

## Formulation and evaluation of floating beads of esomeprazole magnesium USP

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### Abstract

The aim of this study was to develop and evaluate floating beads of Esomeprazole Magnesium USP. Floating beads of Esomeprazole were prepared by ionotropic Gelation method using sodium alginate as the polymer. Five different formulations were developed. The developed floating beads were evaluated for percentage yield, particle size, *in vitro* buoyancy, scanning electron microscopy and drug release. Stability studies were carried for 45 days. There are no significant change in the drug entrapment, buoyancy, and drug release of floating beads Esomeprazole Magnesium after 45 days. The polymer used was Sodium alginate. FTIR study results showed that there were no incompatibility between drug and polymer. Solubility study was performed and recorded the results. Results of our present study suggest that floating beads of Esomeprazole Magnesium can be successfully designed for controlled drug delivery which can reduce dosing frequency making the formulation an effective alternative to conventional dosage forms.

**Keywords:** Floating beads, Esomeprazole magnesium, Buoyancy, In vitro.

### Introduction

<sup>1</sup>Oral route is the most preferable route of drug administration due to better patient compliance. However there arises a problem by oral route with the use of certain types of dosage form i.e., fluctuation in plasma drug level. By the use of controlled drug delivery system we can prolong the action of drugs in our body. Gastric emptying is a complex process in our body variable in different individuals. The aim of designing oral controlled drug delivery system is to increase the bioavailability of drugs. A major problem associated with the oral controlled drug delivery system is limited gastric residence time. To improve the retention of an oral dosage form in the stomach various approaches have been developed, eg. Floating systems, swelling and expanding systems, bioadhesive system, altered density systems and other delayed gastric emptying devices. Gastro retentive dosage form prolongs the gastric residence time of drug by remaining in the gastric region for several hours. Floating Beads are one of the gastro retentive dosage forms that float over gastric contents due to their buoyancy and remain in the stomach for prolonged period. Suitable drugs that can be used in gastro retentive system include

1. Drugs with narrow absorption window in the stomach.
2. Drugs locally acting in the stomach
3. Drugs which are unstable in intestinal and colonic environment<sup>2</sup>

Floating drug delivery system is a type of gastro retentive drug delivery system. This system remain buoyant in the stomach without affecting the gastric emptying rate for a prolonged period time because they have a bulk density less than gastric fluids.<sup>3</sup> From these system the drug is released slowly at a desired rate, which results in increased gastro retention time. And there is also reduction in fluctuation of plasma drug concentration. The aim of using floating drug delivery system is to retain the drug in the stomach. And

this system is very useful for drugs that are poorly soluble and unstable in the stomach. The principle of floating drug delivery system is to make the dosage form less dense than gastric fluids. Floating systems are hydro dynamically balanced low density system. Gastric retention of floating drug delivery system increases the bioavailability and therapeutic benefit of the dosage form.

### Materials and Methods

Esomeprazole Magnesium was purchased from Southern Chemicals, Trissur. Sodium Alginate was purchased from Loba Chemi. Sodium Bicarbonate, Calcium Chloride, Glacial Acetic Acid was purchased from Nice Chemicals. All the chemicals used in the study belong to the analytical grades.<sup>4</sup>

### Preformulation Study

Preformulation studies such as solubility determination, FTIR, were performed to determine the solubility parameters of the drug and to assure the compatibility between the drug and the polymer. Absorption maximum and calibration curve were also determined.

### Formulation of Floating Beads

The Floating Beads was prepared using the ionotropic gelatine method<sup>5</sup>. Sodium alginate is added to 10 ml of distilled water in a beaker and stirred well to obtain a clear solution in a magnetic stirrer. To the above solution 100 mg of Esomeprazole Magnesium is dissolved. To the above solution sodium bicarbonate is added and sonicated for 30 min to remove air bubbles. It is kept aside for 30 min. The resultant dispersion is dropped via 23-gauge needle into 100 ml 2% w/v Calcium chloride solution containing 10% acetic acid. Then washed with distilled water and dried at room temperature. Formulation details are given in table 1.

### Evaluation of Floating Microspheres<sup>6</sup>

#### Percentage yield

The prepared beads were collected and weighed. Percentage yield was obtained by dividing measured weight of floating beads by the total weight of drug and the polymer.

#### Particle Size Analysis

The particle sizes of the floating beads were obtained by optical microscopy method. By using stage micrometer eye piece micrometer was calibrated. The beads were mounted onto the slide and mean particle size was determined by the measuring the sizes of hundred particles.

### In-vitro Buoyancy Study<sup>7</sup>

In-vitro buoyancy studies were done using dissolution test apparatus USP type II (rotating paddle). 50 calcium alginate beads of Esomeprazole Magnesium were taken and added to the dissolution flask containing 0.1 N HCl as medium (900 ml) containing 0.02% tween 80. Temperature was maintained at  $37 \pm 0.5^\circ\text{C}$ . Paddle maintained at  $100 \pm 5$  rpm. At hourly intervals stirring was stopped for 2 min and number of settled beads was counted visually. The floating and the settled portion of beads recovered separately.

Buoyancy percentage was calculated as the ratio of the number of beads that remained floating and the total number of beads taken.

Buoyancy percentage =  $\frac{\text{No. of beads remained floating}}{\text{Total no. of beads}} \times 100$

### Scanning Electron Microscopy

The surface morphology and internal structure of the products were observed by scanning electron microscopy using scanning electron microscope. Pictures of the beads were taken by random scanning of the stub.

### In-vitro drug Release Profile<sup>8</sup>

Dissolution studies were performed using the USP dissolution test apparatus-II at 100 rpm. The dissolution studies of the beads equivalent to 50mg of Esomeprazole were performed using USP type II dissolution test apparatus. The drug release study was carried out in 0.1 N HCl for initial 6 h followed with dissolution in phosphate buffer pH 7.4, each 900 ml, maintained at  $37 \pm 2^\circ\text{C}$  and agitated at 100 rpm. 1 ml samples were collected replaced with 1 ml fresh dissolution medium for 8hrs. After filtration through muslin cloth, it is diluted to 10ml using respective buffer solution and concentration of drug was determined spectrophotometrically at 302 nm.

### Percentage Entrapment Efficiency<sup>9</sup>

Accurately weighed quantities of beads (50mg) of the optimized batch were placed in 100ml phosphate buffer pH 7.4 and mechanically agitated on a shaker at 200 rpm for 24 hrs. Then the resultant dispersion were filtered through What's man no. 41 filter paper and analysed spectroscopically at 302 nm.

Percentage entrapment efficiency (% EE) =  $\frac{\text{AQ} \times 100}{\text{TQ}}$

AQ = actual drug content in the beads

TQ = theoretical drug content in the beads

### Stability Study<sup>10</sup>

Stability studies of various dosage form was conducted to determine the maintenance of product quality, safety and efficacy throughout the shelf life are considered as pre-requisite for the acceptance and approval of any pharmaceutical product. These studies are required to be conducted in a planned way following the guidelines issued by ICH, WHO and or other agencies.

The main aim of stability testing was to provide the evidence of how the quality of a dosage form varies with time under the influence of a variety of environmental factors such as temperature, humidity and light. The stability testing also includes the study of product related factors that influence its quality, for example, interaction of API with excipients, container closure systems and packaging materials.

### Procedure

To find out the effect of floating characteristic, percentage entrapment efficiency and in-vitro drug release, the selected formulation, F5 was exposed up to 30 and 45 days of stability studies at  $40^\circ\text{C}$  and 75% RH.

### Result and Discussion

#### Preformulation Studies

1. Solubility studies that the results lie within the pharmacopeal limits.
2. FTIR results shows that there exists no any incompatibility between drug and the polymer.
3. Absorption maximum was found to be at 302 nm.
4. The calibration curve of Esomeprazole Magnesium was found to be linear in the concentration of 2-10 $\mu\text{m}$ .

### Formulation of Floating Microspheres

Five formulations of Floating beads of Esomeprazole magnesium was prepared by ionotropic gelatin method using Sodium alginate as the polymer.



**Fig. 1:** Prepared floating beads of Esomeprazole magnesium

### Evaluation of Floating Beads

Different evaluation studies are conducted for the prepared floating beads for various desired properties and the results are given in table 2.

**Table 1:** Formulation details

Formulationss	F1	F2	F3,F3	F4	F5,F5
Drug(Mg)	100	100	100	100	100
Sodium Alginate(Mg)	0.2	0.4	0.6	0.8	1.0
Sodium Bicarbonate (Mg)	0.5	0.5	0.5	0.5	0.5
Water(Ml)	100	100	100	100	100
Calcium Hloride(G)	2	2	2	2	2
Acetic Acid(Ml)	10	10	10	10	

**Table 2:** Evaluation of Floating beads

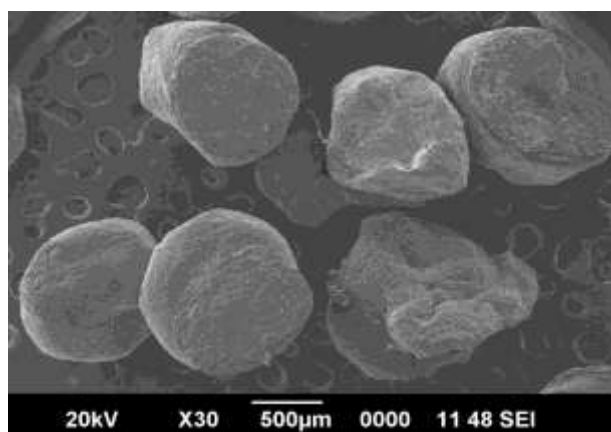
Formulation Code	Percentage yield	Percentage drug entrapment	Percent buoyancy	Mean particle size in nm
F1	37.91	66.43	55.46	150
F2	51.28	69.67	60.33	210
F3	66.35	73.97	76.17	250
F4	70.91	83.12	83.21	335
F5	82.15	94.81	91.40	420

**Table 3:** *In vitro* dissolution study

Time (hrs.)	F1	F2	F3	F4	F5
1	12.82	14.43	16.26	18.01	19.99
2	17.53	19.35	21.59	22.68	24.53
3	24.52	29.51	33.45	35.79	37.61
4	34.36	47.43	46.58	47.23	49.02
5	47.21	53.51	54.22	58.43	59.82
6	55.84	59.78	65.61	69.27	71.01
7	64.95	67.24	73.34	74.25	83.56
8	71.02	75.10	80.19	84.99	91.12

### Scanning Electron Microscopy Analysis

Prepared floating beads are subjected to scanning electron microscopy and the results are depicted in Fig. 2.

**Fig. 2:** Scanning electron microscopy

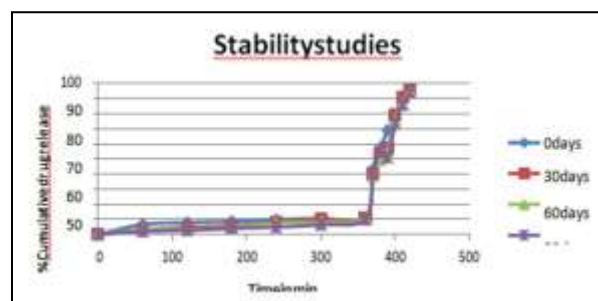
### *In-vitro* Dissolution studies

*In vitro* dissolution study is conducted for the prepared beads for 8 hours and the results shows a satisfactory dissolution pattern (Table 3).

### Stability Studies

In the present study five different formulations were prepared. The best formulation F5 was selected for stability

studies. Stability studies for beads were done by keeping the sample beads from optimized batches at room temperature (30 +/- 2° c, 65 +/- 5% RH) were carried for 45 days. In the interval of each one month the beads were evaluated for different parameters like floating time, % drug entrapment and drug release studies. There are no significant change in the drug entrapment, buoyancy, and drug release of floating beads Esomeprazole Magnesium after 45 days. All the five formulation gave good results within the limits (Fig. 3).

**Fig. 3:** stability studies

Solubility study was performed and recorded the results. A calibration data was obtained by using UV spectrometer and calibration curve was plotted. Evaluation studies such as percentage yield, particle size analysis, percentage buoyancy, and *in vitro* release were conducted.

Percentage yield was calculated and it was in the range of 37.91% -82.15%. Particle size of these microspheres ranges from 183 $\mu$ m-225 $\mu$ m. Percentage buoyancy was in the range of 55.46% -85.92%. Scanning electron microscopy showed that microspheres were spherical in shape and porous in nature. *In vitro* dissolution studies showed that formulation F5 has the release of 90.11% at the end of 8 hours.

### Conclusion

The aim of present study was to formulate floating beads of Esomeprazole Magnesium with different proportions of polymers like sodium alginate for oral drug delivery. From the results obtained from preformulation studies, it can be concluded that there was no incompatibility between drug and polymers. The evaluation studies such as particle size analysis, percentage drug entrapment, floating behavior, *in vitro* drug release and stability studies showed that formulation F5 is the optimized formulation. Stability studies showed that there was no change in the formulation after 45 days. Thus the aim of the study to formulate floating beads of Esomeprazole Magnesium was achieved. In future this system can be developed by using various polymers in various proportions for more better results.

**Conflict of Interest:** None.

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