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FORMULATION AND EVALUATION OF FLOATING MICROBEADS OF LANSOPRAZOLE USING NATURAL POLYMER

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Abstract:
Gastroesophageal reflux disease (GERD) and other acid-related disorders often necessitate prolonged and effective treatment with proton pump inhibitors (PPIs) like lansoprazole. However, the challenge lies in ensuring sustained and controlled release of the drug to optimize therapeutic outcomes while minimizing adverse effects. In this study, we aimed to address this challenge by formulating floating microbeads of lansoprazole using natural polymers, thereby enhancing gastric retention and drug release characteristics. Six formulations (F1-F6) were meticulously developed, employing a blend of natural polymers meticulously selected for their biocompatibility, biodegradability, and swelling properties. Subsequently, the formulations underwent comprehensive evaluation for various parameters, including flow properties, particle size, entrapment efficiency, swelling behavior, and in-vitro drug release kinetics. Among the formulations, F4 emerged as the most promising candidate, exhibiting superior flow properties and the highest entrapment efficiency. Notably, F4 demonstrated sustained drug release kinetics, indicative of its potential for prolonged therapeutic effect. Further analysis revealed a complex interplay of diffusion and erosion-controlled release mechanisms governing drug release from F4, underscoring its suitability for sustained drug delivery. These findings underscore the potential of the formulated microbeads to revolutionize the treatment landscape for acid-related disorders, offering a novel approach to enhance the therapeutic efficacy of lansoprazole while mitigating the challenges associated with conventional dosage forms. Future studies, including in-vivo pharmacokinetic and pharmacodynamic assessments, are warranted to validate these promising results and pave the way for clinical translation.

Keywords: *Lansoprazole, floating microbeads, natural polymers, gastric retention, sustained release, drug delivery, gastroesophageal reflux disease, proton pump inhibitors.*

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INTRODUCTION:

Lansoprazole is a proton pump inhibitor (PPI) commonly used for the treatment of gastroesophageal reflux disease (GERD), peptic ulcer disease, and other acid-related disorders. However, its efficacy is often hindered by its rapid degradation in the acidic environment of the stomach, leading to suboptimal therapeutic outcomes [1-2]. To overcome this limitation, sustained-release formulations of lansoprazole, such as floating microbeads, have been developed. Floating microbeads are gastroretentive drug delivery systems designed to prolong gastric residence time and enhance drug absorption by floating on the gastric contents. These systems offer several advantages, including improved bioavailability, reduced dosing frequency, and enhanced patient compliance [3-4].

Natural polymers, derived from renewable sources such as plants, animals, or microorganisms, have gained significant attention in pharmaceutical formulation due to their biocompatibility, biodegradability, and safety profile. Incorporating natural polymers into floating microbead formulations can provide additional benefits such as improved buoyancy, controlled drug release, and reduced gastric irritation [5].

This study aims to formulate and evaluate floating microbeads of lansoprazole using natural polymers to enhance its gastric retention and therapeutic efficacy. The selection of natural polymers is important to ensure optimal floating properties, drug release kinetics, and stability of the microbeads.

MATERIAL AND METHODS:

Formulation of sustain release microbeads of Lansoprazole

Different batches of drug loaded microbeads (F1, F2, F3, F4, F5 and F6) were prepared using optimized concentration of sodium alginate and gelatin (0.5 to 1.5%) as a coating polymer. To 50ml of deionized water, gelatin was added and stirred with the electric stirrer to form mucilage. Then sodium alginate was added to form uniform dispersion. Weighed quantity of Lansoprazole was added and homogenized for 5 min. The resulting dispersion was dropped through syringe with needle into 100ml of 2% w/v aqueous calcium chloride solution and stirred at 100rpm. After stirring for 1 hour, the formed beads were separated by filtration, washed with distilled water, dried at 50^0C in an oven. The compositions of various formulations designed in the present study are given in Table 1 [6].

Table 1: Composition of various formulations of microbeads

Ingredient (mg)	F1	F2	F3	F4	F5	F6
Drug (mg)	30	30	30	30	30	30
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 microbeads

Evaluation of flow properties of microbeads

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 [7].

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 microbeads was determined using zeta sizer (Malvern zetasizer instrument, India) [8]. The microbeads 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 [9]. The clear supernatant solution was assayed spectrophotometrically for drug content at the wavelength of 296nm. 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 [10]. 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

Scanning electron microscopy (SEM)

The surface morphology of the beads was examined using scanning electron microscope (Jeol, JSM, 35CF, Japan). The beads were mounted onto individual stab and then coated with carbon and gold (100 and 50 Å thickness respectively). The coated samples were then observed under scanning electron microscope operated at 7Kv.

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. One Lansoprazole microbeads was 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 (37°C) was supplanted each time with a similar amount of the sample and takes the absorbance at 296nm using spectroscopy.

RESULTS AND DISCUSSION:

The evaluation of flow properties, particle size, entrapment efficiency, swelling index, and in-vitro drug release kinetics provides valuable insights into the characteristics and performance of the formulated microbeads.

In terms of flow properties, the loose bulk density, tapped bulk density, Carr's index, and Hausner's ratio serve as indicators of the flowability of the microbead formulations. Lower values of Carr's index and Hausner's ratio generally suggest better flowability. Among the formulations, F4 exhibits relatively lower Carr's index and Hausner's ratio, indicating improved flow properties compared to others.

Particle size plays a crucial role in the gastric retention and drug release characteristics of the microbeads. Entrapment efficiency, on the other hand, reflects the proportion of drug encapsulated within the microbeads. Formulation F4 stands out with the highest entrapment efficiency, indicating efficient drug loading within the microbeads.

The swelling index data offer insights into the hydration and swelling behavior of the microbeads over time. Higher swelling indices indicate greater water uptake and swelling capacity. Formulation F3 demonstrates the highest swelling index, suggesting superior hydration and swelling properties compared to other formulations.

The in-vitro drug release profiles depict the cumulative release of the drug from the microbeads over time. The sustained release of lansoprazole from the microbeads is evident, with gradual release

observed throughout the study duration. Notably, formulation F4 exhibits relatively slower drug release kinetics compared to others, indicating sustained and controlled release behavior.

Further analysis of the drug release kinetics for the optimized formulation (F4) reveals that the release follows the First Order and Korsmeyer-Peppas models, suggesting a combination of diffusion and erosion-controlled release mechanisms.

Table 2: Evaluation of flow properties of microbeads

Formulation code	Parameters			
	Loose Bulk density(gm/ml)	Tapped bulk density(gm/ml)	Carr's Index (%)	Hausner's Ratio
F1	0.885	1.985	55.42	2.243
F2	0.895	1.962	54.38	2.192
F3	0.796	1.885	57.77	2.368
F4	0.885	1.896	53.32	2.142
F5	0.965	1.987	51.43	2.059
F6	0.832	1.965	57.66	2.362

Table 3: Results of particle size and entrapment efficiency of microbeads

F. Code	Beads size (nm)	Entrapment Efficiency (%)
F1	385.65	66.45
F2	326.65	69.98
F3	318.85	68.85
F4	285.46	73.36
F5	305.65	71.12
F6	315.96	68.78

Table 4: Results of percentage swelling index of microbeads

F. Code	% Swelling index				
	1hrs	2 hrs	4 hrs	6 hrs	8 hrs
F1	32	54	65	78	110
F2	45	63	89	98	136
F3	55	73	95	120	165
F4	63	89	110	155	196
F5	58	73	88	98	163
F6	62	88	98	125	159

Table 5: *In-vitro* drug release study of microbeads

Time	% Cumulative Drug Release					
(hr)	F1	F2	F3	F4	F5	F6
0.5	36.65	32.23	29.98	25.65	20.23	18.54
1	49.98	45.65	40.23	36.85	33.12	26.65
1.5	66.65	59.98	55.65	45.95	40.56	35.45
2	78.85	73.32	69.98	58.85	51.21	45.85
3	96.65	94.45	88.45	63.32	60.36	55.45
4	99.05	98.85	93.32	75.56	69.98	62.23
6	99.12	99.45	98.85	89.98	86.65	84.45
8	99.65	99.65	99.12	93.32	90.12	88.98
12	99.45	99.82	99.36	99.05	93.32	90.14

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	0.818	0.989	0.936	0.996

CONCLUSION:

In conclusion, the formulation and evaluation of floating microbeads of lansoprazole using natural polymers have shown promising results with regards to their flow properties, particle size, drug entrapment efficiency, swelling behavior, and in-vitro drug release kinetics. The assessment of flow properties indicated that formulation F4 exhibited improved flowability compared to other formulations, which is crucial for manufacturing and handling processes. Moreover, formulation F4 demonstrated the highest entrapment efficiency, suggesting efficient drug loading within the microbeads.

The swelling index data revealed that formulation F3 exhibited superior hydration and swelling properties, which are essential for prolonged gastric retention and controlled drug release. In-vitro drug release studies demonstrated sustained and controlled release behavior of lansoprazole from the microbeads over an extended period. Notably, formulation F4 exhibited relatively slower drug release kinetics, indicating sustained drug release characteristics. Further analysis of drug release kinetics confirmed that the release mechanism of the optimized formulation (F4) followed both diffusion and erosion-controlled mechanisms, as evidenced by the fit to the First Order and Korsmeyer-Peppas models.

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