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DEVELOPMENT AND EVALUTION OF FLOATING MICROSPHERES OF OMEPRAZOLE

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ABSTRACT

The gastro retentive system prolongs the drug's gastric retention time through staying for many hrs in GIT region. The main aim of the present investigation is to formulate Omeprazole loaded Floating microspheres by spray drying technique. The obtained formulations were evaluated for drug content, entrapment efficiency, Buoyancy time and *in vitro* dissolution studies. The entrapment efficiency was found to be increased by increasing the concentration of the polymer. In vitro dissolution studies were conducted for a period of 12 hours. The drug release was continued up to 12 hrs with 99% drug release. From the study it was concluded that formulation with code F4 was yielding the best floating microspheres which were floating for a period of 24 hrs. It decreases drug waste while enhancing the bioavailability and solubility of the medication. These systems possess low density thus remain buoyant for longer time.

KEYWORDS: Omeprazole, floating microspheres, *in vitro* dissolution studies.

INTRODUCTION

The gastro retentive system prolongs the drug's gastric retention time through staying for many hrs in GIT region. It decreases drug waste while enhancing the bioavailability and solubility of the medication. These systems possess low density thus remain buoyant for longer time. These are machines that offer a continuous drug discharge under hydrodynamic control. To make the buoyant systems, granules, powders, capsules, pills, and hollow microspheres were used.[1-5] The duration of the digestive process ranges from 5 to 2 hours on average.[6-8]

Solid spherical particles known as microspheres range in diameter in between 1-1000 µm. They, freely-moving sphere shaped biodegradable comprised of different polymers.Due to the extended duration of effective API concentration in the target tissue made possible by the site-specific microparticulate delivery devices, there are less side effects linked to lower plasma concentrations in the peripheral blood circulation.[9,10] Omeprazole is a selective and irreversible proton pump inhibitor. Stomach acid secretion is decreased as a result of the H+/K+-ATPase system being inhibited on the secretory membrane of gastric parietal cells. Due to the fact that this enzyme system is also referred to as the acid (proton, or H+) pump within the stomach mucosa, omeprazole reduces the last stage of acan id production.[11] Immediately after oral administration, omeprazole has an inhibitory effect. the greatest impact happens in the first two hours. up to 72 hours can pass between inhibitions without omeprazole.[12]

The primary goal of the study was to develop and assess omeprazole gastroretentive floating microspheres, which are anticipated to administer the medication in a regulated manner with reduced frequency of drug administration, enhance patient compliance, and increase omeprazole bioavailability.

Preparation of Omeprazole Microspheres

Omeprazole microspheres were produced by spray drying the drug and polymer solutions. The creation of a drug and polymer ethanolic solution was followed by the addition of a cross-linker to the mixture. The following spray drying parameters were established and determined: Feed Rate: 3 ml/min; Cooling Temperature: 900C; Pressure: 2bar; Inlet Temperature: 1300C; Outlet Temperature: 900C. Peristaltic pumps were used to deliver liquid to the nozzle, where the force of compressed air atomized the liquid and broke it up into small droplets. The droplets were blown into a chamber with hot air, where the solvent evaporated and was evacuated via an exhaust tube. A collection bottle was used to collect the dry goods.[13]

Table 1: Composition of the omeprazole floating microspehres formulations.

S. No.	Incredients	Formulation code			
		F1	F2	F3	F4
1	Omeprazole	0.5 g	0.5 g	0.5 g	0.5 g
2	Ethylcellulose	0.5 g	4 g	0.3g	0.3
3	HPMC E 50	0.3g	0.3g	4 g	-
4	PVP	-	0.3g	-	0.5 g
5	Eudragit RS 100	-	-	-	0.3g
6	Ethanol	15 ml	15 ml	15 ml	15 ml
7	Dichloromethane	15 ml	15 ml	15 ml	15 ml
8	Sodium lauryl sulphate (0.1%)	100ml	100ml	100ml	100ml

Evaluation of Microspheres

1. Percentage yield

Accurate weights of the dried microspheres were used to determine the % yield.[14-17]

% yield = (Practical yield/Theoretical yield) × 100

2. Drug content and entrapment efficiency

Microspheres were precisely weighed at 100 mg, ground in a motar, suspended in 100 ml of phosphate buffer pH-6.8, and then ultrasonically processed for two hours. The samples were then filtered43 and centrifuged for 20 minutes at 1000 rpm to get rid of any supernatant layer. To be spectrophotometrically evaluated at 300 nm, 1 mL of the filtered solution was collected and diluted in 25 mL of phosphate buffer pH-6.8.[18-20]

Theoretical drug content

$$\frac{\text{Weight of drug} - \text{loaded} / \text{Total weight of Microspheres}}{\text{Practical drug content}} X100$$

Encapsulation efficiency = (Actual drug content / Theoretical drug content) X 100

3. In *vitro* buoyancy studies

The USP XXIII dissolution apparatus (type II), which was filled with 900 ml of SGF (pH 1.2) containing 0.02 percent tween 20, was covered with the microspheres, each weighing around 0.3 g. A paddle revolving at 100 rpm was used to stir the medium for 12 hours. Microspheres' floating and settling sections were retrieved separately, dried, and weighed.[21]

4. In-*vitro* dissolution studies

It was done by the means of USP Paddle Type Equipment. A muslin fabric with 100mg of drug-loaded microspheres was put inside of it, then fastened to the paddle. The buffer is used as a dissolving media in 900 ml. In a dissolution medium with 900 ml of buffer, a precisely weighed sample was added, and it was left to dissolve for up to 12 hours. At regular intervals (every 1 hr), 1 ml of the material was collected and filtered through a 0.4 m membrane filter.Every time a sample was taken, the same 1ml of the dissolving medium was substituted to bring the volume of the dissolution media to 900ml4. After that, the materials underwent a 300nm spectrophotometric analysis.[22-24]

RESULTS

Table 2: Micromeritic Properties of formulations.

FORM. CODE	ANGLE OF REPOSE	BULK DENSITY	TAPPED DENSITY	CARR'S INDEX	HAUSNER'S RATIO
F1	19.42±0.20	0.68±0.64	0.74±0.73	10.1±0.84	1.05±0.54
F2	25.82±0.80	0.41±0.042	0.39±0.012	9.52±0.026	1.078±0.32
F3	19.66±0.36	0.69±0.62	0.73±0.72	7.73±0.29	1.14±0.011
F4	18.66±0.20	0.52±0.30	0.58±0.36	10.1±0.84	1.17±0.046

Table 3: Evaluation parameters of Omeprazole floating microspheres.

Code	% Yield	Drug content	Entrapmen efficiency	%Buoyancy
F1	65.9	50	91.1	74.8
F2	68.5	52.8	93.3	75.1
F3	83.1	53.8	86.5	77.9
F4	89.1	62.3	95.2	84.3

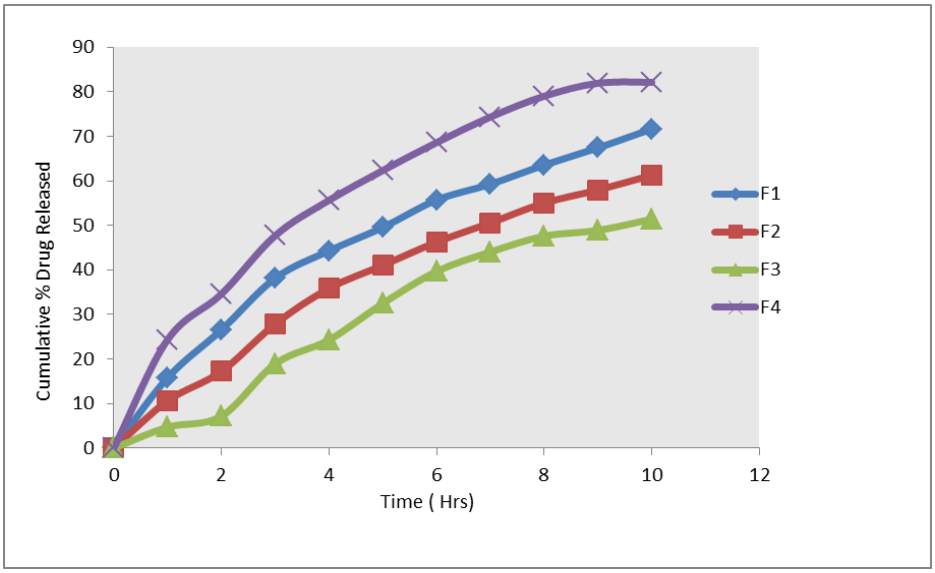

Figure 1: *In vitro* release profile of Omeprazole floating microspheres.

In the present study four different batches of floating microspheres of curcumin were formulated using different polymer by spray drying. The physical characterization, floating behavior and in vitro release studies were studied. Angle of repose, Hausner ratio, and Carr's index can be used to predict flowability. The higher the Hausner ratio the greater the cohesion between particles while the higher the Carr's index of the greater the tendency to form bridges between particles. Floating microspheres of batch F4 were spherical in shape.

Buoyancy for all the formulations was ≥ 74 % after 12 h. The nature of the polymer influenced the floating behavior of the microspheres. In general with 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 increased amount of the polymers present. The good buoyancy behavior of the microspheres may be attributed to the hollow nature of the microspheres. Formulations of batch F4 shows more entrapment efficiency. Due their floating nature, the microspheres were forcibly immersed into the dissolution medium to avoid adherence to the surface of the jar, thus leading to nonparticipation in the dissolution process. The drug release was extended to 12 h. Microspheres prepared of batch F4 showed more release (82%).

CONCLUSION

Omeprazole floating microspheres were successfully developed using spray drying method. The microspheres 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 Omeprazole.

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