, floatability or in vitro dissolution pattern after storage at 35 °C(65%RH) and at 40°C (75%RH) during stability studies for one months.

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