Development and Evaluation of Floating Alginate Beads of Esomeprazole

Bhagyashri P. Mahabale ., *Umesh T. Jadhao., Gunesh. N. Dhembre., D. A. Rathod., S. A. Wathore. S. T. Thoke

Department of Pharmaceutics SDMVMS SVP College of Pharmacy Hatta, Hingoli, India

***Corresponding Author**

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ABSTRACT

The aim of the study was the Development and Evaluation of Floating alginate beads of Esomeprazole. The floating alginate beads of Esomeprazole (F1–F6) were prepared in six different batches using varying concentration of sodium alginate and HPMC K4M using inotropic gelation technique. The floating alginate beads of Esomeprazole (F1–F6) were extensively evaluated. Micrometric properties such as angle of repose, bulk density, tapped density, Carr's index, and Hausner's ratio confirmed good flow and packing behavior across all formulations, with F5 exhibiting the most favorable characteristics. The drug entrapment efficiency increased with polymer concentration, reaching a maximum of 87.96 ± 1.05% for F5.Floating lag time decreased with increasing polymer content, with F5 showing the shortest lag time (33.8 ± 1.4 sec).The total floating duration improved significantly with HPMC content, with F5 and F6 maintaining buoyancy for over 12 hours.Particle size analysis revealed a trend of decreasing size with increasing polymer content, with F5 having the smallest average size (190.1 ± 2.3 µm). Additionally, percent yield improved with higher polymer concentrations, with F5 again demonstrating the highest yield (89.62 ± 1.10%).The optimized formulation F5, containing 2% sodium alginate and 1% HPMC K4M, exhibited maximum sustained release (98.26% over 12 hours), balancing matrix stability and drug dissolution

Keywords-. Alginate beads, Floating Drug Delivery, Esomeprazole, Micrometric properties

INTRODUCTION

A floating drug delivery system (FDDS) is a type of drug delivery system designed to prolong the residence time of drugs within the gastrointestinal (GI) tract, particularly the stomach. The primary objective of FDDS is to enhance the bioavailability and efficacy of drugs, particularly those with narrow absorption windows or those that degrade in the acidic environment of the stomach.[1-3]

In FDDS, the drug is typically incorporated into a formulation that possesses low density or contains gas-generating agents, allowing it to float on the gastric contents after ingestion. This buoyancy ensures that the drug remains in the stomach for an extended period, thereby prolonging its release and absorption.[4-5]

Floating alginate beads are a type of drug delivery system designed to remain buoyant on the surface of gastric fluid for an extended period of time. These beads are typically prepared using sodium alginate, a natural polysaccharide derived from brown seaweed, along with other excipients and active ingredients. The primary component of floating alginate beads, sodium alginate serves as the matrix material responsible for forming the bead structure. Calcium salts, such as calcium chloride or calcium carbonate, are commonly used as cross-linking agents to gel the alginate and form stable beads. Drugs or other active ingredients can be incorporated into the alginate matrix to achieve controlled release or targeted delivery. Additional excipients such as gel-forming agents, pore-forming agents, and release modifiers may be included to optimize bead characteristics and drug release kinetics.[6-7]

Gastroretentive floating beads are small, solid and free flowing particulate carriers, on which the drug is coated

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or encapsulated in the core of beads. Beads can provide controlled / sustained release properties and as such bioavailability of drugs are enhanced. Gastro retentive beads are not just to sustain the drug release, but also to enhance gastric residence of the dosage forms until the entire drugs are completely released at the desired period of time. Gastroretentive floating beads are typically designed using polymers such as alginate, chitosan, or hydroxypropyl methylcellulose (HPMC). The beads are formulated to contain a gas-generating agent like sodium bicarbonate, which releases CO2 in the acidic environment of the stomach. This gas generation reduces the density of the beads, allowing them to float on the gastric fluid. The buoyancy ensures prolonged gastric retention, providing a sustained release of the drug.[8]

MATERIALS AND METHOD

Materials

Esomeprazole was obtained as gift samples from Cipla Ltd, Goa, HPMC purchased from Colorcon Asia Pvt Ltd, Sodium Alginate purchased from S.D. Fine Chem. Ltd, all other chemicals are analytical grade.

Methods

Determination of Melting Point

Melting point of Esomeprazole was determined by capillary method. Fine powder of Esomeprazole was filled in the glass capillary tube which was sealed at end. The capillary tube is tied to thermometer and the thermometer was placed in melting point apparatus. The powder at what temperature it will melt was noticed as melting temperature of drug.

Solubility

Solubility of Esomeprazole was determined in different aqueous and non-aqueous solvents. Solubility studies performed by taking excess amount of Esomeprazole in different beakers containing the solvents.

UV Spectroscopy

A stock solution of Esomeprazole was prepared by using 0.1 N Hcl. Then UV Spectrum was scanned in the range 200-400nm by using Shimadzu 1601.

Drug Excipients Compatibility Studies

Drug-excipient compatibility studies are an essential part of preformulation and formulation development processes in the pharmaceutical industry. These studies assess the compatibility of a drug substance with various excipients that are used to formulate the final dosage form. he primary purpose of drug-excipient compatibility studies is to evaluate potential interactions between the drug substance and excipients. These studies aim to identify any chemical, physical, or mechanical interactions that could affect the stability, efficacy, or safety of the final dosage form. By assessing compatibility early in the development process, formulation scientists can make informed decisions regarding excipient selection, formulation design, and process optimization. Compatibility study of drug with the excipients was determined by I.R. Spectroscopy (Shimadzu, Japan). The pellets were prepared at high compaction pressure by using KBr and the ratio of sample to KBr is 1:100. The pellets thus prepared were examined and the spectra of the drug and other ingredients in the formulations were compared with that of the pure drug.[9-11]

Formulation of Esomeprazole Floating Alginate Beads

Floating alginate beads of Esomeprazole were prepared using the ionotropic gelation technique. Initially, accurately weighed quantities of Esomeprazole were dispersed in distilled water under magnetic stirring to form a uniform drug solution. To this, the required concentration of Sodium Alginate (as per the formulation F1–F6) was slowly added with continuous stirring to obtain a homogenous polymeric solution. For formulations F4 to F6, the required amount of HPMC K4M was also incorporated as a secondary polymer to enhance the gel

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strength and sustain the drug release. To impart floating properties, sodium bicarbonate was added to the polymer-drug dispersion and mixed thoroughly. The final mixture was allowed to hydrate for 30 minutes to remove entrapped air and ensure complete polymer swelling. The prepared dispersion was then extruded dropwise through a 29-gauge hypodermic needle into 2% w/v calcium chloride solution maintained under gentle stirring. Upon contact with the calcium chloride, instantaneous gelation occurred due to ionic cross- linking between calcium ions and alginate chains, forming spherical beads. The beads were allowed to remain in the calcium chloride solution for 30 minutes to complete the curing process, after which they were collected by filtration and washed thoroughly with distilled water to remove excess calcium chloride. Finally, the beads were air-dried at room temperature for 24 hours and stored in airtight containers for further evaluation. The composition of different formulation of Esomeprazole floating beads is shown in the table 1.[12-13]

Table 1: Formulation of Floating Beads of Esomeprazole

Ingredients (mg)	F1	F2	F3	F4	F5	F6
Esomeprazole	40	40	40	40	40	40
Sodium Alginate (%w/v)	1	1.5	2	2	2	2
HPMC K4M (%)	-			0.5	1	1.5
Calcium Chloride (%w/v)	2	2	2	2	2	2
Sodium Bicarbonate (%w/v)	0.5	0.5	0.5	0.5	0.5	0.5
Distilled Water (q.s.) (ml)	100	100	100	100	100	100

Evaluation Floating Beads

Drug Entrapment Efficiency (%):

To determine the drug entrapment efficiency (%DEE) of the prepared floating alginate beads of Esomeprazole, a known weight of the dried beads (usually 100 mg) was accurately weighed and crushed using a mortar and pestle to obtain a fine powder. This powder was then transferred into a 100 ml volumetric flask containing 0.1 N hydrochloric acid (pH 1.2), which serves as the dissolution medium. The mixture was sonicated for 30 minutes to ensure complete extraction of the entrapped drug and then stirred continuously for another 1 hour using a magnetic stirrer to achieve thorough drug release from the polymeric matrix. After complete extraction, the resulting solution was filtered through Whatman filter paper or centrifuged to remove undissolved particles. The clear filtrate was appropriately diluted and analyzed spectrophotometrically at 301 nm (the λmax of Esomeprazole) using a UV-visible spectrophotometer. The actual drug content was calculated using a standard calibration curve of Esomeprazole prepared in the same solvent. The drug entrapment efficiency was then calculated using the following formula.[14]

Entrapment Efficiency % = (Actual drug content/Theoretical drug content) × 100

Floating Lag Time

In this parameter 100 mg of beads formulation were added into the 900 ml dissolution vessel containing 0.1N HCl at 37^0C. It was the time taken by beads to emerge on surface of dissolution medium is noated as floating lag time.[15]

Total Floating Duration

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In this parameter 100 mg of beads formulation was added into the 900 ml dissolution vessel containing 0.1N HCl at 37^0C. The time for which the formulation remains constantly floating on surface of dissolution medium was referred as duration of floating.[16]

Particle Size Analysis

The particle sizes of drug loaded beads were measured by an optical microscope fitted with an ocular and stage micrometer and particle size distribution was calculated. In all measurements at least 50 beads in five different fields were examined. Each experiment was carried out as triplicate.[17]

Determination of Percentage Yield

The prepared beads were collected and weighed. The measured weight was divided by the total amount of all non-volatile components, which were used for the preparation of the beads. Percentage Yield was determined using following formula. [18]

Percentage yield = Actual weight of product / Total weight of drug and polymer X 100

In-vitro Dissolution Studies:

In-vitro dissolution studies were performed for all the formulations using USP type II apparatus. An accurately weighed floating alginate beads were taken into 900ml 0.1 N Hcl buffer (pH 1.2). The temperature was maintained at 37 ˚± 0.5 ℃ and stirred at a speed of 50 rpm. At specified time intervals 5 ml of sample was withdrawn, at the same time 5 ml of fresh dissolution media was added to maintain sink condition. The collected samples were filtered if necessary and analyzed at 301 nm using UV spectrophotometer against 0.1 N Hcl buffer (pH 1.2) taken as blank.[19, 21]

Stability Study

The accelerated stability studies were carried out according to ICH guidelines on optimized formulation. The formulation was packed in strip of aluminum foil and was stored in stability chamber maintained at 40^oC and 75% RH for the period of 3 months. The beads formulation was evaluated before and after 3 months for change in floating behaviors, drug content and in -vitro drug release.[22-23]

RESULTS AND DISCUSSION

Determination of Melting Point

The melting point of Esomeprazole was determined by capillary method, melting point of Esomeprazole was found to be 217 to 220°C. Melting point of drug was compared with pharmacopoeial standards that confirmed the purity of drug sample.

Solubility

Esomeprazole was found to be slightly soluble in water, soluble in methanol, ethanol, acetone, DMSO and DMF.

Compatibility Studies (FT-IR)

Both the polymer and pure drug's infrared spectra are examined. It has been found in this investigation that there is no chemical interaction between the polymer and Esomeprazole. The major peak in the drug and polymer mixture's infrared spectra was found to remain unchanged, indicating that there was no physical interaction due to bond formation between the two substances.

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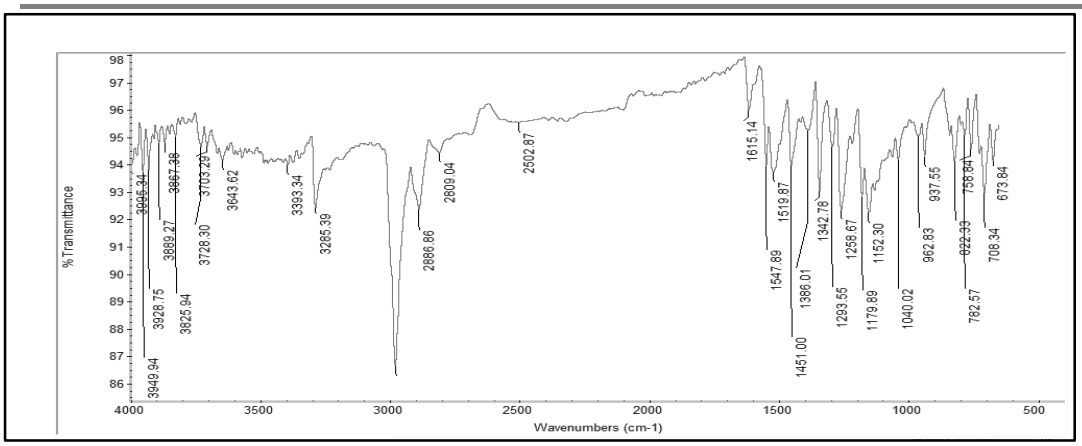

Figure 1 IR Spectra of Pure Drug Esomeprazole

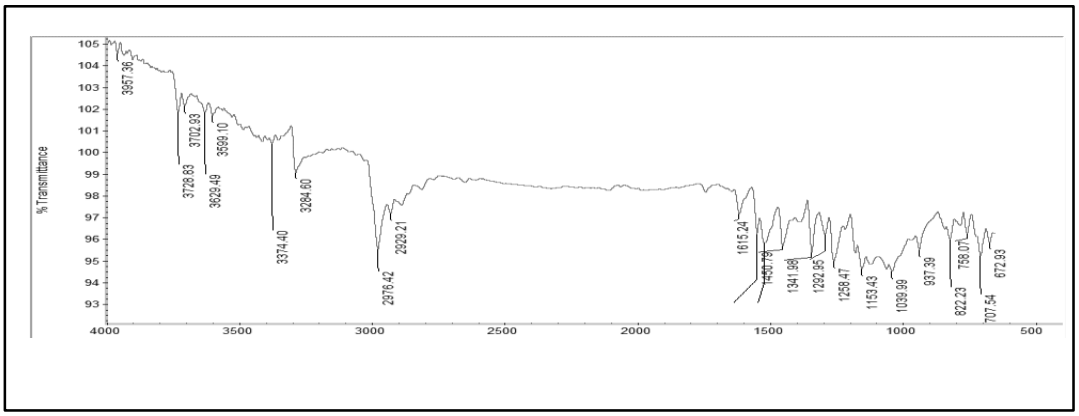

Figure 2.IR Spectra of Esomeprazole Floating Beads

Micromeritics Properties of Floating Beads

The micromeritics properties of the prepared floating alginate beads of Esomeprazole were evaluated to assess the flow characteristics and packing behavior of the formulations. The results for Angle of Repose, Bulk Density, Tapped Density, Carr's Index, and Hausner's Ratio for all six formulations (F1 to F6) are presented in the table 2.

The angle of repose ranged from 24.89° ± 0.31 (F6) to 27.45° ± 0.35 (F1). All formulations exhibited angles less than 30°, indicating good flow properties. The flow improved with increasing concentrations of sodium alginate and HPMC, with F6 showing the best flow behavior.

Bulk density values varied between 0.42 ± 0.01 g/cm³ (F1) and 0.47 ± 0.01 g/cm³ (F6), while tapped density ranged from 0.51 ± 0.01 g/cm³ (F1) to 0.56 ± 0.02 g/cm³ (F6). These values indicate good packing ability and were consistent with increasing polymer content, which contributes to denser and more uniformly packed particles.

Carr's index, a measure of compressibility, was found in the range of 16.07 ± 0.22% (F6) to 17.65 ± 0.22% (F1). Values below 20% suggest excellent flowability, with F6 again showing the best result. This could be due to better particle shape and smoother surface morphology at higher polymer concentrations. Hausner's ratio was within the range of 1.19 ± 0.01 to 1.21 ± 0.02 for all batches, which also supports the conclusion of good to excellent flow behavior. A Hausner's ratio below 1.25 is generally considered acceptable for flowability. Study conclude that, all formulations demonstrated acceptable micromeritic properties with F5 exhibiting the most favorable flow and packing characteristics, likely due to the higher concentration of sodium alginate and HPMC. These results suggest that the developed formulations are suitable for further processing and handling in pharmaceutical dosage form development.

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Table 2: Micromeritics Properties Of Floating Beads (F1 to F6)

Batch Code	Angle of Repose (°)	Bulk Density (g/cm³)	Tapped Density (g/cm³)	Carr's Index (%)	Hausner's Ratio
F1	27.45 ± 0.35	0.42 ± 0.01	0.51 ± 0.01	17.65 ± 0.22	1.21 ± 0.01
F2	26.78 ± 0.28	0.44 ± 0.02	0.53 ± 0.02	16.98 ± 0.31	1.20 ± 0.02
F3	25.34 ± 0.41	0.46 ± 0.01	0.55 ± 0.01	16.36 ± 0.27	1.19 ± 0.01
F4	26.92 ± 0.36	0.43 ± 0.01	0.52 ± 0.02	17.30 ± 0.30	1.21 ± 0.02
F5	24.89 ± 0.31	0.47 ± 0.01	0.56 ± 0.02	16.07 ± 0.22	1.19 ± 0.01
F6	25.65 ± 0.29	0.45 ± 0.02	0.54 ± 0.03	16.67 ± 0.24	1.20 ± 0.01

(SD ± Mean of n=3)

Drug Entrapment Efficiency (%)

The floating beads of Esomeprazole (F1 to F6) were evaluated for various parameters, including drug entrapment efficiency, floating lag time, total floating duration, mean particle size, and percent yield. The results indicated that all formulation parameters were significantly influenced by the concentration of sodium alginate and HPMC K4M. Drug entrapment efficiency increased progressively from 65.12 ± 1.24% in F1 to 87.96 ± 1.05% in F5, suggesting that higher polymer concentrations provided a stronger gel matrix capable of retaining more drug during bead formation. F6 also showed high entrapment efficiency (85.27 ± 1.30%), though slightly less than F5, likely due to increased viscosity causing less uniform drug distribution. .

Floating Lag Time

The floating lag time, which reflects the onset of buoyancy, decreased with increasing polymer concentration. F1 showed the highest lag time (49.3 ± 1.6 sec), while F5 had the shortest (33.8 ± 1.4 sec), indicating quicker floatation due to optimal polymer-gas interaction. F6 exhibited a slightly longer lag time (36.2 ± 1.3 sec) than F5, possibly due to excessive viscosity reducing CO_2 entrapment efficiency.

Total Floating Duration

The total floating duration improved significantly with increasing polymer content; F1 floated for only 4 hours, whereas F5 and F6 remained buoyant for more than 12 hours, highlighting the role of HPMC K4M in enhancing matrix stability and sustained floatation.

Particle Size Analysis

The mean particle size showed a gradual reduction from 215.6 ± 3.5 µm in F1 to 190.1 ±

2.3 µm in F5, attributed to tighter cross-linking and more compact bead formation with increased polymeric content. F6 showed a slight increase in particle size (193.6 ± 2.5 µm)

Compared to F5, again likely due to higher viscosity.

Determination of Percentage Yield

The percent yield increased across the batches, with F1 yielding 75.26 ± 1.32% and F5 achieving the highest yield of 89.62 ± 1.10%, indicating improved bead formation efficiency and minimal drug loss at higher polymer concentrations. F6 showed a slightly reduced yield (87.40 ± 1.26%) compared to F5. The results are showed in

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Table 3: Characterizations of Floating Beads of Esomeprazole (F1 to F6)

Batch	Drug Entrapment Efficiency (%)	Floating Lag Time (Sec)	Total Floating Duration (Hr)	Mean Particle Size (µm)	Percent Yield (%)
F1	65.12 ± 1.24	49.3 ± 1.6	4 hrs	215.6 ± 3.5	75.26 ± 1.32
F2	70.34 ± 1.37	44.1 ± 1.3	6 hrs	210.2 ± 3.2	78.45 ± 1.45
F3	74.88 ± 1.18	40.6 ± 1.2	8 hrs	204.7 ± 2.9	81.33 ± 1.28
F4	79.45 ± 1.22	37.2 ± 1.1	10 hrs	198.4 ± 2.7	84.19 ± 1.16
F5	87.96 ± 1.05	33.8 ± 1.4	> 12 hrs	190.1 ± 2.3	89.62 ± 1.10
F6	85.27 ± 1.30	36.2 ± 1.3	> 12 hrs	193.6 ± 2.5	87.40 ± 1.26

(Values are SD ± Mean of n=3)

In-Vitro Dissolution Study

The in-vitro drug release study of Esomeprazole floating beads (F1 to F6) demonstrated that the release rate was significantly affected by the concentration of sodium alginate and the incorporation of HPMC K4M as a secondary polymer. Formulation F1, containing 1% sodium alginate, exhibited a rapid drug release with 96.34% of the drug released within 4 hours. Increasing the sodium alginate concentration to 1.5% in F2 resulted in a slightly more sustained release profile, reaching 95.46% drug release at 6 hours. F3, formulated with 2% sodium alginate, showed a further extension in the release period, achieving 97.98% drug release over 8 hours, indicating that higher polymer concentration contributes to stronger gel formation and slower drug diffusion. Formulations F4 to F6 included 2% sodium alginate along with increasing concentrations of HPMC K4M (0.5%, 1%, and 1.5%, respectively), which significantly influenced the drug release kinetics. F4, with 0.5% HPMC, released 96.45% of the drug over 10 hours, while F5, containing 1% HPMC, showed the most prolonged and controlled release, with 98.26% of the drug released in 12 hours. F6, having 1.5% HPMC, demonstrated a slightly lower release of 91.34% over 12 hours, likely due to increased gel viscosity forming a denser matrix that hindered complete drug diffusion. These results indicate that the combination of sodium alginate and HPMC K4M effectively modulates the drug release rate. Among all batches, F5 was found to be the optimized formulation, providing a balanced and sustained release over 12 hours with the highest cumulative drug release. This highlights its potential for improved gastric retention and controlled delivery of Esomeprazole. Data for in vitro drug release of floating beads was shown in figure 2

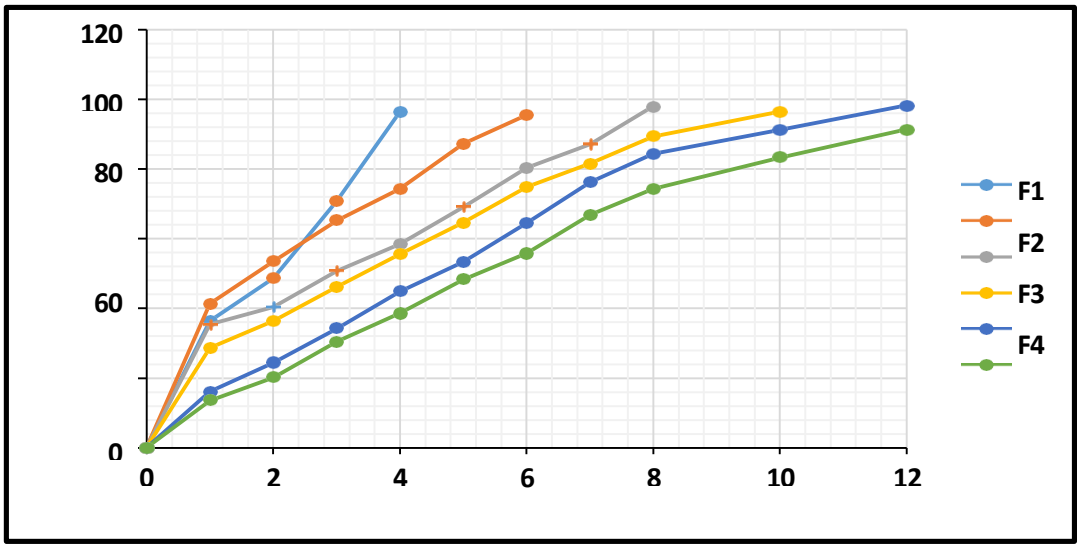

Figure 2: Comparative In Vitro Dissolution Profile Of Formulation F1 to F6

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Stability Study

The optimized formulation F5 was subjected to stability studies for a period of 3 months under standard storage conditions. The parameters evaluated included floating lag time, total floating time, and percentage drug release. Floating lag time showed negligible change over the storage period, with values of 33.8 ± 1.4 seconds initially and 32 ± 0.67 seconds after 3 months. This minimal variation indicates that the formulation retained its buoyancy properties effectively. The total floating time remained unchanged at more than 12 hours before and after the storage period, confirming the formulation's ability to maintain prolonged gastric residence over time. The percentage drug release was 98.26 ± 1.42% at 0 month and slightly decreased to 97.88 ± 1.18% after 3 months. This minor reduction in drug release is within acceptable limits, suggesting that the drug content and release profile were not significantly affected by storage.

Overall, the stability study results indicate that formulation F5 is physically and chemically stable over the 3-month period, maintaining its floating characteristics and drug release profile with no significant degradation or performance loss. The results of stability data were shown in table 4

Table 4: Stability Data of Optimized Formulation F5

Formulation Code	Parameter	Before storage (0 month)	After storage (3 month)
F5	**Floating lag Time (Sec)**	33.8 ± 1.4	32±5.0.67
	Total Floating Time (hr)	> 12 hrs	> 12 hrs
	% Drug Release	98.26 ± 1.42	97.88±1.18

CONCLUSION

The present study successfully demonstrated the development and evaluation of floating alginate beads of Esomeprazole designed for sustained gastric retention and controlled drug release. Preformulation studies confirmed the drug's purity, stability, and compatibility with polymers. The floating beads were formulated using ionotropic gelation, varying the concentrations of sodium alginate and HPMC K4M, and extensively evaluated for physicochemical and performance characteristics. Among the six formulations (F1–F6), formulation F5 emerged as the most optimized stability studies over three months confirmed that formula t ion F5 maintained its buoyancy and release characteristics without significant degradation. Thus, the study concludes that floating alginate beads of Esomeprazole, particularly formulation F5, present a promising gastro retentive drug delivery system capable of enhancing the therapeutic efficacy and patient compliance through sustained drug release and prolonged gastric residence time.

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