RESEARCH PAPER

Development and Evaluation of Stomach-Specific Floating Beads of Metoclopramide Hydrochloride

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Abstract

Background: Gastroretentive floating drug delivery systems are designed to remain buoyant in gastric fluid and to sustain drug release in the upper gastrointestinal tract. Metoclopramide hydrochloride, an antiemetic and prokinetic agent, was selected for development of stomach-specific floating beads. Objective: The study aimed to formulate and evaluate floating beads of metoclopramide hydrochloride using sodium alginate, calcium chloride, calcium carbonate and poloxamer 188. Methods: Floating beads were prepared by ionotropic gelation. A 3^2 factorial design was applied using sodium alginate and poloxamer 188 as independent formulation variables. The prepared beads were evaluated for drug content, entrapment efficiency, particle size, in vitro buoyancy, in vitro dissolution, FTIR, DSC and scanning electron microscopy. Results: The prepared beads showed particle size values from 87.14±0.34 to 113.00±0.34 µm. Percentage yield ranged from 86.76±1.23% to 98.47±1.56%, drug content from 69.28±0.39% to 95.09±0.17%, and entrapment efficiency from 78.42±0.78% to 96.12±0.23%. All formulations floated for more than 12 hours with buoyancy values from 98.66±0.45% to 100±0.68%. The 12-hour drug release ranged from 79.87±0.52% to 92.32±0.38%. FTIR and DSC observations indicated no evident drug-excipient interaction in the selected formulation. SEM images showed spherical beads with rough and wrinkled surface characteristics. Conclusion: The factorially developed alginate-poloxamer floating beads provided prolonged buoyancy and sustained release of metoclopramide hydrochloride in acidic medium, with F9 showing high drug loading, high entrapment and controlled release behavior.

Keywords: Metoclopramide hydrochloride; Floating beads; Gastroretentive drug delivery; Sodium alginate; Poloxamer 188; Ionotropic gelation; Stomach-specific delivery.

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1. Introduction

Oral delivery remains a widely accepted route because it is convenient, economical and suitable for controlled-release pharmaceutical products. However, conventional oral formulations may show limitations when the drug has a narrow absorption window, requires prolonged exposure in the stomach or upper intestine, or exhibits better solubility in acidic medium. Gastroretentive drug delivery systems are developed to improve gastric residence time and to sustain drug release at or near the desired absorption region [1-8].

Floating drug delivery systems are a major class of gastroretentive systems. Their density is lower than gastric fluid, permitting the dosage form to float on gastric contents while releasing the drug at a controlled rate. In such systems, buoyancy and controlled release act together: the formulation remains in the stomach for an extended period while the drug diffuses or erodes from the polymeric matrix. Multi-unit floating systems such as alginate beads reduce the "all-or-none" emptying risk associated with single-unit dosage forms and may reduce inter-subject variability [3,6,8].

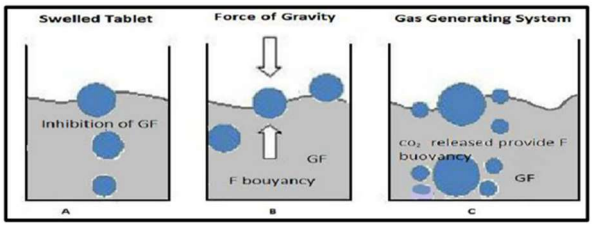

Figure 1. Mechanism of floating drug delivery system as represented in the source thesis.

Gastric retention depends on the physiological behavior of the stomach and the transit time of the dosage form

through different gastrointestinal regions. The source thesis summarized gastric transit as highly variable, with liquids leaving the stomach within 10-30 minutes and solids remaining from less than one hour to more than three hours. This variability is important for controlled-release products because premature gastric emptying may reduce the opportunity for drug release and absorption in the upper gastrointestinal tract.

Table 1. Transit time in different segments of the gastrointestinal tract

Segment	Liquid transit	Solid transit
Stomach	10-30 minutes	<1 to >3 hours
Duodenum	Short	Minutes to hours
Jejunum and ileum	3 h ± 1.5 h	4 h ± 1.5 h
Colon	Not specified	20-50 hours

The key advantages of gastroretentive and floating systems described in the thesis include sustained drug delivery, reduction in dose frequency, improved patient compliance, controlled plasma level fluctuation and localization of the dosage form in the upper gastrointestinal tract. Limitations include dependence on sufficient gastric fluid, unsuitability for drugs unstable in acidic conditions and the need for administration with an adequate volume of water.

Metoclopramide hydrochloride is a prokinetic and antiemetic drug used in nausea, vomiting and motility disorders. The present work converted the thesis investigation into a research article format focused on formulation development, characterization and in vitro performance of stomach-specific floating beads. The development strategy used sodium alginate as a gelling polymer, calcium chloride as a crosslinking agent, calcium carbonate as a gas-forming agent and poloxamer 188 as a formulation variable.

2. Literature Foundation from Source Thesis

The source thesis reviewed previous work on gastroretentive floating beads and related polymeric systems. The studies consistently supported ionotropic gelation, alginate-based matrices, gas-forming agents and polymeric release modifiers as useful approaches for sustained release and gastric retention. The selected literature also showed that multiparticulate systems may improve buoyancy, drug loading, entrapment efficiency and sustained release performance for drugs intended for upper gastrointestinal delivery.

Table 2. Literature foundation supporting the formulation approach

Author/year	System or topic	Key relevance reported in source thesis
Agarwal et al. (2022)	Ketoprofen floating microspheres	Ionotropic gelation was suitable for sustained drug delivery.
Abdelkader et al. (2020)	Modified-release baclofen floating coated beads	Coated beads reduced rapid plasma peaking-related side effects.
Shirsath et al. (2020)	Vildagliptin-loaded gellan gum mucoadhesive beads	Prepared beads were promising for sustained release.
Daihom et al. (2020)	Domperidone/Dowex gastro-floatable effervescent alginate beads	Optimized formulation may increase bioavailability and patient compliance.
Zang Tong et al. (2018)	Gastroretentive beads with Brucea javanica oil	Beads showed oil encapsulation, gastroretention, buoyancy and sustained release.
Hendrika et al. (2018)	Amoxicillin floating beads using banana peel pectin	Prepared beads delivered drug in stomach for a prolonged period.
Naik et al. (2019)	Nanoparticulate sustained-release oral system	System helped reduce limitations of conventional dosage and dosing frequency.
Dangre et al. (2019)	Alginate-Neusilin microcomposite beads for cilnidipine	Microcomposite beads were useful for sustained oral release.
Chan et al. (2017)	Alginate/k-carrageenan hydrogel beads for insulin aspart	Composite beads were reported as promising delivery systems.
Amin et al. (2016)	Floating mucoadhesive microspheres of metronidazole	Microspheres supported site-specific sustained release to

		gastric mucosa.
Cetin et al. (2016)	Alginate and alginate-chitosan beads of metformin HCl	Beads may prolong hypoglycemic action and improve compliance.
Allam et al. (2015)	Metformin-loaded biopolymeric beads	Beads showed high yield and entrapment with sustained release.
Biswas et al. (2015)	Starch-blended alginate beads of metoprolol tartrate	Gas-forming calcium carbonate improved gastric residence.
Wang et al. (2015)	Alginate-chitosan gastric floating beads of oxymatrine	Combined solid dispersion and floating beads supported retention and release.
Zhang et al. (2014)	Gastroretentive floating system for dipyridamole	Prepared beads improved bioavailability.
Ozsoy et al. (2021)	Review of floating gastroretentive dosage forms	Floating systems increase GI transit time and may improve bioavailability.
Abhishek Kumar et al. (2021)	Review of gastroretentive approaches	GRDDS can support prolonged residence and release for narrow-window drugs.
Kumari et al. (2018)	Review of floating drug delivery systems	Floating approach targets upper GI release and supports optimal bioavailability.
Senjoti et al. (2016)	Review of GRDDS and in vivo success	GRDDS can improve conventional oral delivery limitations.

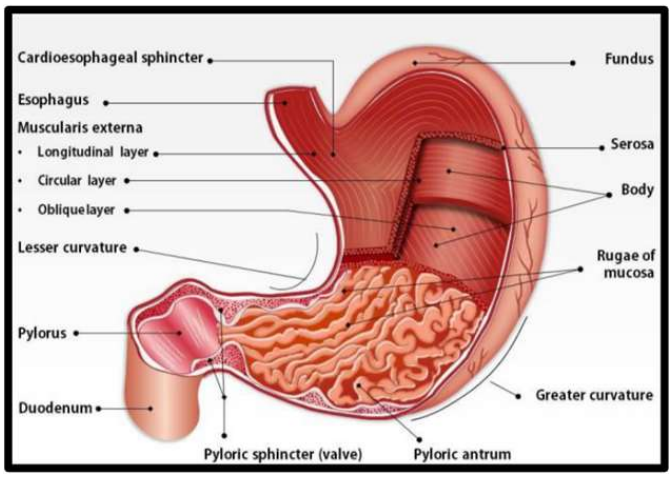

Figure 2. Structure of stomach included in the source thesis to support gastroretentive rationale.

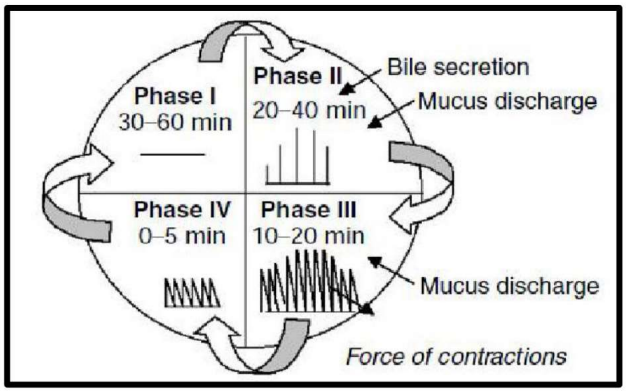

Figure 3. Gastric emptying and motility pattern related to gastric retention.

3. Need and Objective of the Study

The formulation need was to increase gastric residence of metoclopramide hydrochloride so that beads could remain in the stomach for an extended duration, prolong drug release, reduce dosing frequency and support patient compliance. The study objectives were: (i) to formulate gastroretentive floating beads of metoclopramide hydrochloride and (ii) to evaluate the prepared gastroretentive floating beads for physicochemical, buoyancy and dissolution performance.

4. Materials and Methods

3.1 Materials

Metoclopramide hydrochloride was obtained from Ronak Healthcare, Gujarat. Sodium alginate and calcium chloride were obtained from Loba Chemie Pvt. Ltd. Calcium carbonate was obtained from SD Chem Lab India. Poloxamer 188 was obtained from Vishal Chem, Mumbai. The equipment used in the work included a digital analytical balance, magnetic stirrer, UV

spectrophotometer, dissolution apparatus, FTIR, DSC and scanning electron microscope as described in the source dissertation.

4.1.1 Drug profile of metoclopramide hydrochloride

The source thesis described metoclopramide hydrochloride as a prokinetic drug used for stomach and esophageal problems, including nausea and vomiting associated with gastroesophageal reflux disease and diabetic gastroparesis. The drug acts through dopamine D2 and serotonin 5-HT3 receptor antagonism in the chemoreceptor trigger zone, with prokinetic contribution through D2 receptor inhibition and 5-HT4 receptor agonistic action. Drug-specific information used for the formulation rationale is summarized below.

Table 3. Drug profile information taken from the source thesis

Parameter	Source-thesis information
Empirical formula	C14H22ClN3O2.HCl.H2O
Chemical name	4-amino-5-chloro-N-[2-(diethyl-amino) ethyl]-2-methoxy-benzamide hydrate hydrochloride
Molecular weight	336.26 g/mol
Trade names mentioned	Reglan and Metozolv ODT
Description	White solid crystalline powder
Melting point	103°C in drug profile; 102°C observed experimentally
BCS status	Class 3
Solubility	Very soluble in water and freely soluble in alcohol
Log P	1.4
pKa	Acidic 14.45; basic 9.04
Half-life	5-6 hours

Table 4. Materials used for formulation development

Material	Supplier/Source
Metoclopramide hydrochloride	Ronak Healthcare, Gujarat
Sodium alginate	Loba Chemie Pvt. Ltd.
Calcium carbonate	SD Chem Lab India
Calcium chloride	Loba Chemie Pvt. Ltd.
Poloxamer 188	Vishal Chem, Mumbai

Table 5. Equipment used in the source study

Equipment	Make/Model
Digital analytical balance	Shimadzu Japan, Model No. ATX 124
Magnetic stirrer	Remi Motor, Model No. RQT127
Ultrasonicator	Ultrasonic Model (2500 ml), Model No. CD4820, Mumbai
Double-beam UV/Visible spectrophotometer	Shimadzu Double Beam UV1800, Japan
FTIR spectrophotometer	Thermo Fisher Scientific India
Differential scanning calorimeter	KEP Technologies, Japan
Optical microscope	ESAW Optscopes Classic
Scanning electron microscope	JSM 6330 JEOL, Japan
Dissolution apparatus	Lab India Analytical Instrument Pvt. Ltd., Mumbai

Table 6. Software/tools mentioned in the source study

Software/tool	Use
Microsoft Office Excel 2003	Data handling and plotting
Microsoft Office PowerPoint	Presentation/figure preparation
Design-Expert/Stat-Ease software	Factorial design, model fitting and ANOVA

4.2 Drug and excipient rationale

The drug and excipient selection in the source work was based on the role of each component in the bead matrix. Sodium alginate was used as the gelling polymer; calcium chloride was used for ionic crosslinking; calcium carbonate was used as the gas-forming component; and poloxamer 188 was varied as the release-modifying polymer in the factorial design. The structures of the drug and major excipients were included in the thesis and are reproduced below only from the supplied file.

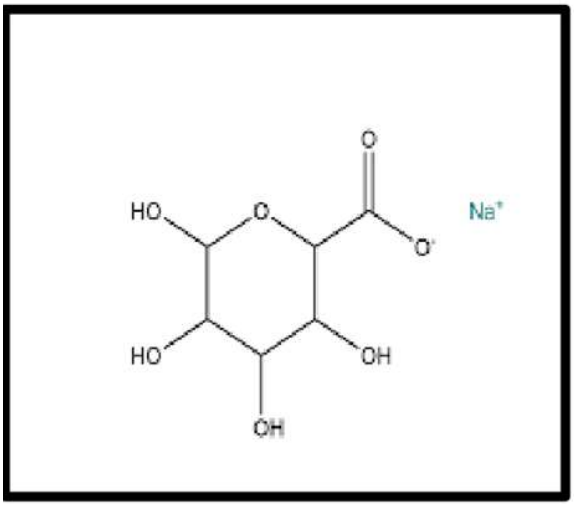

Figure 4. Structure of sodium alginate from the source thesis.

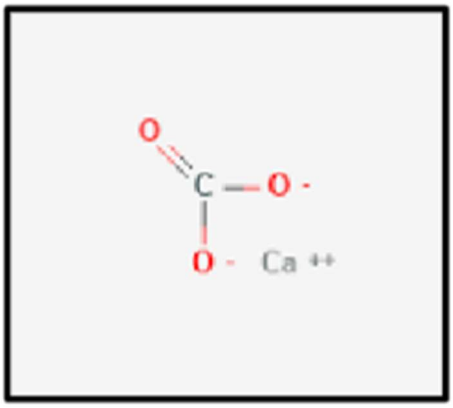

Figure 5. Structure of calcium carbonate from the source thesis.

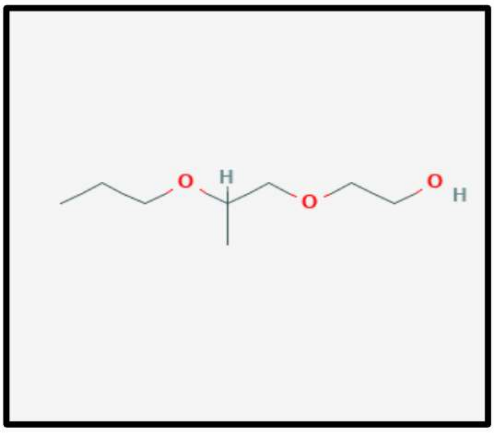

Figure 6. Structure of poloxamer 188 from the source thesis.

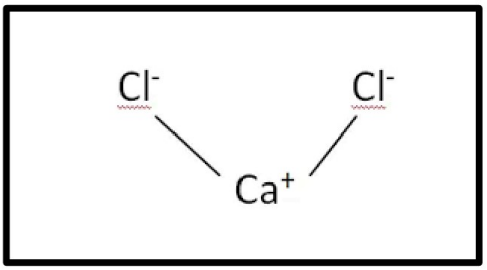

Figure 7. Structure of calcium chloride from the source thesis.

Table 7. Functional role of formulation components

Component	Role in formulation
Metoclopramide hydrochloride	Model antiemetic/prokinetic drug for stomach-specific floating beads
Sodium alginate	Gelling matrix polymer for calcium alginate bead formation
Calcium chloride	Crosslinking agent for ionotropic gelation
Calcium carbonate	Gas-forming floating inducer in acidic gastric medium
Poloxamer 188	Polymeric variable used in factorial design to influence bead characteristics and release

Table 8. Excipient profile details summarized from the source thesis

Excipient	Source profile details relevant to formulation
Sodium alginate	Sodium salt of alginic acid; forms thick colloidal solution in water; used as stabilizing agent, suspending agent, binder, disintegrant and sustained-release excipient.
Calcium carbonate	Fine white powder/crystals; used as diluent, buffering agent and antacid-related pharmaceutical material; acts here as gas-forming agent in acidic medium.
Poloxamer 188	Polyoxyethylene-polyoxypropylene copolymer; used in pharmaceutical systems as polymeric excipient and release modifier.
Calcium chloride	Calcium salt used as crosslinking agent in alginate bead formation through ionotropic gelation.

4.3 Preformulation and analytical characterization

The pure drug was characterized for description, solubility, taste and melting point. The UV spectrum was recorded in 0.1 N HCl and the wavelength of maximum absorbance was determined. A standard calibration curve was prepared in the concentration range of 0-16 µg/ml

and the absorbance was measured at 272 nm. FTIR spectroscopy was performed to identify characteristic functional-group peaks and to assess compatibility. DSC thermograms were recorded to compare the thermal behavior of pure drug and formulated beads.

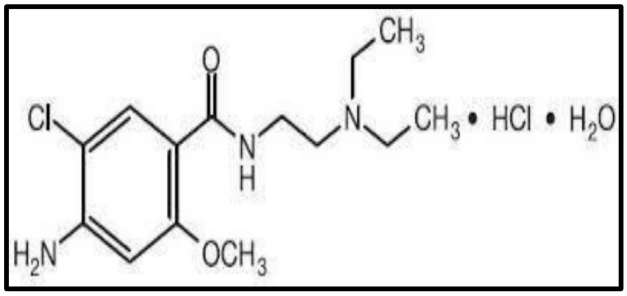

Figure 8. Chemical structure of metoclopramide hydrochloride from the source thesis.

4.4 Formulation design

A 3^2 factorial design was selected to study the influence of sodium alginate and poloxamer 188. Sodium alginate was evaluated at 1%, 2% and 3%, while poloxamer 188 was evaluated at 30 mg, 40 mg and 50 mg. Nine formulations (F1-F9) were prepared. Metoclopramide hydrochloride was kept constant at 40 mg in all batches. Calcium chloride was kept at 3% and calcium carbonate was kept at 1 gm in all formulations.

Table 9. Formulation of floating beads of metoclopramide hydrochloride

Ingredient	F1	F2	F3	F4	F5	F6	F7	F8	F9
Metoclopramide Hydrochloride (mg)	40	40	40	40	40	40	40	40	40
Sodium alginate	1%	1%	1%	2%	2%	2%	3%	3%	3%
Poloxamer 188 (mg)	30	40	50	30	40	50	30	40	50
Calcium chloride	3%	3%	3%	3%	3%	3%	3%	3%	3%
Calcium carbonate (gm)	1	1	1	1	1	1	1	1	1

e 9. Floating Beads of Metoclopramide Hydrochlori

Figure 9. Floating beads of metoclopramide hydrochloride from the source thesis.

Figure 10. Prepared batches of floating beads of metoclopramide hydrochloride.

4.5 Method of preparation: ionotropic gelation

Floating beads were prepared by ionotropic gelation. Sodium alginate was dissolved in 100 ml distilled water and stirred continuously. Poloxamer 188 was then added as per the formulation design and stirred for 20 minutes. Metoclopramide hydrochloride and calcium carbonate were added to the polymeric dispersion. The dispersion was kept aside for 25 minutes to allow removal of entrapped air bubbles. The mixture was then extruded dropwise through a syringe into calcium chloride solution. The formed beads were collected, washed with distilled water and dried.

Table 10. Laboratory workflow followed in the source study

Step	Activity
1	Literature survey
2	Selection of drug and excipients
3	Procurement of drug and excipients
4	Experimental work
5	Preparation of floating beads
6	Optimization of formulation batches
7	Evaluation of floating beads

8	Data analysis and interpretation

4.6 Evaluation of formulated beads

Drug content was determined by triturating accurately weighed beads, dispersing the powder in 0.1 N HCl and measuring absorbance at 272 nm after appropriate dilution and filtration. Entrapment efficiency was determined by dispersing the powdered beads in 0.1 N HCl, keeping the dispersion for 24 hours, filtering, diluting and analyzing spectrophotometrically. In vitro buoyancy was measured by placing 50 beads in simulated gastric fluid (pH 1.2) at 37.5°C with stirring at 100 rpm and counting floating beads hourly up to 12 hours. Dissolution was performed using USP Type II paddle apparatus in 900 ml of 0.1 N HCl at 37±0.5°C and 100 rpm. Samples were withdrawn at predetermined intervals and analyzed at 272 nm.

Table 11. Main evaluation parameters and formulae

Parameter	Experimental basis / calculation
Drug content	Actual drug content / total weight of beads × 100
Entrapment efficiency	Practical drug content / theoretical drug content × 100
In vitro buoyancy	Number of floating beads / total beads × 100
In vitro dissolution	USP Type II paddle, 900 ml 0.1 N HCl, 100 rpm, 37±0.5°C
Data analysis	3^2 factorial design and ANOVA using Design-Expert/Stat-Ease software

5. Results and Discussion

4.1 Drug characterization and UV analysis

Metoclopramide hydrochloride was observed as a white or almost white odorless powder, freely soluble in alcohol and very soluble in water. The drug was intensely bitter in taste. The melting point was found to be 102°C. UV spectrophotometric scanning showed maximum absorbance at 272 nm. The calibration curve in 0.1 N HCl showed linearity with slope 0.031208, intercept 0.002333 and coefficient of correlation (R^2) 0.9965.

Table 12. Observation for standard calibration curve of metoclopramide hydrochloride

Sr. No.	Concentration (µg/ml)	Absorbance
1	0	0
2	2	0.075
3	4	0.125
4	6	0.181
5	8	0.246
6	10	0.32
7	12	0.372
8	14	0.459
9	16	0.49

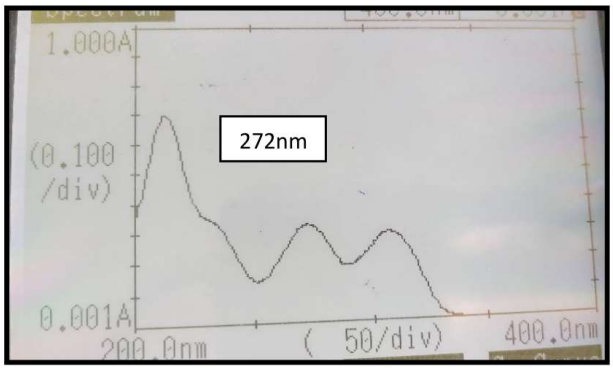

Figure 11. UV spectrum showing λmax of metoclopramide hydrochloride at 272 nm.

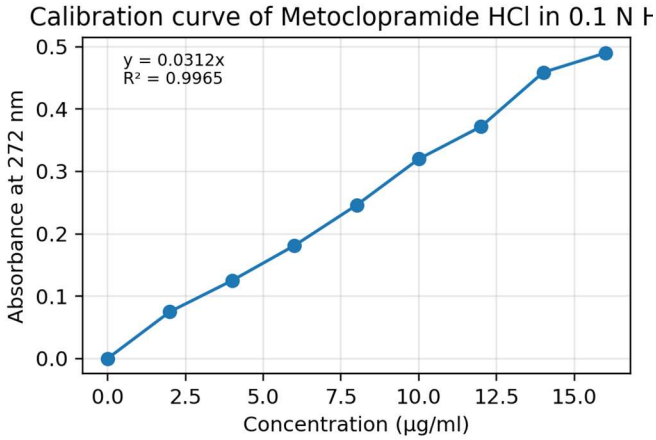

Figure 12. Calibration curve of metoclopramide hydrochloride in 0.1 N HCl reconstructed from the source data.

4.2 FTIR and DSC compatibility study

FTIR spectra of pure drug and formulation F9 showed the characteristic peaks corresponding to OH stretching, NH bending, C=C stretching, -OCH3 stretching and -CN stretching. The same major peaks were retained in the formulation, supporting absence of evident chemical interaction between metoclopramide hydrochloride and selected excipients. DSC analysis showed a sharp endothermic peak of metoclopramide hydrochloride around 105°C. The formulation thermogram did not show a meaningful shift in the drug endothermic response, indicating compatibility between drug and excipients in the selected formulation.

Table 13. FTIR interpretation of metoclopramide hydrochloride and formulation F9

Sr. No.	Wave number range (cm-1)	Interpretation	Pure drug peak (cm-1)	F9 peak (cm-1)
1	3500-3000	OH stretching vibration	3185.95	3188.15
2	2000-1500	NH bending vibration	1589.96	1587.82
3	2000-1500	C=C stretching	1533.66	1533.87
4	1500-1000	-OCH3 stretching	1254.80	1251.28
5	1500-1000	-CN stretching	1208.28	1207.48

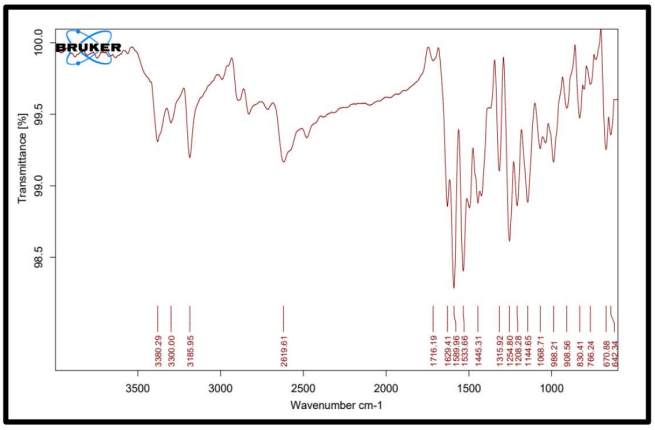

Figure 13. FTIR spectrum of pure metoclopramide hydrochloride.

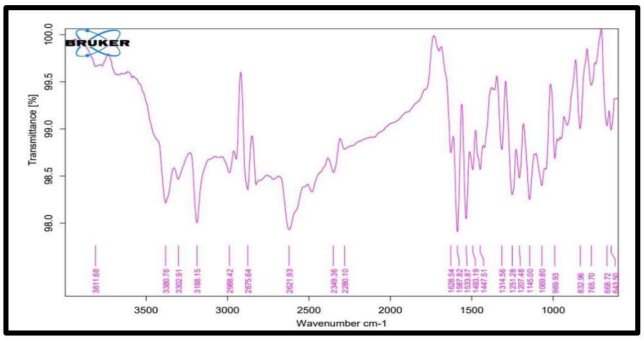

Figure 14. FTIR spectrum of formulation F9.

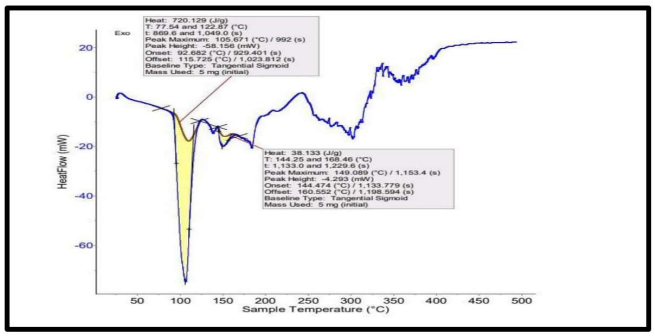

Figure 15. DSC thermogram of pure metoclopramide hydrochloride.

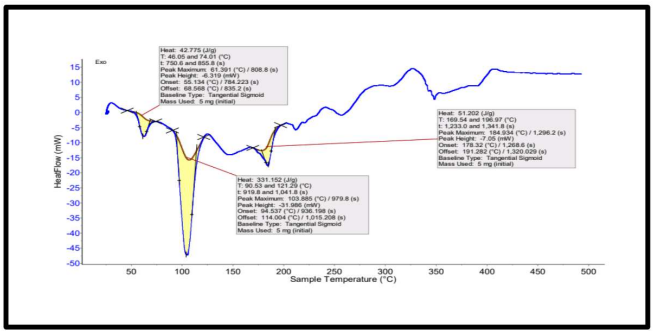

Figure 16. DSC thermogram of metoclopramide hydrochloride beads formulation F9.

Additional compatibility spectra from the source thesis are included to preserve the analytical visual evidence used in the dissertation. These spectra support comparison among pure drug, excipient and selected formulation during compatibility assessment.

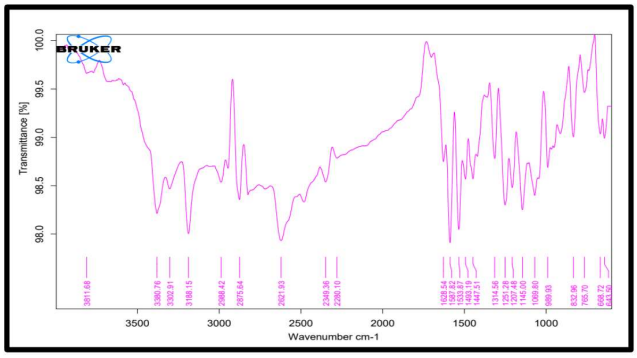

Figure 17. IR spectrum of pure metoclopramide hydrochloride used for compatibility comparison.

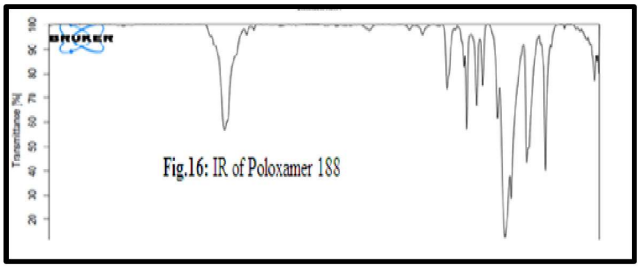

Figure 18. IR spectrum of poloxamer 188.

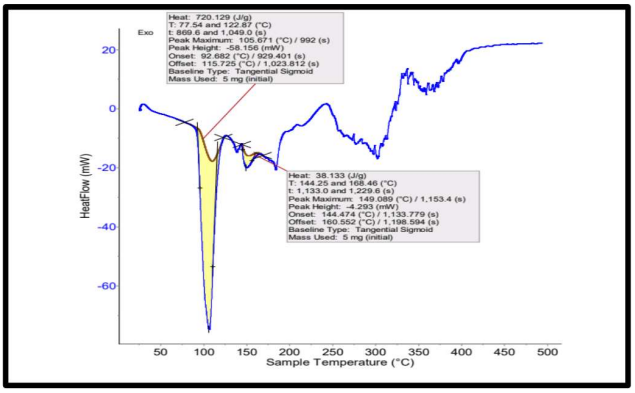

Figure 15. DSC of pure Metoclopramide Hydrochloride

Figure 19. DSC profile of pure metoclopramide hydrochloride from the source thesis.

4.3 Particle size, yield, drug content and entrapment efficiency

The prepared beads were round and free-flowing at higher sodium alginate concentrations. The particle size increased with increasing sodium alginate concentration, which may be related to the higher viscosity of the polymeric dispersion and greater resistance during droplet formation. The particle size ranged from 87.14±0.34 µm to 113.00±0.34 µm. Percentage yield values ranged from 86.76±1.23% to 98.47±1.56%. Drug content increased across formulations and reached 95.09±0.17% in F9. Entrapment efficiency ranged from 78.42±0.78% to 96.12±0.23%, with F9 showing the highest entrapment efficiency.

Table 14. Characterization of formulated floating beads

Formulation	Particle size (µm)	Yield (%)	Drug content (%)	Entrapment efficiency (%)	Floating lag time (min)	Floating time (h)	Buoyancy (%)
F1	87.14±0.34	88.32±0.98	72.49±0.25	80.27±0.075	2:10±0.34	>12	100±0.43
F2	91.86±0.24	91.84±1.09	69.28±0.39	78.42±0.78	1:39±0.12	>12	99±0.28
F3	87.36±0.31	86.76±1.23	75.46±0.17	79.07±0.20	1:52±0.43	>12	99.66±0.11
F4	91.12±0.21	94.98±0.76	79.57±0.08	88.20±0.05	2:21±0.29	>12	99.34±0.37
F5	97.3	98.4	81.5	82.0	2:1	>1	98.6
	2±0.15	7±1.56	6±0.17	0±0.22	2±0.98	2	6±0.45
F6	99.00±0.21	94.98±1.32	85.01±0.10	86.42±0.16	2:20±0.61	>12	99±0.81
F7	101.18±0.09	97.63±0.62	91.73±0.23	91.10±0.07	1:33±0.55	>12	100±0.68
F8	112.28±0.18	94.76±0.98	93.83±0.11	90.60±0.34	1:29±0.23	>12	99±0.39
F9	113.00±0.34	98.20±1.26	95.09±0.17	96.12±0.23	1:14±0.58	>12	100±0.47

4.4 In vitro buoyancy and surface morphology

All formulations demonstrated floating time greater than 12 hours in simulated gastric fluid (pH 1.2). The floating lag time ranged from 1:14±0.58 minutes to 2:21±0.29 minutes. The high buoyancy was attributed to calcium carbonate-mediated gas formation and the porous/entrapped-air structure of the alginate beads. SEM analysis of the optimized batch showed spherical beads with a rough, wrinkled surface. The surface texture and internal porosity were consistent with sustained buoyancy and controlled release behavior.

Figure 21. Floating beads Initial Time (F1, F2, F3)

Figure 20. Floating beads at initial time (F1, F2, F3).

Figure 21. Floating beads after 12 hours (F7, F8, F9).

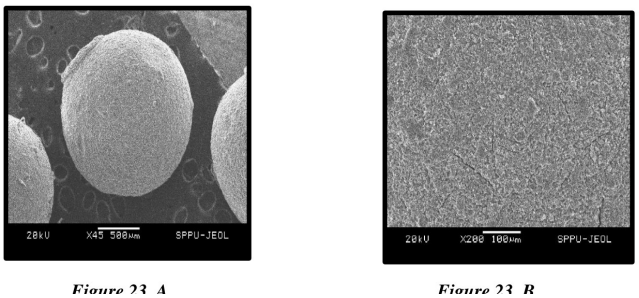

Figure 22. SEM photomicrographs of drug-loaded floating beads (A and B).

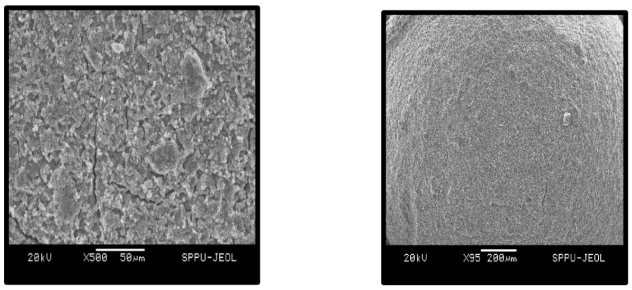

Figure 23. SEM photomicrographs of drug-loaded floating beads (C and D).

4.5 In vitro dissolution

The dissolution profiles demonstrated sustained release of metoclopramide hydrochloride in 0.1 N HCl over 12 hours. Among all formulations, the 12-hour cumulative release ranged from 79.87±0.52% in F9 to 92.32±0.38% in F7. Increasing polymer concentration generally reduced the rate and extent of drug release. Formulation F9 showed slower and more controlled release than lower-polymer formulations while maintaining high drug content, entrapment efficiency and buoyancy.

Figure 24. Dissolution test apparatus used in the source thesis.

Table 15. In vitro dissolution profile of formulations F1-F9

Time	F1	F2	F3	F4	F5	F6	F7	F8	F9
(h)									
0	0	0	0	0	0	0	0	0	0
2	42.7	37.08	36.17	41.12	38.12	39.98	38.67	35.12	33.82
4	69.56	64.07	63.28	64.96	59.83	54.12	68.19	65.7	61.16
6	76.32	71.26	69.14	75.67	73.18	67.97	74.3	71.49	69.46
8	84.56	76.32	72.6	79.09	73.43	71.12	79.96	75.06	72.18
10	86.38	84.8	77.4	82.16	80.35	78.4	89.12	79.98	76.4
12	92.02	86.79	81.75	89.23	83.31	82.28	92.32	84.12	79.87

All dissolution values are cumulative percentage drug release; source values were reported as mean ± SD (n=3).

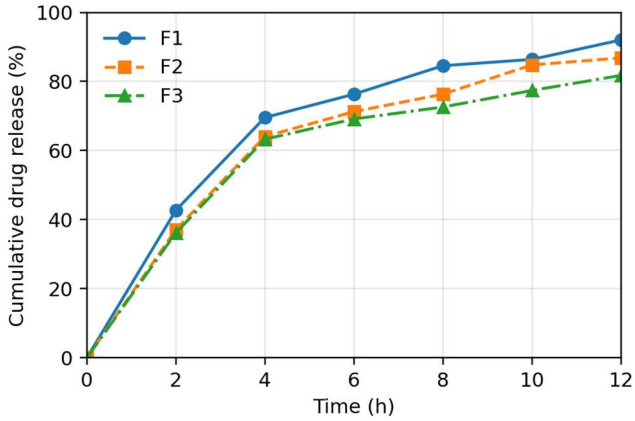

Figure 25. In vitro dissolution profile of formulations F1-F3.

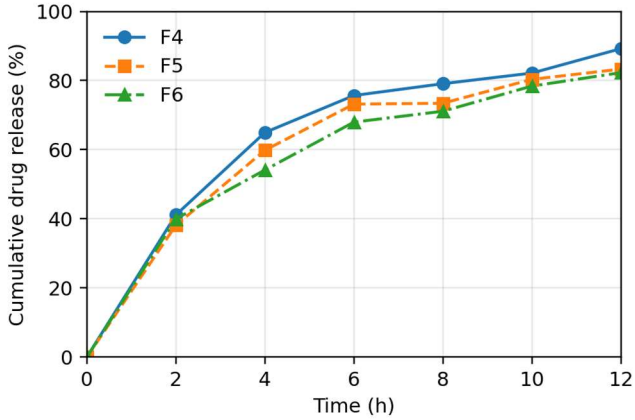

Figure 26. In vitro dissolution profile of formulations F4-F6.

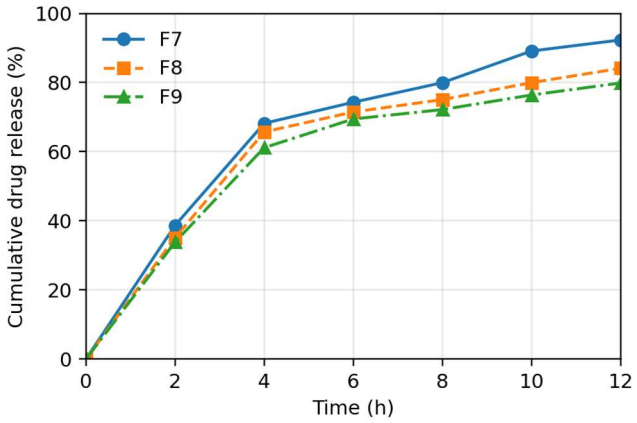

Figure 27. In vitro dissolution profile of formulations F7-F9.

4.6 Factorial design and ANOVA

The 3^2 factorial design was used to evaluate the effect of sodium alginate (X1) and poloxamer 188 (X2) on 12-hour drug release. The observed 12-hour release values across the nine formulations ranged from 79.87% to 92.32%. The overall model for Rel12hr showed F value 3.26 and p value 0.1797, indicating that the model was not statistically significant at the conventional 0.05 level. The linear effect of poloxamer 188 (X2) was significant with p=0.0324, while X1, interaction and quadratic terms were not significant.

Table 16. Factorial design summary

Factor	Name	Unit	Type	Coded levels	Actual levels
X1	Sodium alginate	%	Numerical	-1, 0, +1	1%, 2%, 3%
X2	Poloxamer 188	mg	Numerical	-1, 0, +1	30, 40, 50

Table 17. Response summary for all formulations

Formulation	Sodium alginate (X1)	Poloxamer 188 (X2)	Rel12hr (%)
F1	1%	30	92.02
F2	1%	40	86.76
F3	1%	50	81.75
F4	2%	30	89.23
F5	2%	40	83.31
F6	2%	50	82.28
F7	3%	30	92.32
F8	3%	40	87.50
F9	3%	50	79.87

Table 18. Analysis of variance for Rel12hr

Source	Sum of squares	DF	Mean square	F value	P value	Model status
Model	111.94	5	22.39	3.26	0.1797	Not significant
X1	0.6936	1	0.6936	0.1010	0.7714	
X2	98.09	1	98.09	14.29	0.0324	
X1X2	1.29	1	1.29	0.1876	0.6941	
(X1)^2	11.71	1	11.71	1.71	0.2826	
(X2)^2	0.1568	1	0.1568	0.0228	0.8895	
Residual	20.60	3	6.87			
Core Total	132.54	8				

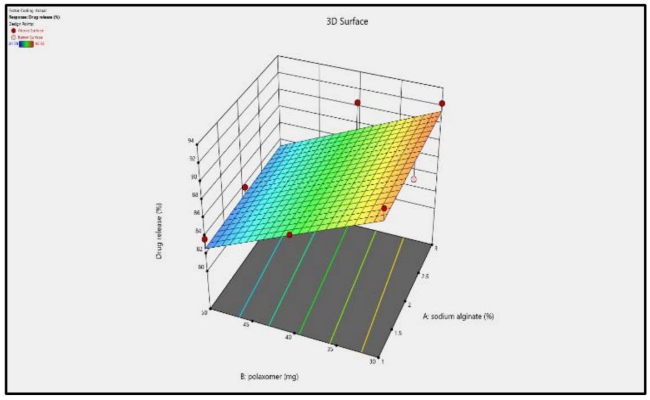

Figure 28. Response 3-D surface plot for drug release.

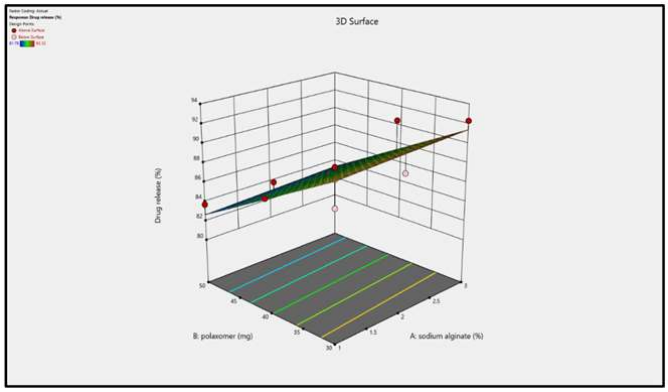

Figure 29. Response 3-D plot/contour representation for drug release.

6. Overall Discussion

The study demonstrated that sodium alginate-calcium chloride ionotropic gelation can produce stomach-specific floating beads of metoclopramide hydrochloride. The constant drug and gas-forming agent levels allowed the factorial design to focus on the polymeric matrix variables. The results indicate that higher polymer content improved drug content and entrapment efficiency, while also modulating the drug release profile. The buoyancy results confirmed the ability of the prepared beads to remain floating for more than 12 hours, which is a central requirement for gastroretentive delivery.

FTIR and DSC results supported compatibility between the drug and excipients. SEM observations showed the bead surface as rough and wrinkled, supporting the role of matrix texture and entrapped gas in buoyancy and release behavior. The dissolution data suggest that the formulations provided sustained drug release in acidic medium. Although F7 showed the highest 12-hour release, F9 showed the most controlled release among the higher-polymer batches while maintaining the highest drug content and entrapment efficiency. Therefore, F9 can be considered the selected formulation based on a balanced profile of yield, loading, entrapment, buoyancy and sustained release.

7. Conclusion

Stomach-specific floating beads of metoclopramide hydrochloride were successfully formulated by ionotropic gelation using sodium alginate, calcium chloride, calcium carbonate and poloxamer 188. The prepared beads showed acceptable particle size, high yield, improved drug content, high entrapment efficiency and excellent floating behavior for more than 12 hours. FTIR and DSC results indicated no evident drug-excipient incompatibility. SEM images showed spherical, rough and wrinkled beads. Formulation F9 showed high drug content (95.09±0.17%), highest entrapment efficiency (96.12±0.23%), 100±0.47% buoyancy and controlled 12-hour drug release (79.87±0.52%). Based on these results, alginate-poloxamer floating beads can be considered a promising stomach-specific delivery system for metoclopramide hydrochloride.

8. Future Perspective

The formulation approach may provide a basis for developing similar stomach-specific controlled-release dosage forms. Further work can focus on scale-up, stability evaluation and in vivo gastric residence confirmation as per the future direction indicated in the source thesis.

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The manuscript was prepared from the experimental data, results, figures and references available in the submitted dissertation. No additional experimental data were inserted.

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