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PREPARATION AND CHARACTERIZATION OF FLOATING ALGINATE BEADS OF LAFUTIDINE AS A GASTRORETENTIVE DOSAGE FORM

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Keywords:

Lafutidine, Alginate floating beads, Floating drug delivery system

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ABSTRACT: Background: Lafutidine floating beads as a gastro-retentive dosage form antagonisms of histamine H2 receptor. It is used as anti-ulcerative agent. It is effective against the oesophageal lesions induced by acid reflux through inhibition of acid secretions. **Objectives:** The objective of the present work was to formulate and evaluate the floating beads of Lafutidine as a model drug. The objective of this study is to develop a simple uncomplicated and easy to manufacture floating beads that are capable of delivering lafutidine at a prolonged release rate of delivery. It has a short half-life (3 h). It has a low bioavailability (60-80%). The frequent dosing, which results in unacceptable patient compliance. **Methods:** Lafutidine was received as a gift sample and a thorough pre-formulation study was performed on a given sample in order to estimate the physicochemical properties like solubility, melting point, partition coefficient to confirm the authenticity of sample and to confirm that there are no significant barriers to the development of dosage forms. 12 different formulation of lafutidine floating alginate beads were successfully developed using the emulsion solvent diffusion method. The beads had good yield and showed high, drug entrapment efficiency. The flow properties of microspheres were within the acceptable range and therefore would be easily filled into capsules. Release properties were satisfactory and the formulations hold promise for further development into drug delivery systems for oral administration of lafutidine. **Results and Discussions:** FT-IR spectra of the physical mixture showed no significant shifting of the peaks, so ingredients used in the study are suitable for the development of lafutidine floating beads formulations. The minimum cumulative percent drug release after 7 h of the Lafutidine floating beads 23.244 ± 0.82% was shown by batch AB3 and the maximum release 72.41 ± 0.09% was shown by the floating beads of batch AB4.

INTRODUCTION: A Drug Delivery System is defined as a formulation or a device that enables the introduction of a therapeutic substance in the body and improves its efficacy and safety by controlling the rate, time, and release of drugs in the body.

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This process includes the administration of the therapeutic products and subsequent transport of the active ingredients across the biological membranes to the site of action. Drug Delivery System is an interface between the patient and the drug. It may be a formulation of a drug to administer it for a therapeutic purpose or a device used to deliver the drug.

The oral route of drug administration is most commonly used for therapeutic drugs because of its cost efficiency and easy administration leads to good patient's compliance [1]. More than 50% of the

drug delivery systems available in the market are oral drug delivery system [1]. The most important objectives of these new drug delivery systems are: first, it would be a single dose, which releases the active ingredient over an extended period of time. Second, it should deliver the active entity directly to the site of action, thus, minimizing or eliminating side effects [2]. To overcome the limitations of conventional drug delivery system, floating drug delivery systems have been developed. Drugs that have a narrow absorption window in the gastrointestinal tract (GIT) will have poor absorption. For these drugs, gastroretentive drug delivery systems offer the advantages in prolonging the gastric emptying time [3].

To increase the gastric emptying time and control over the release of the drug from the devices, the increasing sophistication of delivery technology will ensure the development of an increasing number of gastroretentive drug delivery systems to optimize the delivery of molecules that exhibit low bioavailability and extensive first-pass metabolism [4]. A gastric floating drug delivery system can overcome at least some of these problems and is particularly useful for drugs that are primarily absorbed in the duodenum and upper jejunum segments, and it can prolong retention times of dosage forms in the GIT and thereby improve their oral bioavailability [5]. Beads are distinct spherical microcapsule that works as the solid substrate on which the drug is coated or encapsulated in the core of beads. Beads can provide controlled release properties. Furthermore, the bioavailability of drugs formulated in beads can be enhanced. Floating beads fulfills the aim of the development of a gastro retentive drug delivery system is not only to sustain the drug release but also to prolong gastric residence of the dosage forms until all the drug is completely released at the desired period [6].

These multi particulate dosage forms have many advantages over single-unit preparations, including uniform dispersion in the gastrointestinal tract (GIT), uniform drug absorption, less inter- and intraindividual variability, no chances of dose dumping, improve flow property, and more flexible formulation processes [7].

When floating beads come in contact with gastric fluid, the gel formers, polysaccharides and polymers hydrate to form a colloidal gel barrier that controls the rate of fluid penetration into the device and drug release. As the exterior surface of the dosage form dissolves, the gel layer is maintained by the hydration of the adjacent hydrocolloid layer. The air trapped by the swollen polymer lowers the density and confers buoyancy to the microspheres. However, minimal gastric content is needed to allow the proper achievement of buoyancy [8]. Adherence to the wall of the stomach will be possible during the emptying process in the fed and the fasted state, assuming that the mucoadhesive properties of the particles have not been modified by the stomach contents, in particular, non-adherent mucus [9].

Lafutidine2-[(furan-2-yl)methanesulfinyl]-N-[(2Z)-4- ({4- [(piperidin-1- yl) methyl] pyridine- 2-yl}oxy)but-2-en-1-yl]acetamide is an antihistamine medicine, which is used for treating peptic, duodenal and gastric ulcers. It is also prescribed for the treatment of gastro-oesophageal reflux disease (GERD). Lafutidine blocks or reduces gastric acid secretion [10]. Common side effects of Lafutidine include diarrhea, vomiting, nausea, constipation and dizziness. It can also cause an increase in liver enzymes, an increase in the level of blood urea or even hallucinations. It has also been reported to cause breast enlargement in male [11].

MATERIALS AND METHODS:

Materials: Lafutidine was procured as a gift sample from Sun Pharmaceuticals, Gujarat. Potassium Di-Hydrogen Orthophosphate, Sodium Hydroxide pellets, Di-Sodium Hydrogen Phosphate A.R. were purchased from Central Drug House, Delhi, India. Octanol was procured from Merck, India, Ltd, Mumbai, India all other chemicals used were of analytical grade.

Development of Floating Beads of Lafutidine by Emulsion Solvent Diffusion Method: Sodium alginate and solutions of other ingredients of different concentrations were prepared by dissolving the required amount of alginate **Table 1** in 100 ml of distilled water under gentle agitation. Lafutidine and calcium carbonate (as gas-forming agent) were dispersed in alginate solution under constant stirring for uniform mixing. The resultant dispersion was dropped through a syringe needle into 100 ml of 15% (w/v) calcium chloride solution

containing 10% (v/v) acetic acid at room temperature. For 10 min, the beads formed were allowed to remain in the stirred solution. The beads were filtered and subsequently oven-dried at 50 ºC for 4 h [12].

TABLE 1: SOLUBILITY PROFILE OF LAFUTIDINE

Medium	Concentration (µgm/ml), N=3
Distilled water	0.243 mg/mL
Glacial acetic acid	1 mg/ml
Methanol	0.564 mg/ml
Phosphate buffer Ph 7.4	0.352 mg/ml

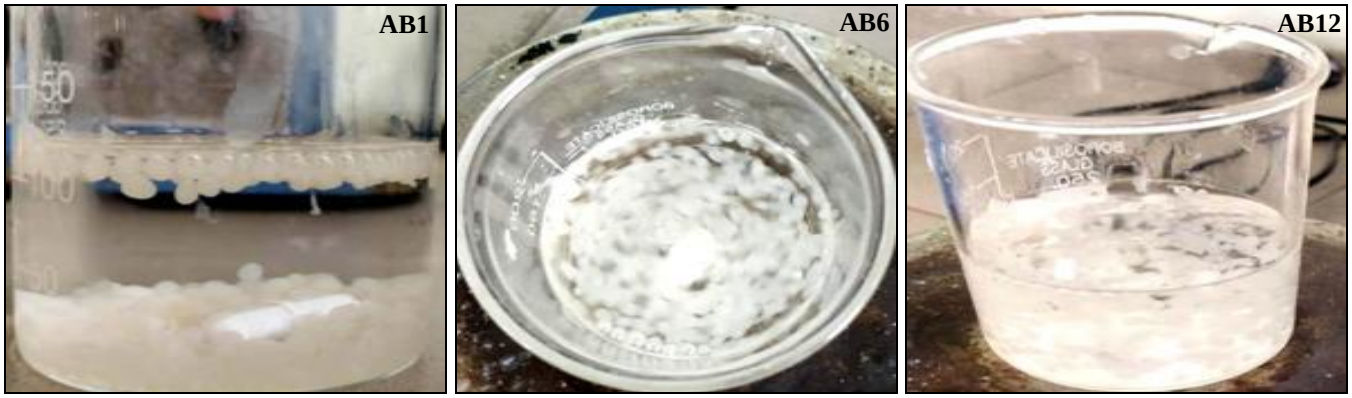

FIG. 1: ALGINATE FLOATING BEADS OF LAFUTIDINE

Evaluation Parameters of Floating Beads of Lafutidine: The prepared beads were evaluated by measurement of particle size, bulk density, tapped density, angle of repose, determination of percentage yield, carr's (compressibility) index, Hausner's ratio, drug entrapment efficiency, assessment of *in-vitro* buoyancy, *in-vitro* drug release studies, drug release kinetic data analysis.

Measurement of Particle Size: The particle size was measured by microscopic technique. In this method suspension of floating beads was prepared using castor oil. A drop of suspension was mounted on a slide and observed under optical microscope about 600 particles were measured with the help of the eyepiece micrometer. The floating beads were uniformly spread on a slide. The particle size of the beads was measured, along the longest axis and the shortest axis (cross-shaped measurement). Average of these three readings was given as mean diameter of particles. The particle size was calculated by multiplying the number of division of the ocular disc occupied by the particle with the calibration factor. All the beads in a field were counted [13].

Determination of Percentage Yield: The prepared beads were collected and weighed. The measured weight was divided by the total amount of all non-volatile components, which were used for the preparation of the beads [14].

Percentage yield = Actual weight of products × 100 / Weight of drug and excipients

Measurement of Bulk Density: Bulk density is determined by pouring pre-sieved floating beads into a graduated cylinder *via* a large funnel and measure the volume and weight. This volume is bulk volume and it includes the true volume of the powder and the void space among the floating beads [15].

Bulk density = Mass of microbeads / Bulk volume

Measurement of Tapped Density: In this method floating beads were transferred to a measuring cylinder and tapped for 100 times. After tapping the volume of floating beads was visually examined. The ratio of the mass of floating beads to the volume of floating beads after tapping gives tapped density floating beads [16].

Tapped density = Mass of microbeads / Volume after tapping

Determination of Carr's (Compressibility) Index: This parameter was calculated from bulk density (the ratio of weighed quantity of microbeads to its volume), DP, and tapped density as follows [17].

Compressibility index = DT – DP / DT × 100

Determination of Hausner,s Ratio: Hausner,s ratio of floating beads was determined by comparing tapped density to bulk density using the equation [18].

Hauser's ratio = Tapped density / Bulk density

Values less than 1.25 indicate good flow (= 20% Carr), whereas greater than 1.25 indicates poor flow (= 33% Carr).

Measurement of Angle of Repose: The angle of repose is defined as the maximum angle possible between the surface of the pile of the powder and the horizontal plane. The angle of repose (θ) of the floating beads, which measures the resistance to particle flow, was determined by a fixed funnel method. The height of the funnel was adjusted in such a way that the tip of the funnel just touches the heap of the blends. Accurately weighed floating beads were allowed to pass through the funnel freely on to the surface. The height and radius of the powder cone were measured and the angle of repose was calculated using the following equation.

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

Where, θ - angle of repose, h - Height of granules above the flat surface, r - Radius of the circle formed by the granule heap.

Determination of Drug Entrapment Efficiency: The amount of drug entrapped was estimated by crushing the floating beads and extracting with aliquots of 0.1N HCl repeatedly. The extract was transferred to a 100 ml volumetric flask and the volume was made up using 0.1N HCl. The solution was filtered and the absorbance is measured by spectrophotometer against appropriate blank. The amount of drug entrapped in the microbeads was calculated by the following formula:

DEE = Amount of drug actually present × 100 / Theoretical drug load expected

Assessment of *In-vitro* Buoyancy: Microbeads (200 mg) were spread over the surface of a USP XXIV dissolution apparatus type II filled with 900 ml of 0.1 N hydrochloric acid containing 0.02% tween 80. The medium was agitated with a paddle rotating at 100 rpm for 12 h.

The floating and the settled portions of microbeads were recovered separately. The microbeads were dried and weighed. The buoyancy percentage was calculated as the ratio of the mass of the microbeads that remained floating and the total mass of the microbeads [19].

Buoyancy (%) = WF × 100 / WF + WS

Where WF and WS are the weight of floating and settled microbeads, respectively.

***In-vitro* Drug Release Studies:** A USP basket apparatus has been used to study *in-vitro* drug release from floating beads. In the present study, drug release was studied for 10 h using a modified USP XXIV dissolution apparatus type I (basket) at 100 rpm in distilled water and 0.1 mol L-1 HCL (pH 1.2) as dissolution fluids (900 ml) maintained at 37 ± 10 ºC. Samples were withdrawn at periodical intervals and analyzed spectrophotometrically at 251 nm. The volume was replenished with the same amount of fresh medium to maintain the sink condition. All experiments were performed in triplicate for 7 h. Cumulative percentage drug release was calculated using an equation obtained from a standard curve [20].

Drug Release Kinetic Data Analysis: The release data obtained from various formulations is studied for their fitness of data in different kinetic models like Zero-order, Higuchi's and Peppa's [21].

RESULTS AND DISCUSSIONS: Lafutidine was received as a gift sample from Sun Pharmaceuticals, Gujarat. The drug was authenticated by different test *i.e.* solubility, melting point, test according to Indian Pharmacopoeia and analytical methodology was performed on the sample to justify the authenticity of sample. The melting point of the obtained drug sample was found to be 94-98 ºC, which complies with the one specified in Indian pharmacopeia. This justifies the authenticity of a given sample of Lafutidine. Lafutidine was found to be freely soluble in glacial acetic acid, soluble in methanol, sparingly soluble in dehydrated ethanol, very slightly soluble in ether, practically insoluble in water. The solubility profile justifies the authenticity of a given sample of Lafutidine.

The absorption spectrum of the pure drug was scanned over the range of 200-500 nm with 10 µg/ml concentration prepared in phosphate buffer pH 7.4. The absorption spectra of Lafutidine showed a peak at 251 nm, which represents the maximum absorption (λ_{max}). There is always a possibility of drug ingredients interaction in any formulation due to their intimate contact. The technique employed in the present study for this

purpose is FTIR spectroscopy **Fig. 3**. FTIR studies were performed for Lafutidine and a mixture of Lafutidine and different ingredients. There is no change in peak indicating compatibility of drugs and polymers. Although there were some mild changes in bandwidth this may be due to the formation of the band between drug and surfactants but all other peaks and band shows in presence of the drug in the formulation. From the FTIR spectra of pure drug and the combination spectra of drug with the surfactants, it was observed that all the characteristic peaks of a drug are present in the combination spectra as well thus indicating the compatibility of the drug with the polymers used. 12 floating beads formulations of Lafutidine were prepared by using different ingredients *i.e.* Pectin, Sodium alginate, Calcium chloride, $CaCO_3$ and Coconut oil in a different ratio by emulsion solvent diffusion method. The benefits of preparation technique include low processing time, lack of exposure of the drug to high temperature due to which stability of drug increased during the processing leading to high percentage entrapment efficiency of the drug in floating beads.

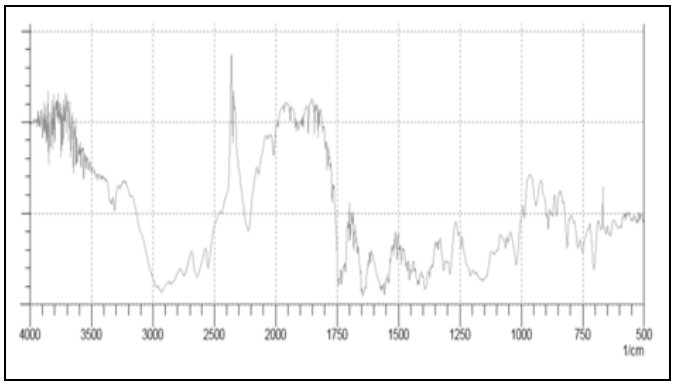

FIG. 2: FTIR SPECTRA OF LAFUTIDINE

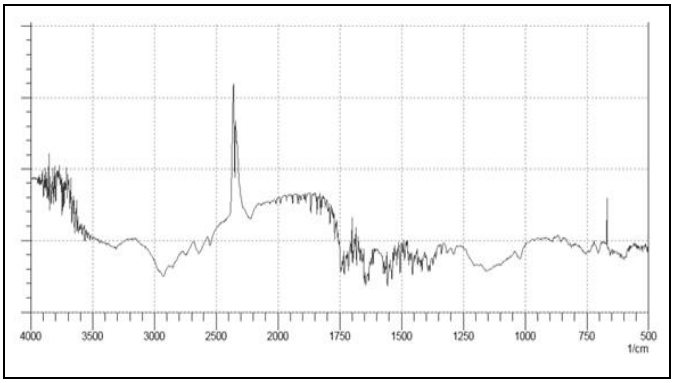

FIG. 3: FTIR SPECTRUM OF MIXTURE OF LAFUTIDINE, SODIUM ALGINATE

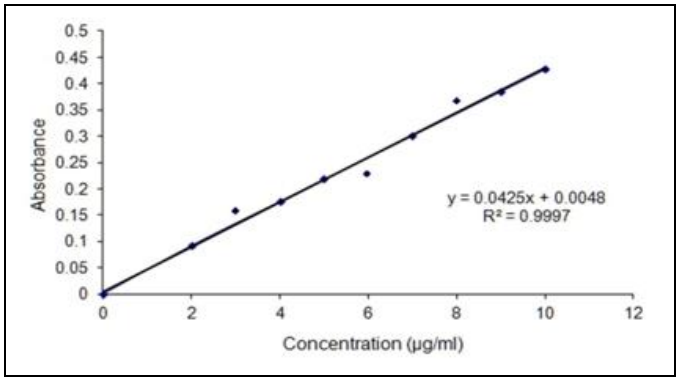

FIG. 4: STANDARD CALIBRATION OF LAFUTIDINE IN PHOSPHATE BUFFER PH 7.4

The mean particle diameter of the floating beads was between 1126.22 ± 0.82-1195.47 ± 0.32 µm **Table 3**. As the polymer concentration increases, the particle size also increases. An increase in particle size diameter was also due to an increase in the concentration of calcium carbonating as a gas-forming agent. As the amount of calcium chloride was increased, the more cross-linking structure was observed that lead to a decrease in particle size 105. The result of bulk density (g/cm^3) ranged from 0.404 ± 0.0062 to 0.498 ± 0.0041 **Table 3**. Bulk density of different formulations of beads was found to be much less than the density of the gastric fluid (1.004 g/ml) and 0.1 N HCl, pH 1.20 (0.997 g/ml). The low density of beads increased the porosity and indicates good packing capacity of beads. Being less in density, the beads were expected to float immediately with less or no floating lag time. The higher amount of effervescent agent caused faster and higher CO_2 generation. This may be attributed to a decrease in bulk density [8]. The tapped density of floating beads of all formulation was found to be in the range of 0.454 ± 0.0038–0.618 ± 0.0009 g/cm^3. Therefore, it was expected to be suitable for the formulation of floating beads as they were having less density than

0.1 N HCl, pH 1.20. Values of tapped density also have shown good packability of beads. The flow properties of all the formulations were found out by measuring the angle of repose and compressibility index. A higher Hauser's ratio indicates greater cohesion between particles while a high Carr's index is indicative of the tendency to form bridges [9].

TABLE 2: COMPOSITION OF ALGINATE BEADS OF LAFUTIDINE

Batch code	Amount of Lafutidine (mg)	Amount of Pectin (mg)	Amount of Sodium alginate (%)	Amount of Calcium chloride (%)	Amount of $CaCO_3$ (gm)	Amount of Coconut oil
AB1	250	500	1	4	2	2
AB2	250	500	2	4	2	2
AB3	250	500	3	4	2	2
AB4	250	500	1	4	2	2
AB5	250	500	2	5	5	5
AB6	250	500	3	5	5	5
AB7	250	500	1	5	5	5
AB8	250	500	2	5	5	5
AB9	250	500	3	6	10	10
AB10	250	500	1	6	10	10
AB11	250	500	2	6	10	10
AB12	250	500	3	6	10	10

TABLE 3: MICROMERITIC PROPERTIES OF LAFUTIDINE LOADED FLOATING ALGINATE GEL BEADS

Batch code	Particle size (µm)	Angle of repose	Bulk density (g/cm^2)*	Tapped density (g/cm^2)*	Carr's compressibility index (%)*	Hausner's ratio
AB1	1145.42 ± 0.46	12.45 ± 0.09	0.451 ± 0.0048	0.501 ± 0.0042	9.98 ± 0.26	1.11
AB2	1175.31 ± 0.24	13.53 ± 0.08	0.463 ± 0.0081	0.513 ± 0.0061	9.74 ± 0.18	1.10
AB3	1165.38 ± 0.52	12.48 ± 0.14	0.422 ± 0.0009	0.477 ± 0.0009	11.53 ± 0.09	1.13
AB4	1161.34 ± 0.57	14.62 ± 0.21	0.475 ± 0.0043	0.525 ± 0.0015	9.52 ± 0.08	1.10
AB5	1159.24 ± 0.32	16.28 ± 0.36	0.447 ± 0.0045	0.497 ± 0.0032	10.06 ± 0.07	1.11
AB6	1141.51 ± 0.68	13.81 ± 0.41	0.456 ± 0.0004	0.506 ± 0.0081	9.88 ± 0.37	1.10
AB7	1195.47 ± 0.32	20.38 ± 0.09	0.486 ± 0.0055	0.532 ± 0.0063	8.64 ± 0.42	1.09
AB8	1164.31 ± 0.58	15.63 ± 0.07	0.498 ± 0.0041	0.618 ± 0.0009	8.09 ± 0.58	1.08
AB9	1188.46 ± 0.78	17.49 ± 0.11	0.404 ± 0.0062	0.454 ± 0.0038	11.01 ± 0.27	1.12
AB10	1126.22 ± 0.82	18.56 ± 0.15	0.463 ± 0.0042	0.522 ± 0.0062	11.30 ± 0.42	1.12
AB11	1139.64 ± 0.28	19.25 ± 0.41	0.482 ± 0.0038	0.532 ± 0.0084	9.39 ± 0.38	1.10
AB12	1191.68 ± 0.58	17.47 ± 0.28	0.426 ± 0.0009	0.476 ± 0.0068	10.50 ± 0.58	1.11

The values of the angle of repose **Table 3** were between 12.45 ± 0.09 to 20.38 ± 0.09 which are within the normal acceptable range of 20 to 40. The porous floating beads thus showed reasonably good flow potential, indicating good flow characteristics of the floating beads. This also implies that the floating beads are non-aggregated. Carr's compressibility index of floating beads of all twelve formulations ranged from 8.09 ± 0.58 to 11.53 ± 0.09 % indicating excellent compressibility of beads **Table 3**. Therefore, floating beads showed good packability inside the capsules with ease of filling the beads. Hausner's Ratio for all eight formulations was in the range of 1.08-1.12 (<1.25) indicating good flow properties of floating beads 108. The percentage of entrapment efficiency in **Table 4** of the floating beads was between 40.21-58.37%. Encapsulation efficiency was found to be increased with the increase in the concentration of gelatine solution (calcium chloride) due to a cross-linking structure. DEE of some formulation was low due to high porosity ($CaCO_3$) because of the leakage of the drug.

Such data may be due to low solubility of Lafutidine in water which facilitates the diffusion of a part of the entrapped drug to the surrounding medium during the preparation of floating beads. The percentage yield of the floating beads was between 90.28 ± 0.41-97.14 ± 0.19%. The purpose of pre-paring floating beads was to extend the gastric residence time of a drug. The floating ability test was carried out to investigate the floatability of the prepared floating beads. The mean percentage buoyancy of the floating beads was between 86.15-95.48%. *In-vitro* buoyancy studies reveal that in spite of stirring the dissolution medium for more than 12 h formulations were still

continued to float without any apparent gelation, thus indicating that floating beads exhibit excellent buoyancies which can be attributed to the pores and cavities present in them. In general, with an increase in the amount of polymers, there is an increase in the buoyancy percentage. The increase in the buoyancy percentage may be attributed to air which caused swelling because of an increased amount of the polymers present. The good buoyancy behavior of the floating beads may be attributed to the hollow nature of the floating beads. *In-vitro* buoyancy study shown that the incorporation of a high concentration of calcium carbonate helped in floating properties when it comes in contact with an aqueous fluid, produce carbon dioxide gas which reduces the density of dosage form due to the entrapment of CO_2 gas in hydrophilic matrices [10].

TABLE 4: CHARACTERISTICS OF ALGINATE BEADS OF LAFUTIDINE

Batch code	Percentage yield (%)	% Drug content	% Buoyancy	DEE (%)	Swelling index (%)
AB1	96.51 ± 0.36	88.54 ± 0.46	86.15	40.21	1371.2 ± 0.09
AB2	95.44 ± 0.13	97.34 ± 0.78	88.17	42.58	1395 ± 0.08
AB3	92.32 ± 0.23	95.56 ± 0.09	91.48	45.36	1374.4 ± 0.03
AB4	90.28 ± 0.41	99.01 ± 0.08	92.58	45.38	1400.8 ± 0.01
AB5	92.18 ± 0.18	97.32 ± 0.14	94.39	53.25	1377.4 ± 0.04
AB6	91.42 ±0.17	96.41 ± 0.26	95.48	51.48	1404.4 ± 0.04
AB7	93.61 ± 0.14	92.52 ± 0.37	89.31	54.64	1380.4 ± 0.07
AB8	93.15 ± 0.15	91.81 ± 0.42	86.57	55.62	1402.4 ± 0.08
AB9	96.48 ± 0.16	89.44 ± 0.09	91.52	55.24	1377.2 ± 0.07
AB10	97.14 ± 0.19	97.82 ±0.05	93.82	56.42	1411 ± 0.06
AB11	94.46 ± 0.31	98.02 ± 0.11	94.82	56.39	1382 ± 0.02
AB12	96.57 ± 0.28	96.53 ± 0.17	91.37	58.37	1397.4 ± 0.04

TABLE 5: DRUG RELEASE KINETIC PARAMETERS FOR DIFFERENT ALGINATE BEADS OF LAFUTIDINE

Batch	Zero order model		First order model		Higuchi model		Korsmeyer-Peppas model		
Code	R	K	R	K	R	K	Slope(n)	R	K
AB1	0.8982	3.6384	0.9564	-0.0575	0.9837	10.3572	0.6236	0.9981	7.8471
AB2	0.9646	2.6360	0.9545	-0.0348	0.9735	8.8942	0.7077	0.9977	4.7378
AB3	0.9643	2.0220	0.9574	-0.0243	0.9266	10.3901	0.8265	0.9947	2.8016
AB4	0.8549	4.2181	0.9310	-0.0768	0.9744	8.9465	0.5721	0.9954	11.5969
AB5	0.9231	2.6472	0.9530	-0.0348	0.9354	10.4172	0.6184	0.9967	7.1554
AB6	0.9590	2.0263	0.9543	-0.0232	0.9644	8.6148	0.7018	0.9978	4.5353
AB7	0.9632	1.6734	0.9564	-0.0189	0.9527	10.5321	0.8415	0.9930	2.5079
AB8	0.8847	3.3740	0.9350	-0.0515	0.9830	9.8362	0.5407	0.9976	10.7404
AB9	0.9141	2.3780	0.9443	-0.0307	0.9426	10.2571	0.6153	0.9943	11.1949
AB10	0.9596	1.9233	0.9237	-0.0225	0.9563	10.3641	0.7688	0.9966	5.1982
AB11	0.9624	1.5861	0.9168	-0.0181	0.9642	9.8363	0.9635	0.9921	2.2810
AB12	0.8787	2.8712	0.9310	-0.0430	0.9711	9.4781	0.5417	0.9890	15.8121

In the present study drug release was studied using a modified USP XXIV dissolution apparatus type I (basket) at 100 rpm in distilled water and 0.1 mol/L HCL (pH 1.2) as dissolution fluids (900 ml) maintained at 37 ± 10 ºC. The minimum cumulative percent drug release after 7 h of the Lafutidine floating beads 23.244 ± 0.82% was shown by batch AB3 and the maximum release 72.41 ± 0.09% was shown by the floating beads of batch AB4 **Fig. 5**, **Fig. 6** and **Fig. 7**. Release profile showed initial burst release up to 1 h due to the surface associated drug, followed by a sustained release phase as the entrapped drug slowly diffused into the dissolution medium. There was the sustained release of a drug at a constant rate. The *in-vitro* drug release studies revealed that the formulation having less concentration of $CaCl_2$ made the swollen beads, which ensured floating and slow diffusion of lafutidine from floating beads, for example.

Sodium alginate itself released in a slow manner and has the main role in entrapment of drug due to which it also lead information of sustained-release floating beads. The response variables of different formulations were calculated from *in-vitro* dissolution profiles to characterize the drug release rate from the floating beads [11]. The results obtained in the *in-vitro* drug release studies were plotted in three models *i.e.* first-order kinetic model and

Korsemeyer's and Peppas release model. The kinetic treatment of the drug release data was used as an indicator of the release mechanism from matrix delivery systems. In this study, the *in-vitro* drug release data were fitted to four commonly employed release kinetic models, namely zero-order, first-order and Higuchi and Peppas models to analyze drug release mechanisms from the polymeric system **Table 5**. The highest regression coefficient (r_2) value was obtained for Korsmeyer–Peppas (0.9981) followed by the Higuchi model (0.9830), by, zero-order (0.9646), and first-order (0.9574) model using PCP disso version 2 software. It indicates diffusion to be the predominant mechanism of drug release from floating beads [22].

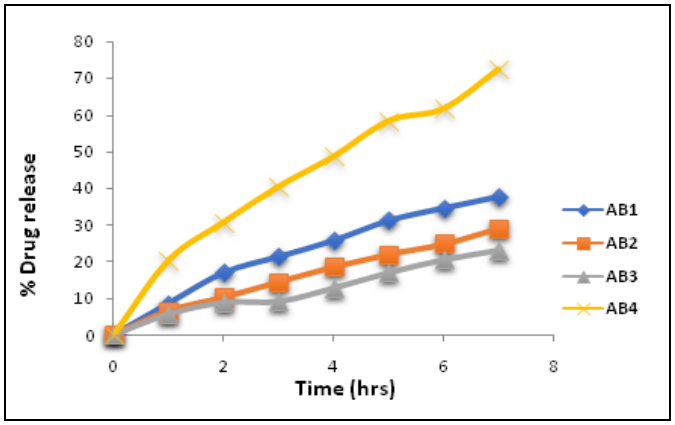

FIG. 5: PERCENTAGE OF LAFUTIDINE RELEASED FROM ALGINATE BEADS OF BATCH AB1-AB4

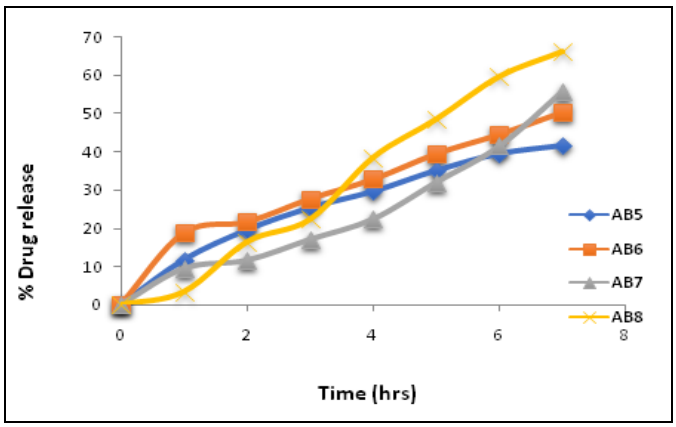

FIG. 6: PERCENTAGE OF LAFUTIDINE RELEASED FROM ALGINATE BEADS OF BATCH AB5-AB8

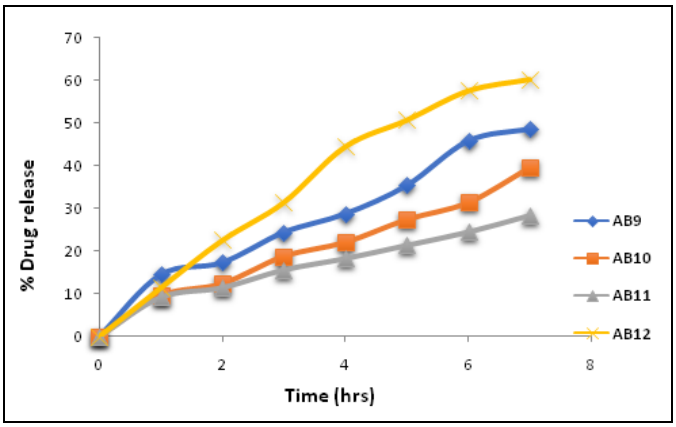

FIG. 7: PERCENTAGE OF LAFUTIDINE RELEASED FROM ALGINATE BEADS OF BATCH AB9-AB12

CONCLUSION: The present study has been a satisfactory attempt to formulate Lafutidine floating beads formulations with a view of improving its oral bioavailability and giving a prolonged release of the drug. From the experimental results, it can be concluded that Different pre-formulation tests performed on a gift sample of Lafutidine, indicates the authenticity of the sample. FT-IR spectra of the physical mixture showed no significant shifting of the peaks, so ingredients used in the study are suitable for the development of Lafutidine floating beads formulations. Lafutidine floating beads formulations were successfully developed by using different ingredients like calcium carbonate, sodium alginate. All floating beads formulations were found to be transparent and were free from the presence of particles. The cumulative percent drug release after 10 h in between 46.158 to 85.114%.

In-vitro drug release studies showed that the maximum drug release was shown by formulations AB4 72.41 ± 0.09%. The data of various models revealed that floating microspheres formulations followed first order and Peppas kinetic models. On the basis of drug content, *in-vitro* release, it can be concluded that the formulation of batch AB4 was an optimum formulation.

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CONFLICTS OF INTEREST: Nil

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