"Development and Evaluation of Oil-Entrapped Gastro-Retentive Floating Beads of Esomeprazole for the Treatment of Ulcers"

Mr. Paras Rathore

Student of M.Pharm, Department of Pharmaceutics, J. K. College of Pharmacy, Bilaspur (C.G.), India

[1]Ms. Lata Choudhary

Associate Professor, Department of Pharmacognosy, J. K. College of Pharmacy, Bilaspur (C.G.), India

[2]Dr. Yogesh Pounikar

Principal, Department of Pharmacognosy, J. K. College of Pharmacy, Bilaspur (C.G.), India

Corresponding Author's

Address- Department of Pharmaceutics, J.K. College of Pharmacy, Bilaspur (C.G.), India

ABSTRACT

Background: *Esomeprazole, a proton pump inhibitor, is primarily absorbed in the upper gastrointestinal tract and exhibits instability in the intestinal environment. Gastro-retentive drug delivery systems are an effective approach to enhance gastric residence time and improve therapeutic efficacy. The present study aimed to develop a gastro-retentive floating bead formulation of Esomeprazole for sustained drug release.*

Methods: *Floating beads of Esomeprazole were prepared using the ionotropic gelation technique with sodium alginate as the polymer and calcium carbonate as the gas-forming agent. The prepared formulations (F1-F6) were evaluated for particle size, floating behavior, drug entrapment efficiency, surface morphology, and in-vitro drug release. The optimized formulation was subjected to release kinetic modeling using zero-order, first-order, Higuchi models.*

Results: *Among all formulations, F5 was identified as the optimized batch, exhibiting high drug entrapment efficiency (98.05%), short floating lag time, prolonged floating duration (>12 h), and*

sustained drug release (98.69% over 12 h). Drug release kinetics of F5 showed the best fit with the Higuchi model, indicating a diffusion-controlled release mechanism. Stability studies confirmed formulation stability under accelerated conditions.

Conclusion: *The developed gastro-retentive floating beads of Esomeprazole demonstrated prolonged gastric retention and controlled drug release, making them a promising delivery system for improving patient compliance and therapeutic efficacy.*

Keywords: *Esomeprazole; Gastro-retentive drug delivery; Floating beads; Ionotropic gelation; Higuchi kinetics; Sustained release etc.*

1. INTRODUCTION:

Gastro-Retentive Drug Delivery Systems (GRDDS)

Gastro-retentive drug delivery systems are designed to remain in the stomach for extended periods, thereby enabling the drug to be released in a sustained and controlled manner. This prolonged gastric retention is particularly beneficial for drugs that are absorbed predominantly in the stomach or proximal part of the small intestine, or those that are unstable in the alkaline pH of the intestine [1,2].

Floating Drug Delivery Systems (FDDS)

Floating drug delivery systems are characterized by their ability to maintain buoyancy in the gastric environment. This is typically achieved by either generating gas (effervescent systems) or by incorporating polymers that swell and trap air (non-effervescent systems). FDDS are especially useful for drugs that act locally in the stomach or are absorbed in the upper GI tract [4,6].

2. MATERIALS AND METHOD:

Materials:

Smart Laboratories Pvt. Ltd. provided a gift sample of esomeprazole, which was utilised exactly as received without additional purification. The provided drug sample was used in every study.

Method:

- **Pre-formulation Studies:**

1. Organoleptic Character:

Esomeprazole's organoleptic qualities were assessed using visual and sensory analysis in a typical laboratory setting. To verify the drug sample's fundamental physical attributes, direct observation was used to evaluate its colour, odour, physical condition, and look [13].

2. Solubility Studies:

Esomeprazole's qualitative solubility was assessed in a variety of solvents in accordance with USP-NF (2007) criteria. Ten milligrams of the medication, each precisely weighed, were added to ten millilitres of various solvents, such as pure water, ethanol, methanol, chloroform, and DMSO, in test tubes. Visual observation was used to evaluate the solubility, and solubility behaviour was used to qualitatively express the results [14].

3. Melting Point:

The melting point was measured using the open capillary tube method. A small quantity of the drug was packed into a thin-walled capillary tube (10-15 mm in length and approximately 1 mm internal diameter), sealed at one end. The capillary tube was then heated gradually, and the temperature at which the drug melted was noted as its melting point [18].

4. Determination of Partition Coefficient:

The partition coefficient of Esomeprazole was evaluated using an n-octanol and water system. A known amount (5 mg) of the drug was added to a separating funnel containing equal volumes (20 ml each) of n-octanol and water. The funnel was agitated for 2 hours using a wrist action shaker to allow equilibrium. After separation, the aqueous phase was analyzed spectrophotometrically at 292 nm to calculate the partition coefficient [17].

5. Preparation of Standard Solution:

A standard stock solution of Esomeprazole (1000 µg/ml) was prepared by dissolving 10 mg of the drug in methanol:water (1:1) in a 10 ml volumetric flask, and the volume was adjusted to 10 ml with the same

solvent. From this stock solution, 1 ml was diluted to 10 ml to obtain a working standard solution of 100 µg/ml [16].

6. Determination of λmax:

From the working standard solution, 2 ml was further diluted to 10 ml with methanol:water (1:1) to obtain a concentration of 20 µg/ml. The solution was scanned in a UV–Visible spectrophotometer over the range of 200-400 nm using the solvent as blank [14]. The wavelength corresponding to maximum absorbance was recorded as λ max and used for further analysis.

7. Calibration curve of Esomeprazole

Aliquots corresponding to concentrations of 5, 10, 15, 20, 25, 30, and 35 µg/ml were taken from the working standard solution and diluted to 5 ml with the solvent in calibrated flasks. Absorbance readings were taken at 292 nm against a blank [17].

8. FTIR Studies:

The FTIR spectrum of Esomeprazole was recorded using the KBr pellet method in the range of 4000-400 cm^{-1}. A pellet was prepared by mixing 1 mg of the drug with 100 mg of spectroscopically pure, IR-dried KBr, followed by compression under high pressure to form a transparent disc [22]. The prepared pellet was scanned using an FTIR spectrophotometer to identify characteristic functional group peaks.

- **Formulation of Floating Beads of Esomeprazole**

Six formulations (F1-F6) of Esomeprazole floating beads were prepared by the ionotropic gelation method using varying concentrations of polymers and gas-forming agents. Sodium alginate was dissolved in distilled water to form a uniform polymeric solution, and Esomeprazole was dispersed under continuous stirring. Calcium carbonate was incorporated as a buoyancy-enhancing agent. The resulting dispersion was extruded dropwise through a syringe into a calcium chloride solution with gentle stirring, leading to instantaneous bead formation due to ionic cross-linking. The beads were allowed to cure for a specified period, collected, washed with distilled water, and dried at room temperature. All six formulations were subsequently evaluated for physicochemical and floating characteristics [27].

- **Optimization of Floating Beads:**

The bead size, buoyancy (floating lag time), floating duration, and morphology of all formulations (F1-F6) were evaluated to identify the optimized formulation. Bead diameter was measured using a screw gauge (least count 0.005 mm) by randomly selecting 20 dried beads from each batch and calculating the mean particle size. Buoyancy was determined by recording the floating lag time, while the total floating time was noted visually. Among all formulations, F5 exhibited an optimal mean particle size (2.11 mm), short floating lag time (21 s), and the longest floating duration (12.03 h), along with uniform spherical shape and acceptable physical appearance. Based on these results, formulation F5 was selected as the optimized formulation for further evaluation [29].

- **Evaluation of Floating Beads of Esomeprazole:**

1. Scanning Electron Microscopy (SEM) of Optimized Formulation

The surface morphology of the optimized F5 alginate beads was examined using scanning electron microscopy (SEM). Prior to analysis, the beads were coated with a thin conductive layer (2-20 nm) of gold/platinum using a sputter coater under vacuum. SEM imaging was carried out to observe surface characteristics and morphological features based on secondary electron emissions resulting from electron–sample interactions [29].

2. Drug Entrapment Efficiency

The drug entrapment efficiency of Esomeprazole-loaded floating beads (F1–F6) was determined by accurately weighing a known quantity of beads, which were crushed and dissolved in a suitable solvent. The solution was filtered, diluted appropriately, and analyzed spectrophotometrically at 292 nm. Entrapment efficiency was calculated as the percentage ratio of the actual drug content to the theoretical drug content [30].

3. *In-Vitro* Drug Release Study

In-vitro drug release from the calcium alginate floating beads was evaluated using a USP Type II dissolution apparatus. The study was conducted in 900 ml of 0.1 N HCl (pH 1.2) maintained at 37 ± 0.5°C and stirred at 50 rpm. Samples were withdrawn at predetermined time intervals and replaced with an equal volume of fresh dissolution medium. The withdrawn samples were analyzed using a UV-Visible

spectrophotometer (Shimadzu UV-1700) at 292 nm. Only formulations showing drug content and entrapment efficiency above 90% were selected for dissolution studies [31].

4. Drug Release Kinetics Study

The drug release kinetics of the optimized formulation F5 was analyzed by fitting the dissolution data into different kinetic models, including zero-order, first-order, Higuchi, and Korsmeyer–Peppas models. The cumulative percentage drug release data were plotted against time, log percentage drug remaining, square root of time, and log time, respectively. The correlation coefficient (R^2) values were calculated to determine the best-fitting kinetic model and to elucidate the mechanism of drug release [26].

5. Stability Study:

The optimized F5 formulation was subjected to accelerated stability studies in accordance with ICH guidelines. The beads were stored at 25 ± 2°C / 60 ± 5% RH and 40 ± 2°C / 70 ± 5% RH for a period of 3 months. At predetermined intervals (30, 45, 60, and 90 days), the formulation was evaluated for floating lag time, entrapment efficiency, and in-vitro drug release (12 h). The results obtained at each interval were compared with those of the initial (0-day) formulation. No significant changes in floating behavior, drug entrapment, or release profile were observed, indicating good stability of the optimized formulation during the study period [34].

3. RESULTS:

- **Pre-formulation Studies:**

1. **Organoleptic Characters:**

Table 1: Organoleptic Characters of Esomeprazole

Drug	Organoleptic properties	Observation
	Colour	**White**
	Odour	**Characteristic**

Esomeprazole	State	**Solid**
	Appearance	**Solid powder**

2. Solubility Studies:

Table 2: Solubility Studies of Esomeprazole

S. No.	Solvent	Solubility Observation	Approx. Solubility (mg/mL)
1	Distilled Water	Slightly soluble	0.8
2	Ethanol	Soluble	5.0
3	Methanol	Soluble	4.5
4	Chloroform	Slightly soluble	0.9
5	DMSO	Freely soluble	12.0

3. Melting Point Determination:

Table 3: Melting point of Esomeprazole

Drugs	Observed	Reference
Esomeprazole	**170^{0}C**	**165to170^{0}C**

4. Determination of Partition Coefficient:

Table 4: Partition Coefficient of Esomeprazole

S.No.	Drug	Solvent	Partition coefficient
1	Esomeprazole	n-Octanol:water	0.29

5. Determination of λmax:

Table 5: λ max of Esomeprazole

S. No	Drug	UV absorption maxima (Lambda max)
1.	**Esomeprazole**	**292.0 nm**

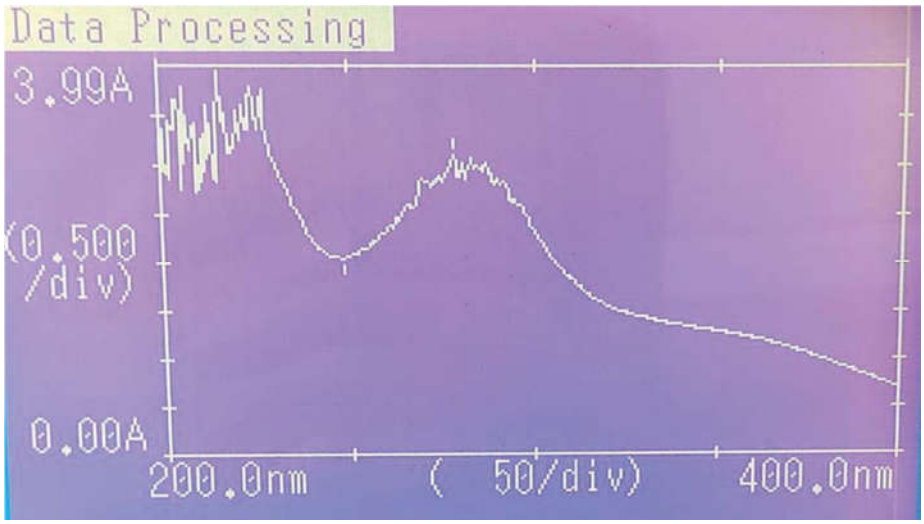

Figure 1: λ max of Esomeprazole

6. Calibration curve of Esomeprazole:

Table 6: concentration and Absorbance of Esomeprazole

Concentration(µg/ml)	Absorbance (292.0nm)
5	0.130
10	0.204
15	0.362
20	0.432
25	0.607
30	0.752
35	0.976
Mean	0.477714286
SD	0.255152709
%RSD	53.45

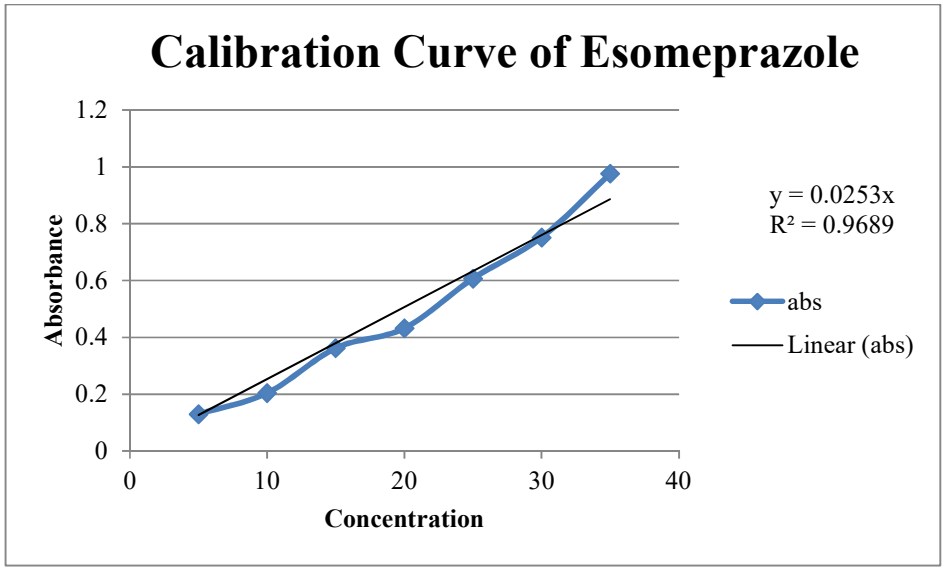

Figure 2: Calibration Curve of Esomeprazole

7. FTIR Studies:

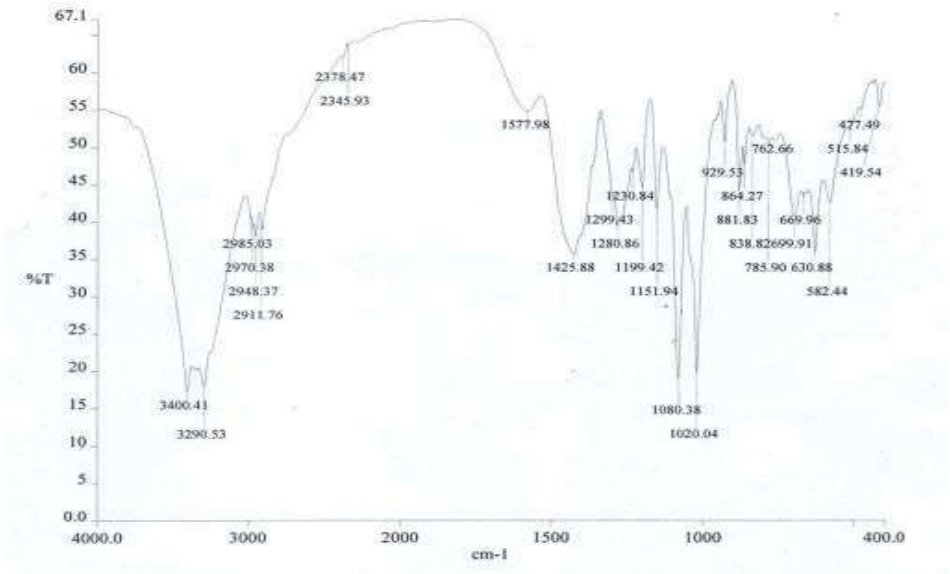

Figure 3: FTIR of Esomeprazole

- **Formulation of Floating Beads of Esomeprazole**

Table 7: Formulation table for Floating Beads of Esomeprazole

S. No.	Formulation Code	Sodium Alginate (% w/v)	Calcium Carbonate (% w/w of polymer)	Drug (mg)	Calcium Chloride Solution (%)
1	F1	2.0	10	100	5
2	F2	2.0	15	100	5
3	F3	2.5	10	100	5
4	F4	2.5	15	100	5
5	F5	3.0	15	100	5
6	F6	3.0	10	100	5

- **Optimization of Floating Beads:**

Table 8: Evaluation of Particle Size, Buoyancy, and Floating Time of Esomeprazole Floating Beads

S. No	Formulation code (F)	Particle size(mm)	Buoyancy (Floating lag time)	Floating Time (hrs)
1.	F1	2.13	30 sec.	**11.29**
2.	F2	2.17	27 sec.	**11.07**
3.	F3	1.97	19 sec.	**11.37**
4.	F4	2.12	29 sec.	**11.47**
5.	F5	2.11	21 sec.	**12.03**
6.	**F6**	**2.18**	**27 sec.**	**11.50**

- **Evaluation of Floating Beads of Esomeprazole:**

1. Scanning Electron Microscopy (SEM) of Optimized Formulation

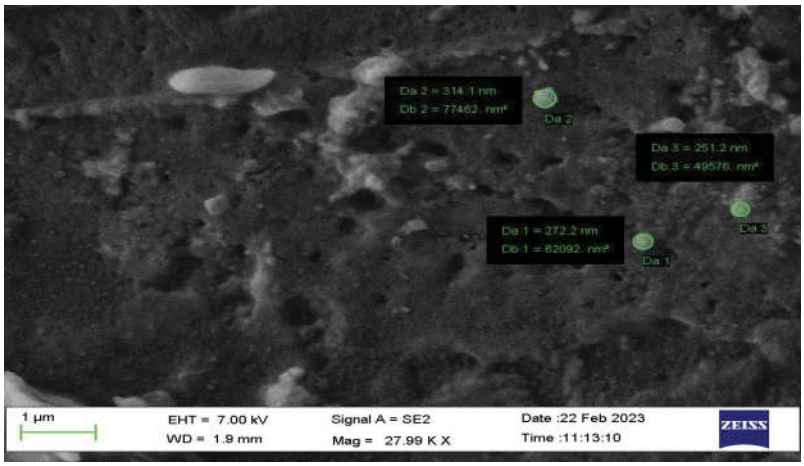

Figure 4: SEM of Optimized Floating Bed Formulation

2. Drug Entrapment Efficiency:

Table 9: Entrapment Efficiency of Floating Bed Formulation

S.No	Formulation Code	Entrapment Efficiency (%)
1.	F1	**95.23**
2.	F2	**93.65**
3.	F3	**96.11**
4.	F4	**97.61**
5.	F5	**98.05**
6.	**F6**	**97.17**

4. Drug Release Kinetics Study:

Table 10: Drug Release kinatics of floating bed formulation

S.No	Time(hr)	F1	F2	F3	F4	F5	F6
1	0	0	0	0	0	0	**0**
2	1	23.27	16.00	19.32	20.46	21.01	**22.54**
3	2	33.97	28.48	35.12	46.43	42.71	**37.23**

4	4	41.04	39.90	47.67	57.18	58.83	**46.76**
5	6	63.78	53.51	58.24	62.69	64.25	**59.11**
6	8	79.11	79.80	73.11	74.22	80.88	**70.60**
7	10	87.20	88.18	89.17	86.65	91.11	**86.87**
8	**12**	**96.09**	**97.11**	**95.10**	**95.27**	**98.69**	**97.34**

Table 11: Release kinetics study of optimized (F5) formulation (Correlation value)

Formulation	Model	Kinetic parameter values
Floating beads	ZeroOrder	**R^2=0.824**
	FirstOrder	**R^2=0.840**
	Higuchi	**R^2=0.961**

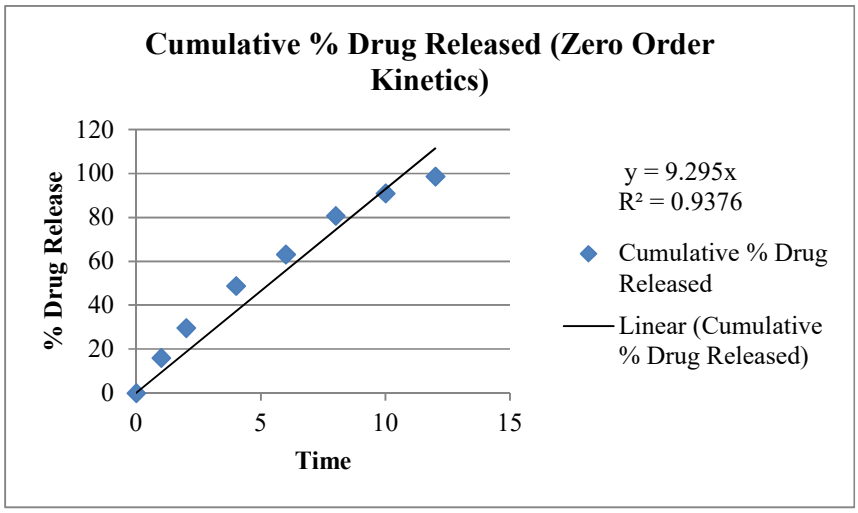

Figure 5: Cumulative % Drug Released (Zero Order Kinetics)

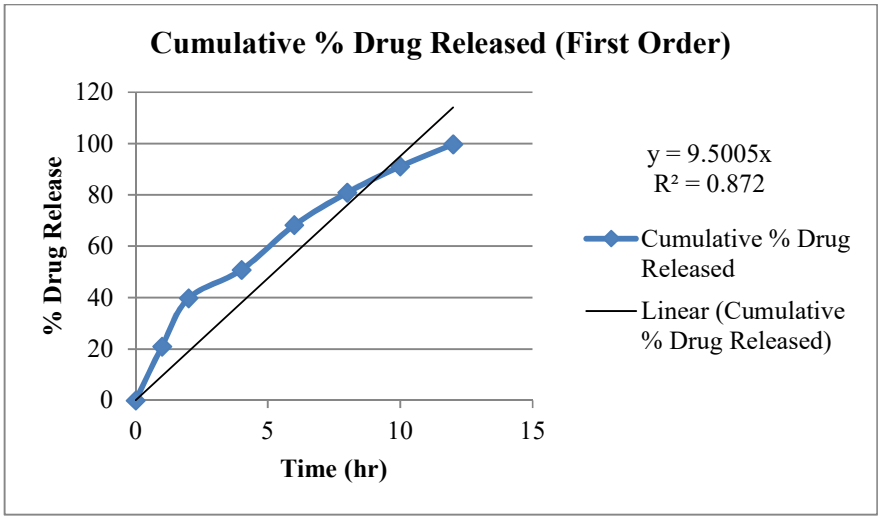

Figure 6: Cumulative % Drug Released (First Order Kinetics)

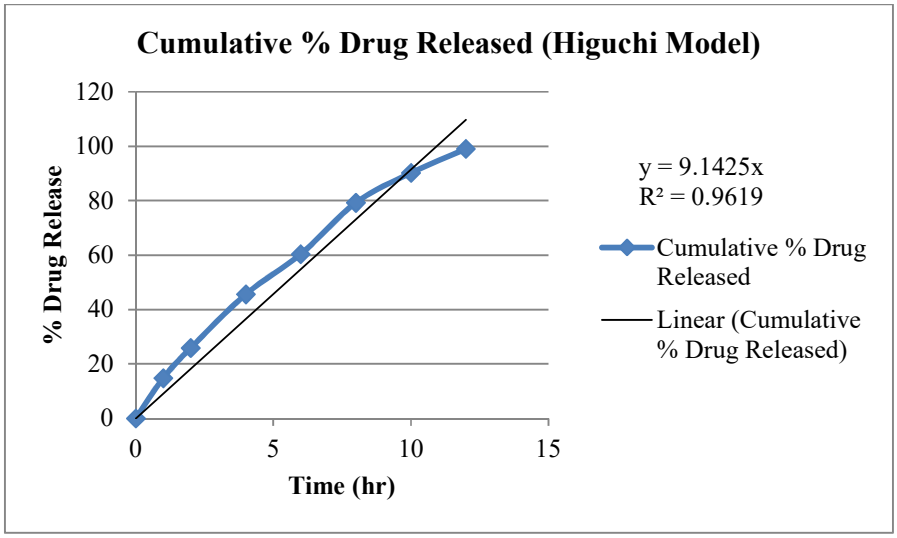

Figure 7: Cumulative % Drug Released (Higuchi Model)

5. Stability Studies:

Table 12: Stability Studies of Floating Optimized Formulation

S.No	Time (Days)	$25^0C \pm 2\ ^0C$ and 60 ± 5%RH			$40^0C \pm 2^0C$ and 70 ±5%RH		
		Floating lag time	Entrapment efficiency	In-vitro release studies (%) 12 hr	Floating lag time	Entrapment efficiency	**In-vitro release studies (%) 12 hr**

1.	0	21 sec.	98.05%	98.69	397.4 nm	67.49%	**98.69**
2.	30	22 sec.	98.01%	98.07	396.9 nm	67.53	**98.05**
3.	45	25 sec.	98.17%	98.10	397.4 nm	67.44	**98.00**
3.	60	18 sec.	97.97%	98.12	397.4 nm	67.50	**98.01**
4.	**90**	**22 sec.**	**98.10%**	**98.08**	**397.4 nm**	**67.48**	**97.96**

4. CONCLUSION:

The present study was successfully undertaken to formulate and evaluate a gastro-retentive floating drug delivery system of Esomeprazole using the ionotropic gelation technique. Floating beads were developed using sodium alginate as the polymer and calcium carbonate as the gas-forming agent to enhance gastric residence time and provide controlled drug release. Pre-formulation studies confirmed the identity, purity, and compatibility of Esomeprazole, indicating its suitability for formulation. Six formulations (F1-F6) were prepared and evaluated for physicochemical properties, buoyancy, drug entrapment efficiency, and in-vitro drug release. Among them, formulation F5 was optimized, showing an ideal particle size, short floating lag time, prolonged floating duration, high drug entrapment efficiency (98.05%), and sustained drug release up to 12 hours (98.69%). Drug release kinetic analysis of the optimized formulation F5 demonstrated the best fit with the Higuchi model ($R^2 = 0.961$), indicating a diffusion-controlled release mechanism, with acceptable correlation to first-order kinetics. Stability studies confirmed that the formulation remained stable under accelerated conditions without significant changes in performance.

5. REFERENCES:

1. Mishra, S., Shukla, P., Chumbhale, D. S., Dutta, P., Vellingiri, D., & Tiwari, R. (2025). Exploring the Potential of Gastro Retentive Drug Delivery Systems: An Insightful Perspective. International Journal of Pharmaceutical Investigation, 15(3).
2. Ramavath, V. N. (2025). A review on gastro retentive drug delivery system. International Journal of Indigenous Herbs and Drugs, 13-17.
3. Gajbhiye, M. L. S., Bhute, M. A. W., Kothari, M. K. S., Lokhande, V. K., & Bijwar, R. REVIEW ON GASTRO RETENTIVE DRUG DELIVERY SYSTEMS. Journal of Pharmaceutical Research, 14(23), 315-339.
4. Sankhe Lochani, D., Khaire Rahul, D., Kathale Ankita, A., Bhandare Tejaswini, S., & Ghude Samiksha, K. (2025). Formulation Strategies and Recent Advances in Floating Drug Delivery

System (FDDS): A Comprehensive Review. Asian Journal of Pharmaceutical Research and Development, 13(5), 76-82.

5. Singh, R., Patel, A., & Patel, S. FLOATING DRUG DELIVERY SYSTEMS: A COMPREHENSIVE REVIEW ON FORMULATION, CHARACTERIZATION, AND THERAPEUTIC APPLICATIONS. World Journal of Pharmaceutical Research, 15(1), 1636-1648.
6. Shankar, S. J., Akshatha, R. S., Kushal, N., Deepika, U., & Ashwini, K. V. (2025). Evaluation of Floating Drug Delivery Systems for Gastroretentive Applications. Journal of Pharmaceutical Research and Integrated Medical Sciences, 40-51.
7. Kawashima, Y., Niwa, T., Takeuchi, H., Hino, T., & Itoh, Y. (1992). Development of hollow microspheres as a stomach-specific controlled drug delivery system. *Journal of Pharmaceutical Sciences*, 81(2), 135–140.
8. Sahakian, A. B., Jee, S. R., & Pimentel, M. (2010). The role of methane in gastrointestinal function. *Digestive Diseases and Sciences*, 55(8), 2135–2143.
9. Alexander, S., Juergen, S., & Roland, B. (2006). A review on gastroretentive drug delivery systems. *Expert Opinion on Drug Delivery*, 3(2), 217–233.
10. Khoder, G., Al-Menhali, A. A., Al-Yassir, F., & Karam, S. M. (2016). Evaluating the role of probiotics in managing gastric ulcers. *Experimental and Therapeutic Medicine*, 12(1), 3–17.
11. Garg, S., & Sharma, S. (2003). Overview of oral drug delivery systems. *Business Briefing: Pharmatech*.
12. Oth, M., Franz, M., Timmermans, J., &Möes, A. (1992). Bilayer floating capsules for targeted gastric delivery of misoprostol. *Pharmaceutical Research*, 9(3), 298–302.
13. Katayama, H., et al. (1999). Sustained-release liquid formulations using sodium alginate for *Helicobacter pylori* eradication. *Biological and Pharmaceutical Bulletin*, 22(1), 55–60.
14. Singh, B. N., & Kim, K. H. (2000). Floating systems for gastric retention and controlled drug release. *Journal of Controlled Release*, 63(3), 235–259.
15. Ji, J., et al. (2017). In vitro and in vivo evaluation of berberine hydrochloride floating tablets. *AAPS PharmSciTech*, 18(6), 2149–2156.
16. bnMadhavi, B. B., et al. (n.d.). Formulation and evaluation of oil-entrapped floating beads of piperine for peptic ulcer treatment.

17. Rani, R., et al. (2022). Berberine hydrochloride-loaded chitosan microspheres: characterization and anti-ulcer study. *Drug Delivery Letters*, 12(4), 287–301.
18. Jain, A., et al. (2015). Development of floating microballoons of nizatidine for ulcer treatment. *Drug Delivery*, 22(3), 306–311.
19. Singh, P. K., & Kaur, I. P. (2011). Gastroretentive system for ginger extract with improved antiulcer activity. *Journal of Drug Targeting*, 19(9), 741–751.
20. Singh, B., Sharma, V., & Chauhan, D. (2010). Floating sterculia–alginate beads for ulcer therapy. *Chemical Engineering Research and Design*, 88(8), 997–1012.
21. Abourehab, M. A., et al. (2015). Evaluation of famotidine with quercetin in peptic ulcer: in vivo study. *Drug Design, Development and Therapy*, 9, 2159.
22. Chandra, A. (2018). Design and evaluation of multiple-unit floating beads of antiulcer drugs. *Asian Journal of Pharmaceutics*, 12(2).
23. Fallone, C. A., et al. (2016). Toronto consensus on *H. pylori* infection treatment. *Gastroenterology*, 151(1), 51–69.e14.
24. Tommasi, S., et al. (2017). PPI-induced DDAH-1 inhibition and cardiovascular risk implications. *Scientific Reports*, 7(1), 2871.
25. Ghebremariam, Y. T., et al. (2013). PPIs and increased levels of ADMA: cardiovascular concerns. *Circulation*, 128(8), 845–853.
26. Haastrup, P. F., et al. (2018). Long-term PPI use and associated side effects. *Basic & Clinical Pharmacology & Toxicology*, 123(2), 114–121.
27. Reimer, C., et al. (2009). Acid rebound after PPI withdrawal in healthy volunteers. *Gastroenterology*, 137(1), 80–87.e1.
28. Prakash, P., Porwal, M., & Saxena, A. (2011). Natural polymers in sustained-release drug delivery. *International Research Journal of Pharmacy*, 2(9), 6–11.
29. Kumar, R., et al. (2017). Advances in multiple-unit floating bead systems. *World Journal of Pharmaceutical Research*, 6, 238–259.
30. Rakesh, P., et al. (2015). Formulation of alginate beads using ionotropic gelation. *Research Journal of Chemical Sciences*, 2231-606X.
31. Ranvirsingh, T. A., et al. (2013). Floating alginate beads of antiulcer drugs: formulation and evaluation. *International Journal of Pharmaceutical Sciences Review and Research*, 21(2), 120–124.

32. Jaiswal, D., et al. (2009). Oil-entrapped floating alginate beads of ranitidine HCl. *International Journal of Pharmacy and Pharmaceutical Sciences*, 1(3), 128–140.
33. Patil, J. S., et al. (2010). Ionotropic gelation and PEC: hydrogel drug delivery strategies. *Digest Journal of Nanomaterials and Biostructures*, 5(1), 241–248.
34. Setia, M., Kumar, K., &Teotia, D. (2018). Floating beads: an emerging drug delivery trend. *Journal of Drug Delivery and Therapeutics*, 8(3), 169–180.
35. Choudhury, A., et al. (2019). A comprehensive view on floating drug delivery systems. *Journal of Applied Pharmaceutical Research*, 7(3), 01–08.
36. Gupta, P., et al. (2015). Review on floating drug delivery systems. *International Journal of Pharma Research & Review*, 4(8), 37–44.
37. Tripathi, P., et al. (2012). Floating DDS: A formulation overview. *International Journal of Research and Development in Pharmacy and Life Sciences*, 1(1), 1–10.