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DEVELOPMENT AND CHARACTERIZATION OF REBAMIPIDE LOADED GASTRO RETENTIVE FLOATING MICROSPHERE FOR ENHANCED GASTRIC RESIDENCE

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Abstract:
Rebamipide-loaded floating microspheres were successfully formulated and evaluated to develop a gastroretentive drug delivery system with improved retention and controlled release. Preformulation studies confirmed the physicochemical identity of Rebamipide, obtained as a white powder with a melting point of 290–292°C. Solubility analysis across multiple solvents and FT-IR characterization verified drug purity and compatibility with ethyl cellulose and HPMC, ensuring excipient safety. Analytical validation demonstrated linearity in the concentration range of 2–10 µg/mL with a regression equation of y = 0.064x + 0.002, confirming method reliability. Formulations F1–F6 were prepared and evaluated for percentage yield, drug entrapment efficiency, buoyancy and floating lag time. Among all batches, F5 exhibited the highest percentage yield (86.65 ± 0.52%), maximum drug entrapment efficiency (83.32 ± 0.65%), shortest floating lag time (48 ± 5 sec), and greatest buoyancy (84.25 ± 0.27%). Particle size analysis of F5 indicated microspheres (231.4 nm) with uniform distribution, while zeta potential (12.2 mV) suggested moderate stability supported by steric hindrance of polymers. In-vitro drug release studies demonstrated biphasic release with initial rapid release followed by sustained release up to 96.85% at 12 hours, fitting the Peppas–Korsmeyer kinetic model. Stability studies under accelerated conditions of formulation F5. Overall, optimized formulation (F5) demonstrated reproducible preparation, high yield, excellent drug entrapment, nanoscale particle size and superior floating behavior, making it a promising candidate for gastroretentive delivery of Rebamipide. These findings provide a strong foundation for further in vivo evaluation and clinical translation.

KEYWORDS: *Rebamipide, Gastroretentive, microspheres buoyancy and floating, Preformulation*

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INTRODUCTION:

The gastroretentive drug delivery system is a member of the class of oral controlled drug delivery systems that can pass through the gastric transit and remain in the stomach[1]. These dosage forms are also known as floating drug delivery systems because they have the ability to float in the stomach's contents and release the medication over an extended period of time in a regulated manner[2]. Depending on the kind and concentration of the swelling polymer that causes the medicine to diffuse and erode, the release rate will be regulated[3].

Rebamipide is a gastroprotective agent widely used in the treatment of gastric ulcers and gastritis[4]. However, it has a relatively short gastric residence time and limited bioavailability due to rapid gastric emptying[5]. Since Rebamipide primarily acts locally on the gastric mucosa, prolonged retention in the stomach can significantly enhance its therapeutic effectiveness[6].

Gastroretentive floating microspheres are designed to remain buoyant in gastric fluid for extended periods, thereby increasing gastric residence time and sustaining drug release[7]. This approach improves drug absorption at the site of action, reduces dosing frequency, enhances patient compliance, and minimizes systemic side effects[8]. Therefore, the development of Rebamipide-loaded floating microspheres is a promising strategy to improve gastric retention, controlled drug release, and overall therapeutic performance.

MATERIALS AND METHOD:

Preparation of floating microsphere of Rebamipide

Floating microspheres containing Rebamipide were successfully prepared by the solvent evaporation method, employing various proportions of hydroxypropyl methylcellulose (HPMC), ethyl cellulose (EC), and guar gum as polymeric carriers. The formulations (F1– F6) are outlined in Table 7.1, wherein the drug-to-polymer ratio was systematically varied to study its impact on microsphere characteristics.

For each formulation, Rebamipide (150 mg) along with respective amounts of HPMC, EC, and Guar gum (as per Table 7.1) were accurately weighed and dissolved in a solvent system composed of ethanol and dichloromethane in a 1:2 ratio. This resulted in a homogenous polymer-drug solution.

The resulting solution was slowly poured in a thin stream into an aqueous solution of 1% polyvinyl alcohol (PVA) under continuous stirring. The emulsification process was maintained at a stirring speed of 500 rpm and temperature of 27 ± 2°C for a duration of 3 hours, allowing for complete evaporation of the organic solvents. During the stirring process, floating microspheres were formed and gradually separated by decantation. Non-floating microspheres settled at the bottom and were discarded. The floating microspheres were collected, washed with distilled water, and then dried in a hot air oven at 40 ± 2°C overnight. The final product was stored in a desiccator for further evaluation.

Table 7.1: Formulations of floating microspheres of Rebamipide

Formulation Code	Rebamipide (mg)	HPMC (mg)	EC (mg)	Guar gum (mg)
F1	150	50	100	-
F2	150	50	150	-
F3	150	50	200	-
F4	150	100	50	10
F5	150	150	50	20
F6	150	200	50	30

RESULTS AND DISCUSSION:

It refers to the evaluation by sensory characters-taste, appearance, odor, feel of the drug. Solubility of the drug was determined by taking some quantity of drug in the test tube separately and added the 5 ml of the solvent (Water, ethanol, methanol, 0.1 N HCl, 0.1 N NaOH, chloroform and Phosphate buffer pH 7.2). Melting point of Rebamipide was found 290-292°C. Rebamipide was obtained as white powder. It was identified from the result of IR spectrum as per specification. The IR spectrum of sample drug shows the peak values which are characteristics of the drug. the FT-IR analysis confirms that Rebamipide is compatible with ethyl cellulose and HPMC, and the excipients do not induce any structural modification of the drug, supporting their safe use

in the formulation. loss on drying of Rebamipide was found to be 0.625±0.005. Moisture content of Rebamipide was 0.058. The linearity of the analytical method for Rebamipide was evaluated in the concentration range of 2–10 µg/mL. The calibration curve was constructed by plotting concentration versus absorbance (or peak area), and the regression analysis yielded the equation: y = 0.064x + 0.002.

Percentage yield: The percentage yield of formulations F1–F6 was determined to evaluate the efficiency of the preparation method. The results revealed noticeable variation among the batches, indicating the influence of formulation variables on product recovery. Formulation F5 exhibited the highest percentage yield (86.65 ± 0.52%), suggesting optimal polymer concentration and processing conditions, which minimized material loss during preparation. The high yield reflects efficient drug entrapment and reduced handling loss. Formulation F3 (83.32 ± 0.45%) and F2 (78.85 ± 0.36%) also demonstrated comparatively good yields, indicating satisfactory formulation performance. In contrast, F6 showed the lowest yield (70.23 ± 0.63%), followed by F4 (75.21 ± 0.33%) and F1 (75.65 ± 0.85%). The reduced yield in these batches may be attributed to higher polymer viscosity, aggregation, loss during filtration, adhesion to equipment surfaces, or inefficient crosslinking/encapsulation conditions. The low standard deviation values (±0.33 to ±0.85) indicate good reproducibility of the preparation method. Overall, the results suggest that formulation variables significantly affect production efficiency and F5 represents the optimized batch in terms of % yield.

Drug entrapment: The drug entrapment efficiency of Rebamipide-loaded microspheres (F1–F6) was evaluated to determine the ability of the polymer system to incorporate and retain the drug within the matrix. The results demonstrated variation among the formulations, reflecting the influence of formulation variables such as polymer concentration, drug–polymer ratio, and preparation conditions. Among all batches, F5 showed the highest drug entrapment efficiency (83.32 ± 0.65%), suggesting optimal formulation parameters that enhanced drug incorporation and minimized drug loss during preparation. The improved entrapment may be attributed to an appropriate polymer concentration, which facilitated effective matrix formation and reduced drug diffusion into the external phase during solvent evaporation. Formulations F2 (75.65 ± 0.25%) and F4 (74.65 ± 0.85%) exhibited satisfactory entrapment efficiency, indicating stable microsphere formation with moderate drug retention. F1 (73.32 ± 0.36%) also demonstrated acceptable encapsulation performance. However, F6 (69.85 ± 0.74%) and F3 (71.15 ± 0.45%) showed comparatively lower entrapment efficiency. The reduced drug loading in these batches may be due to insufficient polymer content, higher porosity, rapid solvent diffusion, or improper emulsification conditions, leading to drug leakage during preparation. The low standard deviation values across all batches indicate good reproducibility and reliability of the preparation method. The results suggest that formulation variables significantly influence drug entrapment efficiency, and F5 was identified as the optimized formulation based on maximum encapsulation efficiency.

Percentage Buoyancy and floating lag time of floating microsphere: The floating behavior of Rebamipide-loaded microspheres was evaluated by determining the floating lag time (FLT) and percentage buoyancy, which are critical parameters for gastroretentive drug delivery systems. The floating lag time represents the time required for microspheres to rise to the surface of the dissolution medium. Among all formulations, F5 showed the shortest floating lag time (48 ± 5 sec), indicating rapid buoyancy due to optimal polymer concentration and efficient entrapment of air within the microsphere matrix. In contrast, F1 exhibited the highest lag time (88 ± 5 sec), suggesting relatively slower hydration and swelling behavior. Percentage buoyancy indicates the ability of microspheres to remain floating over a specified period. F5 demonstrated the highest buoyancy (84.25 ± 0.27%), confirming its excellent floating capacity and prolonged gastric retention potential. The higher buoyancy may be attributed to the appropriate balance of hydrophilic and hydrophobic polymers, leading to lower density and improved matrix integrity. Formulations F2, F4, and F6 showed moderate floating performance, while F3 exhibited comparatively lower buoyancy (70.36 ± 0.35%), possibly due to insufficient polymer concentration or faster medium penetration leading to partial sinking. The results indicate that polymer composition and formulation variables significantly influence floating characteristics. Based on both floating lag time and percentage buoyancy, F5 was identified as the optimized formulation, demonstrating rapid floating and sustained buoyancy suitable for gastroretentive drug delivery. The maximum percentage yield, drug entrapment, percentage buoyancy and less floating lag time was found to be formulation F5 in floating microsphere. The optimized formulation of batche subjected to further studies.

Particle size analysis:

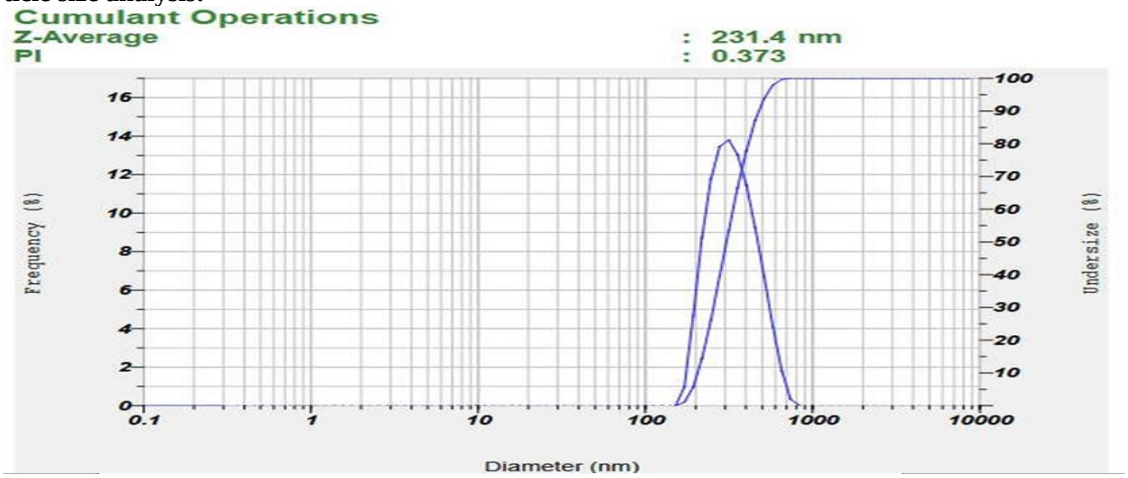

Figure 8.4: Particle size data of optimized microsphere formulation F5

Zeta Potential

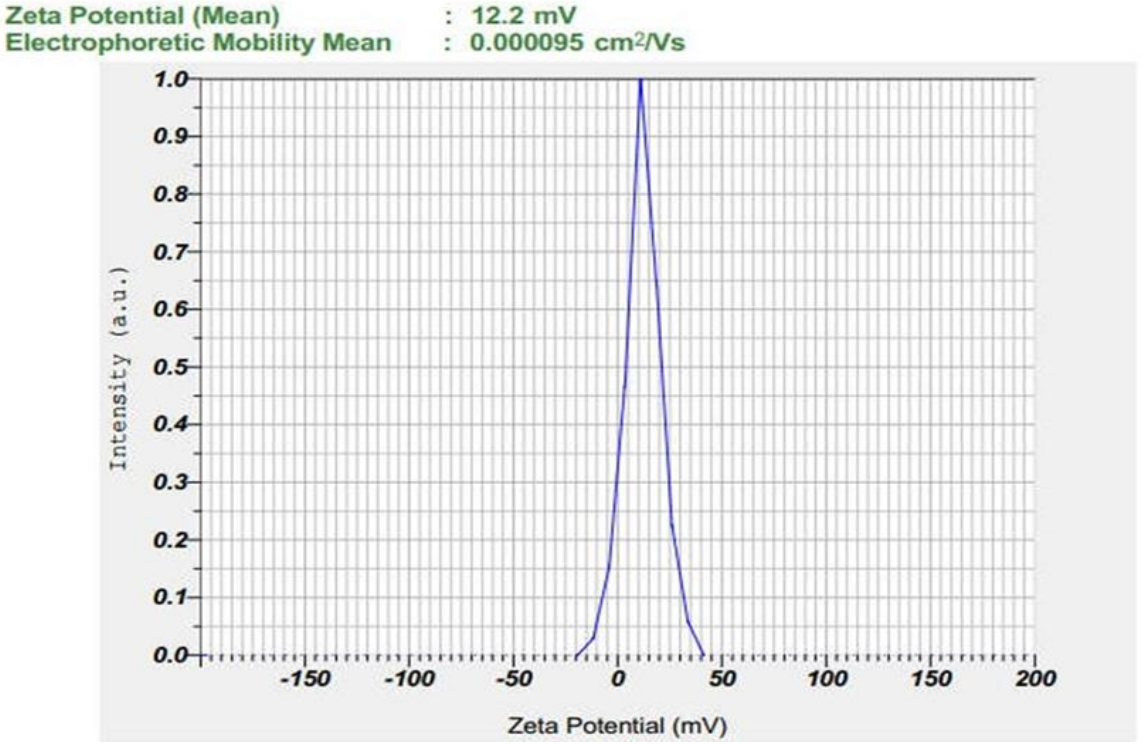

Figure 8.5: Zeta potential data of floating microsphere F5

The optimized formulation (F5) showed a mean particle size of 231.4 nm, indicating the formation of uniformly distributed nanosized particles. The particle size plays a crucial role in drug release behavior, stability, and bioavailability. A particle size in the nanometer range enhances surface area, promotes better drug dissolution, and contributes to improved gastric retention in floating drug delivery systems. The obtained size suggests efficient emulsification and appropriate polymer concentration during formulation development. The zeta potential of F5 was found to be 12.2 mV, which reflects the surface charge and stability of the formulation. Zeta potential is an important parameter in determining colloidal stability, as it indicates the degree of electrostatic repulsion between particles. Although absolute values above ±30 mV generally indicate high electrostatic stability, the observed value of 12.2 mV suggests moderate stability, which may be supported by steric stabilization provided by polymers such as HPMC or ethyl cellulose. In polymeric systems, steric hindrance often contributes significantly to stability even when zeta potential values are moderate. The combination of nanoscale particle size and acceptable zeta potential indicates that formulation F5 possesses suitable physicochemical properties, contributing to improved drug entrapment, controlled drug release, and floating behavior.

Shape and surface of microspheres by scanning electron microscopy (SEM)

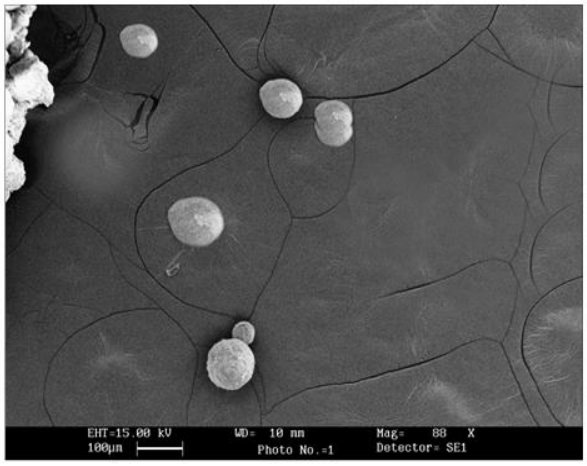

Figure 8.6: Graph of scanning electron microscopy of optimized formulation F5

***In-vitro* drug release study of Rebamipide loaded microsphere**

Table 8.4: Release Study data of formulation F1-F6

Time (Hrs)	F1	F2	F3	F4	F5	F6	Marketed Formulation (Rebamipide 100 mg Tablet)
0.5	38.45	41.32	39.85	24.65	12.45	16.85	72.65
1	52.36	54.85	50.65	34.25	18.75	22.36	88.45
2	61.85	66.32	63.25	45.85	28.65	33.45	97.85
4	73.25	78.65	72.45	58.36	42.85	49.65	–
6	84.32	87.45	82.65	71.25	56.98	63.25	–
8	92.65	95.32	90.85	86.45	68.75	74.85	–
10	97.85	98.65	97.25	96.85	78.45	83.65	–
12	99.25	99.65	99.12	99.05	96.85	89.45	–

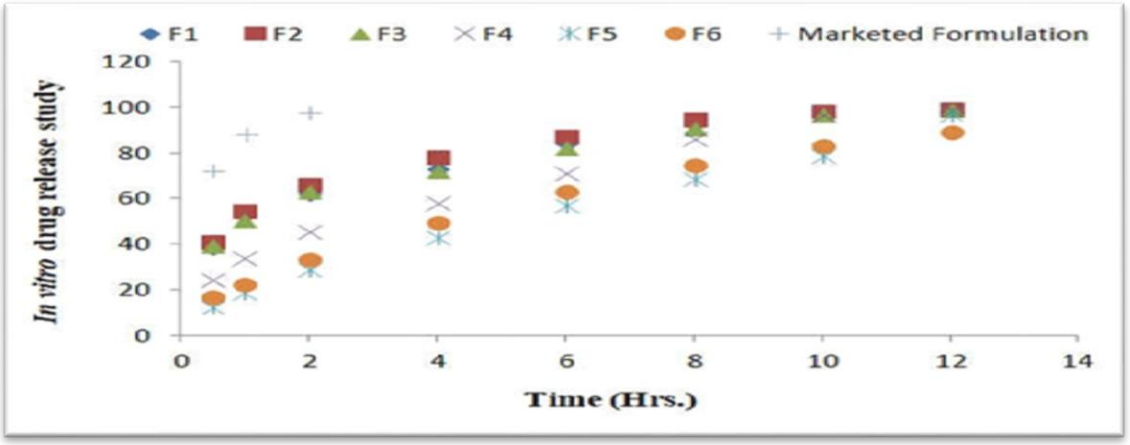

Figure 8.7: Graph of release study of formulation F1-F6

Table 8.5: Release Kinetics of optimized formulation of microsphere F5

Time (h)	Square Root of Time (h)1/2	Log Time	Cumulative% Drug Release	Log Cumulative % Drug Released	Cumulative % Drug Remaining	Log Cumulative % Drug Remaining
0.5	0.707	-0.301	12.45	1.095	87.55	1.942
1	1	0	18.75	1.273	81.25	1.910
2	1.414	0.301	28.65	1.457	71.35	1.853
4	2	0.602	42.85	1.632	57.15	1.757
6	2.449	0.778	56.98	1.756	43.02	1.634
8	2.828	0.903	68.75	1.837	31.25	1.495
10	3.162	1	78.45	1.895	21.55	1.333
12	3.464	1.079	96.85	1.986	3.15	0.498

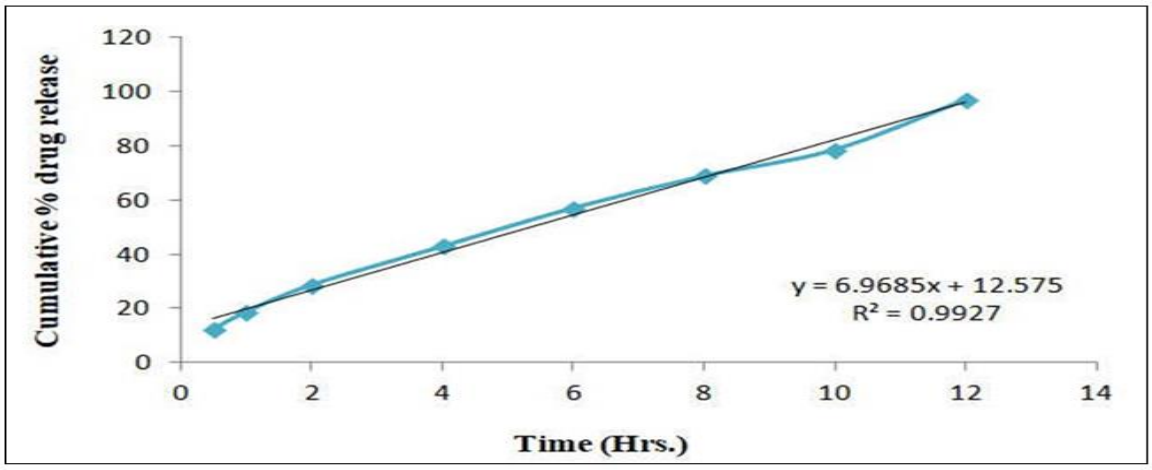

Figure 8.8: Zero order release kinetics graph of optimized formulations

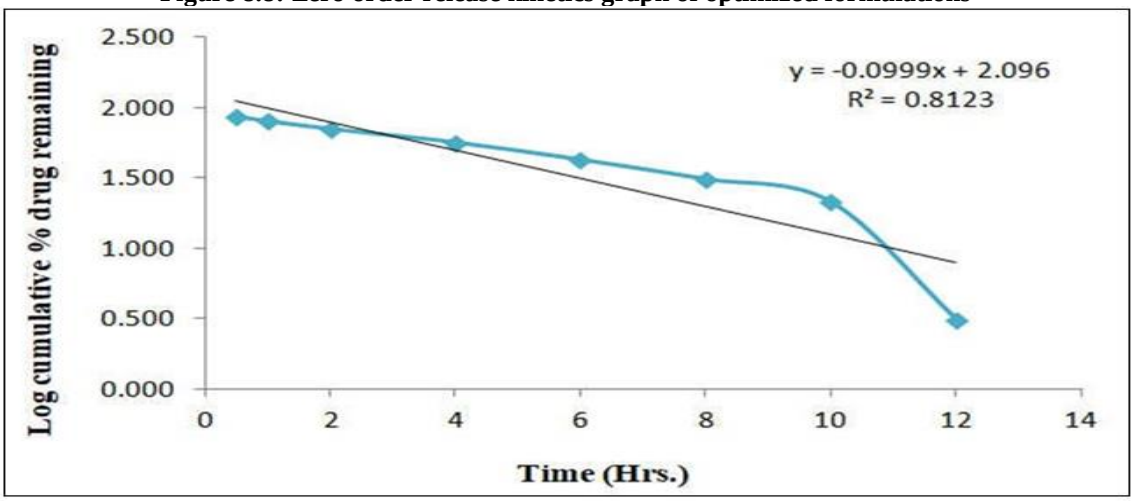

Figure 8.9: First order release kinetics graph of optimized formulations

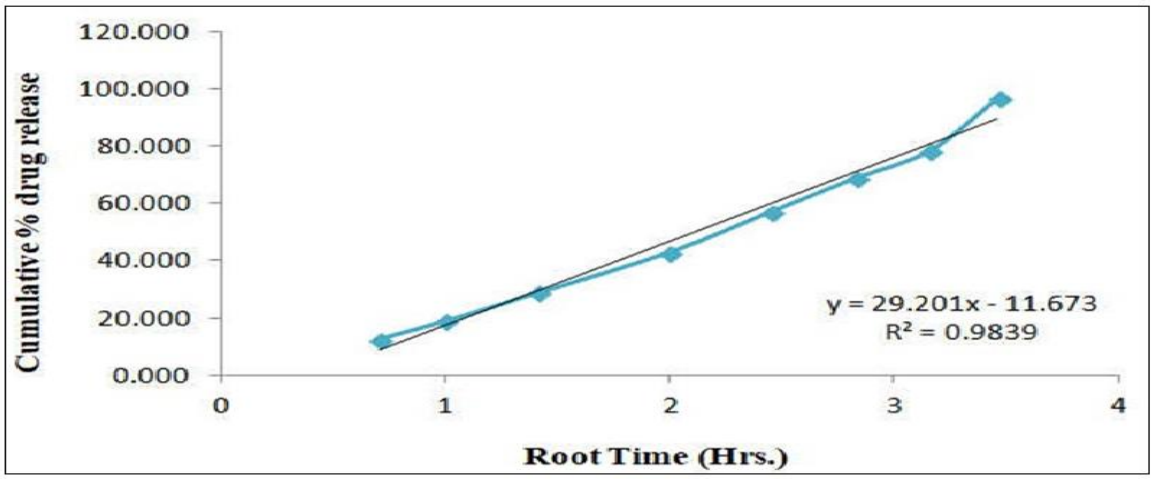

Figure 8.10: Higuchi release kinetics graph of optimized formulations

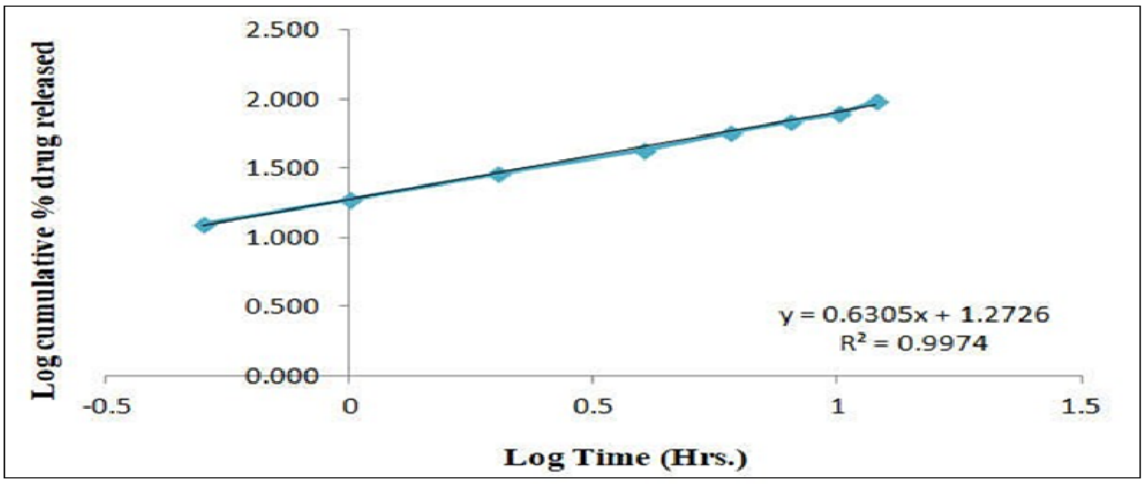

Figure 8.11: Graph of Korsmeyer Peppas release kinetics of optimized formulations

Stability studies of final formulation

The stability study of the optimized formulation (F5) was carried out under accelerated conditions (40 ± 2°C / 75 ± 5% RH) for a period of three months to evaluate its physicochemical stability and performance. Throughout the study period, no change in physical appearance was observed, and the microspheres remained white and spherical, indicating good physical stability and absence of aggregation or degradation. The percentage drug content showed a slight decrease from 99.12% (initial) to 97.25% at the end of 3 months. However, the reduction was minimal and within acceptable pharmacopeial limits (90–110%), suggesting that the drug remained chemically stable under accelerated conditions. Similarly, drug entrapment efficiency showed a marginal decrease from 83.32% to 81.65%, which may be attributed to minor moisture uptake or slight polymer relaxation during storage. The reduction was not significant, indicating that the polymer matrix effectively retained the drug. The floating lag time increased slightly from 48 sec to 54 sec over 3 months. This minor increase may be due to slight changes in surface characteristics or hydration behavior of the polymer. However, the values remained within acceptable limits, confirming maintained floating performance. The percentage buoyancy showed a minimal decrease from 84.25% to 82.36%, indicating that the formulation retained its gastroretentive capability during storage. The drug release at 12 hours decreased slightly from 96.85% to 94.85%, suggesting negligible impact of storage conditions on the sustained release profile.

CONCLUSION:

From the overall evaluation, it can be concluded that Rebamipide-loaded floating microspheres were successfully formulated and characterized. Among all the formulations, F5 was identified as the optimized batch due to its highest percentage yield, maximum drug entrapment efficiency, rapid floating with prolonged buoyancy, controlled and sustained drug release profile, appropriate particle size, acceptable zeta potential, and satisfactory stability under accelerated conditions.

The developed floating microspheres demonstrate promising potential as a gastroretentive drug delivery system for Rebamipide, which may improve therapeutic efficacy, prolong gastric

residence time, and enhance patient compliance. The optimized formulation may be considered suitable for further in-vivo studies and scale-up development.

CONFLICT OF INTERESTS

There no any Conflict of interests.

REFERENCES:

1. Bardonnet PL, Faivre V, Pugh WJ, Piffaretti JC, Falson F. Gastroretentive dosage forms: Overview and special case of Helicobacter pylori. Journal of controlled release. 2006 Mar 10;111(1-2):1-18.
2. Mayavanshi, A. V., & Gajjar, S. S. (2008). Floating drug delivery systems to increase gastric retention of drugs: A review. Research Journal of Pharmacy and Technology, 1(4), 345-348.
3. Desai S, Bolton S. A floating controlled-release drug delivery system: in vitro-in vivo evaluation. Pharmaceutical research. 1993 Sep; 10(9):1321-5.
4. Dubey S, Datt N, Alka, Saraf SK, Chaudhri SK. Colon-Targeted Eudragit-S-100 Coated Nanostructured Lipid Carriers for Enhanced Rebamipide Delivery in Ulcerative Colitis. BioNanoScience. 2025 Dec;15(4):597.
5. Kak M. Rebamipide in gastric mucosal protection and healing: An Asian perspective. World Journal of Gastrointestinal Pharmacology and Therapeutics. 2025 Mar 5;16(1):101753.
6. Mizobuchi S, Hirose K, Ishii N, Kawano Y, Hanawa T. Preparation and characterization of the ground mixture of rebamipide commercial tablets and hydroxypropyl Cellulose-SSL by ball-milling: application to the dispersoid of mouthwash suspension. European Journal of Pharmaceutics and Biopharmaceutics. 2025 Jan 1;206:114584.
7. Yadav R, Bhowmick M, Rathi V, Rathi J, Design and characterization of floating microspheres for rheumatoid arthritis, Journal of Drug Delivery and Therapeutics 2019; 9(2-s):76-81.
8. Andrew EC, et al., Preparation and In Vitro Evaluation of Ranitidine Floating Microspheres in The Treatment of Gastrointestinal Infections. Mathews J Pharma Sci.2024; 8(2):1-13.