



Received on 26 June 2018; received in revised form, 28 September 2018; accepted, 05 October 2018; published 01 March 2019

FORMULATION AND EVALUATION OF FLOATING GEL BEADS OF LORATADINE

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Keywords:

Floating,
Gel beads, Loratadine,
Ionic gelation, Zero-order release

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ABSTRACT: A floating controlled drug delivery system of loratadine was formulated to enhance the retention time in the stomach and to modify the release characteristics of loratadine. Loratadine loaded floating gel beads were prepared by ionic gelation technique using different polymers such as HPMC K4M, HPMC K15M, and carbopol 934P in different proportions and sodium bicarbonate as the gas forming agent. FT-IR spectra revealed that there was no significant interaction of loratadine with the carriers and other excipients. The prepared beads were evaluated for particle size analysis, bulk density, tapped density, compressibility index, hausner's ratio, the angle of repose, swelling index, drug entrapment efficiency, % yield, % buoyancy of loratadine floating beads, *in-vitro* drug release studies, kinetic modeling of drug release and stability studies. Results of the *in-vitro* drug release study indicated sustained release of loratadine for up to 12 h. The drug release kinetics of optimized formulation F7 was best fitted with the zero order and Peppas model with $n > 0.45$.

INTRODUCTION: The oral route is increasingly being used for the delivery of therapeutic agents because the low cost of the therapy and ease of administration lead to high levels of patient compliance. More than 50% of the drug delivery systems available in the market are oral drug delivery systems¹. A major drawback in oral controlled drug delivery is that not all drug candidates are absorbed uniformly throughout the GIT. Some drugs are absorbed only in a particular portion of GIT or are absorbed to a different extent in various segments of GIT.

An absorption window exists because of physiological, physicochemical or biochemical factors. Recent scientific and patent literature reveals increased interest in novel dosage forms that can be retained in the stomach for a prolonged and predictable period.

One of the most feasible approaches is to control the gastric residence time using gastro-retentive dosage forms (GRDDS) that can provide newer therapeutic options. GRDDS can improve the controlled delivery of drugs by continuously releasing the drug for a prolonged period before it reaches its absorption site, thus ensuring its optimal bioavailability². Loratadine is an antihistamine that reduces the effects of natural chemical histamine in the body. Histamine can produce symptoms of sneezing, itching, watery eyes, and runny nose. Loratadine is absorbed in the proximal part of the

QUICK RESPONSE CODE 	DOI: 10.13040/IJPSR.0975-8232.10(3).1289-99
	The article can be accessed online on www.ijpsr.com
DOI link: http://dx.doi.org/10.13040/IJPSR.0975-8232.10(3).1289-99	

gastrointestinal tract; it is stable in acidic pH, has a narrow therapeutic absorption window in the GIT and the presence of food enhances its bioavailability³, meeting the primary criterion for selection of loratadine as the drug candidate to be formulated as a floating multiple unit dosage forms.

The purpose of designing a floating multiple unit dosage forms is to develop a reliable formulation of loratadine that has all the advantages of a floating single unit dosage form but is devoid of disadvantages of single unit dosage forms, namely sticking to or being obstructed in the GIT. In spite of all sophisticated formulations, the retention time of the single unit floating drug delivery system (FDDS) depends on many physiological factors, and it is a well-known fact that early gastric emptying of a monolithic device causes rapid lack of therapeutic efficacy, especially with drugs having an absorption window only in the stomach⁴. The floating beads have been employed to make a sustained release of the drug in the stomach to decrease the dose of the drug and overcome its side effects. The common benefits of the floating beads were ease of preparation without the need for high temperature and a high percentage of the drug entrapment.

The present research was mainly focused on the development and evaluation of gastroretentive, multiple units and controlled release formulations of loratadine. Various batches of floating beads were prepared by ionotropic/emulsion gelation method using different polymers in different proportions to achieve the controlled release of drug from developed floating beads.

MATERIALS AND METHODS:

Materials: Loratadine was received as a gift sample from Granules India Ltd., Hyderabad, India. Sodium alginate and Calcium chloride were procured from Sd Fine-Chem Ltd., Mumbai. Hydroxypropyl methylcellulose (HPMC K4M & 15M), Carbopol 934P were obtained from Rolex Chemical., Mumbai. Sodium bicarbonate was purchased from Quaikem Fine Chem Pvt. Ltd., Vadodara.

Methods: Drug - Carrier - Excipients Compatibility Checking: The drug and the excipients compatibility studies were carried out by checking the physical appearance as well as using

FT-IR spectral analysis. The compatibility studies were performed to ascertain any incompatibility of the drug with the excipients/ additives used in the formulation of floating gel beads of loratadine.

Fourier Transform Infra Red (FT-IR) Analysis:

⁵ An FT-IR spectrophotometer was employed for infrared analysis of the samples. Approximately 4-5 mg of the sample was mixed with dry potassium bromide (KBr), and the sample was analyzed at transmission mode over the 4000-400 cm^{-1} wavenumber range.

Calibration of Standard Curve of Loratadine:

Preparation of Standard Graph of Loratadine in

pH 1.2 Buffer: 100 mg of loratadine was weighed accurately and dissolved in 100 ml of pH 1.2 buffer in 100 ml volumetric flask. The resulting solution had a concentration of 1 mg/ml (1000 $\mu\text{g/ml}$). From the stock solution, 1 ml was taken in a 10 ml volumetric flask, and the volume was made up to 10 ml with pH 1.2 buffer (Secondary stock - 100 $\mu\text{g/ml}$). From the secondary stock solution, 0.5 ml, 1 ml, 1.5 ml, 2.0 ml, 2.5 ml and 3.0 ml were taken and volume made up to 10 ml with pH 1.2 buffer to get concentrations of 5 $\mu\text{g/ml}$, 10 $\mu\text{g/ml}$, 15 $\mu\text{g/ml}$, 20 $\mu\text{g/ml}$, 25 $\mu\text{g/ml}$ and 30 $\mu\text{g/ml}$ concentrations, respectively. The absorbance of each solution was measured by UV - Visible spectrophotometer at 214 nm using a pH 1.2 buffer as blank. The graph of concentration versus absorbance was plotted.

Method of Preparation of Loratadine Floating

Gel Beads: Loratadine floating gel beads were formulated using ionic gelation technique. 10 mg of loratadine was dissolved in 5 ml of purified water to prepare a loratadine solution. The prepared loratadine solution was added to 95 ml of sodium alginate solution (3% w/v) containing HPMC K4M / HPMC K15M / Carbopol 934P as polymers. Sodium bicarbonate was used as a gas forming agent and added to a sodium alginate solution in a ratio of 1:1.

The mixture was dropped into 100 ml of calcium chloride solution (1% w/v) using 24G syringe needle. The beads formed in the solution were then agitated for 10 min to improve the rigidity of floating gel beads. The beads were collected and washed with purified water followed by drying for 48 h.

TABLE 1: FORMULATION OF LORATADINE FLOATING GEL BEADS

Formula code	Drug (mg)	Sodium alginate (g)	HPMC K4M (g)	HPMC K15M (g)	Carbopol 934P (g)	NaHCO ₃ (g)	CaCl ₂ (g)
F1	100	3	-	-	-	3	1
F2	100	2	1	-	-	3	1
F3	100	1.750	1.250	-	-	3	1
F4	100	1.500	1.500	-	-	3	1
F5	100	2	-	1	-	3	1
F6	100	1.750	-	1.250	-	3	1
F7	100	1.500	-	1.500	-	3	1
F8	100	2.950	-	-	0.050	3	1
F9	100	2.900	-	-	0.100	3	1
F10	100	2.850	-	-	0.150	3	1
F11	100	2.500	0.250	0.250	-	3	1
F12	100	2.500	-	0.250	0.250	3	1

Evaluation of Loratadine Floating Gel Beads:

Particle Size Analysis: Average particle size of beads was determined using sieve analysis method. Twenty-gram beads were weighed carefully and placed on the first screen and shaken for a certain time. Each fraction is then taken and weighed. The experiment was performed in triplicate. The particle size was determined as follows:

$$d_{ave} = \sum nd / \sum n$$

Where, d_{ave} = Average diameter of beads; n = Percent of each fraction retained on each sieve and d = Arithmetic mean size of sieve opening.

Flow Properties:

Bulk Density (D_b): It is the ratio of the total mass of powder to the bulk volume of powder. It was measured by pouring the weighed powder (passed through standard sieve # 20) into a measuring cylinder, and initial weight was noted this initial volume is called the bulk volume. From this, the bulk density was calculated according to the formula mentioned below. It is expressed in g/ml and is given by,

$$D_b = M / V_b$$

Where M is the mass of powder, V_b is the bulk volume of the powder and D_b is the bulk density of the powder.

Tapped Density (D_t): It is the ratio of the total mass of the powder to the tapped volume of the powder. Volume was measured by tapping the powder for 750 times, and the tapped volume was noted if the difference between these two volumes is less than 2%. If it is more than 2%, tapping is continued for 1250 times, and tapped volume was noted. Tapping was continued until the difference

between successive volumes is less than 2 % (in a bulk density apparatus). It is expressed in g/ml and is given by,

$$D_t = M / V_t$$

Where M is the mass of powder and V_t is the tapped volume of the powder.

Carr's Index (or) % Compressibility Index: It indicates powder flow properties. It is expressed in percentage and is given by

$$\text{Carr's Index} = \frac{\text{Tapped density} - \text{Bulk density}}{\text{Tapped density}} \times 100$$

Hausner's Ratio: Hausner's ratio is an indirect index of ease of powder flow. It is calculated by the following formula,

$$\text{Hausner's ratio} = \frac{\text{Tapped density}}{\text{Bulk density}}$$

Lower Hausner's ratio (< 1.25) indicates better flow properties than higher ones (> 1.25)

The angle of Repose: The frictional forces in loose powder or granules can be measured by angle of repose. This is the maximum angle possible between the surface of a pile of powder or granules and the horizontal plane. The granules were allowed to flow through the funnel fixed to a stand at definite height (h). The angle of repose was then calculated by measuring the height and radius of the heap of granules formed.

$$\theta = \tan^{-1} (h/r)$$

Where, θ = angle of repose, h = height of the heap and r = radius of the heap.

Swelling Studies: Known weight (50 mg) of floated beads was soaked in 100 ml of buffer 1.2 pH at $37 \pm 0.5 \text{ }^\circ\text{C}$. Then the beads were removed at specified time intervals, dried and weighed to determine the swelling index^{6, 7}. Swelling index was determined from the following equation:

$$\text{Swelling index} = \frac{\text{The weight of swollen beads} - \text{Initial weight of beads}}{\text{The initial weight of beads}} \times 100$$

Percentage Drug Entrapment Efficiency: The encapsulation efficiency was determined from the following equation,

$$\% \text{ Drug Entrapment Efficiency} = \frac{\text{The actual amount of drug}}{\text{The theoretical amount of drug}} \times 100$$

Percentage Yield: Percentage yield for the formulated beads was calculated from the following^{8, 9}:

$$\text{Percentage yield} = \frac{\text{The weight of the beads}}{\text{The weight of drug + Polymer weight}} \times 100$$

Scanning Electron Microscopy (SEM) Studies:

The prepared floated beads were examined for its surface morphology by SEM. The samples were fixed in individual stubs and coated uniformly with gold⁸.

Percentage Drug Loading: 50 mg of the loratadine prepared beads were weighed and dissolved in 50 ml of pH 1.2 buffer centrifuged, filtered and then the filtrate was analyzed at 214 nm using a UV/visible spectrophotometer (Lab India). The experiment was carried out in triplicate, and drug loading was calculated from the following equation:

$$\text{Drug Loading} = \frac{\text{The weight of drug in beads}}{\text{Total weight of beads}} \times 100$$

Buoyancy Study: *In-vitro* floating ability can be determined by calculating percentage buoyancy and performed in USP type II dissolution test apparatus by spreading the floating microspheres in 0.1N HCl. The media is stirred at 100 revolutions per minute (rpm) at $37 \pm 0.5 \text{ }^\circ\text{C}$. After specific intervals of time, both the fraction of microspheres (floating and settled microspheres) is collected, and buoyancy of the floating microspheres is determined by using formula¹⁰.

$$\% \text{ Floating microspheres} = \frac{\text{Weight floating microspheres} \times 100}{\text{The initial weight of floating microspheres}}$$

***In-vitro* Drug Release Studies:** The dissolution rate of the prepared beads was studied using USP rotating paddle dissolution apparatus II (Lab India). A known weight of beads containing an equivalent amount of 10 mg of loratadine was placed in the dissolution medium (900 ml of buffer pH 1.2). The temperature was adjusted to $37 \pm 0.5 \text{ }^\circ\text{C}$ at 50 rpm. 5 ml of samples were withdrawn at specified time intervals and replaced with fresh dissolution medium. The samples were filtered with 0.45 μm Whatman membrane filter and the quantity of the drug released was determined using spectrophotometer at 214 nm.

Kinetic Studies of Drug Release: The release data were analyzed using different kinetic equations which include zero-order, first-order kinetics, Higuchi diffusion, and Korsmeyer - Peppas models. The dissolution release kinetics and result of the best fit model among the preparations were also compared.

To study the mechanism of drug release from the optimized formulation of matrix tablets, the release data were fitted to the following equations:

$$\text{Zero-order equation } Q_t = Q_0 + k_0 t$$

Where, Q_t is the amount of drug release in time t , Q_0 is the initial amount of drug in the solution (most times, $Q_0 = 0$) and k_0 is the zero order release rate.

$$\text{First-order equation } \ln Q_t = \ln Q_0 + k_1 t$$

Where, Q_t is the amount of drug released in time t , Q_0 is the initial amount of drug in the solution, and k_1 is the first order release rate constant.

$$\text{Higuchi's equation (Higuchi, 1962), } Q = k_H t_{1/2}$$

Where, Q is the amount of drug release at time t , and k_H is the Higuchi diffusion rate constant.

Korsmeyer *et al.*, 's equation

$$\text{(Korsmeyer et al., 1983): } M_t/M_\infty = K_n$$

Where M_t is the amount of drug released at time t , M_∞ is the amount of drug released after an infinite time, and k is a kinetic constant incorporating

structural and geometric characteristics of the floating gel beads, and n is the diffusion exponent indicative of the drug release mechanism. The mechanism of drug release was dependent on the value of 'n'.

Stability Studies: The stability of loratadine floating beads was studied at 25 °C and 60% relative humidity in closed high-density polyethylene bottles for 3 months. The drug content and the floating behavior were determined at different time intervals such as 1, 2 and 3 months¹¹.

RESULTS AND DISCUSSION:

Pre-Formulation Studies of Loratadine: The drug and the excipients interaction studies were evaluation by checking the physical appearance and by FT-IR analytical method.

The following pre-formulation studies were performed on loratadine and excipients.

Interpretation of Loratadine:

Analytical Report for API:

TABLE 2: ANALYTICAL REPORT FOR LORATADINE

Pre-formulation test	Results
Description	Colorless
Nature	Odorless
Description	Colorless, odorless crystalline powder
Solubility	Soluble in DMSO (50 mg/ml), ethanol (77 mg/ml at 25 °C), water (<1 mg/ml at 25 °C), chloroform and methanol
Category	Antihistamine drug
Melting point	128 °C

TABLE 3: LORATADINE CHARACTERIZATION

Test	Result
Particle Size (µm)	10.35 ± 0.40
Bulk Density (g/cc)	0.457 ± 0.02
Tapped Density (g/cc)	0.539 ± 0.02
Carr's Index	18.58 ± 0.04
Hausner's Ratio	01.26 ± 0.02
The angle of Repose (°)	27.35 ± 0.04

Drug-Polymer -Excipients Compatibility Studies: The interaction studies were carried out to ascertain any interaction of the drug with the excipients used in the preparation of floating gel beads.

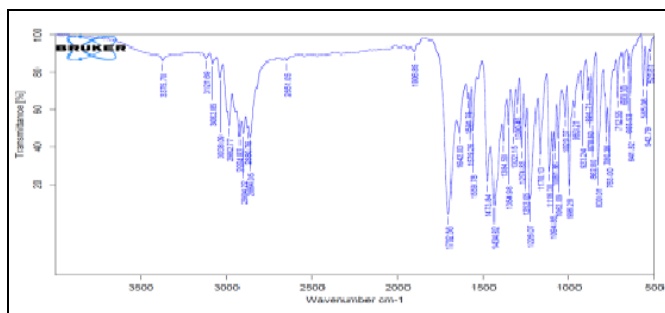


FIG. 1: FT-IR SPECTRA FOR LORATADINE PURE DRUG

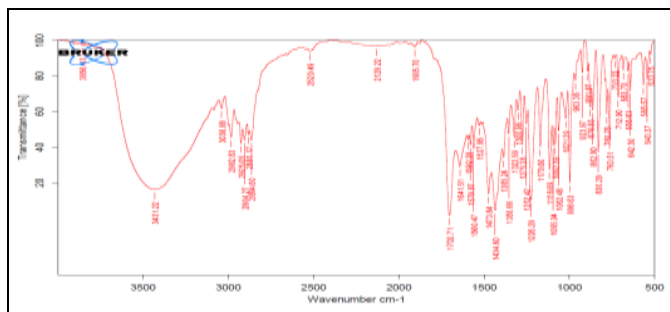


FIG. 2: FT-IR SPECTRA FOR FORMULATION F1

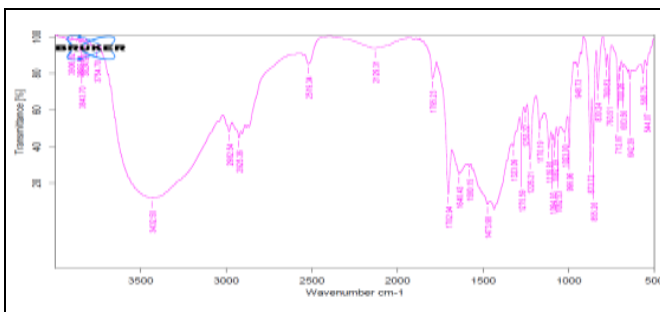


FIG. 3: FT-IR SPECTRA FOR FORMULATION F4

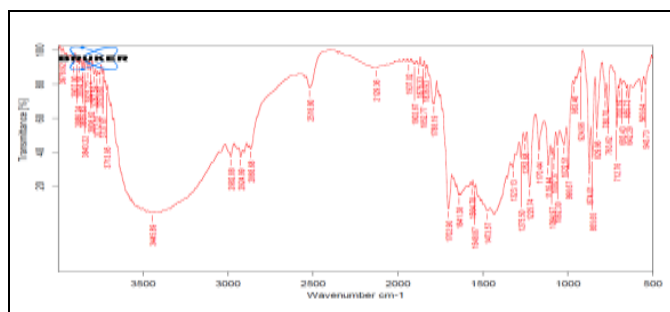


FIG. 4: FT-IR SPECTRA FOR FORMULATION F7

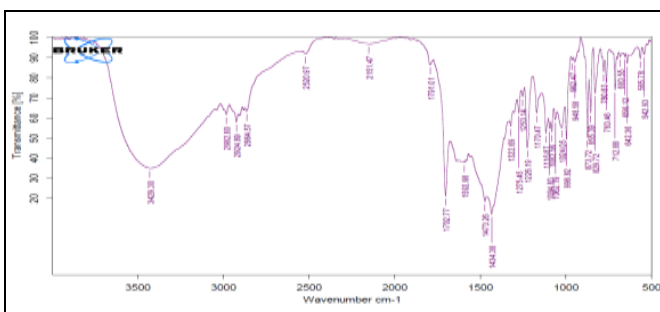


FIG. 5: FT-IR SPECTRA FOR FORMULATION F10

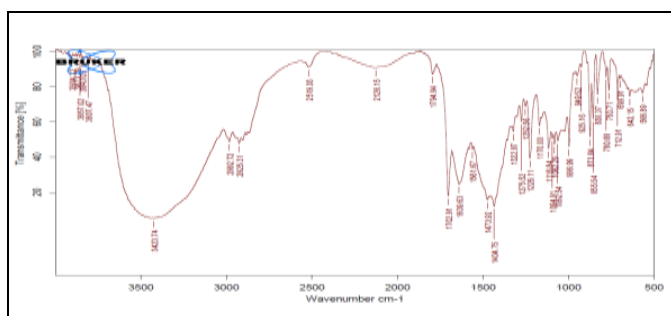


FIG. 6: FT-IR SPECTRA FOR FORMULATION F11

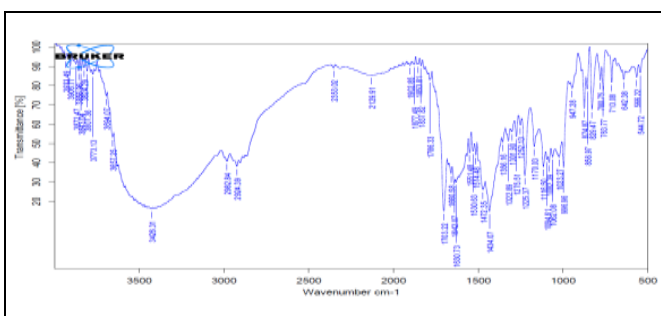


FIG. 7: FT-IR SPECTRA FOR FORMULATION F12

TABLE 4: FT-IR SPECTRA FOR LORATADINE AND LORATADINE FORMULATIONS

Interpretation	Loratadine pure drug	IR absorption bands (cm ⁻¹)					
		F1	F4	F7	F10	F11	F12
C=O stretching & N-H bending	1702.56	1702.71	1702.94	1702.90	1702.77	1702.91	1703.22
C-Cl stretching	996.28	996.63	996.96	996.67	996.82	996.99	996.96
N=O stretching	1434.62	1434.60	1473.98	1473.57	1434.38	1434.75	1434.07
Saturated aliphatic & side chain aromatic groups	1226.07	1226.29	1226.21	1225.74	1226.19	1226.11	1225.37

Based on FT-IR spectra obtained, it was evident that there was no significant interaction of loratadine with the carriers and other excipients.

Formulation Development:

Standard Curve of Loratadine: In the current study, loratadine in pH 1.2 buffer showed good reproducibility in the concentration range of 5 µg/ml - 30 µg/ml at 214 nm as shown in **Table 5** and **Fig. 8**. Correlation ($R^2 = 0.999$) between concentration and absorbance was found to be closer to 1 indicating that the method obeyed Beer-Lambert’s Law.

TABLE 5: STANDARD CALIBRATION CURVE OF LORATADINE

Concentration (µg/ml)	Absorbance at 214 nm (in a buffer solution, pH 1.2)
0	0
5	0.201
10	0.389
15	0.569
20	0.748
25	0.929
30	1.098

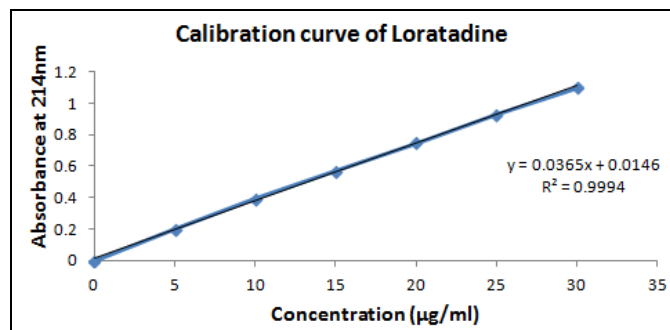


FIG. 8: STANDARD CALIBRATION CURVE OF LORATADINE IN pH 1.2 BUFFER

Preparation of Loratadine Floating Beads: Total twelve formulations of loratadine floating gel beads with the dose of 10 mg were prepared by ionotropic gelation technique using polymers such as HPMC K4M, HPMC K15M, and Carbopol 934P and the resulting beads were shown in **Fig. 9**.



FIG. 9: PREPARATION OF LORATADINE FLOATING ALGINATE BEADS BY IONIC GELATION METHOD

Evaluation of Loratadine Floating Beads: The prepared beads were evaluated for particle size analysis, bulk density, tapped density, compressibility index, Hausner’s ratio, the angle of repose, swelling index, drug entrapment efficiency & % yield, % buoyancy, *in-vitro* drug release studies, kinetic modeling of drug release and Stability studies.

Particle Size Analysis: The particle size of floating loratadine gel beads was affected by the amount of polymer used and its ratio concerning alginate in the formulations. The mean particle size of loratadine floating gel beads significantly increased with the increasing polymer concentration and found to be in the range from $725.23 \mu\text{m} \pm 0.02$ to $929.09 \mu\text{m} \pm 0.04$ as represented in **Table 6**. The effect of polymer type on the size of loratadine beads was observed to be in the following order and may be related to variations in the molecular weight as well as the structure of polymers that resulted in the polymeric solutions of different viscosities.

HPMC K4M > HPMC K15M > Carbopol 934P

Micromagnetic Properties of Loratadine Floating Gel Beads: All the formulations were

evaluated for their micrometric properties as well as physical characteristics and found to be within the limits as shown in **Table 6**. The bulk density was found in the range of $0.48 \text{ g/cm}^3 \pm 0.14$ - $0.79 \text{ g/cm}^3 \pm 0.34$. The tapped density ranged between $0.54 \text{ g/cm}^3 \pm 0.16$ - $0.79 \text{ g/cm}^3 \pm 0.42$. Carr's index of all the formulations existed in the range of 08.75 ± 0.03 to 15.38 ± 0.04 . The result of the Hausner's ratio of all the formulations was between 1.00 ± 0.01 and 1.19 ± 0.01 . The angle of repose of all formulations was within the range of $25.02^\circ \pm 0.27$ to $27.78^\circ \pm 0.12$. These values indicate that the powder blend exhibited good flow properties. These values indicate that the prepared loratadine floating beads exhibited good flow properties. Based on the results obtained, formulation F7 was found to be the best formulation compared to other formulations.

TABLE 6: MEAN PARTICLE SIZE AND MICROMERETIC PROPERTIES OF LORATADINE FLOATING GEL BEADS

Formula code	Mean particle size (μm)	Bulk density (g/cm^3)	Tapped density (g/cm^3)	Carr's index	Hausner's ratio	Angle of repose ($^\circ$)
F1	725.23 ± 0.02	0.53 ± 0.17	0.60 ± 0.12	11.66 ± 0.18	1.13 ± 0.005	25.32 ± 0.52
F2	693.57 ± 0.06	0.48 ± 0.14	0.54 ± 0.16	14.28 ± 0.36	1.12 ± 0.01	26.65 ± 0.27
F3	666.71 ± 0.04	0.51 ± 0.17	0.61 ± 0.14	16.39 ± 0.28	1.19 ± 0.01	26.48 ± 0.62
F4	752.22 ± 0.06	0.48 ± 0.35	0.56 ± 0.12	14.28 ± 0.35	1.16 ± 0.01	26.32 ± 0.24
F5	785.97 ± 0.02	0.54 ± 0.17	0.62 ± 0.44	12.90 ± 0.34	1.15 ± 0.005	27.78 ± 0.12
F6	728.28 ± 0.04	0.52 ± 0.07	0.60 ± 0.04	15.38 ± 0.04	1.15 ± 0.01	26.42 ± 0.36
F7	834.39 ± 0.08	0.79 ± 0.34	0.79 ± 0.42	13.90 ± 0.22	1.00 ± 0.01	25.02 ± 0.27
F8	692.05 ± 0.09	0.60 ± 0.16	0.68 ± 0.15	13.79 ± 0.22	1.13 ± 0.015	26.75 ± 0.35
F9	657.84 ± 0.07	0.71 ± 0.48	0.74 ± 0.24	12.34 ± 0.41	1.04 ± 0.005	25.42 ± 0.12
F10	729.56 ± 0.11	0.70 ± 0.18	0.76 ± 0.14	11.90 ± 0.34	1.09 ± 0.01	26.35 ± 0.42
F11	929.09 ± 0.04	0.68 ± 0.22	0.75 ± 0.16	10.76 ± 0.11	1.10 ± 0.005	27.18 ± 0.25
F12	884.37 ± 0.06	0.53 ± 0.27	0.60 ± 0.26	11.66 ± 0.12	1.13 ± 0.005	26.53 ± 0.19

Swelling Studies: The swelling behavior of the all prepared loratadine floating beads remained intact in pH 1.2 buffer during the experimental time and observed to appear white. From the results of the swelling study, it was evident that the swelling ratios found to increase with the increasing polymer concentrations as shown in **Table 7** and **Fig. 10**. Polymers used may be placed in the following order as per their swelling ratios in pH 1.2 buffer as followed:

Carbopol 934P > HPMC K15M > HPMC K4M

Percentage Drug Entrapment Efficiency: From the results, it was evident that the drug encapsulation efficiency was found to be low for the loratadine floating gel bead formulation F1, while the values were significantly increased with

the increasing concentration of the polymer HPMC K4M as shown in **Table 7**. Further, the results of the study showed that the encapsulation efficiencies were dependent on the type as well as the concentration of polymer used in the preparation of loratadine floating gel beads.

The results were also dependent on the viscosity of the polymer used, the diffusion of loratadine from the gel beads decreased as the viscosity increased.

Percentage Yield: The % yield of loratadine floating gel beads ranged from $84.12\% \pm 1.25$ to $92.51\% \pm 1.35$ for formulations F1 and F12 respectively. Based on the results obtained, it was observed that the yield increased with the increase in polymer concentration and polymer type.

Percentage Drug Loading: The % drug loading of different beads was ranged from 79.25% ± 1.16 to 95.85% ± 1.27 for formulations F1 to F12. The % encapsulation efficiency was found to be highest for formulation F7, i.e. 95.85% ± 1.27.

Percentage Buoyancy: The results showed that all developed loratadine floating beads had % buoyancy from 79.40% ± 1.65 to 96.19% ± 1.12 of beads remained floated for 12 h.

TABLE 7: RESULTS OF SWELLING STUDY OF LORATADINE FLOATING GEL BEAD FORMULATIONS

Formulation code	Swelling index (%)	Drug entrapment efficiency (%)	Percentage yield	% Drug loading	% Buoyancy
F1	75.52 ± 1.25	78.12 ± 1.05	84.12 ± 1.25	79.25 ± 1.16	86.22 ± 0.96
F2	78.49 ± 1.08	80.47 ± 0.96	89.68 ± 1.19	81.09 ± 0.63	85.65 ± 1.25
F3	82.41 ± 0.98	83.68 ± 1.26	90.49 ± 1.35	82.15 ± 1.54	84.26 ± 1.32
F4	84.96 ± 0.87	86.25 ± 1.34	82.27 ± 0.86	85.27 ± 1.31	92.15 ± 1.06
F5	87.64 ± 1.14	91.62 ± 0.89	89.65 ± 0.66	91.36 ± 0.72	82.67 ± 1.18
F6	88.35 ± 1.35	92.36 ± 1.09	90.43 ± 1.29	91.29 ± 1.11	88.48 ± 1.34
F7	89.47 ± 0.84	96.30 ± 1.28	92.51 ± 1.35	95.85 ± 1.27	96.19 ± 1.12
F8	83.24 ± 0.79	85.75 ± 1.46	90.26 ± 1.08	84.26 ± 1.05	78.54 ± 1.07
F9	85.05 ± 1.26	84.59 ± 0.85	88.05 ± 1.24	83.45 ± 0.76	79.82 ± 1.16
F10	87.19 ± 1.08	83.08 ± 0.78	85.57 ± 1.05	82.48 ± 0.37	79.40 ± 1.65
F11	88.36 ± 0.88	85.66 ± 1.12	87.92 ± 1.63	84.28 ± 1.61	86.26 ± 1.38
F12	90.65 ± 0.65	86.29 ± 0.66	87.34 ± 1.51	85.35 ± 0.42	91.35 ± 1.46

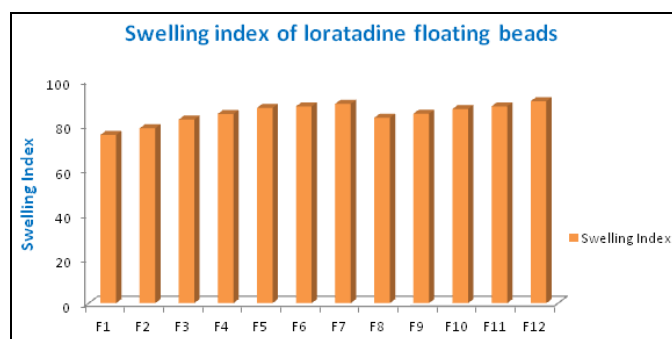


FIG. 10: SWELLING STUDY OF LORATADINE FLOATING GEL BEADS

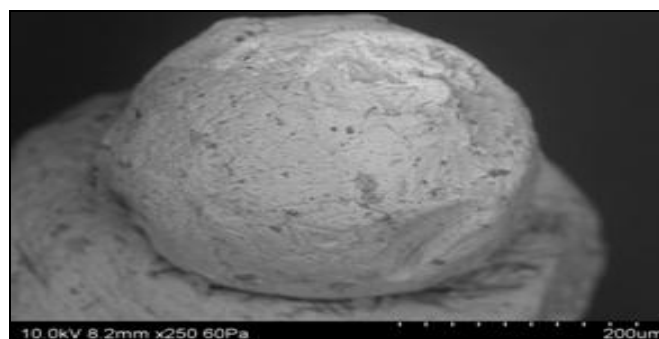


FIG. 11: SEM IMAGE OF LORATADINE FLOATING GEL BEAD FORMULATION F7

SEM of Floating Loratadine Beads: The SEM image for the optimized formulation of loratadine floating gel beads was shown in Fig. 11. SEM graph of beads showed that the beads were spherical with a uniform texture and slightly smooth surface. The slightly smooth surface was due to the use of optimum concentration ratio of sodium bicarbonate as a gas forming agent to sodium alginate (1:1 w/w) for the bead formation.

In-vitro Drug Release Studies: Loratadine floating gel beads were evaluated for *in-vitro* drug release studies in pH 1.2 buffer, and the results were presented in Table 8 and 9.

The formulation F7 showed best drug release of 98.85% ± 0.15 within 12 h when compared to other formulations.

TABLE 8: IN-VITRO CUMULATIVE % DRUG RELEASE OF LORATADINE BEADS F1 TO F6

Time (h)	F1	F2	F3	F4	F5	F6
0	0	0	0	0	0	0
1	10.68 ± 0.18	08.45 ± 0.17	09.64 ± 0.15	08.99 ± 0.20	09.24 ± 0.19	09.75 ± 0.18
2	19.58 ± 0.06	16.68 ± 0.12	17.56 ± 0.09	16.99 ± 0.18	17.86 ± 0.14	17.99 ± 0.14
3	28.11 ± 0.14	24.54 ± 0.09	26.15 ± 0.12	24.99 ± 0.19	26.21 ± 0.17	25.01 ± 0.12
4	39.55 ± 0.11	31.68 ± 0.11	32.24 ± 0.18	30.59 ± 0.14	35.12 ± 0.19	33.58 ± 0.09
5	48.69 ± 0.09	40.01 ± 0.08	41.02 ± 0.09	39.99 ± 0.09	43.32 ± 0.11	41.36 ± 0.18
6	60.01 ± 0.08	48.23 ± 0.05	49.31 ± 0.05	48.68 ± 0.06	51.36 ± 0.09	49.07 ± 0.19
7	69.10 ± 0.10	57.99 ± 0.06	58.42 ± 0.14	59.68 ± 0.11	59.98 ± 0.10	58.36 ± 0.11
8	75.12 ± 0.07	65.28 ± 0.12	64.58 ± 0.16	65.32 ± 0.12	64.89 ± 0.08	66.01 ± 0.15
9	81.54 ± 0.11	72.15 ± 0.05	71.56 ± 0.09	72.15 ± 0.18	73.12 ± 0.09	75.02 ± 0.19
10	88.72 ± 0.12	79.13 ± 0.16	78.99 ± 0.11	79.25 ± 0.10	80.01 ± 0.14	80.36 ± 0.09
11	94.21 ± 0.14	87.12 ± 0.04	86.59 ± 0.16	87.32 ± 0.05	88.12 ± 0.16	89.01 ± 0.05
12	95.12 ± 0.09	94.58 ± 0.11	93.99 ± 0.10	94.02 ± 0.07	93.01 ± 0.15	94.01 ± 0.09

TABLE 9: IN-VITRO CUMULATIVE % DRUG RELEASE OF LORATADINE BEADS F7 TO F12

Time (h)	F7	F8	F9	F10	F11	F12
0	0	0	0	0	0	0
1	08.65 ± 0.19	09.98 ± 0.18	10.01 ± 0.15	10.26 ± 0.11	09.98 ± 0.15	10.21 ± 0.16
2	13.23 ± 0.15	14.01 ± 0.14	14.23 ± 0.13	14.69 ± 0.18	15.01 ± 0.13	14.99 ± 0.09
3	18.15 ± 0.09	18.99 ± 0.16	18.56 ± 0.18	19.65 ± 0.16	18.99 ± 0.19	19.01 ± 0.12
4	20.12 ± 0.05	20.56 ± 0.09	20.23 ± 0.11	22.12 ± 0.09	21.06 ± 0.16	22.01 ± 0.18
5	31.21 ± 0.11	30.99 ± 0.05	29.65 ± 0.09	33.32 ± 0.12	31.65 ± 0.09	32.01 ± 0.13
6	39.99 ± 0.15	38.23 ± 0.13	39.45 ± 0.05	44.19 ± 0.15	40.01 ± 0.05	42.21 ± 0.05
7	49.51 ± 0.17	50.12 ± 0.11	51.01 ± 0.13	52.00 ± 0.06	51.99 ± 0.11	52.01 ± 0.09
8	60.01 ± 0.08	59.65 ± 0.08	60.23 ± 0.07	60.99 ± 0.09	61.01 ± 0.16	60.98 ± 0.16
9	68.33 ± 0.15	68.77 ± 0.13	69.33 ± 0.16	71.95 ± 0.12	72.01 ± 0.09	71.65 ± 0.07
10	75.32 ± 0.06	74.36 ± 0.08	75.32 ± 0.18	81.99 ± 0.09	80.12 ± 0.15	80.01 ± 0.16
11	85.12 ± 0.12	84.32 ± 0.11	85.96 ± 0.12	91.32 ± 0.11	92.01 ± 0.06	91.99 ± 0.19
12	98.85 ± 0.15	94.56 ± 0.05	94.01 ± 0.11	96.01 ± 0.05	96.32 ± 0.19	95.22 ± 0.15

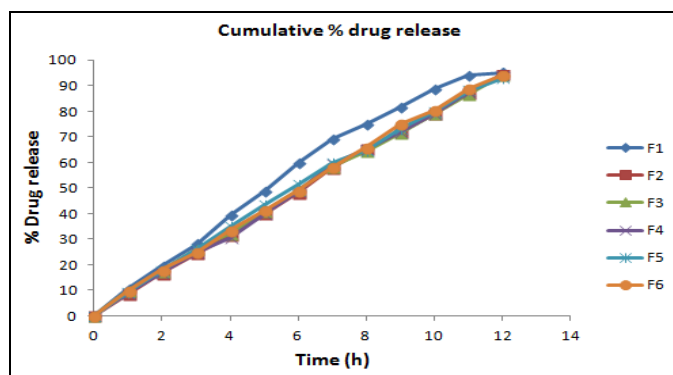


FIG. 12: IN-VITRO DRUG RELEASE PROFILES OF FORMULATIONS F1 - F6

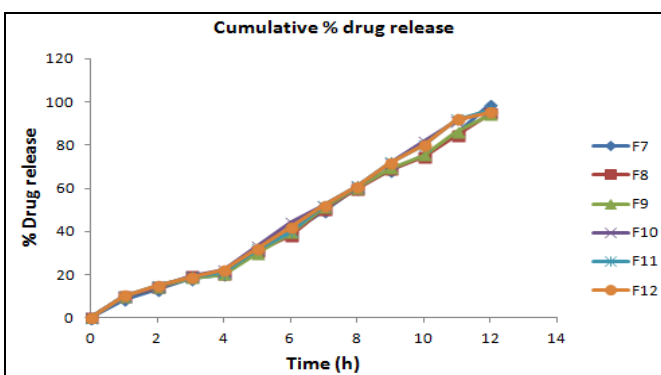


FIG. 13: IN-VITRO DRUG RELEASE PROFILES OF FORMULATIONS F7 - F12

Kinetic Studies of Drug Release:

Release Order Kinetics of Optimized Formulation of Floating Gel Beads: To determine the drug release mechanism; the data of the *in-vitro* drug release of all developed loratadine formulations (F1–F12) were fitted in various kinetic models such as zero, first order, Higuchi and Korsmeyer-Peppas models. The kinetic rate constant (k) the coefficient of determination (R^2) were computed and were depicted in **Table 10**. The best fit with the highest coefficient of determination (R^2) for all formulae was shown with the Higuchi model followed by Peppas release model and then zero-order equation. These results revealed that the kinetic release pattern was best

fitted to Higuchi equation which describes drug release from a polymeric system by the mechanism of diffusion. Fickian diffusion mechanism of release was the drug release controlling mechanism for the optimized formulation F7. The *in-vitro* drug release profiles from optimized formulations F7 were applied on different kinetic models. The best fit with the highest correlation coefficient was observed in zero order and Higuchi model, indicating a diffusion controlled principle. Moreover, the ‘n’ value obtained from the Korsmeyer - Peppas plot, *i.e.* 0.825 suggested that the drug release from loratadine floating gel beads was by an anomalous non-fickian diffusion mechanism.

TABLE 10: DRUG RELEASE KINETICS FOR OPTIMIZED FORMULATION F7

Formulation Code	Zero Order		First Order		Higuchi		Korsmeyer -Peppas	
	R^2	K	R^2	K	R^2	K	R^2	n
F7	0.983	8.090	0.650	0.108	0.860	29.26	0.966	0.825

Stability Studies: The optimized loratadine floating bead formulation F7 was subjected to stability studies at 25 °C / 60% Rh for 3 months. After storage under these conditions, loratadine floating gel beads were analyzed for the change in

physical appearance, drug content, and floating behavior. Results of stability study indicated that there were no significant changes in the physical characteristics of the optimized formulation F7 concerning color and shape by the visual

examination. The drug content of the floating beads also did not alter until the end of 3 months after storage. In the case of floating behavior also, it was

found that there was no change in lag time and the floating time was more than 12 h.

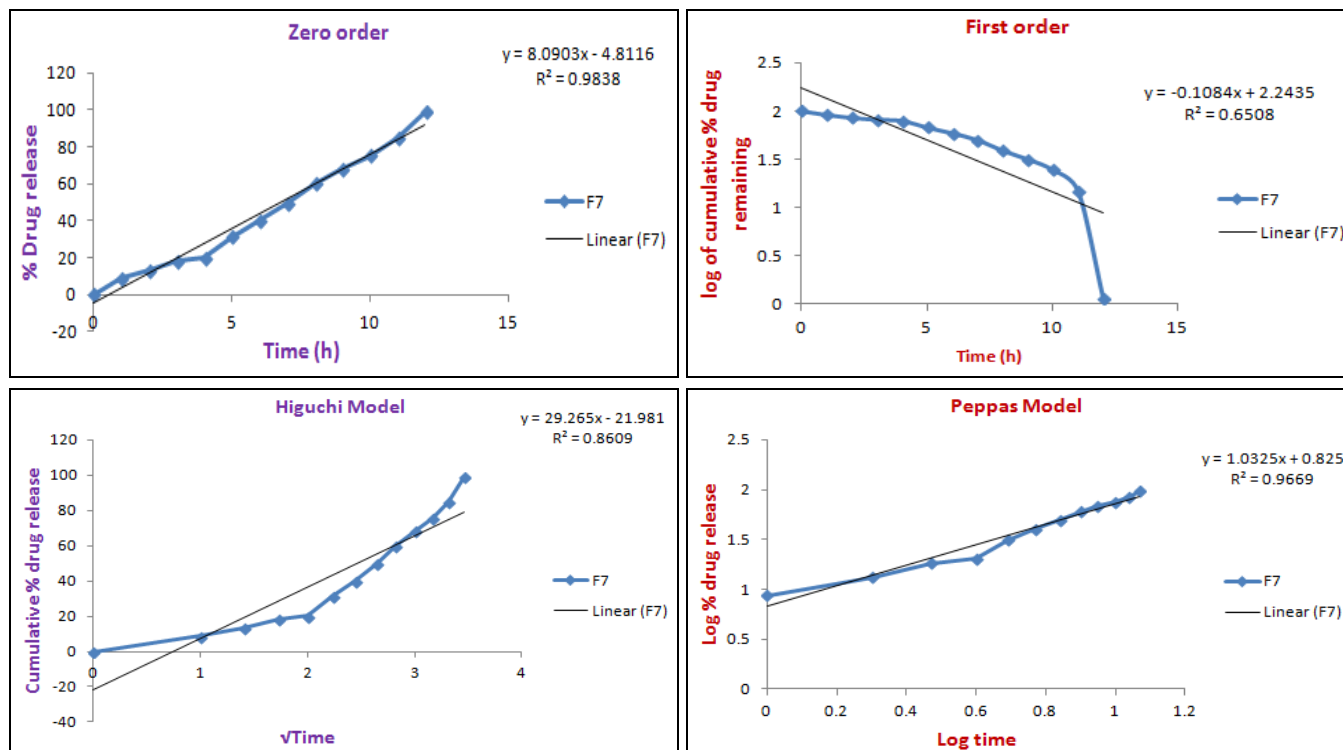


FIG. 14: DRUG RELEASE KINETICS OF OPTIMIZED FORMULATION F7

TABLE 11: EVALUATION OF OPTIMIZED LORATADINE FLOATING BEADS (F7) AFTER SHORT TERM STABILITY PERIOD

Parameters	Before	After
<i>In-vitro</i> Drug release (%)	98.37 ± 0.02	98.05 ± 0.08
Floating lag time (min)	7.4 ± 0.2	7.4 ± 0.1
Floating time (h)	> 12	> 12

n=3; values are expressed as mean ± SD

CONCLUSION: In the current research study, floating beads of loratadine were formulated using different polymers in different proportions by ionic gelation technique to achieve sustained release of the drug. The sodium alginate beads prepared with hydroxyl propyl methyl cellulose (HPMC) K15M in higher concentration, *i.e.*, formulation F7 showed comparatively better drug loading and floating characteristics. The *in-vitro* drug release studies proved that the gel beads exhibited sustained drug release.

ACKNOWLEDGEMENT: The authors are grateful to the Management of Vijaya Institute of Pharmaceutical Sciences for Women, Enikepadu, Vijayawada for providing the necessary facilities to carry out the research work.

CONFLICT OF INTEREST: The authors declare that they have no conflicts of interest.

REFERENCES:

- Arora S, Ali A, Ahuja A, Khar RK and Baboota S: Floating drug delivery systems: a review. *AAPS Pharm Sci Tech* 2005; 6(3): E372-E390.
- Yeole PG, Khan S and Patel VF: Floating drug delivery system: need and development. *Indian J Pharm Sci* 2005; 67: 265-272.
- Goodman and Gilman's *The Pharmacological Basis of Therapeutics*, 10th ed; McGraw-Hill, New York 2006: 638-639.
- Talukder R and Fassihi R: Gastro retentive delivery systems: hollow beads. *Drug Dev Ind Pharm* 2004; 30: 405-412.
- Torrado JJ and Augsberger LL: Tableting of multiparticulate modified release systems. In: *Pharmaceutical Dosage Forms - Tablets Vol. 2. Rational Design and Formulation* (Augsberger LL and Hoag SW, eds.), Edi 3, Informa Healthcare, London 2008: 509-533.
- Whitehead L, Fell JT, Collett JH, Sharma HL and Smith A. *In-vivo* study demonstrating prolonged gastric retention. *J Control Release* 1998; 55: 3-12.
- Whitehead L, Collett JH and Fell JT: Amoxycillin release from a floating dosage form based on alginates. *Int J Pharm* 2000; 210: 45-49.
- Ichikawa M, Watanabe S and Miyake Y: A new multiple-unit oral floating dosage system. II: *in-vivo* evaluation of floating and sustained-release characteristics with para-amino benzoic acid and isosorbide dinitrate as model drugs. *J Pharm Sci* 1991; 80: 1153-1156.

9. Bulgarelli E, Forni F and Bernabei MT: Effect of matrix composition and process conditions on casein gelatin beads floating properties. Int J Pharm 2000; 198: 157-165.
10. Srivastava A, Ridhurkar K and Wadhwa DN: Floating microspheres of cimetidine: formulation, characterization

- and *in-vitro* evaluation. Acta Pharm 2005; 55: 277-285.
11. El-Kamel AH, Sokar MS, Al Gamal SS and Naggar VF: Preparation and evaluation of ketoprofen floating oral drug delivery system. Int J Pharm 2001; 220: 13-21.

How to cite this article:

Begum SA, Jhansi J and Padmalatha K: Formulation and evaluation of floating gel beads of loratadine. Int J Pharm Sci & Res 2019; 10(3): 1289-99. doi: 10.13040/IJPSR.0975-8232.10(3).1289-99.

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