

FORMULATION AND EVALUATION OF FLOATING MICROSPHERES OF CURCUMIN

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ABSTRACT

The objective of present study was to develop multiparticulate gastro retentive drug delivery system of Curcumin. The gastro retentive drug delivery system can be prepared to improve the absorption and bioavailability of curcumin by retaining the system in to the stomach for prolonged period of time. The floating drug delivery system of curcumin was prepared by emulsion solvent diffusion method by using ethyl cellulose, HPMC E5LV, Eudragit L 100, Eudragit S 100 polymers in varying concentration. Formulations were evaluated for percent yield, particle size, entrapment efficiency, *in vitro* buoyancy and *in vitro* release studies. The optimized formulations show good buoyancy and *in vitro* controlled release of Curcumin.

Keywords: Floating microsphere, Ethyl cellulose, HPMC E5LV, Eudragit L 100, Eudragit S100.

INTRODUCTION

Many different kinds of sustained drug delivery systems have been proposed for various routes of administration, since they require less frequent drug administration, provide more therapeutic effects, and reduce the incidence of side effects. To develop a drug delivery system for oral administration, the preferred route of administration, it is necessary to optimize not only the release rate from the system but also the residence time of the system in gastrointestinal tract [1]. Various oral delivery systems have been developed including osmotic tablets, polymeric matrices and microcapsules. However, limited number of approaches has been pursued to extend the residence time of the delivery system within the GIT. Floating drug delivery system (FDDS) or Hydrodynamically Balanced System (HBS) are among the several approaches that have been developed in order to increase the gastric residence time (GRT) of dosage forms [2-4]. Single unit systems possess a disadvantage of "all or nothing" effect leads to high intersubject variability [5, 6]. Still the multiple unit dosage forms may be better suited because they are claimed to reduce the intersubject variability in absorption and lower the probability of dose dumping [7, 8]. Development of floating delivery system involves use of many low density polymers. EC, HPMC and Eudragit L and S are such low density polymers. Many controlled release dosage forms utilize hydrophilic polymers for retarding drug release. The mechanism of drug release is dependent on the swelling and dissolution process. In this case the early part of

the release process is marked by swelling due to conversion of the polymer from a glassy to a rubbery state due to water penetration.

Curcumin is a potent phytochemical with wide range of biological activity [9, 10] possess a low absorption [11]. It is poorly absorbed in the lower GIT and has short elimination half life ~0.39 h. The object of the present investigation was to formulate floating microspheres of curcumin in order to achieve a prolonged retention in the upper GIT, which may result in enhanced absorption and thereby improved bioavailability. The prepared microspheres were evaluated for yield, size, *in vitro* release, and buoyancy and incorporation efficiency. The effect of various formulation variables on the size and drug release was studied.

MATERIALS AND METHODS

Curcumin was purchased from Loba chemie, Mumbai, Ethyl Cellulose from Central drug house, New Delhi, Eudragit L100, Eudragit S100 from Rohm Pharm, Germany, HPMC E5LV also from Loba chemie, Mumbai.

Preparation of Microspheres

Microspheres were prepared by emulsion solvent diffusion method. Drug and polymers are mixed in organic solvent of dichloromethane and ethanol. That mixture was added in to 0.2 % w/v aqueous solution of SLS at temp 40°C. Prepared microspheres were filtered, washed with water and dried at room temperature.

Table 1: It shows Composition of batches of floating microspheres of Curcumin

Batch	Curcumin (mg)	Ethyl Cellulose(mg)	HPMC E5LV(mg)	Eudragit L100(mg)	Eudragit S100(mg)
IN ₁	100	200	-	-	-
IN ₂	100	400	-	-	-
IN ₃	100	800	-	-	-
IN ₄	100	100	100	-	-
IN ₅	100	200	200	-	-
IN ₆	100	400	400	-	-
IN ₇	100	-	-	100	100
IN ₈	100	-	-	200	200
IN ₉	100	-	-	400	400

In-vitro evaluation of floating microspheres of Curcumin

Determination of percent yield

Thoroughly dried microspheres were collected and weighed accurately. The percentage yield was then calculated.

Determination of entrapment efficiency

The drug content of Curcumin loaded microspheres was determined by dispersing 100 mg microspheres in 10 ml of ethanol, which was

stirred with a magnetic bead for 8 h to extract the drug. The samples were diluted and analyzed spectrophotometrically at 421 nm and the percentage drug entrapment was calculated.

Particle size analysis

Particle size of prepared microspheres was measured using an optical microscope, and the mean particle size was calculated by measuring 100 particles with the help of a calibrated ocular micrometer.

Floating behaviour (buoyancy)

50 mg of the microspheres were placed in 100 ml of simulated gastric fluid (pH 1.2) containing 0.02% w/v tween 20. The mixture was stirred at 100 rpm on a magnetic stirrer. After 4 h, the layer of buoyant microspheres was pipetted and separated by filtration; particles in the sinking particulate layer were also separated by filtration. Particles of both types were dried in desiccators. Both the fractions of microspheres were weighed and buoyancy was determined by the weight ratio of floating particles to the sum of floating and sinking particles.

SEM study

The surface topography and internal textures of the microspheres was observed by scanning electron microscopy.

In-vitro dissolution studies in 0.1N HCl

The *in-vitro* dissolution studies were carried out by using USP XXIV paddle type dissolution apparatus. Weighed amount of drug loaded floating microspheres was introduced into 900 ml 0.1 N HCl, used as a dissolution medium, maintained at $37 \pm 0.5^\circ\text{C}$ at a rotation speed of 100 rpm. The samples were withdrawn at predetermined time intervals. First two samples were withdrawn at 30 min. interval and next eleven samples were withdrawn at 1 h interval. The samples were analyzed spectrophotometrically at 430 nm to determine the concentration of drug present.

RESULT AND DISCUSSION

Percent yield

All batches showed a percentage yield of greater than 70%, whereas five batches showed a yield of more than 80%. Percentage yield is found to be higher with formulation of high amount of polymer. Results showed that percentage yield increases with increase in the amount of polymer.

Entrapment efficiency

All batches show percent entrapment more than 50% and it is found that entrapment of drug increases with an increase in the amount of the polymer. Formulation IN₆ shows maximum entrapment whereas formulation IN₇ shows minimum entrapment of the curcumin in the polymer as shown in table 2.

Particle size analysis

Results showed that particle size of prepared microspheres was in the range of $130 \pm 20\mu\text{m}$ to $226 \pm 25\mu\text{m}$. It was concluded that with increase in polymer concentration, particle size of prepared microspheres increases as shown in table 2.

SEM study

Results showed that ethyl cellulose microspheres of ketorolac trometamol were predominantly spherical in shape with smooth surface. The porous nature and characteristics internal structure of the microspheres, a hollow cavity inside enclosed with the rigid shell constructed with drug and polymer was clearly evident. Ethyl cellulose and HPMC E5LV based floating microspheres were found to be much more elongated in nature than microspheres prepared by using Eudragit S100 and Eudragit L100. The porous nature and cavity formed in the microspheres would dictate the floating behaviour of microspheres of Curcumin as shown in figure 1.

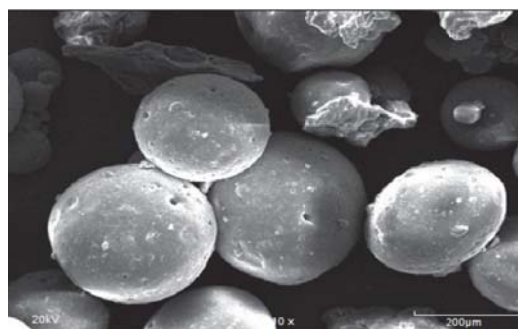


Fig. 1: It shows SEM photomicrographs of batch IN₆

Floating ability (Percent buoyancy)

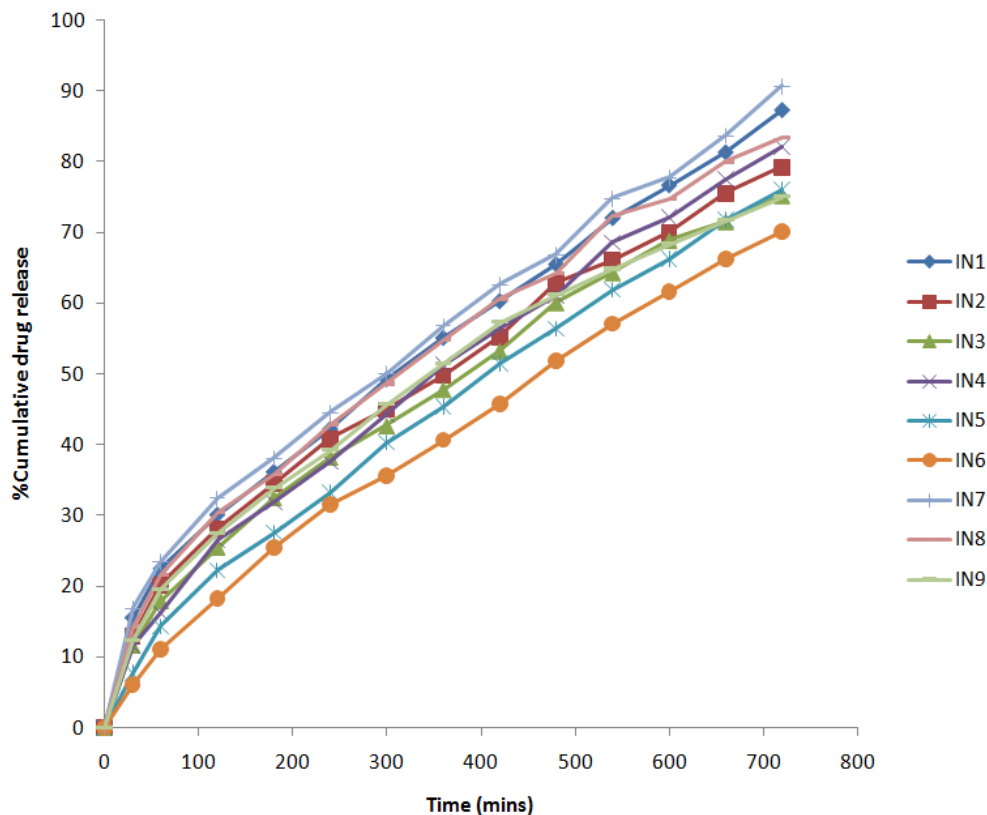
The formulated batches of floating microspheres of curcumin showed average buoyancy more than 53%. Amongst the batches of prepared microspheres, batch IN₆ showed highest buoyancy (74%). Further it was observed that in case of ethyl cellulose and HPMC E5LV based microspheres, buoyancy was high, as compared with only ethyl cellulose based microspheres as shown in table 2.

Table 2: It shows Characterisation of various batches of floating microspheres of Curcumin

formulation code	Production yield (%)	Entrapment efficiency (%)	Drug loading (%)	Buoyancy % age	Mean particle size (μm)
IN ₁	83.9	54.13	21.50602	65.85	10
IN ₂	85.2	66.5	15.57229	63.82	18
IN ₃	86.9	73.01	9.337349	69.23	25
IN ₄	78.3	63.89	27.16867	60	32
IN ₅	81.2	73.49	18.10241	70.1	38
IN ₆	83.1	81.53	10.87349	73.52	45
IN ₇	73.2	50.73	23.07229	53.85	49
IN ₈	76.9	61.92	16.11446	56.09	55
IN ₉	78.8	78.01	10.99398	59.52	60

Table 3: It shows Dissolution profiles of batches of Floating microspheres of Curcumin

Time (mins)	% Cumulative drug release								
	IN ₁	IN ₂	IN ₃	IN ₄	IN ₅	IN ₆	IN ₇	IN ₈	IN ₉
0	0	0	0	0	0	0	0	0	0
30	15.58	12.97	11.67	11.67	7.76	6.13	16.89	14.28	12.32
60	22.52	20.22	17.93	16.3	14.33	11.05	23.5	21.53	19.56
120	30.14	28.16	25.53	26.52	22.24	18.28	32.44	30.45	27.5
180	36.18	34.51	32.52	31.88	27.58	25.56	38.16	35.84	33.85
240	42.25	40.89	38.24	37.6	33.27	31.57	44.56	42.88	39.25
300	49.32	45	42.69	44.33	40.3	35.65	50.03	48.66	45.66
360	55.14	49.81	47.81	51.42	45.42	40.74	56.82	54.8	51.45
420	60.33	55.31	53.29	56.59	51.53	45.85	62.67	60.64	57.28
480	65.55	62.81	60.1	61.14	56.38	51.97	66.93	64.23	61.18
540	72.1	66.08	64.34	68.64	61.9	57.15	74.79	72.4	64.77
600	76.73	70.02	68.93	72.28	66.16	61.69	77.8	74.75	68.38
660	81.38	75.62	71.58	77.56	71.72	66.27	83.76	80.05	71.68
720	87.36	79.28	75.23	82.22	76.02	70.21	90.73	83.41	75



Graph 1: It shows effect of different Polymers on Dissolution profiles

CONCLUSION

The percentage yield of all the formulated batches of microspheres was more than 70 %. Among the prepared batches, batch IN₃ showed highest percentage yield. The percentage entrapment of the formulated batches of microspheres was more than 50%. Amongst the batches, batch IN₆ showed highest (81.53 %) entrapment efficiency. The particle size of all the formulated batches of microspheres was ranged from 10 μm to 60 μm . SEM study showed that the microspheres prepared by using ethyl cellulose alone were predominantly spherical in shape with smooth surface than the microspheres prepared by using Eudragit S100, Eudragit L100, and ethyl cellulose + HPMC E5LV based microspheres. The formulated floating microspheres showed average percentage buoyancy more than 53 %. Amongst the formulated batches, batch IN₆ showed highest percentage buoyancy (74%). In-vitro dissolution studies in 0.1N HCl buffer solution showed polymer concentration dependent release of curcumin.

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