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FORMULATION AND EVALUATION OF FLOATING MICROBALLOONS FOR ANTI GOUT DRUG

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ABSTRACT

Microballoons are considered as one of the most promising buoyant drug delivery systems as they possess the advantages of both multiple-unit systems and good floating properties. The purpose of the present investigation was to characterize and evaluate microballoons of Allopurinol and to increase its boioavailability by increasing the retention time of the drug in the gastrointestinal tract. Sustained release floating microballoons containing allopurinol was formulated by solvent evaporation method using different polymer, DCM and ethanol as organic solvents and tween 80 as a processing medium. The prepared batches were evaluated for particle size, % entrapment efficiency, drug loading, floating time, total floating time and *in-vitro* drug release. The % entrapement efficiency was found to be 63.6 % to 84.83 %. Drug loading was found the range of 55.81 to 88.56 %. All the prepared microballoons remain on float condition over a period of 12 hrs. Formulation F1 showed the highest drug release of 83.93 % in 12 hrs. All other physical parameters were found satisfactorily. The results showed that the prepared floating microballoons of Allopurinol prove to be potential multiple-unit delivery devices for safe and effective sustained drug delivery.

KEYWORDS: Allopurinol, Floating, Microballoons, Sustained Rrelease.

INTRODUCTION

Gastroretentive drug delivery is an approach to prolong gastric residence time, thereby targeting site-specific drug release in the upper gastrointestinal tract (GIT) for local or systemic effects.[1] Floating drug delivery systems are hydrodynamically balanced among the several approaches that have been developed in order to increase the gastric residence time of dosage form. Oral drug delivery system is most convenient system for the patients. Microballoons (hollow microsphere) are in strict sense, spherical empty particles without a core. These microballoons are characteristically free flowing powder. It consists of proteins or a synthetic materials and ideally having size less than 200 micrometer. These are low density systems that have sufficient buoyancy to float over gastric contents, remain in stomach for the prolonged period. The drug is released slowly at the desire rate resulting in increased gastric retention with reduced fluctuation in the plasma drug concentration.[2-4] Microballoons are considered as one of the most promising buoyancy systems, as they possess the unique merits of multiple unit system as well as better floating properties, because of the central hollow space inside the microsphere.[5-6] Allopurinol is a white powder. Allopurinol is an ideal drug for treatment of gout. Allopurinol reduces the production of uric acid in your body. Uric acid buildup can lead to gout or kidney stones. It is potent xanthine oxidase inhibitor. Chemically it is analogue of hypoxanthine.[7-8] It having short half life of 1.62 hrs, hence more suitable for sustained release.

MATERIAL AND METHODS

Allopurinol was obtained as a gratis sample from Harman Finochem Ltd., Aurangabad, Maharashtra. All other chemicals were used of analytical grade.

Formulation of Floating Microballoons

The floating microballoons were prepared by using different ratio of Allopurinol and polymers as shown in table no. 1. Drug polymer mixture was dissolved in the dichloromethane and ethanol (1:1) as a solvent system. Mixture was poured in the distilled water containing surfactant tween 80 at a room temperature consequently with continuous stirring at 300 rpm to allowed evaporation of volatile solvent . After that the solution

was filtered and washed with distilled water and dried at 40°c.

Table 1: Formulation composition of batches F1-F12.

Ingredients	F1	F2	F3	F4	F5	F6	F7	F8	F9	F10	F11	F12
Allopurinol (mg)	100	100	100	100	100	100	100	100	100	100	100	100
Allopurinol: Eudragit RS 100	1:1	1:2	1:3	-	-	-	-	-	-	-	-	-
Allopurinol:HPMC	-	-	-	1:1	1:2	1:3	-	-	-	-	-	-
Allopurinol:HPMC K4M	-	-	-	-	-	-	1:1	1:2	1:3	-	-	-
Allopurinol: Ethyl Cellulose	-	-	-	-	-	-	-	-	-	1:1	1:2	1:3
DCM :Ethanol	1:1	1:1	1:1	1:1	1:1	1:1	1:1	1:1	1:1	1:1	1:1	1:1
Tween 80 (%)	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1
Distilled water (ml)	200	200	200	200	200	200	200	200	200	200	200	200

Evaluation of Floating Microballoons

Production yield

The production yield of the micro particles was determined by calculating accurately the initial weight of the raw materials and the last weight of the microballoons obtained.[9]

% yield = (Weight of microballoons collected / Weight of all non-volatile components using for the preparation) ×100

Loading efficiency

The loading efficiency (%) of the micrballoons was calculated according to the following equation.[10]

Loading Efficiency=Amount of drug in microballoons/ Weight of Microballoons*100

Drug entrapment efficiency (DEE)[11]

The amount of drug can be estimated by crushing the microballoons and extracting with aliquots of 0.1 N HCl repeatedly. The extract is further transfer in to a 100 ml volumetric flask and the volume is made up using 0.1 N HCl. The solution is filter and absorbance is measure by the spectrophotometer against the appropriate blank. The amount of entrapped in microballoons was calculated by;

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

Particle size

Particle size of microballoon formulation was performed by optical microscopy.[12]

Floating lagtime

The 100 mg of floating microballoons were placed in the 500ml of 0.1N HCl and it's raised to upper of the beaker. The duration of time was noted.

Total floating time

100 mg microballoons were dispersed in 0.1 N HCl solution containing Tween 80 (0.1 w/v %) to stimulate gastric fluid and the mixture was stirred with a paddle at 75 rpm. After 12 hours, the layer of the buoyant particles was pipetted and the floating particles were separated by filtration and particles in sinking particulate layer were separated by filtration. Both particles were dried overnight and each weight was measured and buoyancy was determined by the weight ratio of the floating particles to the sum of floating and sinking particles.[11]

Buoyancy (%) = Qf/Qf+ Qs x 100

Where Qf and Qs are the masses of floating and settled microballoons.

In-vitro drug release study

In vitro release rate studies of microballoons were carried out by basket type dissolution apparatus. Floating microballoons equivalent to 100 mg Allopurinol were filled in capsules. Dissolution study was carried in pH 1.2 dissolution media for 12 hrs at 37 °C. Allopurinol amount in withdrawn samples was determined by spectrophotometrically at 250 nm.[13]

RESULTS AND DISCUSSION

All the prepared floating microballoons were evaluated for their physical properties and drug release as shown in table no. 2. All prepared batches were showed satisfactory floating behavior. Highest % entrapment, drug loading and drug release as shown in figure 1 to 4 was found in formulation F1 containing Eudragit RS polymer.

Table 2: Evaluation parameters of batches F1-F12.

Batch No.	Mean Size (µm± S.D., n=3)	Production Yield (%)(% ± S.D., n=3)	Entrapment Efficiency (% ± S.D., n=3)	Drug Loading (% ± S.D., n=3)	Floating lag time (sec)(±S.D., n=3)	Total floating time(hrs)
F1	196.9±0.85	89.5±0.54	84.83±.0.44	88.56±0.03	1.22±0.1	>12
F2	191.6±0.55	91.3±0.26	79.3±0.36	84.36±0.14	1.66±0.57	>12
F3	182.6±0.52	94.6±0.32	75.5±0.51	81.52±0.09	2±0.01	>12
F4	150.6±1.51	78.6±0.31	71.2±0.30	68.31±0.08	2.33±0.57	>12
F5	147±0.80	77.1±0.61	67.1±0.50	62.14±0.01	2.33±0.21	>12
F6	142.8±1.02	80.8±0.43	73.8±0.28	66.81±0.08	3.08±0.09	>12
F7	132.8±1.04	69.5±0.42	63.6±0.32	55.81±0.05	2.33±0.01	>12
F8	125.3±1.12	73.2±0.14	68.1±1.20	58.32±0.12	3±0.07	>12
F9	119.3±1.35	74.5±0.38	62.4±0.70	59.52±0.06	1.33±0.37	>12
F10	169.3±1.45	77.3±0.56	78.2±0.20	69.12±0.04	2.66±0.08	>12
F11	162.5±1.32	81.3±0.64	67.6±0.41	63.19±0.04	2.33±0.02	>12
F12	156.8±1.04	87.9±0.33	74.8±0.20	70.99±0.01	3±0.09	>12

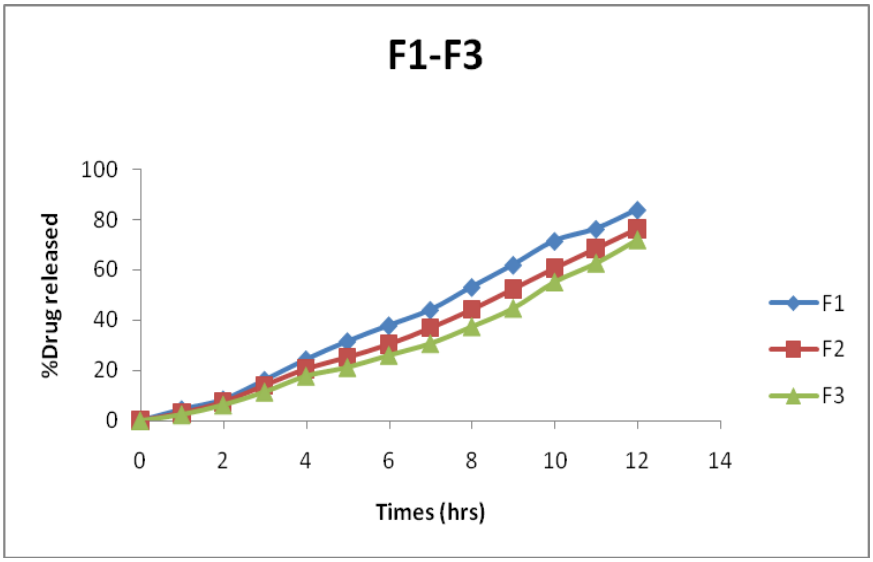

Figure 1: In vitro drug released from F1-F3.

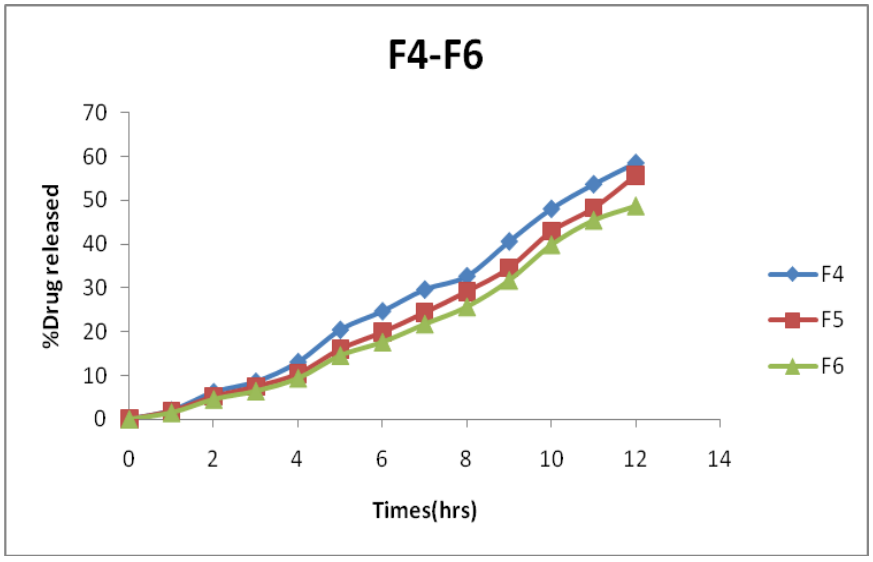

Figure 2: In vitro drug released from F4-F6.

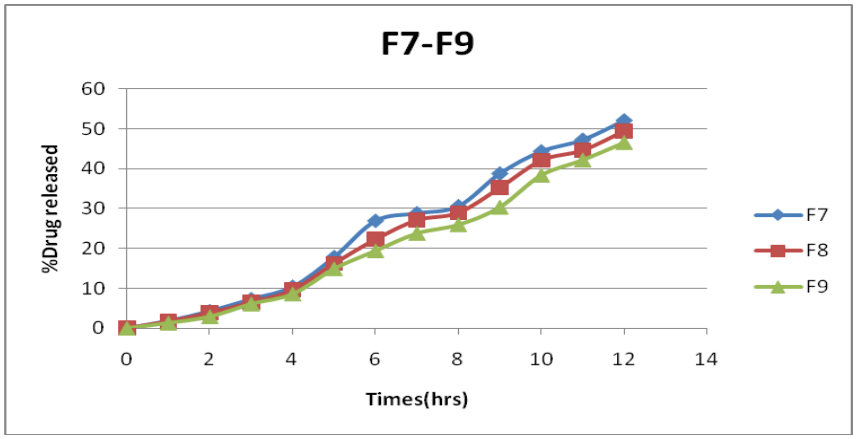

Figure 3: In vitro drug released from F7-F9.

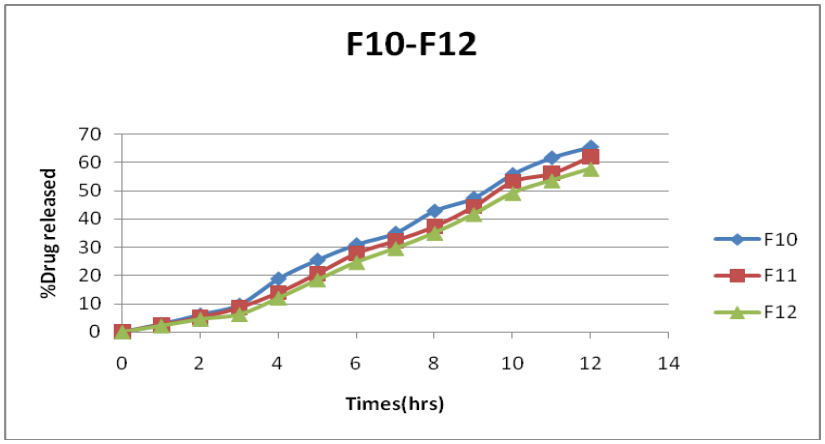

Figure 4: In vitro drug released from F10-F12.

CONCLUSION

Drug absorption in the gastrointestinal tract is a highly variable process, prolonging gastric retention of the dosage forms, and extending the time of drug absorption. Hollow microballoons, gastro retentive controlled release delivery system promises to be a potential approach for gastric retention. Floating microballoons of allopurinol was successfully prepared by taking polymer Eudragit RS 100 by solvent evaporation method. Allopurinol was successfully formulated in floating microballoons to deliver drug up to 12 hours.

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