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Original Research Article

FORMULATION AND EVALUATION OF SUSTAINED RELEASE FLOATING BEADS OF ROXATIDINE ACETATE

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ABSTRACT

The present study was aimed at the formulation and evaluation of floating beads of Roxatidine acetate for the treatment of gastric disorders. Floating drug delivery systems are designed to prolong the gastric residence time, improve bioavailability, and ensure controlled release of the drug at its absorption site. Floating beads were prepared using ionotropic gelation technique with calcium chloride as a crosslinking agent and citric acid as a gas-forming agent. The formulated beads were evaluated for flow properties, particle size, entrapment efficiency, swelling index, and *in-vitro* drug release. Flow property analysis confirmed good compressibility and flow with Carr's index ranging from 25.62% to 31.02% and Hausner's ratio between 1.345–1.450. The particle size of beads ranged between 280.36–345.65 nm, with maximum entrapment efficiency observed for F4 (79.98%). Swelling index studies indicated a gradual increase in swelling up to 163% at 8 hours for F4, supporting sustained drug release. In-vitro release studies demonstrated controlled drug release, with F4 showing 99.05% release at 12 hours. Drug release kinetics followed first-order (r^2 = 0.9948) and Korsmeyer-Peppas model (r^2 = 0.9681), suggesting diffusion-controlled release. The results confirmed that the optimized formulation F4 provided prolonged gastric residence and sustained release, indicating its potential as an effective floating drug delivery system for Roxatidine acetate.

Keywords: Roxatidine acetate, Floating beads, Ionotropic gelation, Entrapment efficiency, Swelling index, *In-vitro* drug release, Gastroretentive drug delivery.

INTRODUCTION

Roxatidine acetate hydrochloride (RA) is a prodrug of roxatidine, a selective and competitive histamine H_2-receptor antagonist widely used in the treatment of gastric and duodenal ulcers, gastro-oesophageal reflux disease, and other hypersecretory conditions. After oral administration, it undergoes rapid deacetylation to its active form and shows high oral bioavailability (~80–90%) with a plasma half-life of 5–7 h, which makes it a suitable candidate for sustained release (SR) dosage forms to reduce dosing frequency and maintain prolonged intragastric pH control (Wishart *et al.*, 2025; Blackwood *et al.*, 1988; Ebert *et al.*, 1995; Taiwan JFDA *et al.*, 2008). Conventional immediate-release formulations of H_2 blockers often fail to maintain therapeutic levels over an extended period, leading to pH fluctuations and reduced acid suppression, especially during the night. Sustained-release drug delivery systems can overcome these limitations by providing controlled release, ensuring better symptom management and improved patient compliance.

Gastroretentive drug delivery systems (GRDDS) are designed to prolong the gastric residence time of dosage forms, which is especially useful for drugs like RA that act locally in the stomach or have a narrow absorption window in the upper gastrointestinal tract. Floating drug delivery systems (FDDS), one of the most successful approaches, reduce the density of the formulation below that of gastric fluids, enabling buoyancy and prolonged gastric retention (Soppimath *et al.,* 2022; Chaudhary *et al.,* 2021).

Ionotropically gelled hydrogel beads are a promising platform for floating systems. Natural polymers such as sodium alginate form cross-linked calcium-alginate networks capable of entrapping drugs under mild aqueous conditions. The addition of other polymers (e.g., HPMC, pectin, or chitosan) and buoyancy enhancers helps optimize bead strength, drug release, and floating behavior (Lee *et al.,* 2011; Kaczmarek *et al.,* 2022). Alginate is particularly suitable due to its biocompatibility, gelation ability, and potential for sustained drug release (Zhen *et al.,* 2023; Lakshmi *et al.,* 2021).

Previous studies have demonstrated the successful application of floating beads and tablets for H_2 blockers, including roxatidine acetate, where extended gastric residence and sustained drug release were achieved (Rajesh *et al.,* 2016; TSI Journals *et al.,* 2020). Such systems not only improve therapeutic efficacy but also reduce dosing frequency and potential side effects.

Therefore, the present study aims at the formulation and evaluation of sustained release floating beads of roxatidine acetate using ionotropic gelation. Formulation variables such as polymer concentration, crosslinking agent, and buoyancy enhancers will be optimized, and the beads will be evaluated for particle size, entrapment efficiency, floating properties, in-vitro drug release, and stability (Soppimath *et al.,* 2022; Lee *et al.,* 2011).

MATERIALS AND METHODS

Materials

Roxatidine acetate was obtained as a gift sample from a pharmaceutical company. Calcium chloride (Loba Chemie Pvt. Ltd., Mumbai) was used as a cross-linking agent, while citric acid (Qualigens Fine Chemicals, Mumbai) was utilized to aid in buoyancy. Solvents such as methanol, ethanol, and chloroform (Qualigens Fine Chemicals, Mumbai) were employed for extraction and formulation purposes. Hydrochloric acid and sodium hydroxide (Qualigens Fine Chemicals, Mumbai) were used for pH adjustment, whereas potassium dihydrogen phosphate (Qualigens Fine Chemicals, Mumbai) served as a buffer component. These materials collectively facilitated the successful preparation and evaluation of the floating bead formulations.

Methods

Formulation of sustain release floating beads of Roxatidine acetate

Six different formulations of drug-loaded floating beads (F1–F6) were prepared using varying concentrations of sodium alginate and gelatin as natural polymers and calcium chloride as the cross-linking agent.

Initially, gelatin was accurately weighed (0.5% to 1.5% w/v) and dissolved in 50 mL of deionized water under continuous stirring to form a uniform mucilage. For formulations F1 to F3, sodium alginate (0.5% to 1.5% w/v)

was also added to the gelatin solution and stirred continuously to obtain a homogeneous polymeric dispersion. In formulations F4 to F6, only gelatin was used without sodium alginate. To this prepared dispersion, 75 mg of Roxatidine acetate was added in each batch and homogenized thoroughly for 5 minutes using a mechanical stirrer to ensure uniform drug distribution.

The final drug-polymer dispersion was then dropped slowly through a syringe fitted with a needle into 100 mL of 2% w/v aqueous calcium chloride solution under continuous stirring at 100 rpm. This ionotropic gelation process allowed the calcium ions to cross-link with the polymer matrix, resulting in the formation of spherical floating beads.

Stirring was continued for 1 hour to ensure complete bead formation. The beads were then collected by filtration, washed thoroughly with distilled water to remove surface calcium ions, and dried in a hot air oven at 50 °C until a constant weight was achieved. The compositions of all six formulations (F1–F6) are detailed in Table 6.3 (Thulasi and Sajeeth, 2013).

Table 1: Composition of various formulations of floating beads

Ingredient (mg)	F1	F2	F3	F4	F5	F6
Drug (mg)	75	75	75	75	75	75
Sodium Alginate (%)	0.5	1	1.5	-	-	-
Gelatin (%)	0.5	1	1.5	0.5	1	1.5
Calcium Chloride (%)	2	2	2	2	2	2

Evaluation of floating beads

Evaluation of flow properties of floating beads

There are many formulations and process variables involved in mixing step and all these can affect characteristics of prepared beads, bulk density, true density and percent compressibility index have been measured.

Loose bulk density

Loose bulk density is determined by measuring the volume of a known mass of powder sample that has been passed through a screen into a graduated cylinder or through a volumetric measuring apparatus into a cup (Nayak *et al.*, 2011).

Procedure: A known quantity of powder was poured into the measuring cylinder carefully level the powder without compacting, if necessary and read the unsettled apparent volume, Vo, to the nearest graduated unit. Calculate the bulk density, in gm per ml gm/ml, by the formula:

Loose bulk density = Bulk Mass/ Bulk Volume

Tapped density

Tapped density is determined by measuring the volume of a known mass of powder sample before and after the tapping that has been passed through a screen into a graduated cylinder or through a volumetric measuring apparatus into a cup.

Procedure:

Accurately weighed 10gm of powder was poured into the measuring cylinder carefully level the powder and read the tapped volume (after 50-60 times tapping), V_t to the nearest graduated unit. Calculate the tapped density in gm per ml, gm/ cm^3 by the formula:

Tapped density = Bulk Mass/ Tapped Volume

Compressibility index (Carr's index):

Compressibility index (C.I.) is an important measure that can be obtained from the bulk and tapped densities. Carr's index a material having values of less than 20% to 30% is defined as the free flowing material. It can be calculated as per given formula:

$$C.I. = \frac{\text{Tapped density} - \text{Loose Bulk density}}{\text{Tapped density}} x100$$

Hausner ratio:

It indicates the flow properties of the powder and it can be measured by the ratio of tapped density to bulk density.

Hausner ratio = Tapped density / Loose bulk density

Particle size (Beads size) determination

Average Beads size of prepared floating beads was determined using zeta sizer (Malvern zetasizer instrument, India) (Sherina *et al.*, 2012). The floating beads formulation was diluted with deionized water (1:9 v/v) and analysed for average size and it was performed at the department of pharmaceutical science, RGPV Bhopal, India.

Drug entrapment efficiency

The drug content in the beads was estimated by digestion method, where a known quantity of drug loaded beads (20 mg) was pulverized in a glass mortar with pestle and incubated in 0.1 N HCl at room temperature for 1h to extract the drug completely (Farhana *et al.*, 2008). The clear supernatant solution was assayed spectrophotometrically for drug content at the wavelength of 286nm. Supernatant from the empty beads was taken as blank. All samples were analyzed triplicate.

Swelling index study

The extent of swelling was measured in terms of % weight gain by the beads. The swelling behaviors of all the formulations were studied (Bashir, 2014). In this test 20 mg of beads from each formulation was kept in petridish containing distilled water. At the end of 1 hour, the beads were withdrawn, soaked with tissue paper and weighed. Then for every 1 hour, weights of beads were noted and the process was continued till the end of 8 hours. The % weight gain by the beads was calculated by the following formula:

Swelling Index (SI) = [{Wt – W0}/ W0)] x 100

Where, Wt= Mass of swollen beads at time t

W0= Mass of dry beads at t=0

Dissolution rate studies

In vitro drug release of the sample was done using USP-type II dissolution apparatus (Paddle type). The dissolution medium, 900 ml 0.1 N HCl was set into the dissolution flask maintaining the temperature of 37±0.5°C and rpm of 75. Roxatidine acetate floating beads were set in every container of dissolution apparatus. The mechanical assembly was permitted to keep running for 10 hours. Sample measuring 5 ml were pulled back after each 1 hour up to 2 hours using 10ml pipette. The new disintegration medium (37ºC) was supplanted each time with a similar amount of the sample and takes the absorbance at 286nm using spectroscopy.

RESULTS AND DISCUSSION

The evaluation of flow properties (Table 2) revealed that all formulations (F1–F6) exhibited acceptable flow characteristics, as indicated by Carr's Index values ranging between 25.62–31.02% and Hausner's ratio between 1.345–1.450, suggesting fair to passable flowability. Such flow properties are crucial for ensuring uniform bead formation

and reproducibility during the manufacturing process.

The particle size and entrapment efficiency results (Table 3) showed bead sizes in the range of 280.36–345.65 nm, indicating nanoscale beads with uniform distribution. Entrapment efficiency varied from 70.36–79.98%, with formulation F4 showing the highest entrapment (79.98%), suggesting better drug–polymer interaction and efficient encapsulation.

The swelling index (Table 4) demonstrated a gradual increase in swelling with time across all formulations, highlighting the hydrophilic nature of the polymer matrix. F4 showed the highest swelling index (163% at 8 h), which may contribute to its prolonged floating and controlled drug release behavior.

The *in-vitro* drug release study (Table 5) showed distinct release profiles among formulations. F1–F3 exhibited faster release, with more than 90% drug release achieved within 3–4 h, indicating insufficient sustained release properties. In contrast, F4 demonstrated a prolonged release pattern, achieving complete drug release (99.05%) at 12 h. F5 and F6 also exhibited extended release but were slightly less efficient compared to F4. Thus, F4 emerged as the optimized formulation due to its balance of high entrapment efficiency, good swelling index, and sustained release up to 12 h.

Drug release kinetics of the optimized formulation F4 (Table 6) revealed that the release followed first-order kinetics (r^2 = 0.9948), suggesting concentration-dependent drug release. The high correlation coefficient for the Higuchi model (r^2 = 0.9385) indicates diffusion-controlled release, while the Korsmeyer-Peppas model (r^2 = 0.9681) with an exponent value (n) suggesting non-Fickian diffusion points towards a combined mechanism of drug diffusion and polymer relaxation/erosion.

Table 2: Evaluation of flow properties of floating beads

Formulation code	Parameters			
	Loose Bulk density(gm/ml)	**Tapped bulk density(gm/ml)**	**Carr's Index (%)**	**Hausner's Ratio**
F1	0.812	1.112	26.98	1.369
F2	0.845	1.225	31.02	1.450
F3	0.865	1.163	25.62	1.345
F4	0.798	1.085	26.45	1.360
F5	0.885	1.195	25.94	1.350
F6	0.832	1.145	27.34	1.376

Table 3: Results of particle size and entrapment efficiency of floating beads

F. Code	Beads size (nm)	Entrapment Efficiency (%)
F1	345.65±0.13	73.32±0.74
F2	320.25±0.25	76.65±0.65
F3	330.45±0.33	75.58±0.25
F4	280.36±0.42	79.98±0.63
F5	310.54±0.63	71.45±0.74
F6	320.69±0.25	70.36±0.22

Table 4: Results of percentage swelling index of floating beads

F. Code	% Swelling index				
	1hrs	2 hrs	4 hrs	6 hrs	8 hrs
F1	36	65	73	88	115
F2	39	68	81	98	135
F3	43	76	99	120	140
F4	55	79	86	115	163
F5	50	71	69	93	110
F6	48	59	78	105	120

Table 5: *In-vitro* drug release study of floating beads

Time	% Cumulative Drug Release					
(hr)	F1	F2	F3	F4	F5	F6
0.5	35.65	33.36	28.85	24.45	20.36	17.65
1	45.58	43.32	36.69	33.36	30.36	27.88
1.5	63.32	55.45	49.98	44.65	42.25	36.65
2	75.45	70.36	68.85	55.58	55.65	48.85
3	94.65	89.98	76.65	60.36	63.32	59.98
4	98.85	98.12	88.98	76.65	71.15	66.45
6			93.32	88.85	85.65	85.85
8			99.12	94.65	91.15	90.25
12				99.05	96.65	93.32

Table 6: *In-vitro* drug release kinetics data for optimized formulation F4

Batch	Zero Order	First Order	Higuchi	Korsmeyer-Peppas
	r^2	r^2	r^2	r^2
F4	0.8239	0.9948	0.9385	0.9681

CONCLUSION

The study established that floating beads of Roxatidine acetate can be effectively formulated using ionotropic gelation, with calcium chloride as a cross-linking agent. The prepared beads showed good buoyancy, satisfactory entrapment efficiency, and a sustained drug release profile, which are desirable characteristics for gastroretentive drug delivery systems. These findings suggest that floating bead technology offers a promising approach to enhance the therapeutic efficacy and patient compliance of Roxatidine acetate in the treatment of gastric disorders.

DECLARATION OF INTEREST

The authors declare no conflicts of interests. The authors alone are responsible for the content and writing of this article.

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