RESEARCH PAPER

Formulation and Optimization of Floating Microsponge-Based Ranitidine Delivery System for Prolonged Gastric Retention and Improved Absorption

Pradeep Kumar[1,2*], Sarvesh Kumar Paliwal[2]

[1] Department of Pharmacy, LLRM Medical College, Meerut - 250001, India.

[2] Department of Pharmacy, Banasthali Vidyapith, Rajasthan - 304022, India.

[*] Corresponding Author: Pradeep Kumar, Department of Pharmacy, Banasthali Vidyapith, Rajasthan - 304022. Email: pky.llrm@gmail.com

Received: 28th Feb, 2026 | **Revised:** 14th Mar, 2026 | **Accepted:** 4th Apr, 2026 | **Available Online:** 20th Apr, 2026

ABSTRACT

Background: Ranitidine hydrochloride belongs to the class of histamine H_2 receptor antagonists. It has a relatively short half-life in the body and is primarily absorbed in the upper region of the gastrointestinal tract. Because of this limited absorption window, its overall bioavailability is reduced, often requiring repeated dosing to maintain effective therapeutic levels. To overcome these limitations, gastro-retentive drug delivery systems are formulated to stay in the stomach for a prolonged period, which increases the duration during which the drug can be absorbed.

Objective: This study aimed to formulate floating microsponges of ranitidine by employing the quasi-emulsion solvent diffusion method. The main goal was to enhance the residence time of the drug in the stomach while ensuring a sustained and controlled release pattern over an extended period.

Methods: Floating microsponges of ranitidine hydrochloride were prepared using the quasi-emulsion solvent diffusion technique, employing various polymers such as Eudragit RS100, Eudragit S, HPMC K100M, ethyl cellulose, and hydroxypropyl cellulose as carrier materials. The internal phase was drug and polymer solubilized in a methanol:dichloromethane (2:8) solution, which was ultrasonicated and added dropwise into an aqueous polyvinyl alcohol solution dissolved in an external phase while stirred to allow solvent evaporation leading to microsponge generation. Twelve formulations (F1–F12) were prepared to improve the microsponge characteristics by changing polymer ratios. The formulation exhibiting the most desirable properties was identified as the optimized batch, based on evaluation parameters including particle size, entrapment efficiency, buoyancy percentage, and in-vitro drug release profile of the prepared microsponges.

Results: The optimized formulation demonstrated particle size of 52.66 ± 1.1 µm, drug content 92.87 ± 0.12%, entrapment efficiency of 63.58 ± 0.74%, buoyancy of 87 ± 1.67% for 8 hours, and sustained drug release (95.89 ± 0.79 at 8 h). According to the coefficients of regression (R^2), most formulations were fit better by the Korsmeyer–Peppas model (81%) suggesting diffusion-controlled drug release. The diffusion exponent (n), which ranges from 0.5 to 1.1, suggests a non-Fickian (anomalous) release pattern, indicating that the drug is released from floating microsponges prepared with Eudragit RS via a synergistic combination of diffusion and polymer relaxation mechanisms. There was no substantial drug-polymer interaction detected.

Conclusion: Floating microsponges of ranitidine successfully achieved prolonged gastric retention and controlled drug release, indicating their potential to enhance gastrointestinal absorption and therapeutic performance.

Keywords: Ranitidine, Floating microsponges, Gastro-retentive system, Factorial design, Controlled release, QbD.

How to cite this article: Kumar P, Paliwal SK. Formulation and Optimization of Floating Microsponge-Based Ranitidine Delivery System for Prolonged Gastric Retention and Improved Absorption. Int J Drug Deliv Technol. 2026;16(30s):558-573. DOI: 10.25258/ijddt.16.30s.56

Source of support: Nil.

Conflict of interest: The authors declare no conflict of interest.

1. Introduction

However, oral administration validates as the most preferred one among all systemic therapies in terms of convenience, economical and better patient adherence. Controlled drug delivery systems (CDDS) were created to maintain plasma concentration of drug and minimize dosing frequency. However, these systems may have limited utility when a drug demonstrates variability in intestinal pH stability, narrow absorption windows or poor gastrointestinal absorption. Gastro-retentive drug delivery systems (GRDDS) aim to prolong the retention of dosage forms within the stomach, which in turn enhances the absorption of drugs that are preferentially absorbed in the upper region of the gastrointestinal tract (Alqahtani MS et al., 2021).

GRDDS are especially beneficial for drugs that are primarily absorbed in the stomach or proximal small intestine. unstable under alkaline conditions and those with decreased solubility at higher pH. Examples would be drugs including ranitidine, metformin, furosemide, diazepam, riboflavin and levodopa (Zanke AA et al., 2022). These systems can prolong gastric residence time, which impacts dissolution profiles in acidic environments and lowers degradation of the drug to increase bioavailability and reduce concentration deviation on plasma. Additional benefits include decreased dosing frequency, improved therapeutic efficacy for drugs with short half-lives, and mitigation of dose-dumping risks.

Ranitidine hydrochloride acts as a competitive antagonist at histamine H_2 receptors and is commonly used in the treatment of conditions such as peptic ulcer disease, gastroesophageal reflux disease (GERD), and Zollinger–Ellison syndrome (Ahmad S et al., 2016). Despite its clinical effectiveness in suppressing gastric acid secretion, ranitidine exhibits several biopharmaceutical challenges. It has an oral bioavailability of approximately 50% due to presystemic metabolism and incomplete absorption, along with a relatively short elimination half-life of about 2.5–3 h. Furthermore, ranitidine demonstrates chemical instability under neutral, alkaline, and oxidative conditions, while remaining comparatively stable in acidic gastric environments (Mandal UK et al., 2016). These properties make it a suitable candidate for gastro-retentive formulations aimed at prolonging gastric retention and improving therapeutic performance.

Various GRDDS approaches such as floating systems, mucoadhesive formulations, and swellable matrices have been investigated for ranitidine delivery. These systems have demonstrated sustained release profiles and prolonged gastric residence; however, limitations such as suboptimal drug loading, variable entrapment efficiency, and limited retention time remain concerns.

Microsponge drug delivery systems represent an advanced alternative within gastro-retentive technologies. Microsponges are highly porous polymer-based microspheres, generally having a particle size in the range of 5–300 μm, and possess a network of interconnected pores that allows efficient incorporation of significant quantities of drug. Their highly porous structure provides large internal surface area, facilitating controlled and sustained drug release. Compared to conventional microspheres, microsponges offer advantages such as higher drug loading capacity, improved formulation stability, reduced risk of dose dumping, and extended release duration (Sharma P et al., 2019; Darekar A et al., 2019).

Floating microsponge drug delivery systems (FMDDS) further enhance therapeutic potential by combining buoyancy with a porous matrix architecture. The low density of microsponges enables them to remain suspended in gastric fluid, thereby prolonging gastric residence time. Their porous structure increases the effective surface area of the incorporated drug, improving dissolution rate and enhancing absorption within the optimal absorption window of the upper GI tract (Kaity S et al., 2010). Additionally, microsponges exhibit favorable stability characteristics, compatibility with various excipients, good flow properties, and cost advantages compared to more complex systems such as liposomes and nanocapsules.

Considering these advantages, the present study intends to develop floating microsponges of ranitidine hydrochloride using biocompatible polymers such as ethyl cellulose, Eudragit S, and Eudragit RS100. Optimization of polymer composition is aimed at attaining high drug entrapment efficiency, sustained drug release and long gastric buoyancy. Thus, this newly developed system is designed to improve the

bioavailability and therefore therapeutic potency of ranitidine by retaining the dosage form in the acidic gastric lumen close to its major absorption site.

2. Materials and Techniques

2.1. Ingredients

Ranitidine hydrochloride, hydroxypropyl methylcellulose, ethyl cellulose, Eudragit® RS 100, Eudragit® S 100, and HPC K100M were purchased from Pure and Cure Healthcare Pvt. Ltd. in Haridwar, Uttarakhand, India. The supplier of polyvinyl alcohol was SD Fine Chemicals Ltd. in Mumbai, India. Merck Life Science Pvt. Ltd. in Mumbai, India provided analytical-grade ethanol and dichloromethane. Analytical-grade chemicals and reagents were all used in the examination without further purification.

2.2 Pre-formulation studies

The API will go through a comprehensive investigation of its physical features, melting point, solubility studies, maximal absorption characteristics, and drug□excipient interactions in accordance with the methods outlined by **Anurup et al., 2019.**

2.2.1 Physical Properties

The organoleptic properties of ranitidine hydrochloride, including appearance, colour, and odour, will be evaluated according to the specifications outlined in the Indian Pharmacopoeia (2007).

2.2.2 Determination of Melting Point

Our department will measure the melting point of ranitidine hydrochloride using a capillary tube method and/or a melting point apparatus. Melting of the drug sample will be performed and temperature at which melting is recorded.

2.2.3 Determination of solubility

The solubility of ranitidine hydrochloride will be evaluated in different solvents, including methanol, ethanol, distilled water, acetic acid, and 0.1N HCl, as per the Indian Pharmacopoeia (2007) guidelines. Excess drug will be added to each solvent, shaken adequately, and the solubility will be determined after equilibrium.

2.2.4 Determination of λ max

For this a stock solution of ranitidine hydrochloride (RTZ), method must be prepared in 100 mg RTZ dissolved in 100 mL of 0.1N methanolic hydrochloric acid to give a concentration about at 1 mg/mL (read literature). It will end up being diluted to an arbitrary concentration of 100 µg/mL. Scanning the prepared solution with a UV–Visible spectrophotometer in the 200–400 nm range (λmax).

2.2.5 The Ranitidine hydrochloride standard calibration curve

100 mg of ranitidine hydrochloride dissolved in 20 mL of phosphate buffer (pH 1.2) to make a stock solution. The volume was then raised to 100 mL using the same buffer. A series of working standard solutions with concentrations of 20, 40, 60, 80, and 100 µg/mL were collected from this stock in 10 mL volumetric flasks. Phosphate buffer (pH 1.2) was used as the blank to measure the absorbance of each solution at 313 nm. Plotting concentration against the necessary absorbance values offered the build of a calibration curve.

2.2.6 Drug-excipients interaction studies by FTIR

To assess compatibility, FTIR analysis of both pure ranitidine hydrochloride and its physical mixtures with chosen excipients will be conducted. The samples were scanned over a spectrum range of 4000–400 cm^{-1} using an FTIR spectrophotometer and the potassium bromide (KBr) pellet technique. The acquired spectra will be examined for characteristic peaks and relevant shifts or loss of one or more peaks to identify possible drug–excipient interactions.

Method

3.1 Floating Microsponge Preparation

By using a quasi-emulsion solvent diffusion technique, floating microsponges were formed. Prior to a formation of spherical microsponges, the within and external phases were developed separately using this technique. The drug-loaded nanoformulations of ranitidine hydrochloride were subsequently developed through this approach.

Step-1: At this stage, the polymer(s) selected for this internal phase have been dissolved in methanol:dichloromethane (2:8 ratio), step-1The polymer solution was then sonicated with an ultrasonic probe for 1 minute to obtain a homogeneous and homogeneous solution. Next, the ranitidine hydrochloride was introduced to polymer solution, followed by ultrasonication for 2 min. to the same temperature (35 °C) until completely dissolved and drug well dispersed.

Step 2: The external phase was formulated by dissolving 200 mg of polyvinyl alcohol (PVA) in

200 mL of distilled water with continuous stirring at 60 °C until a clear and homogeneous solution was obtained. The solution was then cooled and kept at a temperature range of 25–27 °C for subsequent use.

Step-3: The internal phase (drug–polymer solution) was then dropped into the external phase PVA solution) and blended. Stirring was continued for 3h afterwards to allow for diffusing and evaporating of the organic solvent from internal phase droplets.

The resin of the evaporated solvent was obtained from adrenal extracts and characterized after vacuum filtration. subsequent to multiple washes of filtration in order to eliminate unattached PVA and un-entrapped drug though hot air oven at 40 °C for 12 hours. Floating dried product was obtained microsponges of ranitidine hydrochloride.

Table 3.1: Formulation of Floating Microsponges Using Various Ratios of Different Polymers

Ingredients	**FM1**	**FM2**	**FM3**	**FM4**	**FM5**	**FM6**	**FM7**	**FM8**	**FM9**	**FM10**	**FM11**	**FM12**
Ranitidine HCl	150	150	150	150	150	150	150	150	150	150	150	150
Eudragit RS100	350	-	-	-	350	350	-	-	350	350	350	350
HPMCK100M	250	-	-	-	-	-	250	-	250	-	-	250
Eudragit S	-	350	-	350	350	-	-	-		-	-	350
Ethyl cellulose	-	-	250	250	-	250	-	-		-	-	250
Hydroxy Propyl cellulose	200	-	-	-	-	-	-	200		200	-	200
Polyvinyl alcohol	200	200	200	200	200	200	200	200	200	200	200	200
Dichloromethane (%)	8	8	8	8	8	8	8	8	8	8	8	8
Ethanol	2	2	2	2	2	2	2	2	2	2	2	2

3. Characterization of Floating Microsponge

3.1 Particle Size Analysis

The particle size of the developed microsponge formulations was evaluated using an optical microscope. Before analysis, calibration of the eyepiece micrometer was carried out with the help of a stage micrometer to determine the calibration factor. A small amount of the microsponge sample was then mounted on a clean glass slide, and the particle size was measured using the calibrated eyepiece scale.

3.2 Surface Morphology

The surface morphology of the optimized formulation was analyzed using scanning electron microscopy (SEM). The samples were carefully fixed onto aluminum stubs and coated with a thin layer of gold in an argon atmosphere using a sputter coating unit (VG Microtech, high vacuum evaporator) before examination. The coated samples were then observed at varying magnifications ranging from 100× to 1000× to evaluate their surface features and porosity.

3.2 Percentage Yield

The production yield of the prepared microsponges was determined by comparing the actual weight of the final product with the total

theoretical weight of all the ingredients used in the formulation. The percentage yield was calculated using the following expression:

% Yield = Practical Yield/Theoretical Yield×100

3.3 Entrapment Efficiency

To determine the % drug entrapment efficiency, crushed microsponges were subjected to extraction through treatment with 0.1 N HCl. The volume of the solution was adjusted to 100 mL using the same solvent. The resulting solution was filtered, and its absorbance was recorded using a UV–Visible spectrophotometer. The entrapment efficiency (EE) was then calculated as the percentage ratio of the measured drug content to the theoretical amount of drug incorporated in the formulation.

3.4 Drug Content

The drug loading of ranitidine hydrochloride in the prepared microsponges was quantified using a UV–Visible spectrophotometric method at its maximum absorption wavelength (λmax). An accurately weighed 50 mg sample of microsponges was taken, finely crushed, and dispersed in 100 mL of 0.1 N HCl. The mixture was stirred at 75 rpm for 2 hours to ensure complete extraction of the drug. Afterward, the solution was filtered, and the absorbance of the filtrate was measured at 313 nm using a UV–Visible spectrophotometer.

3.5 Buoyancy Study

The floating ability of the prepared microsponges was assessed using a USP dissolution apparatus II (paddle method). An accurately weighed sample of 50 mg was placed in 900 mL of 0.1 N HCl containing 0.02% Tween 80 as a surfactant. The dissolution medium was maintained at 37 ± 0.5 °C, and the paddle was rotated at 100 rpm to ensure consistent mixing and uniform conditions throughout the study.The microsponges that were floating and settled after 12 h were then separately collected. The floating fraction was ashed in a oven #80 for 15 minutes, weighed to measure percentage buoyancy.

3.6 Evaluation of Micromeritic Properties of Prepared Microsponges

3.6.1 Angle of Repose

The flow properties of the prepared microsponges were assessed by measuring the angle of repose using the fixed funnel method (as presented in Table 3.2).

An inert substrate surface was built where microsponges were poured from a funnel in which only a small defined quantity of microsponges is freed to flow without hindering the formation of geometric piles through heaps of stacked conical shapes.

After complete flow, a circle was drawn on the ground around the base of each heap formed. The height of the formed powder cone and the radius of its base were measured using suitable instruments. The angle of repose (θ) was then determined using the standard mathematical relationship (Dang et al., 2015; Shabaraya et al.)..

$\tan \theta = h/r$

Table 3.2: Correlation between Angle of Repose and Flow Characteristics

Angle of repose	Type of flow
<25	Excellent
25-30	Good
30-40	Satisfactory
>40	Very Poor

3.6.2 Bulk density

Bulk density is defined as the mass of a powder divided by its total volume, which includes both the particle volume and the spaces between the particles. It is influenced by factors such as particle shape, size, and the manner in which the particles are arranged. If bulk density is high, It will mean that particle shape is spherical. When the particle size is bigger then in this case the bulk density will be smaller. 10 ml measuring cylinder was taken and then 1 g of powder was added. Bulk density was measured by determining the volume occupied by the powder in its loose, untapped form. It was calculated using the standard equation, and the results were expressed in g/mL.

$$\textbf{Bulk density} = \frac{weight\ of\ sample}{volume\ of\ sample}$$

3.6.3 Tapped Density

To measure tapping density we use mechanical method by tapping the powder sample in a measuring cylinder. The process is carried out by using gravitational force. The cylinder is. Cylinder is tapped from 2 cm height for 20 times. The given formula is used to calculate the tapped density.

$$Tapped\ density = \frac{weight\ of\ sample}{Tapped\ volume}$$

3.6.4 Carr's Index (CI)

The bulk density (ρb) and tapped density (ρt) of the microsponge formulations were measured using a 10 mL graduated cylinder. We filled the

cylinder with 1 g of prepared microsponges and recorded its initial volume. It was then pounded 100 times against a wood surface from 1 inch above. After tapping, the amount of the microsponges [in graduated cylinder were measured. This process was performed three times to take triplicate measurements. Each sample density is based on the average of three replicate measurements. Density was computed as the mass-to-volume ratio (Dang et al., 2015). Equation 2 and equation 3 were used to calculate the car's index and Hausner's ratio respectively.

CI = {(ρt – ρb)/ρt}100 …… … (2)

HR = (ρt/ρb)100 …….... (3)

Table 3.3: Relationship between Percentage Compressibility and Flow Characteristics

S. No.	% Compressibility	Flow ability
1	5-15	Excellent
2	12-16	Good
3	18-21	Fair passable
4	23-35	Poor
5	33-38	Very poor
6	>40	Very very poor

3.6.5 Hausner's Ratio

Hausner's ratio is a useful parameter for evaluating the flow behavior of powders, based on the relationship between tapped density and bulk density. It is calculated as the ratio of tapped density to bulk density. Lower values of Hausner's ratio are indicative of improved flow characteristics. The equation for Hausner's ratio is displayed in the table below. Hausner's ratio for classification of the flow properties powder or granule, 1.5 poor-flow [6]. Represented by specific classifications (See Table 3.4 in appendix).

Table 3.4: Correlation between Hausner's Ratio and Flow Properties

Hausner's ratio	Flow property
<1.25	Good flow
1.25-1.5	Moderate
>1.5	Poor flow

3.7 In-Vitro Drug Release Study of Floating Microsponges

The in-vitro release profile of the prepared floating microsponges was studied using a USP dissolution apparatus II (paddle method). The experiment was conducted in 900 mL of 0.1 N HCl as the dissolution medium. A sample of microsponges equivalent to 400 mg of ranitidine hydrochloride was added to the medium. The temperature was maintained at 37 ± 0.5 °C, and the paddle speed was adjusted to 50 rpm to ensure uniform mixing throughout the study.

At specified time intervals, 5 mL aliquots were withdrawn from the dissolution medium and immediately replaced with an equal volume of fresh medium to maintain constant volume and sink conditions. The samples collected were filtered, and their absorbance was determined at 313 nm using a UV–Visible spectrophotometer (Dandagi et al., 2009; Patel and Amin, 2011).

3.8 *In-Vitro* Kinetic Data Analysis

The drug release data were analyzed using different kinetic models, namely zero-order, first-order, Higuchi, and Korsmeyer–Peppas models. The applicability of each model was evaluated by comparing their correlation coefficient (R^2) values. The model with the highest R^2 value was considered to best describe the drug release behavior. The following mathematical models were employed:

3.8.1 Zero-Order Kinetics

This model is suitable for dosage forms where the drug dissolution is slow and does not involve disaggregation or changes in surface area or equilibrium conditions. The equation used is:

Qt=Q0+K0t

In this model, Qt represents the amount of drug released at time t,

Q0 is the initial amount of drug present in the solution, and

K0 denotes the zero-order release rate constant.

3.8.2 First-Order Kinetics

This model is commonly used to describe drug release systems where the release rate is dependent on the concentration of the drug remaining. The release data were fitted to the following equation:

logQt=log

Q0+K1t2.303\log Qt = \log Q0 + K1 t}{2.303}logQt=logQ0+2.303K1

Here, Qt indicates the amount of drug released at time t, Q0 is the initial drug concentration, and K1 represents the first-order release rate constant.

3.8.3 Higuchi Model

For poorly soluble drugs and highly water-soluble drugs, this model involves the evaluation of their release upon incorporation into solid or semi-solid matrices. Further analysis was conducted using the following formula

Qt = KH t1/2

Where Qt is the total drug released at time t and The KH is noted Higuchi rate constant.

3.8.4 Korsmeyer and Peppas Model

When the release mechanics is not well established or multiple release mechanism may be involved in pharmaceutical polymeric dosage forms this model can be used. Further analysis is performed based on the following formula

$Mt / M = Ktn$

Where Mt/M is the fraction of drug released

K is the release constant

T is the release time, and

n is the diffusion exponent that describes morphological of matrix dosage form

In the present study, the in-vitro drug release data were analyzed using four widely accepted kinetic models in pharmaceutical research. To understand the mechanism of drug release, the dissolution data were fitted into different models. Zero-order kinetics was assessed by plotting cumulative percentage drug released versus time. First-order kinetics was evaluated by plotting the logarithm of the cumulative percentage of drug remaining against time. The Higuchi model was analyzed by plotting cumulative percentage drug release versus the square root of time. Furthermore, the Korsmeyer–Peppas model was applied by plotting the logarithm of cumulative percentage drug release against the logarithm of time.

These models are useful for describing drug release behavior and assist in identifying the kinetic model that best represents the release profile based on the goodness of fit.

RESULTS & DISCUSSIONS

4.1. Pre-formulation studies

4.1.1 Physical properties

Table represents the outcome of Physical characterization of Silver sulphadiazine. The COA specification and the observations recorded at each of the experiments reflect differences.

TABLE: 2. Physical properties of Ranitidine HCL

Colour	White to off white
Odour	Odourless
Taste	Bitter taste

4.1.2 Melting point

The experimentally determined melting point was found to be in close agreement with the value reported in the Certificate of Analysis (COA) provided by Sigma-Aldrich, India.

Table:3. Melting point of Ranitidine HCL

SI. No	**Reported**	**Observed**		
1	**141–143°C**.	Trail-I	Trail-I	Trail-I
		141°C.	141°C.	142°C.

4.1.3 Solubility analysis

Solubility criteria of drug are important to check whether it is soluble or not. Ranitidine was freely soluble in water, alcohol, acetic acid, distilled water, slightly soluble in 0.1N HCL and dichloromethane.

4.1.3 Determination of λmax

Assayed between 200-400 nm in UV (λ max determination of ranitidine) spectrophotometer. It was found to be 313 nm.

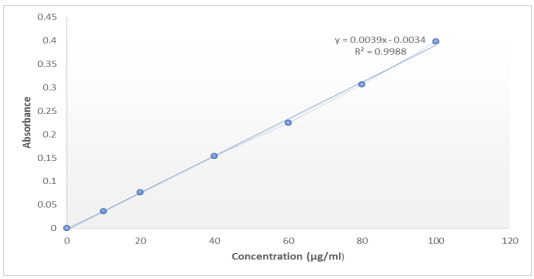
4.1.4 Calibration Curve of Ranitidine Hydrochloride

The standard solution for ranitidine HCL (0-100 µg/ml) of drug shows the absorbance in table 4.1. The standard calibration curve is illustratively displayed in figure 4.1 which have slope and regression coefficient of 0.0039 and 0.9988 respectively. Absorbance (µg/ml) A =0.005× + 0.856 with a linear range of 0-100 µg/ml at 313 nmThis calibration curve is employed for calculating the drug content and *in-vitro* drug release

Table 4.1: Calibration Data of Ranitidine Hydrochloride

Concentration in (µg/ml)	**Absorbance (±SD)**
00	0 ± 00
10	0.036 ± 0.005
20	0.076 ± 0.003
40	0.154 ± 0.010
60	0.225 ± 0.042
80	0.307 ± 0.064
100	0.398 ± 0.073

Each reading is an average of three determination ± SD



4.1.6 FTIR interpretation

FTIR spectroscopy is a powerful technique, which is used for the identification of drug substances. The characteristic IR absorption peaks of ranitidine were observed as: 2909 and 2944 (C-H), 3350 and 3166 (N-H), 1220 and 1045 (C-N), 1555 and 1379 (N-O), 1616 (C=C of C=C-NO2) as showed in figure 4.2. The characteristic IR absorption peaks of HPMC were observed as: 2942 and 3450 (O-H), 2942 and 2839 (C-H), 1121 and 1052 (C-O) as showed in figure 4.3. The characteristic IR absorption peaks of HPC are: 3596 (O-H), 2920 and 2874 (C-H), 1156,1090 and 1045 (C-O) as showed in figure 4.4. The characteristic IR absorption peaks of ethyl cellulose were observed as: 3400 (O-H), 2974 and 2873 (C-H), 1156, 1090 and 1109 and 1055 (C-O) as showed in figure 4.5. The characteristic IR absorption peaks of ERS were observed as: 2962 and 2839 (C-H), 1732 (C= O), 1339 and 1233 (C-N), 1141 (-C-O) as showed in figure 4.6.

The distinct IR absorption peaks of prepared formulations (F1-F12) were observed as illustrated in figure 4.7 to figure 4.18. The spectra of all prepared formulations (F1-F12) exhibited all the characteristic peaks of ranitidine at those particular wavelengths range. These findings suggest good compatibility between the drug and the selected polymers, indicating that the chemical integrity of the drug remained unaffected.

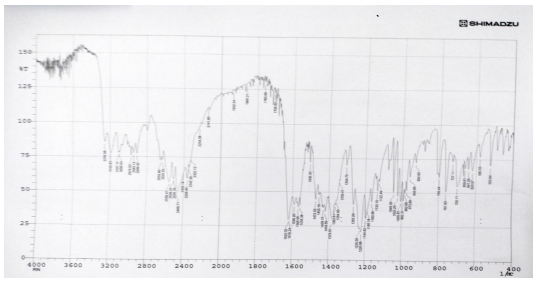


Figure 4.2: IR Spectra of Ranitidine HCl

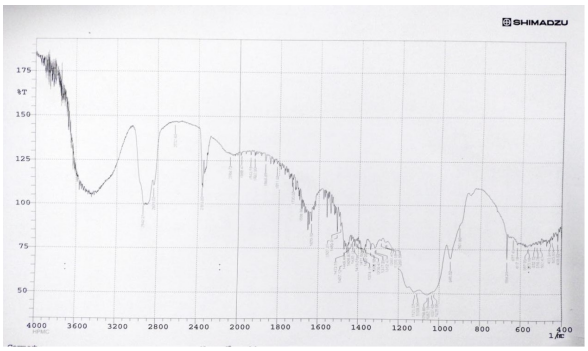


Figure 4.3: IR Spectra of HPMC

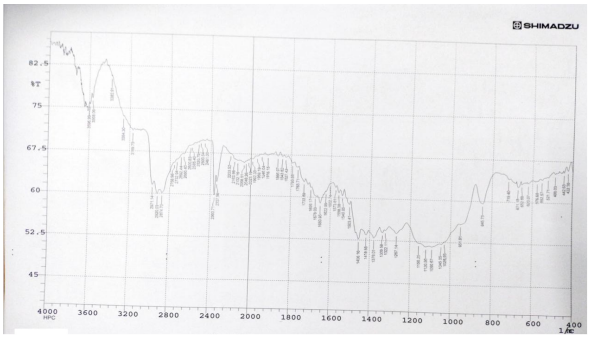
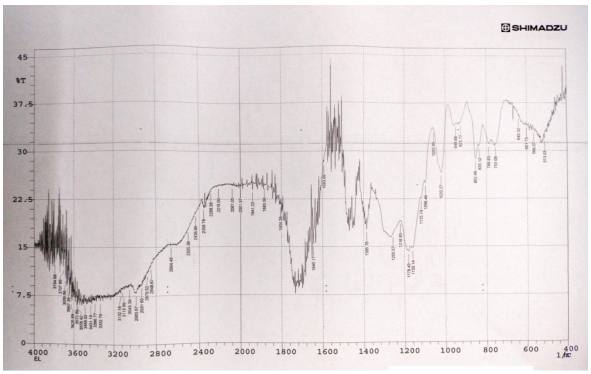


Figure 4.4: IR Spectra of HPC



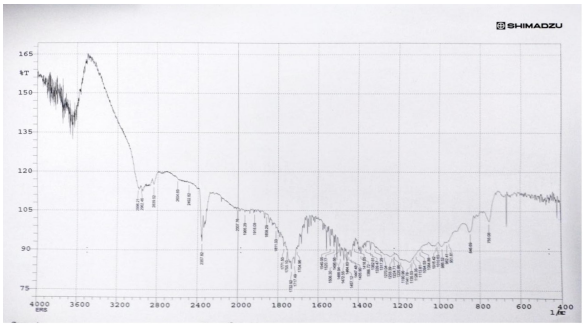


Figure 4.5: IR Spectra of EL

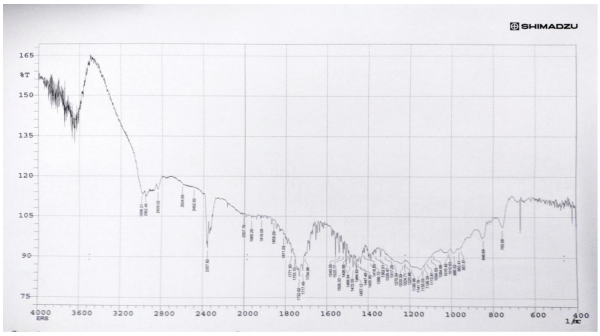
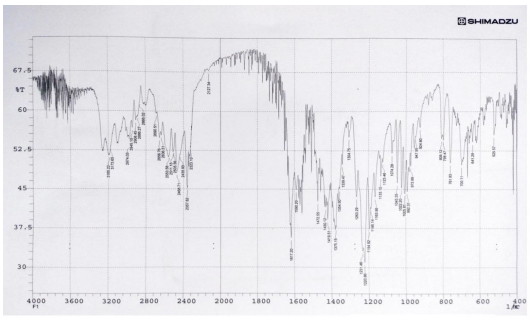


Figure 4.6: IR Spectra of ERS



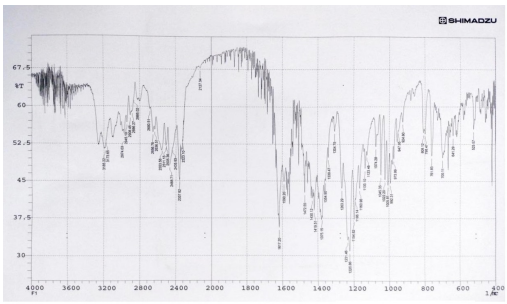


Figure 4.7: IR Spectra of F1

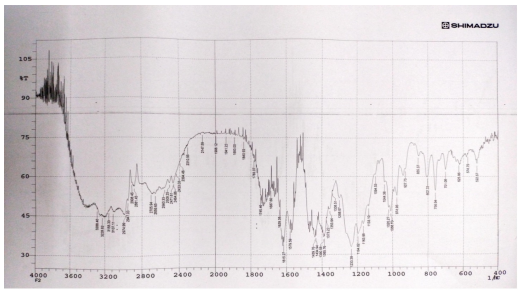


Figure 4.8: IR Spectra of F2

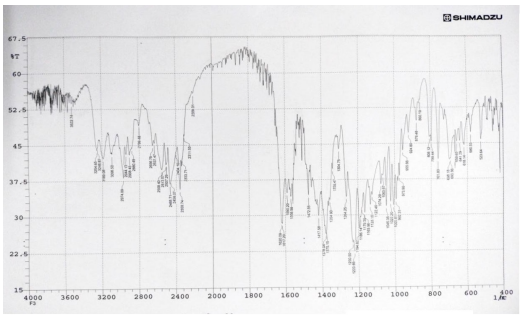


Figure 4.9: IR Spectra of F3

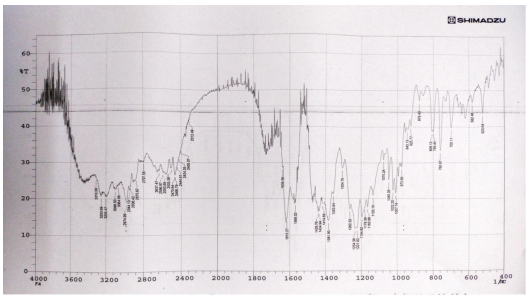


Figure 4.10: IR Spectra of F4

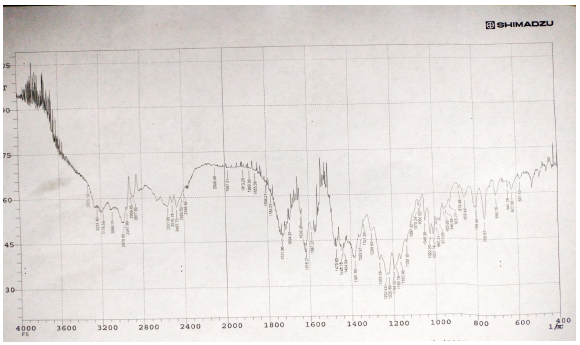


Figure 4.11: IR Spectra of F5

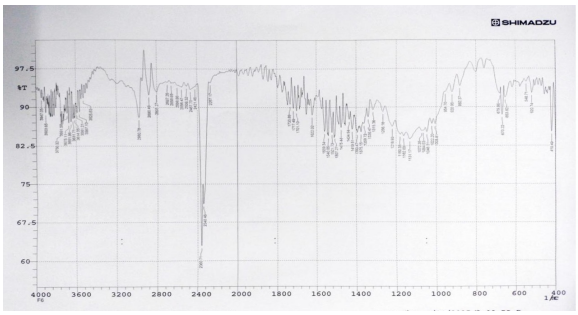


Figure 4.12: IR Spectra of F6

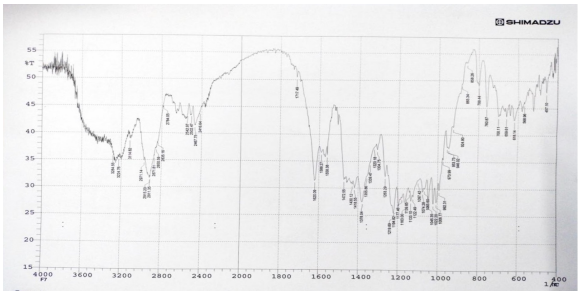


Figure 4.13: IR Spectra of F7

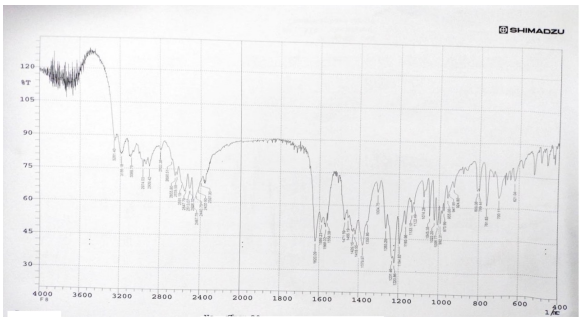


Figure 4.14: IR Spectra of F8

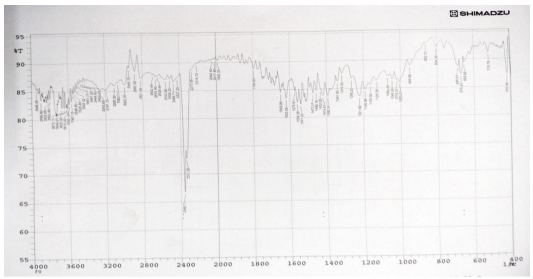


Figure 4.15: IR Spectra of F9

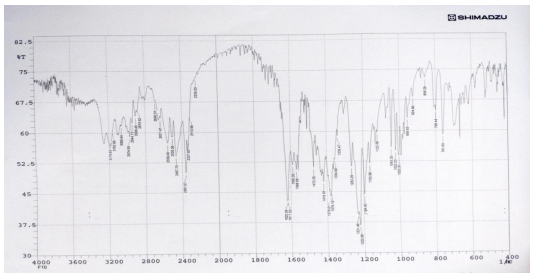


Figure 4.16: IR Spectra of F10

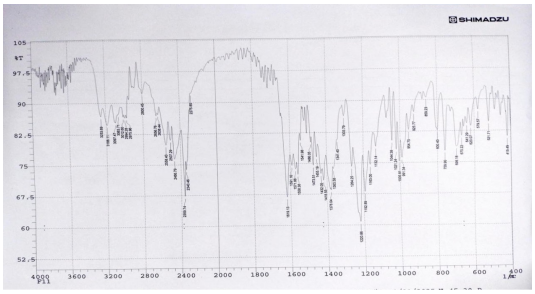


Figure 4.17: IR Spectra of F11

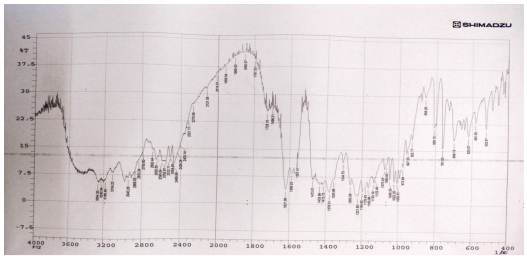
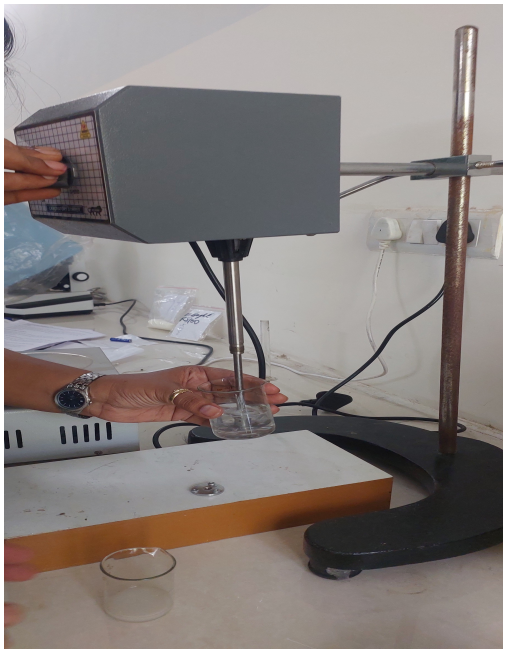


Figure 4.18: IR Spectra of F12

DEVELOPMENT METHODOLOGY OF RANITIDINE MICRO-SPONGES:

Ranitidine-loaded microsponges were formulated using the quasi-emulsion solvent diffusion technique, as illustrated in Figures 4.19, 4.20, and 4.21.



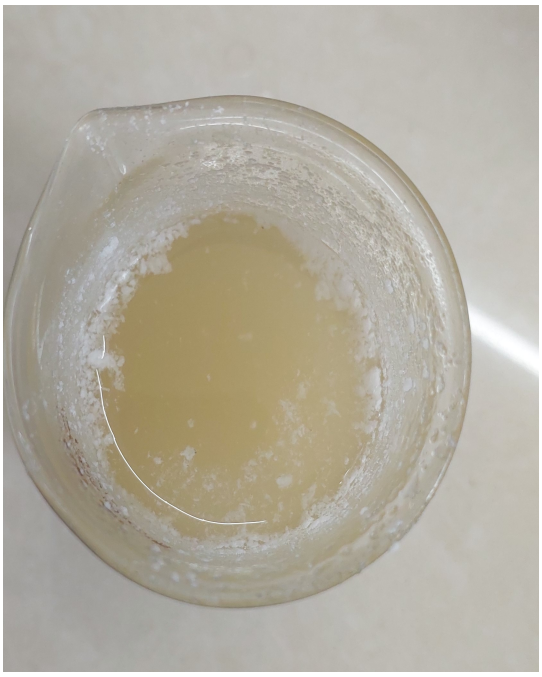


Figure 4.19: Quasi Emulsion Solvent Diffusion Method

Figure 4.20: Ranitidine Microsponges F7

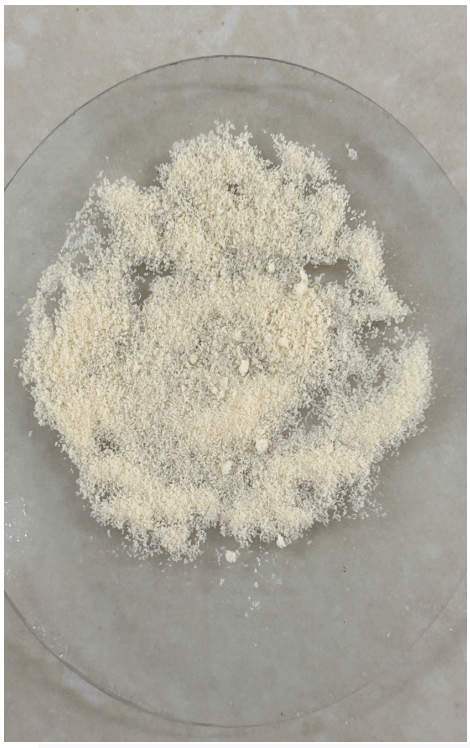


Figure 4.21: Ranitidine Microsponges F11

ASSESSMENT OF RANITIDINE FLOATING MICROSPONGES

Particle Size

The particle size of the formulated microsponges ranged from 25.50 ± 1.4 to 52.66 ± 1.1 µm. Among the formulations, F11 exhibited the largest particle size (52.66 ± 1.1 µm), whereas F6 showed the smallest size (25.50 ± 1.4 µm). The observed increase in particle size can be attributed to the rise in viscosity associated with higher polymer concentration, which results in the formation of larger droplets and consequently larger floating microsponges. The output can be found in the table 4.2 and figure 4.35 respectively.

Surface Morphology of Ranitidine HCl Microsponges

Microsponges in suspension were investigated for their external and internal morphology using scanning electron microscopy (SEM). Microsponges are symmetric in shape with smooth surface, porous architecture comprised of void space. Thus, the surface morphology of ranitidine HCl loaded floating microsponges was analyzed by SEM for all formulations from F1 to F12. Fig.38 shows the SEM image of formulations F1, F8 and F11. 12, the SEM analysis suggested that the microsponges formed were porous and nearly spherical. Pores were induced by solvent diffusion from microsponges surface. It was also showing the specific inside model of a cavity made of F1 and F11. They had a structure consisting of many internal pores which qualified them quite well to be called microsponges (see Figures 4.22 to 4.34).

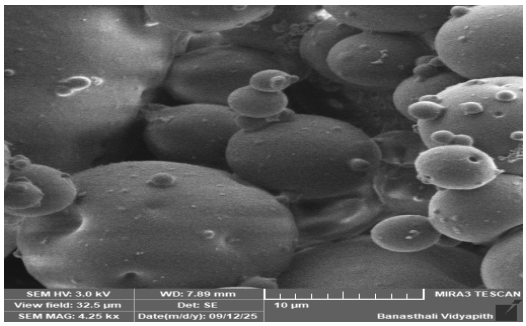


Figure 4.28: SEM Images of Floating microsponges of Formulation F7

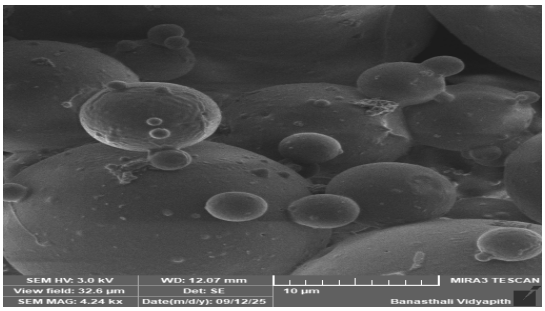


Figure 4.32: SEM Images of Floating microsponges of Formulation F11

% Yield

The % yield was found to be satisfactory in the range of 43.65 ±1.2% to 74.46±1.21% which is shown in the table 4.2 and figure 4.36. The formulation F11 shows the highest value containing the polymers eudragit RS 100.

Drug Content

The ranged from 67.74±0.14% − 92.87±0.12%. F11 showed to have the highest value having 92.87±0.12%. Table 4.2 and figure 4.37 display the results.

Drug Encapsulation Efficiency

The encapsulation efficiency was ranged from 48.18±0.69% to 63.58±0.74%. Entanglement efficiency was determined for all formulations and among them highest inefficiency always turned out to be F11 formulation, 63.58±0.74%. These results were revealed in the table 4.2 and the graph plotted as figure 4.38

Percentage Buoyancy

The results of this study are tabulated in table (4.2) and plotted graph shown as figure (4.39). Its results were between 60± (1.13)% andα87±(1.67)%, which is an acceptable range for any analytical tests. The highest value for F11 prepared with eudragit RS100 was 87±1.67%.

Table 4.2: Evaluation Data of Ranitidine Floating Microsponges

Formulation code	% Yield	Particle size (µm)	Drug content	Drug Encapsulation Efficacy	% Buoyancy
F1	43.65±1.20	42.25±1.0	78.52±0.15	53.08±0.11	83±1.50
F2	59.83±1.30	34.67±1.2	82.59±0.72	55.41±0.52	71±1.20
F3	73.23±1.50	32.60±1.1	90.15±0.04	62.0±0.83	69±1.10
F4	65.42±1.40	35.91±1.0	85.62±0.02	57.41±0.61	81±1.40
F5	67.79±1.50	32.50±1.3	84.25±0.22	56.45±0.44	75±1.60
F6	59.34±1.10	25.50±1.4	67.74±0.14	51.07±0.54	69±1.30
F7	45.37±1.30	32.48±1.2	78.32±0.15	54.98±0.31	71±1.16
F8	48.91±1.10	38.60±1.6	67.12±0.18	57.49±0.43	66±1.40
F9	49.62±1.11	42.64±1.1	71.92±0.15	56.08±0.54	68±1.51
F10	52.65±1.01	49.66±1.7	71.94±0.19	48.18±0.69	60±1.13
F11	74.46±1.21	52.66±1.1	92.87±0.12	63.58±0.74	87±1.67
F12	62.61±1.43	49.40±1.9	71.92±0.15	50.66±0.21	66±1.21

Figure 4.39: % Buoyancy of Ranitidine Floating Microsponges

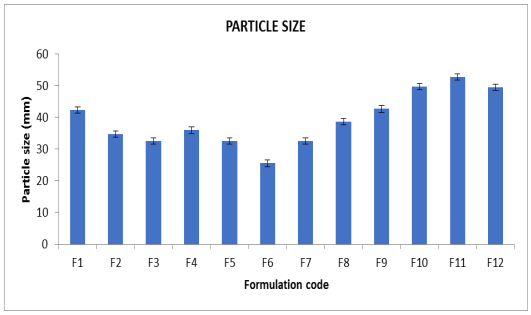


Figure 4.35: Particle Size of Ranitidine Floating Microsponges

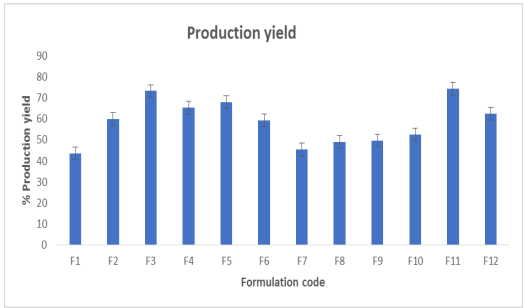


Figure 4.36: % Yield of Ranitidine Floating Microsponges

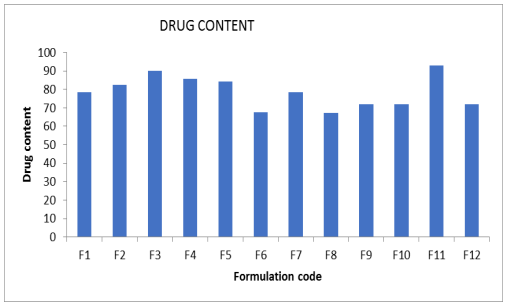


Figure 4.37: Drug Content of Ranitidine Floating Microsponges

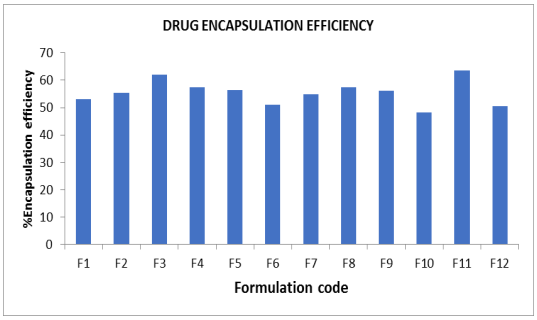


Figure 4.38: Drug Encapsulation Efficiency of Ranitidine Floating Microsponges

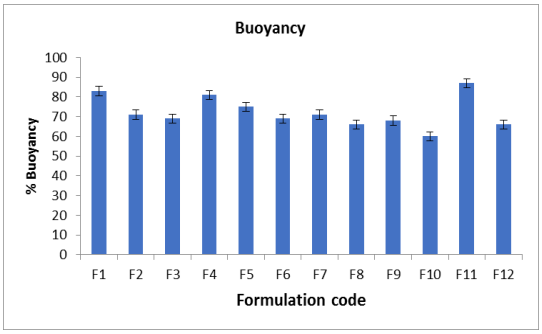


Figure 4.39: % Buoyancy of Ranitidine Floating Microsponges

Micromeritic Properties

The flow behavior of the microsponge powder blends was evaluated, and the findings are summarized in Table 4.3 and Figures 40–44. The bulk density values were found to range from 0.32 ± 0.01 to 0.39 ± 0.03 g/mL, while the tapped density varied between 0.37 ± 0.05 and 0.44 ± 0.03 g/mL. Carr's index was observed in the range of 8.33 to 16.21, and the Hausner's ratio ranged from 1.08 ± 0.03 to 1.16 ± 0.08. The angle of repose values were recorded between 20.5 ± 0.16° and 28 ± 0.61°.

These values indicate that the prepared microsponges possess acceptable micromeritic characteristics and exhibit good flow properties. The corresponding parameters for angle of repose and Hausner's ratio are presented in Tables 5 and 6, respectively.

Table 4.3: Micromeritic Properties

Formulation code	Bulk density	Tapped density	Hausner ratio	Carr's index	Angle of repose
F1	0.32 ±0.11	0.37 ±0.51	1.15±0.63	15.62 ±0.42	25.4 ±0.61

F2	0.33 ±0.3 5	0.37 ±0.5 3	1.12±0 .32	12.12 ±0.87	24.8 ±0.2 7
F3	0.37 ±0.2 4	0.41 ±0.1 2	1.11±0 .45	10.81 ±0.23	21.5 ±0.3 4
F4	0.36 ±0.4 3	0.42 ±0.2 1	1.13±0 .71	13.89 ±0.54	28.0 ±0.6 1
F5	0.39 ±0.3 6	0.43 ±0.3 6	1.10±0 .36	10.25 ±0.81	25.5 ±0.3 4
F6	0.38 ±0.2 7	0.44 ±0.3 4	1.15±0 .71	15.78 ±0.34	20.5 ±0.1 6
F7	0.37 ±0.2 4	0.43 ±0.3 4	1.16±0 .08	16.21 ±0.65	23.5 ±0.2 6
F8	0.38 ±0.2 6	0.41 ±0.4 3	1.13±0 .23	13.15 ±0.38	21.4 ±0.2 2
F9	0.37 ±0.2 1	0.42 ±0.3 4	1.13±0 .54	13.51 ±0.19	23.9 ±0.1 6
F10	0.35 ±0.2 6	0.40 ±0.3 5	1.11±0 .62	11.42 ±0.72	26.5 ±0.2 6
F11	0.36 ±0.2 5	0.39 ±0.3 3	1.08±0 .34	08.33 ±0.52	23.8 ±0.2 9
F12	0.38 ±0.2 9	0.44 ±0.3 7	1.15±0 .44	15.78 ±0.78	24.9 ±0.2 8

*Each reading is an average of 3 determination ± Standard deviation (SD)

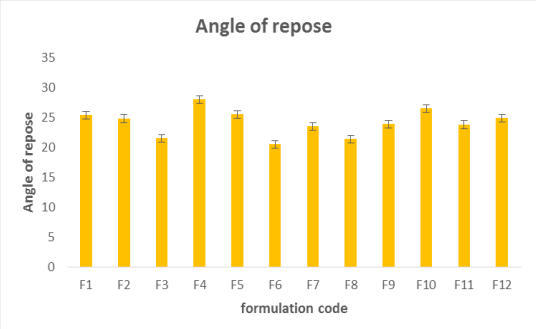


Figure 4.40: Angle of Repose Properties of Microsponges Formulation F1 to F12

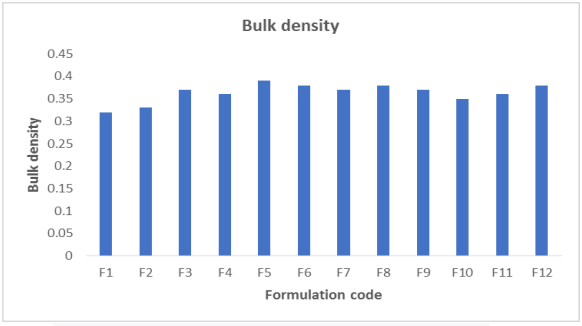


Figure 4.41: Bulk Density Properties of Microsponges Formulation F1 to F12

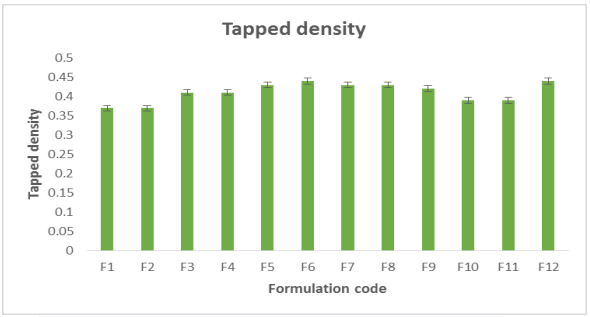


Figure 4.42: Tapped Density Properties of Microsponges Formulation F1 to F12

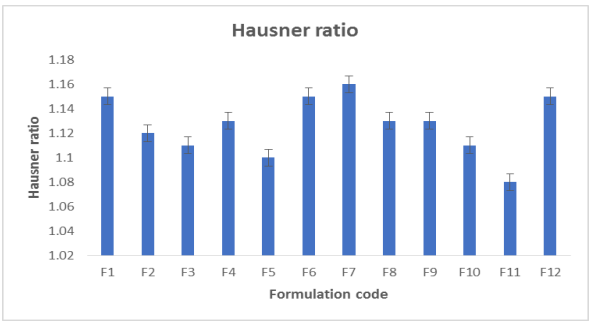


Figure 4.43: Hausner's Ratio Properties of Microsponges Formulation F1 to F12

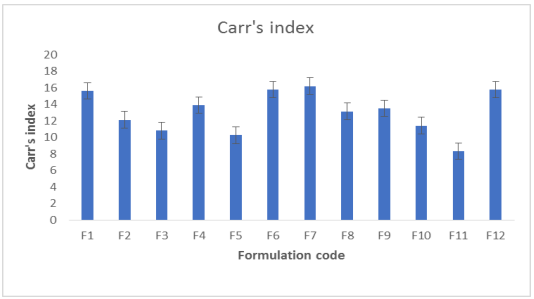


Figure 4.44: Carr's Index Properties of Microsponges Formulation F1 to F12

***In-Vitro* Dissolution Studies of Ranitidine Hydrochloride Floating Microsponges**

All formulation of ranitidine floating microsponges was study for in-vitro drug release, which were carried out at 0.1N HCl using (USP type-II) apparatus and the results are depicted in table 4.4 and table 4.5. The drug release obtained from the eighth hour formulation F1 (62.78±0.61) prepared with the polymers eudragit RS100,

HPMC K100 M and hydroxyl propyl cellulose is shown below. After which 49.5±1.1% drug release was observed at eighth hour formulation F2 prepared with polymers eudragit S. The maximum drug release was found out to be 73.5±1.09% with the eighth hour formulation F3 which had been prepared with the assistance of polymers ethyl cellulose. With the assistance of polymers eudragit S and ethyl cellulose, formulation F4 was observed to have 61.6±0.98% drug release. Polymer eudragit RS100 aided formulation F5 demonstrated with a 87.95±1.03% drug release. Among them the drug release of formulation using polymers eudragit RS and ethyl cellulose (formulation F6) was found to be 71.78±1.06% respectively. The drug release was found to be 58.56±0.99% for F7 prepared with the aid of polymers HPMC K100 M. It noted 64.12±1.4% drug release of form F8 theophylline was prepared by using polymer hydroxyl propyl cellulose. Eudragit RS100 and HPMC K100 M assisted formulation F9 exhibited a drug release of 66±0.99%. All the polymer eudragit RS and hydroxyl propyl cellulose Formulation F10 were found to have drug release of 62±1.2%. Release profile of F11 was 95.89±0.79% after eight hours while drug release for F12 was found to be67.45±1.4%. The curves of % Cumulative the %drug release (%) v/s time (hr) were drawn, as shown in figures 4.45 to figure 4.50.

Table 4.4: *In-vitro* Drug Dissolution Studies from formulation F1-F6

S. No.	Time (hr)	Cumulative Percent of drug release (%)					
		F1	F2	F3	F4	F5	F7
1	0	0±0	0±0	0±0	0±0	0±0	0±0
2	1	12.80±0.67	6.00±1.07	11.00±1.30	9.50±0.45	6.50±0.67	10.85±0.99
3	2	18.89±0.56	12.76±0.97	24.90±0.98	12.00±1.40	16.98±0.91	23.98±0.77
4	3	29.50±0.98	16.98±0.85	35.80±0.76	17.80±1.30	26.15±0.92	36.99±0.59
5	4	34.87±1.02	25.65±1.03	46.70±1.11	37.50±1.02	32.98±0.68	44.85±0.84
6	5	45.0	28.8	52.5	43.5	40.6	57.5
		0±0.89	7±1.23	0±0.88	0±1.01	7±1.10	0±0.79
7	6	54.50±0.35	35.00±0.98	65.67±0.76	47.95±0.99	55.50±0.95	62.84±0.89
8	7	60.50±0.78	39.50±1.11	69.82±0.99	54.50±0.76	64.85±1.05	71.78±1.01
9	8	62.78±0.61	49.50±1.10	73.50±1.09	61.60±0.98	87.95±1.03	76.78±1.06

*Each reading is an average of 3 determination ± Standard deviation (SD)

Table 4.5: *In-vitro* Drug Dissolution Studies from formulation F7-F12

S. No.	Time (Hr)	Cumulative Percent of drug release (%)					
		F7	F8	F9	F10	F11	F12
1	0	0±0	0±0	0±0	0±0	0±0	0±0
2	1	3.87±0.99	5.55±0.68	9.78±1.60	7.87±1.10	11.58±1.01	5.65±1.10
3	2	7.56±1.06	12.76±0.96	21.00±1.10	12.45±1.40	26.83±0.99	12.67±0.04
4	3	12.88±1.02	18.00±1.02	25.12±1.01	15.98±1.30	43.87±0.87	26.78±1.03
5	4	24.85±1.08	22.87±1.01	31.67±1.04	25.13±1.20	57.95±0.95	33.85±1.10
6	5	32.76±1.10	32.64±1.10	38.54±1.03	34.65±0.98	72.85±0.76	45.89±1.30
7	6	42.85±1.12	39.87±0.99	45.00±1.10	42.66±0.78	82.89±0.88	52.00±1.10
8	7	50.87±1.14	54.99±1.10	55.23±1.20	55.87±1.10	94.97±0.69	60.12±1.20
9	8	58.56±0.99	64.12±1.40	66.00±0.99	62.00±1.20	95.89±0.79	67.45±1.40

*Each reading is an average of 3 determination ± Standard deviation (SD)

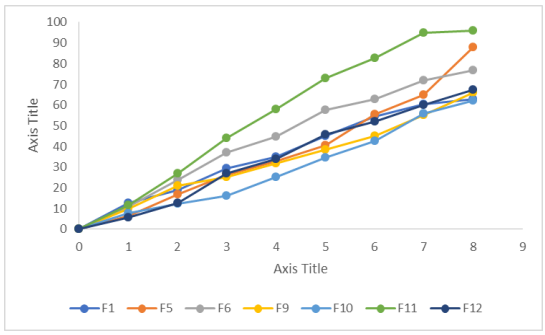


Figure 4.45: *In-vitro* Drug Profile of ERS 100+HPMC+HC, ERS 100+ES, ERS 100+EC, ERS 100+HPMC, ERS 100+HPC, ERS 100, ERS 100+ES+HPMC

Figure 4.46: *In-vitro* Drug Profile of F1, F8, F9 and F12

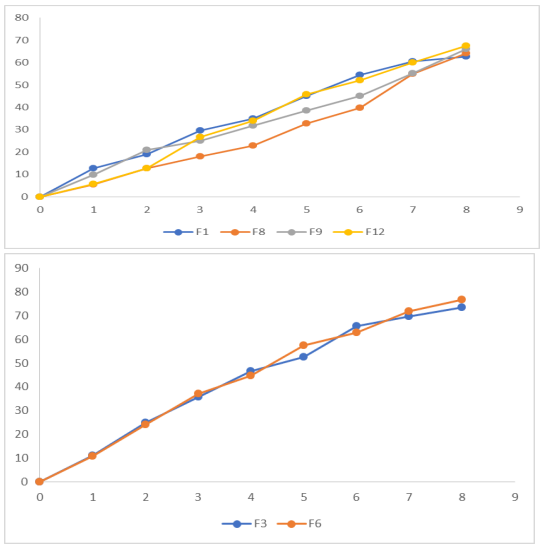


Figure 4.47: *In-vitro* Drug Profile of F3 and F6

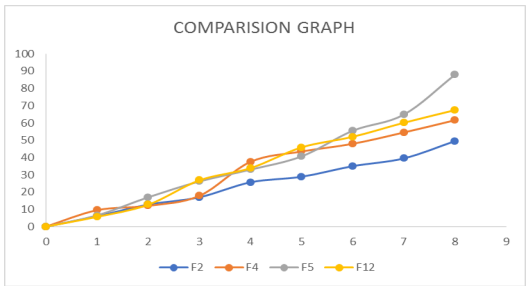


Figure 4.48: *In-vitro* Drug Profile of F2, F4, F5 and F12

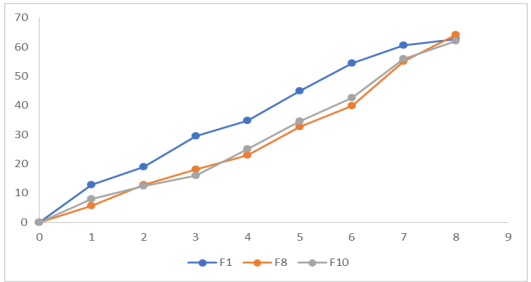


Figure 4.49: *In-vitro* Drug Profile of F1, F8 and F10

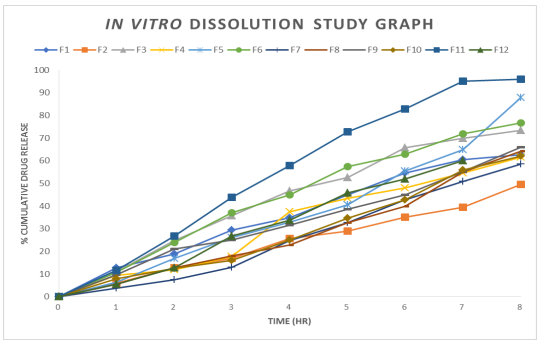


Figure 4.50: *In-vitro* Drug Profile of F1 to F12

Table 4.6: R^2 Value for Kinetic Modelling of Various Formulations

S. NO	Formulation code	R^2 Value			
		Zero order	First order	Higuchi	Korsemeyer Peppas
1.	F1	0.9864	0.9913	0.9541	0.9889
2.	F2	0.9932	0.9772	0.909	0.9948
3.	F3	0.9775	0.9877	0.9530	0.9855
4.	F4	0.9731	0.9732	0.8899	0.9383
5.	F5	0.9715	0.7904	0.8364	0.9912
6.	F6	0.9843	0.9912	0.9500	0.9885
7.	F7	0.9802	0.9497	0.8313	0.9869
8.	F8	0.9723	0.8950	0.8314	0.9891
9.	F9	0.9895	0.9448	0.9176	0.9864
10.	F10	0.9803	0.9380	0.8469	0.9655
11.	F11	0.9815	0.9157	0.9328	0.9869
12.	F12	0.9928	0.9814	0.9012	0.9881

Conclusion

Ranitidine hydrochloride is a competitive antagonist of histamine H_2 receptors and is commonly employed in the management of gastroesophageal reflux disease (GERD). and gastric ulcers is associated with some formulation-related limitations that can negatively impact its therapeutic efficacy. To overcome these shortcomings, floating

microsponge-based gastroretentive delivery system were developed to achieve retention in the gastric region for extended periods of time and improved drug release properties.

The present work focused on the formulation of floating microsponges of ranitidine hydrochloride using the quasi-emulsion solvent diffusion technique. Initial trials were carried out to select and optimize the appropriate polymer concentration. The developed formulations were then evaluated for various parameters, including drug content, percentage buoyancy, production yield, micromeritic properties, in vitro drug release behavior, and surface morphology using scanning electron microscopy (SEM). Furthermore, the formulations were also investigated for their *in-vivo* anti-ulcer activity.

FM11 was found to be the best of all formulations having desired drug release and good extent of buoyancy. The floating microsponge system was successfully developed for gastroretentive drug delivery.

FUTURE SCOPE

Further investigations are required to establish a reliable *in vitro–in vivo* correlation (IVIVC) in order to better predict the *in-vivo* performance of the developed formulation using suitable animal models are recommended to strengthen clinical applicability. Scale-up studies and clinical evaluation may further support the development of this gastroretentive microsponge system for improved management of gastric ulcers.

References

1. Alqahtani MS, Kazi M, Alsenaidy MA, Ahmad MZ. Advances in oral drug delivery. *Front Pharmacol.* 2021;12:618411.

2. Zanke AA, Shendge RS, Gaikwad DD. Gastroretentive drug delivery systems: A review. *J Drug Deliv Sci Technol.* 2022;68:102992.

3. Ahmad S, Ali M, Ali A, Sheikh S. Formulation and evaluation of ranitidine hydrochloride gastroretentive dosage forms. *Int J Pharm Sci Res.* 2016;7(3):1050–1058.

4. Mandal UK, Chatterjee B, Senjoti FG. Gastro-retentive drug delivery systems and ranitidine hydrochloride: Formulation approaches and evaluation. *Int J Pharm Investig.* 2016;6(3):119–126.

5. Sharma P, Singh A, Jain S. Microsponge drug delivery system: A comprehensive review. *Int J Pharm Sci Drug Res.* 2019;11(4):141–150.

6. Darekar AB, Saudagar RB. Microsponge drug delivery system: A review. *J Drug Deliv Ther.* 2019;9(3):491–498.

7. Nire N, Derle DV. Development and evaluation of floating microsponge of ranitidine hydrochloride. *Int J Pharm Pharm Sci.* 2014;6(6):477–482.

8. Shwetha TL, Biharee A, Prasad MP. Microsponge drug delivery system: An updated review. *Int J Appl Pharm.* 2022;14(4):1–9.

9. Biharee A, Shwetha TL, et al. Recent advances in microsponge-based drug delivery systems. *Asian J Pharm Clin Res.* 2023;16(2):15–23.

10. Kaity S, Maiti S, Ghosh AK, Pal D. Microsponge: A novel strategy for drug delivery system. *J Adv Pharm Technol Res.* 2010;1(3):283–290.

11. Sareen R, Nath K, Jain N. Microsponge drug delivery system: A review. *Int J Pharm Sci Rev Res.* 2014;24(1):73–82.

12. Srivastava R, Pathak K. Microsponge-based drug delivery systems: A review. *Drug Dev Ind Pharm.* 2012;38(9):1135–1145.