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Formulation and Evaluation of Gastro-Retentive Effervescent Floating Tablets of Ranitidine Hydrochloride Using HPMC K100M as a Rate-Controlling Polymer

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Abstract:

Background: Ranitidine hydrochloride (HCl), a Histamine H_2-receptor antagonist, exhibits pharmacokinetic limitations including a short biological half-life (2–3 h), narrow absorption window confined to the upper gastrointestinal tract, and low oral bioavailability (~50%), necessitating twice- daily conventional dosing. A gastro-retentive floating drug delivery system (GFDDS) offers a rational approach to prolong gastric residence, sustain drug release, and improve bioavailability.

Objective: To develop and evaluate effervescent floating matrix tablets of Ranitidine HCl using HPMC K100M as a hydrophilic rate-controlling polymer and sodium bicarbonate as a gas-generating agent, with the goal of achieving once-daily therapeutic delivery.

Methods: Six formulation batches (F1–F6) were prepared by direct compression with systematically varied HPMC K100M (30–50% w/w) and $NaHCO_3$ (10–17.5% w/w) concentrations at a fixed Ranitidine HCl dose of 150 mg. Tablets were evaluated for preformulation characterisation (FTIR, DSC, UV spectrophotometry), pre-compression flow properties, post-compression pharmacopoeial parameters, in vitro buoyancy, in vitro drug release (USP Type II, 0.1N HCl, 24 h), drug release kinetic modelling, and accelerated stability (40°C/75% RH, 3 months, ICH Q1A(R2)).

Results: FTIR and DSC confirmed absence of drug–excipient interactions. Batch F3 (HPMC K100M 40%, $NaHCO_3$ 15%) was identified as the optimised formulation with floating lag time (FLT) of 1.9 ± 0.2 min, total floating time (TFT) of 19.4 ± 0.7 h, drug release of 19.8% at 1 h and 96.8% at 24 h, and anomalous (non-Fickian) drug transport (Korsmeyer–Peppas n = 0.543, R^2 = 0.9968). Stability testing confirmed drug content ≥ 97.9% with unchanged release profiles (f_2 > 50) over 3 months.

Conclusion: A once-daily effervescent floating tablet of Ranitidine HCl was successfully developed using directly compressible excipients. Batch F3 fulfilled all buoyancy, release, and

stability criteria, demonstrating the feasibility of GFDDS for bioavailability enhancement of narrow-absorption-window drugs.

Keywords: Gastro-retentive drug delivery; floating tablets; Ranitidine hydrochloride; HPMC K100M; sodium bicarbonate; effervescent; controlled release; floating lag time.

Introduction

Oral drug delivery remains the most widely accepted and patient-compliant route for systemic therapeutic administration owing to its convenience, non-invasiveness, and cost-effectiveness. However, the pharmacokinetic performance of many orally administered active pharmaceutical ingredients (APIs) is significantly limited by the complex physiology of the gastrointestinal (GI) tract, particularly the variable and often rapid gastric emptying that constrains the time available for drug dissolution and absorption. For certain drug molecules, this pharmacokinetic challenge is compounded by a phenomenon termed the "narrow absorption window" (NAW), wherein the compound demonstrates optimal or exclusive absorption from a restricted anatomical region principally the stomach and proximal small intestine.

Ranitidine hydrochloride, a potent competitive and reversible Histamine H_2-receptor antagonist, exemplifies such a drug candidate. Extensively prescribed for the management of peptic ulcer disease, gastroesophageal reflux disease (GERD), Zollinger–Ellison syndrome, and related acid-hypersecretory conditions, its clinical efficacy is constrained by a short biological half-life of 2–3 hours and an oral bioavailability of approximately 50%, arising directly from its narrow upper GI absorption window.

Conventional immediate-release tablets, typically prescribed at 150 mg twice daily, produce characteristic peak-and-trough plasma concentration profiles that result in periods of subtherapeutic drug exposure between doses. Gastro-retentive drug delivery systems (GRDDS) have emerged as a rational and pharmacokinetically justified approach to address these limitations. By intentionally prolonging the residence time of the dosage form within the stomach, GRDDS ensures that drug release occurs continuously at or proximal to the optimal absorption window, maximising absorption efficiency and producing a more sustained and predictable plasma concentration profile. Among the various gastro-retentive strategies including mucoadhesive, high-density, expandable, and floating systems effervescent floating drug delivery systems (EFDDS) have attracted considerable research attention owing to their mechanistic simplicity, predictable performance, and favourable safety profile.

The effervescent floating mechanism relies on the generation and entrapment of carbon dioxide (CO_2) gas within a polymer matrix. When the tablet contacts gastric acid (0.1N HCl), sodium bicarbonate undergoes rapid acid–base neutralisation, and the evolved CO_2 is entrapped within the viscous gel matrix formed by concurrent HPMC hydration, reducing tablet bulk density below that of gastric fluid (~1.004 g/cm³). Hydroxypropyl Methylcellulose K100M (HPMC K100M), owing to its high viscosity (75,000–140,000 mPa·s at 2% w/v), is the benchmark hydrophilic matrix polymer for such systems simultaneously acting as a structural scaffold for CO_2 entrapment and as a diffusion barrier governing controlled drug release.

The present investigation was therefore designed to systematically evaluate the influence of HPMC K100M and $NaHCO_3$

concentrations on the physicochemical performance, buoyancy, and release characteristics of Ranitidine HCl floating tablets, with the aim of identifying an optimised formulation suitable for once-daily gastro- retentive delivery.

Materials and Methods

Materials

Ranitidine Hydrochloride was supplied by Sun Pharmaceutical Industries Ltd., India. HPMC K100M and PVP K30 were procured from Loba Chemie Pvt. Ltd., Mumbai. Sodium Bicarbonate, Microcrystalline Cellulose PH101 (Avicel PH101), Magnesium Stearate, and Talc were obtained from S D Fine-Chem Ltd., Mumbai.

All materials were of pharmacopoeial grade and used as received. A complete summary of materials, grades, suppliers, and functional roles is presented in Table 1.

Table 1: Materials

Material	Supplier	Role in Formulation
Ranitidine HCl	Sun Pharma, India	Active Pharmaceutical Ingredient
HPMC K100M	Loba Chemie, Mumbai	Rate-controlling matrix polymer; CO_2 scaffold
Sodium Bicarbonate	S D Fine-Chem, Mumbai	Gas-generating agent; buoyancy driver
Avicel PH101 (MCC)	S D Fine-Chem, Mumbai	Diluent; directly compressible filler
PVP K30	Loba Chemie, Mumbai	Dry binder; tablet cohesion
Magnesium Stearate	S D Fine-Chem, Mumbai	Lubricant
Talc (purified)	S D Fine-Chem, Mumbai	Glidant

Preformulation Studies

UV Spectrophotometric Analysis

A stock solution of 1000 µg/mL Ranitidine HCl was prepared in 0.1N HCl. A 10 µg/mL working solution was scanned from 200–400 nm against a 0.1N HCl blank to determine the wavelength of maximum absorption (λmax). Standard solutions (2–20 µg/mL) were prepared and absorbances measured in triplicate at the confirmed λmax to construct a calibration curve. Method linearity was accepted when $R^2 \geq 0.999$.

FTIR Spectroscopic Analysis

Drug–excipient compatibility was assessed by FTIR spectroscopy. Physical binary mixtures of Ranitidine HCl with each excipient were prepared at 1:1 w/w ratios. Spectra of pure drug, individual excipients, and binary mixtures were recorded over 4000–400 cm^{-1} using 16 scans at 4 cm^{-1} resolution with KBr disc preparation. Compatibility was concluded when no significant peak shifts (< ±10 cm^{-1}), disappearances, or new interaction bands were observed.

Differential Scanning Calorimetry (DSC)

DSC analysis was performed on pure Ranitidine HCl, individual excipients, and 1:1 drug excipient physical mixtures. Approximately 5– 10 mg samples were sealed in aluminium pans and heated from 30–300°C at 10°C/min under nitrogen purge (50 mL/min). Thermal compatibility was inferred when the drug's characteristic endothermic peak remained essentially unchanged (shift < 5°C) and no new thermal transitions appeared.

Pre-compression Powder Flow Characterisation

Bulk density (BD), tapped density (TD), Carr's Compressibility Index (CI), Hausner Ratio (HR), and angle of repose (θ) were

determined for all six formulation blends. CI and HR were calculated from BD and TD measurements.

Angle of repose was determined by the fixed funnel method. Blends with CI ≤ 15% and HR ≤ 1.25 were considered acceptable for direct compression.

Formulation Design

Six tablet batches (F1–F6) were prepared using a one-variable-at-a-time (OVAT) approach, varying HPMC K100M (30–50% w/w) and $NaHCO_3$ (10–17.5% w/w) concentrations while keeping all other excipients constant. Each tablet contained a fixed dose of 150 mg Ranitidine HCl. The complete formulation matrix is presented in Table 2.

Table 2: Formulation Composition of Tablet Batches F1–F6

Ingredient	F1	F2	F3 (Optimized)	F4	F5	F6
Ranitidine HCl (mg)	150	150	150	150	150	150
HPMC K100M (mg, %)	120 (30%)	140 (35%)	160 (40%)	160 (40%)	180 (45%)	200 (50%)
$NaHCO_3$ (mg, %)	40 (10%)	50 (12.5%)	60 (15%)	70 (17.5%)	60 (15%)	60 (15%)
Avicel PH101 (mg)	64	40	18	—	—	—
PVP K30 (mg)	12	12	12	12	12	12
Magnesium Stearate (mg)	4	4	4	4	4	4
Talc (mg)	10	10	10	10	10	10
Total Weight (mg)	**400**	**406**	**414**	**406**	**416**	**436**

Manufacturing Procedure: Direct Compression

All six batches were manufactured by direct compression under humidity-controlled conditions (< 40% RH, < 25°C) to preclude premature activation of the effervescent reaction.

Drug and all functional excipients were sifted and blended by geometric dilution for 15 minutes, followed by addition of Talc and Magnesium Stearate (2–3 minutes). The lubricated blend was compressed on a single- punch tablet press (10 mm flat-faced round punches) to produce tablets with hardness of 5– 7 kg/cm².

Post-Compression Evaluation

All batches were evaluated for tablet weight and weight variation (IP, n = 20), thickness and diameter (n = 10), hardness (Monsanto/Pfizer hardness tester, n = 10), friability (Roche friabilator, 4 min, 25 rpm; acceptance criterion < 1.0%), and drug content uniformity (spectrophotometric assay at 314 nm, n = 10; acceptance criterion 95–105% of label claim).

In Vitro Buoyancy Studies

Floating lag time (FLT) and total floating time (TFT) were determined by placing one tablet in a 900 mL beaker containing 0.1N HCl (37 ± 0.5°C) with gentle agitation. FLT was recorded as the time from tablet immersion to complete ascent to the medium surface. Performance targets were FLT ≤ 2 min and TFT ≥ 12 h (n = 3).

In Vitro Dissolution Studies

Dissolution profiles were generated using USP Type II (paddle) apparatus (900 mL, 0.1N HCl, pH 1.2, 37 ± 0.5°C, 50 rpm). Aliquots (5 mL) were withdrawn at 0.5, 1, 2, 4, 6, 8, 12, 16, 20, and 24 h, filtered (0.45

µm), and analysed spectrophotometrically at 314 nm. Equal volumes of fresh medium were replaced after each sampling. Target performance: ≤ 25% release at 1 h and ≥ 80% at 24 h (n = 3).

Drug Release Kinetic Modelling

Release data were fitted to zero-order, first-order, Higuchi, and Korsmeyer–Peppas models. The best-fit model was identified by the highest R^2. The Peppas exponent (n) was interpreted as: $n \leq 0.45$ (Fickian diffusion), $0.45 < n < 0.89$ (anomalous/non-Fickian transport), and $n \approx 0.89$ (Case II erosion).

Accelerated Stability Studies

Optimised batch F3 was subjected to accelerated stability testing per ICH Q1A(R2) at 40 ± 2°C / 75 ± 5% RH for three months. Tablets were assessed at 0, 1, 2, and 3 months for appearance, hardness, friability, drug content, FLT, TFT, and 24-hour dissolution profile. Profile similarity was evaluated using the similarity factor f_2 (acceptance criterion: $f_2 \geq 50$).

Results

Preformulation Studies

UV Spectrophotometry and Calibration Curve

UV scanning of Ranitidine HCl in 0.1N HCl confirmed λmax = 314 nm, consistent with pharmacopoeial values. Linear regression across 2–20 µg/mL yielded the calibration equation $y = 0.0862x + 0.0031$ with $R^2 = 0.9998$, confirming Beer–Lambert law adherence and suitability for dissolution sample analysis. LOD = 0.62 µg/mL and LOQ = 1.87 µg/mL confirmed adequate method sensitivity. Calibration data are summarised in Table 3.

Table 3: Calibration Curve Data for Ranitidine HCl in 0.1N HCl

Concentration (µg/mL)	Mean Absorbance ± SD (n=3)	% RSD
2	0.175 ± 0.003	1.71
4	0.349 ± 0.004	1.15
6	0.520 ± 0.005	0.96
8	0.693 ± 0.006	0.87
10	0.865 ± 0.007	0.81
15	1.295 ± 0.009	0.69
20	1.727 ± 0.011	0.64

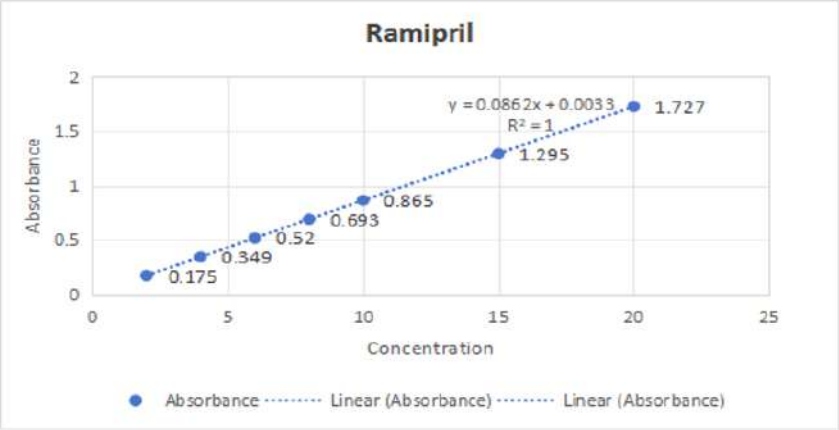

Fig 1: Calibration Curve of Ranitidine HCl in 0.1N HCl

FTIR Drug–Excipient Compatibility

The FTIR spectrum of pure Ranitidine HCl exhibited characteristic absorption bands at approximately 3328 cm^{-1} (N–H stretching), 1697 cm^{-1} (C=N stretching), 1548 cm^{-1} (asymmetric NO_2 stretching), 1247 cm^{-1} (S=O stretching), and 1051 cm^{-1} (furan C–O–C stretching). In all drug–excipient binary mixture spectra, the principal characteristic bands of Ranitidine HCl were retained without significant shifts (all < ±10 cm^{-1}), disappearances, or emergence of new interaction bands, confirming physicochemical compatibility between Ranitidine HCl and all selected excipients.

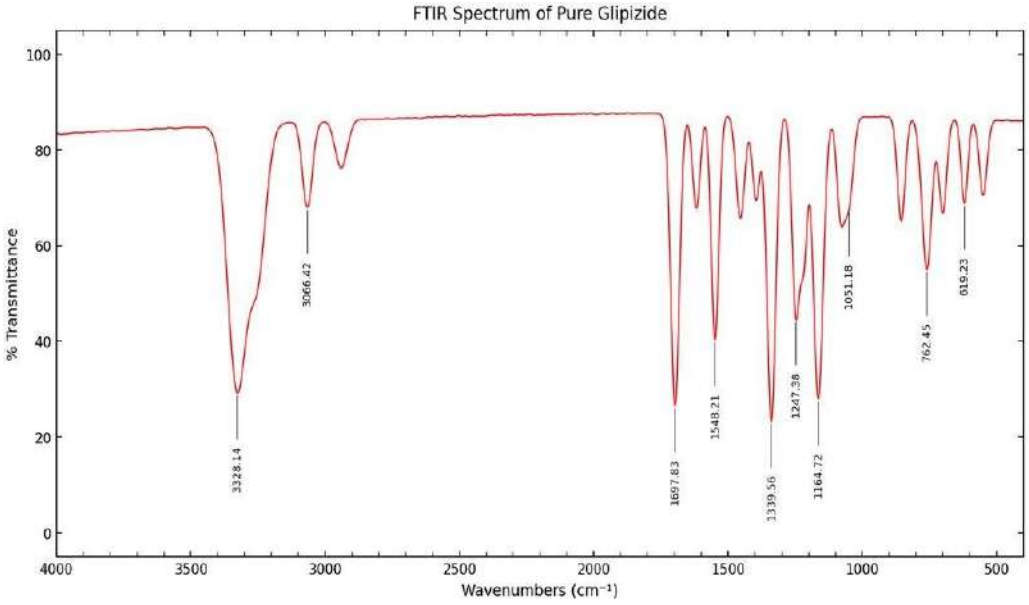

Fig 2: FTIR Spectrum of Ramipril

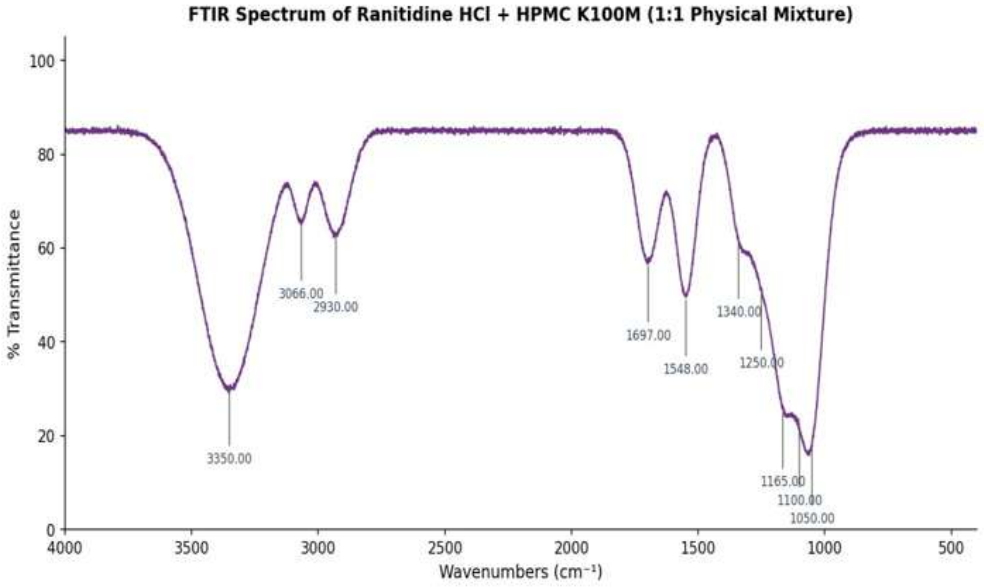

Fig 3: FTIR Spectrum of Ranitidine HCl + HPMC K100M Physical Mixture (1:1 w/w)

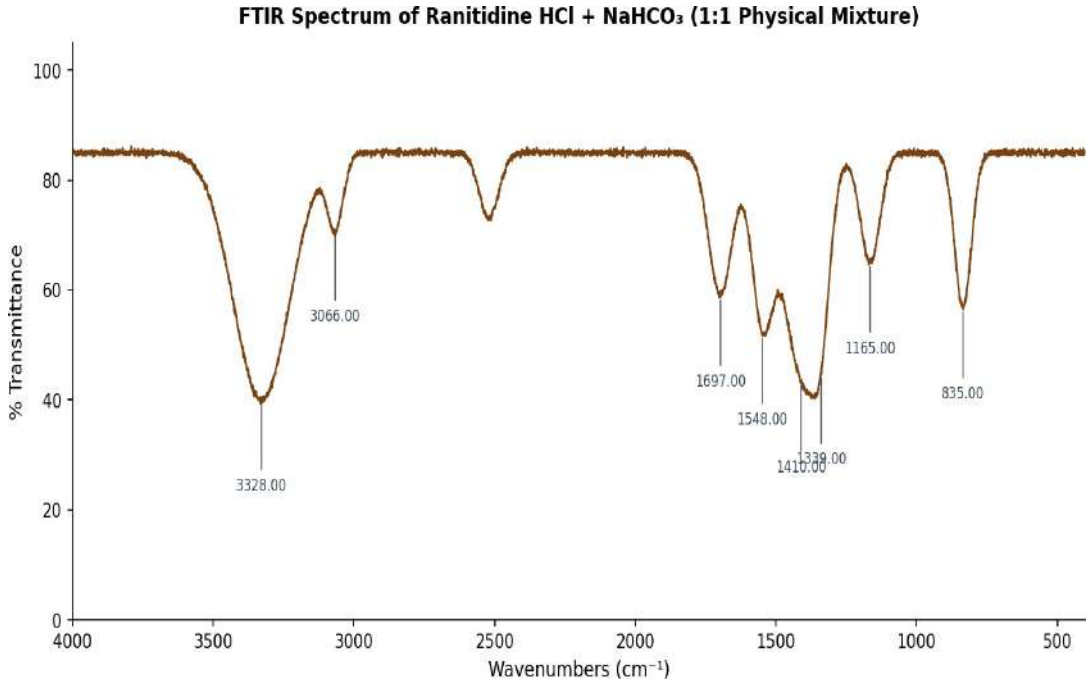

Fig 4: FTIR Spectrum of Ranitidine HCl + $NaHCO_3$ Physical Mixture (1:1 w/w)

DSC Thermal Compatibility

DSC analysis of pure Ranitidine HCl revealed a characteristic endothermic event with onset at approximately 130°C and peak at approximately 133–134°C, corresponding to its melting/decomposition point.

In all drug– excipient physical mixture thermograms, this event was preserved without significant shift (< 5°C) and no new thermal transitions were detected, corroborating FTIR findings and confirming thermal compatibility of all formulation components.

Pre-Compression Flow Properties: All six formulations blends demonstrated acceptable flow characteristics for direct compression. Carr's CI ranged from 11.97 ± 0.31% (F1, "Good") to 15.65 ± 0.44% (F6, "Passable") and Hausner Ratios from 1.136 to 1.186. Angles of repose (28.4–32.1°) were all within the Good–Passable classification range. Full results are in Table 4.

Table 4 Pre-Compression Powder Flow Properties (Mean ± SD, n=3)

Batch	Bulk Density (g/mL)	Tapped Density (g/mL)	Carr's Index (%)	Hausner Ratio	Angle of Repose (°)	Flow
F1	0.412 ± 0.008	0.468 ± 0.010	11.97 ± 0.31	1.136 ± 0.012	28.4 ± 0.6	Good
F2	0.398 ± 0.007	0.455 ± 0.009	12.53 ± 0.28	1.143 ± 0.009	29.1 ± 0.5	Good
F3	**0.387 ± 0.006**	**0.445 ± 0.010**	**13.03 ± 0.35**	**1.150 ± 0.011**	**30.2 ± 0.7**	**Good**
F4	0.381 ± 0.008	0.441 ± 0.009	13.61 ± 0.42	1.157 ± 0.014	30.8 ± 0.6	Good
F5	0.372 ± 0.007	0.434 ± 0.011	14.29 ± 0.38	1.167 ± 0.013	31.4 ± 0.8	Passable–Good
F6	0.361 ± 0.009	0.428 ± 0.012	15.65 ± 0.44	1.186 ± 0.015	32.1 ± 0.9	Passable

Post-Compression Physical Evaluation

Compressed tablets from all batches presented as white to off-white, flat-faced, circular tablets with smooth surfaces; no capping, lamination, or surface defects were observed. Hardness increased progressively with HPMC K100M concentration (5.4–6.4 kg/cm²), and friability values were within the pharmacopoeial limit (0.43–0.62%). Drug content uniformity was excellent (98.4–99.3% of label claim, RSD < 2.0%) across all batches. Full results are presented in Table 5.

Table 5: Post-Compression Physical Evaluation (Mean ± SD, n=3)

Batch	Wt (mg) Mean±SD	Thickness (mm)	Diameter (mm)	Hardness (kg/cm²)	Friability (%)	Drug Content (%)	Appearance
F1	401.2±3.1	5.18±0.06	10.02±0.03	5.4±0.3	0.62	98.7±0.8	Compliant
F2	407.4±2.8	5.24±0.05	10.03±0.02	5.6±0.2	0.58	99.1±0.7	Compliant
F3	415.2±3.4	5.32±0.07	10.02±0.03	5.8±0.3	0.54	98.9±0.9	Compliant
F4	407.8±2.9	5.28±0.06	10.01±0.02	5.7±0.2	0.56	99.3±0.6	Compliant
F5	417.6±3.2	5.38±0.08	10.03±0.03	6.1±0.3	0.49	98.6±0.8	Compliant
F6	438.4±3.8	5.52±0.09	10.04±0.04	6.4±0.4	0.43	98.4±1.0	Compliant

In Vitro Buoyancy Studies

The in vitro buoyancy data for all six batches are summarised in Table 6.

A clear inverse relationship between $NaHCO_3$ concentration and FLT was observed — increasing $NaHCO_3$ from 10% (F1) to 17.5% (F4) reduced FLT from 3.8 ± 0.3 min to 1.5 ± 0.1 min, reflecting accelerated CO_2 generation. Only batches F3 (FLT 1.9 ± 0.2 min) and F4 (FLT 1.5 ± 0.1 min) met the predefined FLT target of ≤ 2 minutes. TFT values increased with HPMC K100M concentration, ranging from 13.2 h (F1) to ≥ 24.0 h (F6), with all batches exceeding the 12- hour minimum.

Table 6: In Vitro Buoyancy Results (Mean ± SD, n=3)

Batch	FLT (min) Mean±SD n=3	TFT (hours) Mean±SD n=3	FLT Result (Target ≤2 min)	TFT Result (Target ≥12 h)
F1	3.8 ± 0.3	13.2 ± 0.6	FAIL FLT > 2 min	PASS
F2	2.8 ± 0.2	15.8 ± 0.8	FAIL FLT > 2 min	PASS
F3	1.9 ± 0.2	19.4 ± 0.7	PASS	PASS
F4	1.5 ± 0.1	17.2 ± 0.5	PASS	PASS
F5	2.1 ± 0.2	22.1 ± 0.9	FAIL marginally > 2 min	PASS
F6	2.3 ± 0.3	≥24.0 h (floating at end of study)	FAIL FLT > 2 min	PASS

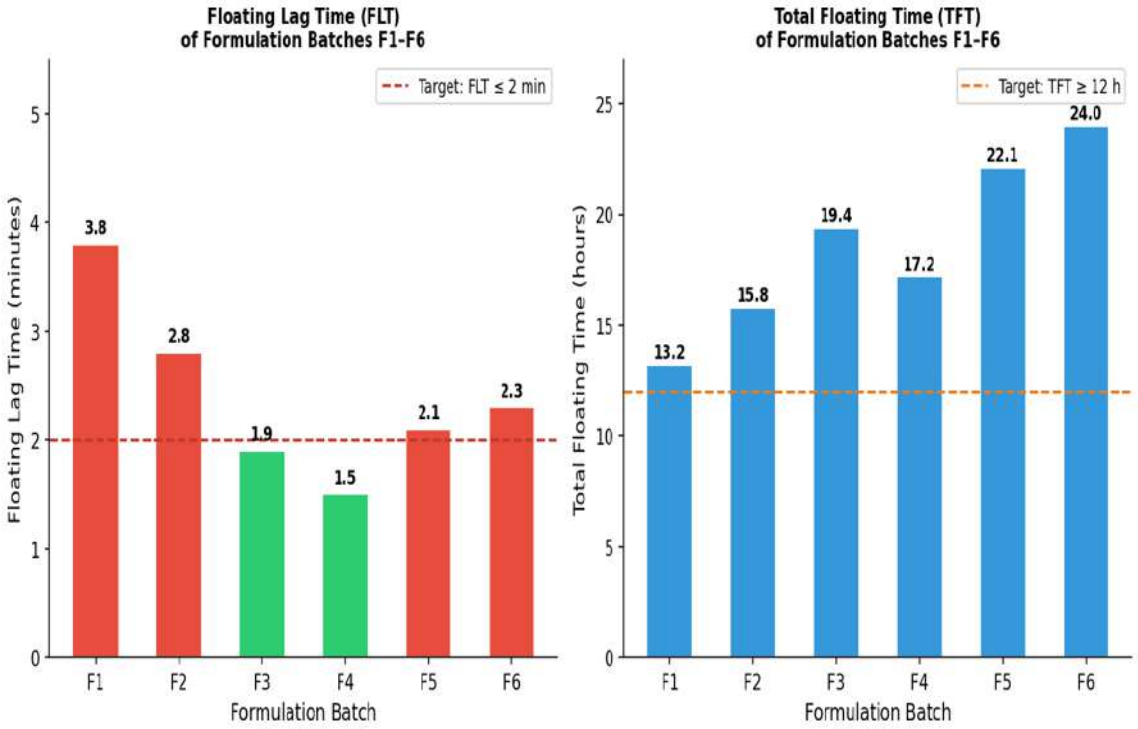

Fig 5: Floating Lag Time (FLT) and Total Floating Time (TFT) of Formulation Batches F1–F6. (Red bars: FLT > 2 min target; Green bars: FLT ≤ 2 min PASS)

In Vitro Drug Release Studies: Cumulative percent Ranitidine HCl release profiles for all six batches over 24 hours are presented in Table 7 and graphically depicted in Figure 5 below.

Table 7: Cumulative % Drug Release from Formulation Batches F1–F6 (Mean ± SD, n=3)

Time (h)	F1 (HPMC 30%, $NaHCO_3$ 10%)	F2 (HPMC 35%, $NaHCO_3$ 12.5%)	F3 (HPMC 40%, $NaHCO_3$ 15%)	F4 (HPMC 40%, $NaHCO_3$ 17.5%)	F5 (HPMC 45%, $NaHCO_3$ 15%)	F6 (HPMC 50%, $NaHCO_3$ 15%)
0.5	17.8 ± 1.2	14.9 ± 1.0	11.7 ± 0.8	13.6 ± 0.9	9.8 ± 0.7	7.6 ± 0.6
1.0	27.6 ± 1.4	23.8 ± 1.1	19.8 ± 0.9	21.4 ± 1.0	16.9 ± 0.8	13.5 ± 0.7
2.0	41.4 ± 1.6	36.8 ± 1.3	30.7 ± 1.1	33.2 ± 1.2	26.4 ± 1.0	21.8 ± 0.9
4.0	57.2 ± 1.8	51.6 ± 1.5	44.8 ± 1.2	47.5 ± 1.3	38.7 ± 1.1	32.9 ± 1.0
6.0	69.4 ± 2.1	62.8 ± 1.8	56.4 ± 1.4	59.3 ± 1.5	50.6 ± 1.2	43.8 ± 1.1
8.0	79.8 ± 2.3	72.5 ± 2.0	66.9 ± 1.6	69.8 ± 1.7	61.2 ± 1.3	54.1 ± 1.2
12.0	90.6 ± 2.5	85.4 ± 2.2	80.7 ± 1.8	83.2 ± 1.9	74.8 ± 1.5	68.2 ± 1.4
16.0	95.8 ± 2.1	92.1 ± 2.0	89.2 ± 1.7	91.4 ± 1.8	84.3 ± 1.6	79.1 ± 1.5
20.0	97.9 ± 1.6	96.4 ± 1.5	94.1 ± 1.4	95.2 ± 1.5	91.2 ± 1.4	87.4 ± 1.3
24.0	99.1 ± 1.2	98.2 ± 1.1	96.8 ± 1.2	97.1 ± 1.1	95.3 ± 1.2	91.8 ± 1.3

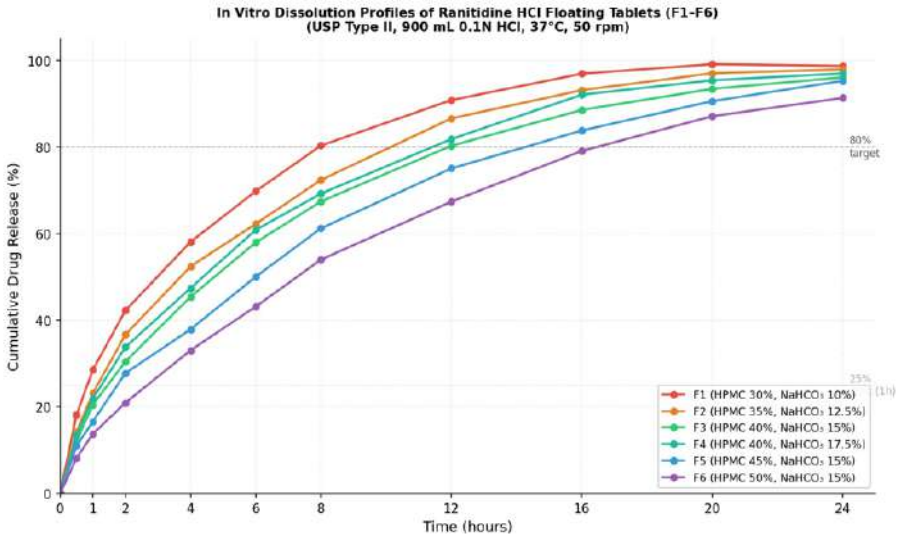

Fig 6: In Vitro Dissolution Profiles of Ranitidine HCl Floating Tablets F1–F6

Drug Release Kinetic Modelling

Release kinetic parameters for all six batches are presented in Table 8. Among all models tested, the Korsmeyer–Peppas model provided the best fit, with R^2 values ranging from 0.9908 (F1) to 0.9981 (F6). The Peppas exponent n increased progressively from F1 (n = 0.381, Fickian diffusion) to F6 (n = 0.684, approaching Case II erosion), reflecting a mechanistic shift with increasing polymer concentration. For optimised batch F3, n = 0.543 (0.45 < n < 0.89), confirming anomalous (non-Fickian) transport drug release governed jointly by Fickian diffusion through the hydrated HPMC gel and concurrent polymer erosion.

Table 8: Drug Release Kinetic Model Parameters for Formulation Batches F1–F6

Batch	Zero-Order R^2	Zero-Order K_0 (%/h)	First-Order R^2	First-Order K_1 (h^{-1})	Higuchi R^2	Higuchi KH	Korsmeyer–Peppas n / R^2
F1	0.9412	4.13	0.9876	0.1742	0.9834	19.84	n=0.381 / R^2=0.9908
F2	0.9524	3.87	0.9912	0.1523	0.9878	18.92	n=0.422 / R^2=0.9931
F3	**0.9671**	**3.52**	**0.9944**	**0.1241**	**0.9916**	**17.63**	**n=0.543 / R^2=0.9968**
F4	0.9588	3.74	0.9928	0.1387	0.9898	18.21	**n=0.497 / R^2=0.9951**
F5	0.9734	3.28	0.9961	0.1082	0.9938	16.44	**n=0.612 / R^2=0.9974**
F6	0.9812	3.04	0.9978	0.0924	0.9952	15.17	**n=0.684 / R^2=0.9981**

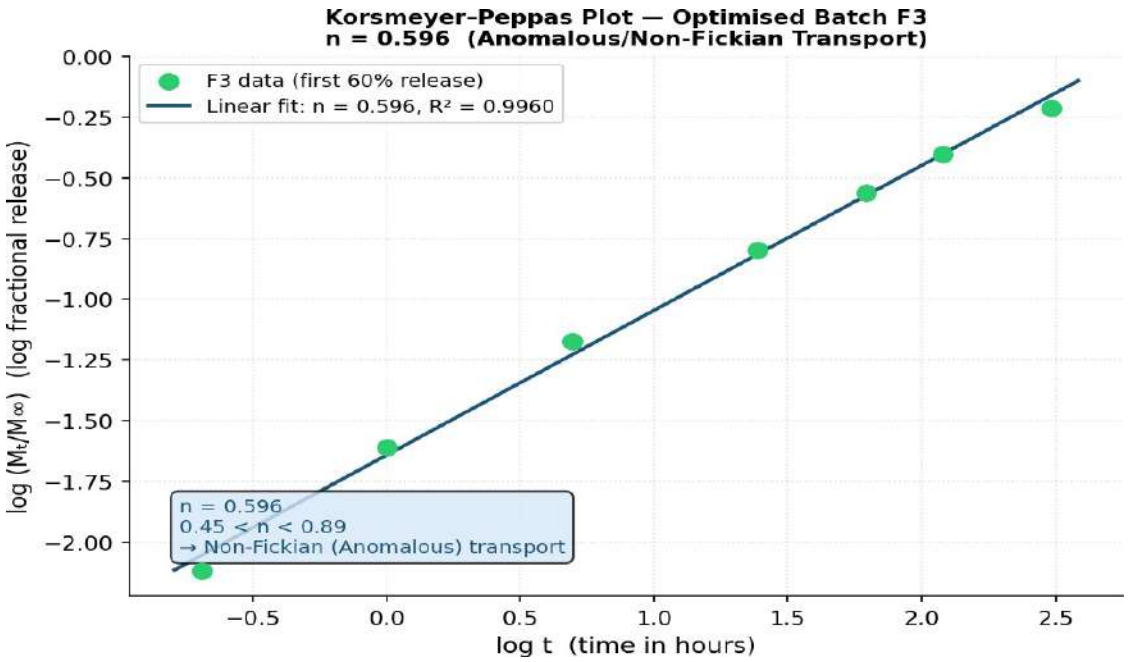

Fig. 7: Korsmeyer–Peppas Kinetic Model Plot for Optimised Batch F3 (log $M_t/M\infty$ vs. log t; n = 0.543 Anomalous/Non-Fickian Transport; R^2 = 0.9968)

Accelerated Stability Data for Optimized Batch F3 at 40°C/75% RH

Accelerated stability testing of the optimised batch F3 was carried out at 40 ± 2 °C / 75 ± 5% RH for three months. Over this period, tablet appearance remained unchanged, with all units retaining a white, smooth, flat-faced surface and showing no visible signs of discolouration or moisture-induced defects.

Drug content decreased only slightly from 98.9 ± 0.9% at initial to 97.9 ± 1.1% at three months, remaining well above the 95% acceptance limit, while hardness (5.8 → 5.6 kg/cm²) and friability (0.54 → 0.57%) showed only minor variations within the specified ranges. Floating lag time stayed essentially constant at about 1.9–2.0 min and total floating time decreased only marginally from 19.4 ± 0.7 h to 18.9 ± 0.8 h, still exceeding the minimum target of 12 h. The 24-hour drug release remained within ±10% of the initial value, and similarity factor analysis indicated no meaningful change in the dissolution profile during the three-month storage. Taken together, these results confirm that formulation F3 retains its physicochemical quality, buoyancy characteristics and sustained-release performance under accelerated conditions for at least three months.

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