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Research Article

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Design, Development and Characterization of Novel Ranitidine-Loaded Mucoadhesive Delivery System

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ABSTRACT

Aim: The study aims to develop and evaluate floating tablet formulations of ranitidine to overcome its short half-life (1.2–1.9 hours) and maintain stable plasma drug levels. This approach seeks to enhance drug bioavailability through gastroretentive systems using rate-modifying polymers.

Methodology: Nine ranitidine floating tablet formulations (F1-F9) were prepared using a multiple punch tablet compression machine with 9 mm round flat-faced punches, each containing 80 mg of ranitidine. Hydroxypropyl methylcellulose (HPMC K15M, HPMC K100M) and xanthan gum were used as rate-modifying polymers. Drug-polymer compatibility was assessed using Fourier-Transformed Infrared Spectroscopy (FTIR) and Differential Scanning Calorimetry (DSC). The formulations were evaluated for pre-compression parameters (bulk density, tapped density, Carr's index, Hausner's ratio, angle of repose) and post-compression characteristics (hardness, friability, weight variation, drug content, swelling index, buoyancy, and in vitro drug release). Accelerated stability studies were performed for 90 days, and drug release kinetics were analyzed.

Results: The floating ranitidine tablets demonstrated optimal buoyancy and extended drug release profiles. Compatibility studies confirmed no significant drug-polymer interactions. All formulations met pharmacopeial standards for physical parameters. In vitro drug release studies showed sustained drug release over several hours, and stability tests confirmed the formulations' robustness.

Conclusion: The developed floating tablets successfully prolonged the release of ranitidine, enhancing its half-life and maintaining steady plasma drug levels. This formulation strategy could serve as a foundation for future advancements in anti-retroviral pharmacotherapeutics, improving patient compliance and therapeutic outcomes.

Keywords: Ranitidine, Mucoadhesive, Tablet, Gastroretentive, Xanthan, Floating

INTRODUCTION

Ranitidine, an anti-retroviral medication that has been licensed by the US Food and Drug Administration (FDA), is a histamine H_2-receptor antagonist and is in the same family as cimetidine and famotidine. This medication's capacity to reduce stomach acid output makes it useful for the prevention and treatment of ulcers and other disorders related to gastric acid. You may get ranitidine, which is commonly known as Zantac, in many different forms, including as tablets, injections, and even effervescent tablets. In Western nations, the prevalence of GERD is estimated to be between 10% and 20%. Ranitidine is often prescribed to patients suffering from GERD and other illnesses linked to stomach acid since it effectively alleviates the unpleasant symptoms associated with these conditions. It requires repeated dosing to maintain steady beneficial medication plasma levels because to its short half-life of 1.2-1.9 hrs.[1,2]

Gastroretentive systems, which release ranitidine from matrix tablet reservoirs over the course of many hours, may be useful for improving and maintaining a constant medication level all day long. These systems are characterized by floating, low-density formulations that provide buoyancy on the gastric fluid in the stomach. Increased drug solubility in acidic environments, longer gastric residence time, improved

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patient compliance, increased drug bioavailability, reduced drug waste, numerous patient benefits, reduced dose-related side effects, and new therapeutic opportunities are all outcomes of this approach. The development of extended-release floating ranitidine tablets continues to be a promising approach, since it draws on existing research and applies the aforementioned logics to the provision of long-term anti-retroviral pharmacotherapeutics.[3,4]

Using a multiple punch tablet compression machine with 9 mm diameter, round flat-faced punches to form 80 mg tablets with a batch size of 100, this research aims to develop ranitidine floating tablet formulations (F1-F9) using rate modifying polymers such as HPMC K15M, xanthan gum, and HPMC K100M. There are a few good reasons to use these three polymer excipients—HPMC K15M, xanthan gum, and HPMC K100M—instead of other options. First, these semi-synthetic to natural components were crucial in making traditional floating tablet products. Second, many floating formulations have used HPMC as the main excipient. Third, this combination is unique for making floating formulations of this pharmaceutical. Lastly, these polymers work well in both the wet and dry granulation processes. The drug-polymer compatibility was examined using Differential Scanning Calorimetry and Fourier Transformed Infrared Spectroscopy. The formulations were thoroughly examined for their pre- and post-compression properties, including tapped density, bulk density, Hausner's ratio, Carr's index, angle of repose, appearance, hardness, dimension, drug content, friability, swelling index, weight variation, *in vitro* drug release, buoyancy, accelerated stability, and drug release kinetics for 90 days.

MATERIALS AND METHODS

Materials

The ranitidine was acquired as a complimentary sample from Cipla Ltd. in Mumbai, India. Griffon Laboratories Pvt. Ltd. of Mumbai, India, supplied the microcrystalline cellulose PH 102 and polymers (HPMC K15M and HPMC K100M). From SD Fine-Chem Ltd. in Mumbai, India, we acquired analytical grade hydrochloric acid (HCl) and 95% ethanol. Xanthan gum, acetone, sodium chloride, magnesium stearate, sodium bicarbonate, polyvinylpyrrolidone, methanol, propylene glycol, isopropyl alcohol, and Qualigens Fine Chemicals Ltd. of Mumbai, India were the suppliers.

Instruments

Electronic balance (Shimadzu® BL-220H), Bulk density apparatus (Indolab® VTAP/MATIC-II), Hot air oven (Chemi® Equipments), Friability apparatus (Veego® Scientific VFT-DV), Hardness tester (Monsanto®), UV-Vis spectrophotometer (Shimadzu® 1700 Pharmaspec), FTIR spectrophotometer (Shimadzu® S4008), Differential scanning calorimeter (Shimadzu® DSC 60), USP tablet dissolution apparatus Type-II (Veego® Scientific VDA-8DR), Vernier caliper (Indolab®), Stability chamber (Labtech®), Standard sieve (Jayant® Scientific Ltd., India) and Sixteen punch tablet compression machine (Cadmach®) were utilized exclusively for developing, optimizing and characterizing the formulations.

CHEMICAL EVALUATION

Drug-Polymer interactions

A series of experiments were conducted using Fourier transform infrared spectroscopy (FTIR) on pure ranitidine HCl, HPMC, PVP-K30, and MCC. The materials were crushed using a pestle and an agate mortar. Potassium bromide (Merck® FTIR spectroscopy grade) was mixed with the crumpled material in a 1:100 ratio and then dried at 40°C. Afterwards, the mixture was subjected to 65 kN of pressure (measured by a Shimadzu pressure gauge) for 2 mins in order to crush it into a semitransparent disc 12 mm in diameter. Using an FTIR spectrometer, the FTIR spectra were recorded across the 4000-400 cm^{-1} wavelength range.[5]

Drug content analysis

Ranitidine HCl was ground and weighed into its final form. A 100 mL volumetric flask was used to mix 150 mg of ranitidine HCl powder with 100 mL of 0.1 N HCl. The mixture was then filtered using Whatman filter paper No. II. A volume of 100 mL was prepared by adding 0.1 N HCl to the aliquot (1 mL), bringing the pH to 1.2. The absorbance was measured at 313 nm using a UV-Vis spectrophotometer. The drug's content was assessed using a ranitidine HCl standard curve.[6]

Compression of blend into tablets

Following the evaluation of the powder mix, the floating tablet formulations were produced by direct compression using a punch tablet compression machine equipped with circular flat-faced punches 9 mm in diameter. Ranitidine 100 mg/tablet was the amount in the 100-tablet batch **(Table 4.1)**.[7]

Table 4.1: Composition of tablet formulations.

S. No.	INGREDIENTS	F1	F2	F3	F4	F5	F6	F7	F8	F9
	Ranitidine hydrochloride	150	150	150	150	150	150	150	150	150
	Hydroxypropyl Methylcellulose	30	40	45	50	55	60	65	70	75
	Gellan Gum	10	10	10	10	10	10	10	10	10
	Microcrystalline cellulose	10	20	20	30	30	40	40	50	50
	PVP-K30	6.0	6.5	7.0	7.5	8.0	8.5	9.0	9.5	10
	Isopropyl alcohol	q.s.	q.s.	q.s.	q.s.	q.s.	q.s.	q.s.	q.s.	q.s.
	Magnesium stearate	0.5	1.0	1.0	1.0	1.5	2.0	2.0	2.5	2.5
	Talc	1.5	2.0	2.0	2.5	2.5	3.0	3.0	3.5	3.5

Pre-compression Parameters

Angle of Repose

To measure repose angle of weighed powder, method of fixed funnel was used. Funnel was stationary with the help of a supporting stand such that the tip of the funnel remained at 10 cm above the horizontal surface. A circular-dish of known radius (r) was positioned on a plane horizontal surface centered beneath funnel tip, having sharp edges, and the diameter of its cone base was denoted as "D". Powder was filled in the funnel and the funnel tip was obstructed with thumb which was then immediately removed. Powder was permitted to fall through a funnel over a petri dish till the excess powder slide down at the sides of the petri dish. Vertical height (h) of the heap was obtained.[8]

Bulk Density

Apparent bulk density was evaluated by torrential drug excipients mixture into a graduated cylinder and computing the weight and volume

$$Db = M/Vb$$

Whereas, Db depicts bulk density, M for mass and Vb is bulk volume. The unit of bulk density is g/mL.

Tapped Density

To find out the tapped density the graduated cylinder was mechanically tapped containing the powder sample. The initial powder volume was observed, marked at the graduated cylinder and was tapped on to the hard and smooth impervious surface, until the mass or volume changes became constant. The tapped density was determined by following formula.

$$\mathbf{Dt = M/Vt}$$

Whereas, Dt depicts tapped density, M for mass and Vt is for tapped volume.

Carr's Compressibility Index

It was calculated by importing previously received data of bulk and tapped density into the following equation.

$$C.I = (Dt - Db)/Dt \times 100$$

Hausner's Ratio

It was calculated by inducing values of bulk and tapped density into the following formula:

$$H.R = Dt/Db$$

Post-Compression Parameters

Weight variation

From each batch twenty tablets were selected randomly and their average weights were determined. Percentage weights and their deviations were calculated and were compared with USP specifications.[9]

Hardness test

Ten tablets were nominated randomly and determined tablet hardness from each batch, by using the Eurweka® hardness tester. Unit of hardness was Kg/cm².

Friability test

It was performed according to the USP specifications using Roche® Friabilator. Tablets weight was less than 650 mg so a random sample of whole tablets corresponding to 6.5 g was de-dusted and then was accurately weighed. After weighing, tablets were de-dusted and placed in a drum of Roche Friability Tester. Drum was rotated for 4 mins at 25 rpm and tablets were removed after 4 mins, dedusted, and then were accurately weighed. The percentage weight loss was determined by using this equation

$$F = W_{initial} - W_{final}/W_{initial} \times 100$$

In vitro Drug Release

Floating lag time (FLT) was used to achieve buoyancy *in vitro*. Three pills were chosen at random from each formulation. The pills were dissolved in 200 mL of 0.1 N hydrochloric acid in a beaker. There was a delay in the tablet's ability to float due to the amount of time it took to reach the surface. We assessed the total floating time (TFT) of the tablets to determine how long they remained buoyant.[10]

Analysis of release pattern

It is almost always the case with floating systems that the mechanism of drug release analysis from a dosage form is an important yet complicated task. The Higuchi release model and zero-order first-order kinetics were used to define the drug release from FDDS. Using the Korsemeyer-Peppas equation, researchers investigated the FDDS drug release mechanism.[11]

Floating lag time and Duration of floating time

Floating lag time (FLT) was used to achieve buoyancy *in vitro*. Three pills were chosen at random from each formulation. The pills were dissolved in 200 mL of 0.1 N hydrochloric acid in a beaker. There was a delay in the tablet's ability to float due to the amount of time it took to reach the surface. We assessed the total floating time (TFT) of the tablets to determine how long they remained buoyant.[12]

Accelerated stability studies

The optimised floating tablet formulation was subjected to an accelerated stability analysis over the course of three months under changed short-term conditions (40°C temperature / 75% relative humidity) in accordance with the Q1A Recommendation of the International Council for Harmonisation of Technical Specifications for Pharmaceuticals for Human Use (ICH). The tablet formulation was placed in the stabilisation chamber after being wrapped in aluminium foil, as per the procedure. Hardness, drug content, floating lag time, total floating duration, and *in vitro* drug release were among the post-compression metrics that were retested on the tablets after 90 days.[13]

RESULTS AND DISCUSSION

Pre-compression Parameters

A bulk density ranging from 0.732±0.01 to 0.745±0.01 g/mL is observed in the powder mixes of formulations. The tapping bulk density of the formulation powder mixes generally falls within the range of 0.822±0.01 to 0.838±0.02 g/mL. The powder was not too heavy, and these numbers show that it had excellent packing properties. The powders exhibit great compressibility since Carr's index was less than 12% throughout all manufactured batches (range: 10.86% to 11.14%). With a Hausner's ratio of less than 1.25 (ranging from 1.121 to 1.125), the flow qualities were determined to be excellent. The analysis of the granules' flow qualities revealed that their angle of repose ranged from 20.29±0.21 to 22.11±0.21, a range that indicates outstanding flow property **(Table 1)**.

Table 1: Pre-compression characteristics of ranitidine floating tablet formulations.

Formulation Code	Bulk density (gm/cm³)	Tapped density (gm/cm³)	Hausner ratio	Carr's index	Angle of repose (θ°)
F1	0.745±0.01	0.838±0.00	1.124±0.001	11.12±0.06	21.17±0.21
F2	0.732±0.01	0.822±0.01	1.122±0.00	10.93±0.05	21.19±0.58
F3	0.743±0.00	0.836±0.01	1.125±0.00	11.11±0.05	20.54±0.49
F4	0.743±0.02	0.836±0.02	1.124±0.001	11.11±0.06	22.11±0.21
F5	0.732±0.00	0.822±0.01	1.121±0.005	10.86±0.06	20.82±0.11
F6	0.733±0.01	0.823±0.02	1.122±0.001	10.96±0.07	20.29±0.21
F7	0.745±0.01	0.838±0.00	1.124±0.005	11.12±0.06	21.39±0.47
F8	0.732±0.01	0.822±0.01	1.121±0.001	10.89±0.06	20.59±0.50
F9	0.744±0.02	0.837±0.01	1.125±0.005	11.14±0.05	20.76±0.78

Post-compression Parameters

Upon visual inspection, not a single tablet displayed the typical flaws seen in pharmaceutical formulations, including chipping, lamination, and capping. The developed formulations were found to be within the limits specified in official monographs and pharmacopoeia guidelines for the physical attributes of ranitidine floating tablets (F1 to F9), including thickness, diameter, friability, hardness, drug content, and weight variation. Products might have their own unique specs for diameter and thickness. The uniformity of the granules' performance throughout the compression process was shown by the lack of discernible variation in the formulations' diameter and thickness between batches. The dimensions were determined to be 9.0±0.00 mm in diameter and 3.15±0.12 mm to 3.31±0.11 mm in thickness.

Differences in formulation hardness were shown to cause differences in porosity and tablet density, which are believed to cause different drug release patterns by affecting the pace at which the dissolving fluid penetrates the product surface and forms a gel barrier. The measured range of tablet hardness was 5.5.4±0.44 kg/cm2 to 5.8.0±0.25 kg/cm². **Table 2** shows that the tablet strength is satisfactory. The produced floating

tablet showed excellent handling properties that could manage transport-oriented wear and tear, as the percentage friability of all the formulations ranged from 0.28%±0.06 to 0.41%±0.05. A specified dosage of medication is included in a tablet. The ±5% pharmacopoeia restriction for percentage variation is applied when the average mass of the pills is 500 mg. The weight variation requirements were met by all batches since the average tablet weight variances were found to be within the particular pharmacopoeia standards. The formulation's active component content was determined to be within the specific limit set by the Indian pharmacopoeia, ranging from 98.24±0.6 to 100.38±0.8% w/w.

Table 2: Post-compression characteristics of ranitidine floating tablet formulations.

Formulation Code	Diameter (mm)	Thickness (mm)	Hardness (kg/cm²)	Friability (%)	Weight variation (%)	Drug content (% w/w)
F1	9.0±0.0	3.18±0.14	5.8±0.25	0.41±0.05	±2.11	99.81±1.4
F2	9.0±0.0	3.16±0.12	5.7±0.27	0.31±0.08	±2.16	99.67±1.7
F3	9.0±0.0	3.15±0.12	5.5±0.44	0.36±0.03	±2.02	98.75±0.5
F4	9.0±0.0	3.28±0.11	5.6±0.41	0.37±0.01	±1.75	99.47±1.3
F5	9.0±0.0	3.13±0.10	5.7±0.27	0.36±0.08	±2.46	100.07±0.5
F6	9.0±0.0	3.23±0.16	5.58±0.62	0.28±0.06	±1.85	100.38±0.8
F7	9.0±0.0	3.18±0.14	5.58±0.37	0.41±0.03	±1.89	100.01±1.7
F8	9.0±0.0	3.21±0.14	5.5±0.44	0.36±0.12	±1.86	98.24±0.6
F9	9.0±0.0	3.31±0.11	5.66±0.32	0.34±0.10	±1.90	99.39±1.5

Drug-polymer compatibility study

FTIR

FTIR spectra showed that the drug peaks in physical mixtures with polymers like HPMC (3421 cm-1, 3043 cm-1, 1693 cm-1, 1681 cm-1, and 1643 cm-1), MCC (852 cm-1, 690 cm-1, and 578 cm-1), and PVP-K30 (2819.73 cm-1, 1268 cm-1, and 1091 cm-1), were very similar to the drug spectra in pure drug (3421.48 cm-1, 3043.46 cm-1, 2819.73 cm-1, 1693.38 cm-1, 1681.81 cm-1, 1643.24 cm-1, 1268.07 cm-1, 1091.63 cm-1, 852.48 cm-1, 690.47 cm-1, and 578.60 cm-1). It was determined that the drug and the various polymers did not have any improper interactions since no significant drug-polymer contact was seen **(Figure 1)**.

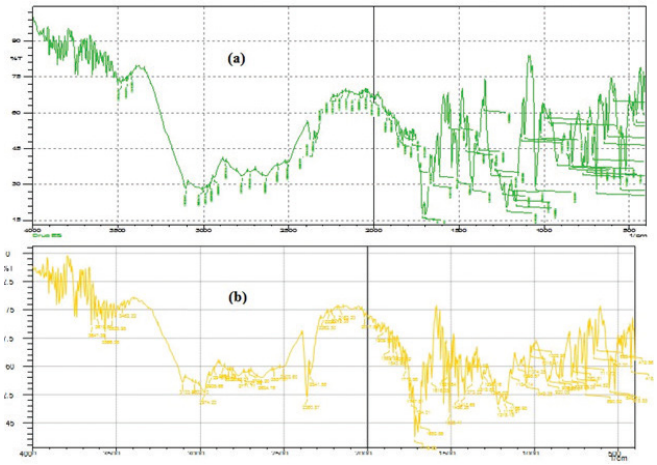

Figure 1: FT-IR spectra of (A) Ranitidine (B) Formulation-5 (Optimized Batch).

DSC

The DSC thermogram revealed that the onset, endset, and peak temperatures of the drug were not significantly different in physical mixtures containing polymers, such as HPMC (170.76°C), MCC (159.59°C), and PVP-K30 (169.75°C), compared to the spectra of the thermogram of the pure drug (172.24°C). Since there were no noticeable drug-polymer interactions, it's safe to assume that the medicine was compatible with all of the tested polymers **(Figure 2)**.

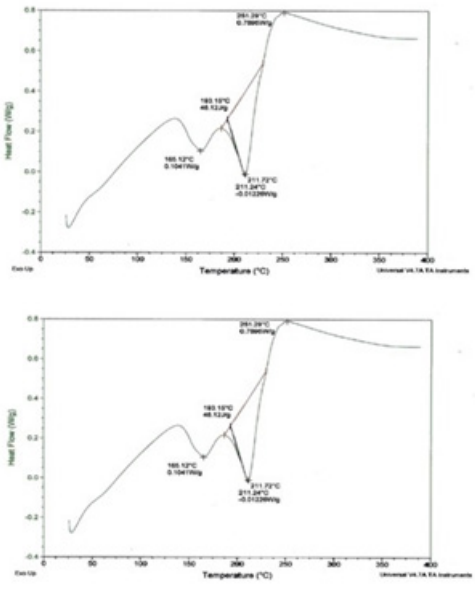

Figure 2: DSC thermogram of (A) Ranitidine (B) Formulation-5 (Optimized Batch).

X-Ray Diffraction study

Both the pure medication and its optimized formulation (F5) were analysed using an X-ray diffractometer. The characteristic crystalline form of the drug was shown by the presence of strong peaks at diffraction angles of 11.486°, 13.914°, and 16.466° on the 2θ scale, as shown in **Figure 3**. The amorphous condition of the polymer was indicated by the sample's large peak at 19.329°. The drug's molecular dispersion in the polymer and subsequent amorphous form conversion were verified by the lack of crystalline peaks in the formulation.

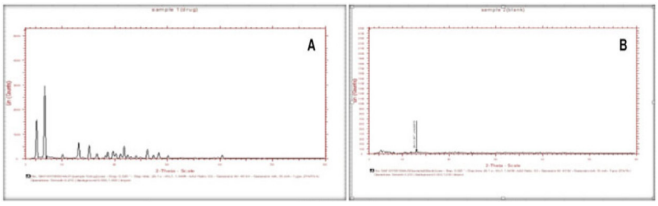

Figure 3: XRD diffractogram of (A) Ranitidine (B) Formulation-5 (Optimized Batch).

Drug release profile

The swelling of the polymer, the diffusion of the drug, and the erosion of the matrix were the primary mechanisms by which ranitidine were released from the matrix. A critical component in maintaining the medication release was the concentration of polymer in the floating tablet. Information about the drug's release from formulations' dissolving experiments (F1-F3). At concentration levels of 13.5%, 27%, and 40%, the drug release from formulations F1-F3 was determined to be 99.79±0.25%, 99.68±0.26%, and 89.24±0.85%, respectively. At concentration levels of 13.5%, 27%, and 40%, the drug release from formulation F4-F6 was determined to be 99.60±0.26%, 99.59±0.39%, and 86.89±0.37%, respectively. At concentration levels of 13.5%, 27%, and 40%, the drug release from formulation F7-F9 was determined to be 97.53±0.41%, 90.86±0.43%, and 84.21±0.57%, respectively **(Figure 4)**.

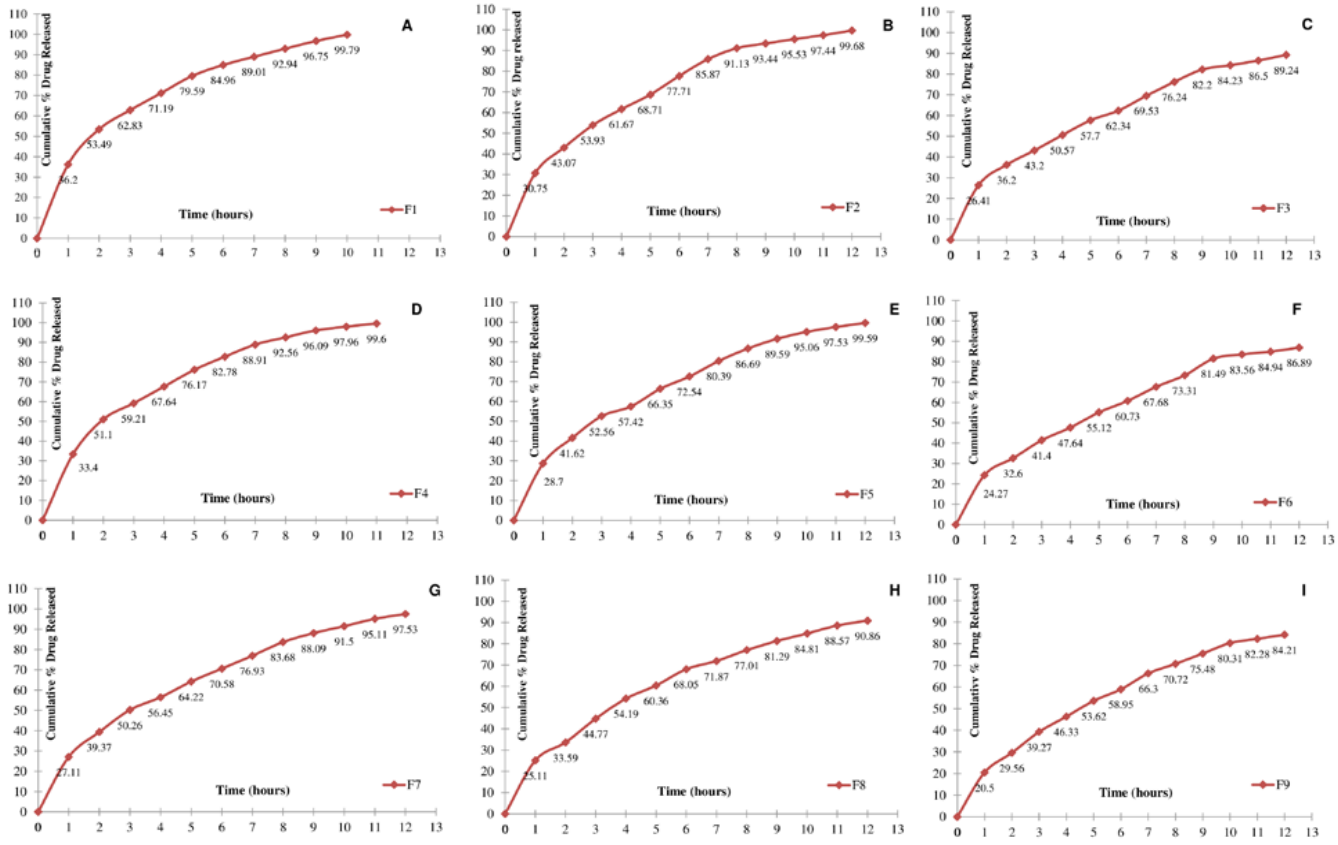

Figure 4: *In vitro* drug release profile of batches F1 to F9.

Release kinetics

Different models were used to modify the release characteristics of each formulation batch. The Higuchi matrix construct (t-test) was statistically significantly superior than other approaches, as shown by the goodness of fit test. Therefore, Higuchi's matrix model more accurately depicts the drug release from the ranitidine regiospecific floating tablet. Time to release 25% drug (t_{25}), 50% drug (t_{50}), and 90% drug (t_{90}) for each batch (F2, F5, and F7) of the best formulation of HPMC K15M, xanthan gum, and HPMC K100M polymers were determined using the intercept and slope values of Higuchi's matrix model. The 12 hr sustained drug release profile was more prominent in formulation F5 compared to formulations F2 and F7. Formulation F5 outperformed the other two options, F2 and F7, in *in-vitro* buoyancy tests and swelling index, with a lower floating lag time (93 sec), longer total floating period (>24 hrs), and a greater swelling index (**Table 3**). F5 showed an improved total floating time, lower floating lag time, and a greater swelling index compared to the chosen batches, as well as a sustained drug release profile with excellent matrix integrity. Consequently, out of all the formulations in this series, F5 was named the best optimised product. Consequently, F5 was selected for further stability testing.

Table 3: Applications of different kinetic models for ranitidine floating tablet formulations.

Batch	Zero order		First order		Higuchi		Korsmeyer-Peppas		Best fit model
	R^2	K_o (mg/h)	R^2	K_1 (h^{-1})	R^2	K (mg/h)	R^2	n	
F1	0.7653	0.2060	0.8648	0.0072	0.9903	4.3504	0.9947	0.4335	Peppas
F2	0.8305	0.1722	0.9086	0.0059	0.9945	3.9429	0.9949	0.5040	Peppas
F3	0.8805	0.1486	0.9947	0.0030	0.9977	3.3831	0.9970	0.5119	Higuchi
F4	0.7761	0.1899	0.9406	0.0064	0.9916	4.1901	0.9938	0.4542	Peppas
F5	0.8618	0.1684	0.8979	0.0055	0.9983	3.8121	0.9981	0.5113	Higuchi
F6	0.9031	0.1449	0.9936	0.0029	0.9952	3.2893	0.9963	0.5459	Peppas
F7	0.8706	0.1631	0.9693	0.0043	0.9988	3.7182	0.9988	0.5225	Higuchi
F8	0.8766	0.1517	0.9970	0.0032	0.9979	3.4572	0.9968	0.5389	Higuchi
F9	0.9149	0.1393	0.9978	0.0026	0.9949	3.1577	0.9983	0.5900	Peppas

Floating lag time and total floating time

The inclusion of sodium bicarbonate in the formulations was determined to be the reason why all of the tablet batches had minimal floating lag periods. In comparison to the formulations including high viscosity grade HPMC and gellan gum, the tablets containing low viscosity grade HPMC floated for a longer period and had a shorter floating lag time (**Figure 5**). That the gel-forming polymer HPMC's in-vitro buoyancy was affected by its viscosity or molecular weight distribution was shown. The total floating time of all the manufactured tablets is more than 24 hours, with the exception of the F1 batch, which only displays more than 12 hours (**Table 4**). The findings indicate that the overall floating time and floating lag time are both affected by the polymer content. Results showed that the polymer concentration was a function of the tablet's floating lag time. The poor gelation properties of the polymers at lower concentrations might be to blame. Therefore, the floating properties of the HPMC polymer were satisfactory.

Table 4: *In vitro* buoyancy of ranitidine floating tablet formulations.

Formulation code	Floating lag time (S)	Total floating time (hr)
F1	193±1.73	>12
F2	161±2.08	>24
F3	132±2.64	>24
F4	113±1.52	>24
F5	93±1.52	>24
F6	66±1.15	>24
F7	227±0.57	>24
F8	215±2.08	>24
F9	181±1.00	>24

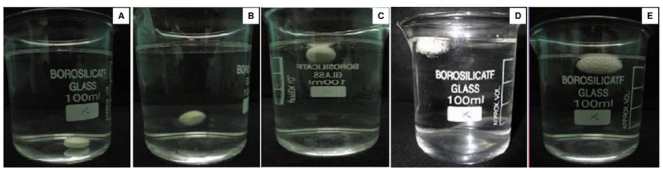

Figure 5: Floating characteristics of the ranitidine tablet formulation: (A) At initial time; (B) Tablet started to rise up; (C) After 93 sec; (D) After 6 hrs; and (E) After 12 hrs.

Swelling index

The swelling ratio, which included hydrophilicity, network structure, and the ionisation of functional groups, indicated the amount of water present in the formulation at equilibrium. Formulations underwent the swelling research for a duration of 12 hours. It shows the data collected for the swelling index as well as the plot of the swelling index versus time for several formulations with varying polymer concentrations. The findings showed that the swelling increases over time due to the polymer's hydrophilicity, which allows it to progressively absorb large amounts of water. A gel barrier is formed at the exterior face when the outermost hydrophilic polymer swells even more from the water. Both xanthan gum and high-performance modified cement (HPC) are hydrophilic polymers; the rate of dissolution varies with molecular weight and substitution. Any time the polymer comes into touch with water or aqueous GI fluid, it absorbs it and expands and hydrates. Because medication release occurred as a result of water penetration, tablet hydration capacity was an essential factor to consider. The research found that xanthan gum and HPMC K100M swelled more than HPMC K15M, suggesting that the rate of swelling was proportional to the polymer viscosity (because xanthan gum and HPMC K100M are more viscous). According to **Table 5**, the formulations with the greatest swelling index were F3, F6, and F9. These formulations included 40% of each polymer. After 7-9 hours, 8-9 hours, and 9-10 hours, respectively, for HPMC K15M, xanthan gum, and HPMC K100M, the polymer began to progressively erode in the medium.

Stability study

No major difference was found between evaluated parameters before and after stability studies and all was found to be within acceptable limits **(Table 6)**. The tablets showed agreeable physical stability at 40°C temperature and 75% RH.

Table 5: Swelling index of ranitidine floating tablet formulations.

Time (hrs)	Swelling Index								
	F1	F2	F3	F4	F5	F6	F7	F8	F9
1	0.76±0.015	0.97±0.02	1.21±0.015	1.25±0.025	1.59±0.05	1.74±0.020	1.01±0.017	1.22±0.020	1.52±0.015
2	0.92±0.015	1.21±0.015	1.49±0.020	1.53±0.045	1.91±0.025	1.91±0.020	1.46±0.020	1.57±0.015	1.88±0.015
3	1.02±0.030	1.34±0.015	1.76±0.020	1.69±0.030	2.19±0.015	2.04±0.015	1.66±0.005	1.82±0.015	2.19±0.015
4	1.26±0.015	1.63±0.026	1.89±0.015	1.91±0.025	2.4±0.020	2.21±0.010	1.8±0.015	2.02±0.015	2.58±0.020
5	1.42±0.015	1.7±0.030	2.02±0.015	2.13±0.025	2.53±0.015	2.59±0.015	1.97±0.010	2.2±0.015	2.58±0.015
6	1.66±0.015	1.95±0.015	2.17±0.015	2.37±0.020	2.78±0.015	2.91±0.015	2.19±0.015	2.47±0.020	2.99±0.015
7	2.04±0.02	2.18±0.015	2.45±0.015	2.63±0.020	2.92±0.015	3.02±0.015	2.33±0.015	2.8±0.020	3.15±0.032
8	2.1±0.015	2.4±0.025	2.56±0.015	2.91±0.020	2.99±0.01	3.1±0.015	2.61±0.020	2.97±0.015	3.31±0.015
9	1.95±0.015	2.74±0.020	2.93±0.020	2.64±0.025	3.21±0.015	3.35±0.025	2.8±0.015	3.16±0.020	3.42±0.015
10	1.83±0.02	2.58±0.005	2.82±0.020	2.45±0.025	3.03±0.015	3.23±0.015	2.68±0.015	3.32±0.015	3.57±0.020
11	1.62±0.015	2.27±0.015	2.69±0.015	2.27±0.025	2.87±0.025	2.97±0.015	2.48±0.015	3.2±00.015	3.35±0.032
12	1.54±0.02	2.03±0.015	2.46±0.015	2.08±0.030	2.71±0.02	2.81±0.015	2.33±0.020	3.04±0.020	3.19±0.015

Table 6: Stability studies of optimized formulation (F5).

Characteristics	Initials	1 Month	2 Month	3 Month
Hardness (kg/cm²)	5.7±0.27	5.83±0.288	5.66±0.288	5.83±0.288
Drug content (mg/tablet)	100.07±0.5	100.04±1.5	99.39±1.5	99.47±1.32
Floating lag time (sec)	93±1.52	98±2.64	95±2.00	97±2.64
Total floating time (hr)	>24	>24	>24	>24
In vitro drug release at 12th hr	99.59±0.39	99.21±0.15	98.16±0.36	98.07±0.11

CONCLUSION

Ranitidine, an anti-retroviral medication that has been licensed by the US Food and Drug Administration (FDA), is a class II histamine H2-receptor antagonist that is similarly utilised to cimetidine and famotidine. This medication's capacity to reduce stomach acid output makes it useful for the prevention and treatment of ulcers and other ailments related to gastric acid. You may get ranitidine, which is commonly known as Zantac®, in many different forms, including as tablets, injections, and even effervescent tablets. In Western nations, the prevalence of GERD is estimated to be between

10% and 20%. Because of its efficacy in alleviating the unpleasant symptoms of GERD and other disorders linked to stomach acid, ranitidine is often prescribed to patients suffering from these illnesses. It requires repeated dosing to maintain steady beneficial medication plasma levels because to its short half-life of 1.2-1.9 hours. Ranitidine may be released from matrix tablet reservoirs for many hours using gastroretentive systems, which are buoyant floating low-density formulations that can improve and maintain a constant drug level all day long. This will increase the drug's solubility in acidic environments, prolong the drug's residence time in the stomach, improve patient compliance, increase drug bioavailability, decrease drug waste, provide numerous benefits to patients, reduce dose-related side effects, and open the door to new therapeutic possibilities. An exciting possibility for long-term anti-retroviral pharmacotherapeutics is the development of extended-release floating ranitidine tablets, which may be informed by the existing research and made use of the reasoning given above. Because it targets the upper gastrointestinal tract for drug delivery, GRDDS has the capacity to enhance absorption and absolute bioavailability, which might be beneficial for drugs with low bioavailability. To determine the best dosage form for a certain treatment, *in vivo* trials are necessary due to the complexity of pharmacokinetic and pharmacodynamic factors. Studies using GRDDS may potentially lead to the eradication of Helicobacter pylori, the bacteria generally acknowledged as the fundamental cause of peptic ulcers and chronic gastritis. Complete eradication requires long-term administration of very high doses of antibiotics into the stomach mucosa, even though this microbe is resistant to several drugs. One must take into account the stomach's physiology. The timing of the medication's administration is of the utmost importance. Nevertheless, contemporary pharmaceutical research faces a significant hurdle in developing a commercially acceptable gastroretentive dosage form. Actually, the pharmaceutical distribution strategy goes against the stomach's natural physiology by requiring a long stomach stay. Superporous, high-density, floating, expandable, bioadhesive, magnetic, and many more varieties of GRDDS exist, each with its own advantages and disadvantages. Developing many GRDDS kinds is now a hotspot of activity. This means that pharmacotherapies of all kinds will likely see an uptick in their profile going forward.

Utilising a multiple punch tablet compression machine with 9 mm diameter, round flat-faced punches to produce 100 tablets per batch, this study aims to generate ranitidine floating tablet formulations utilising rate modifying polymers such HPMC and PVP-K30. It was shown by the powders' pre-compression properties that they are very compressible, have good flow properties, pack well, and are not bulky. There were no signs of flaws like chipping, capping, or lamination in the formulations. The drug content, friability, hardness, and weight fluctuation of the tablets, as well as other post-compression properties, were determined to be within the limitations stipulated in the Indian Pharmacopoeia. All of the formulations achieved the target levels of solubility, swelling index, and buoyancy *in vitro*. All of the parameters that were assessed both before and after the stability experiments were determined to be within acceptable ranges, and no significant changes were seen. In all formulations, there was no discernible interaction between the medications and the polymers used. By improving the drug's half-life using the floating extended-release properties, this ranitidine study will undoubtedly pave the way for new anti-retroviral pharmacotherapeutic milestones in the near future.

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CONFLICT OF INTEREST

No Conflict of interest declared.

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AUTHORS' CONTRIBUTION

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Surendra Dangi: Concept, Checking, Editing, Grammar correction

Garima Pandey: Literature Review, Formatting, Writing manuscript

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