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Design and Characterization of Floating Tablet of Rabeprazole

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ABSTRACT

The present study was aimed at preparing sustained floating drug delivery system of Rabeprazole to increase its gastric residence time and bioavailability after oral administration. Total ten formulations were formulated by direct compression technique using HPMC K15M, HPMC K100M and ethyl cellulose (floating agent) as polymers along with sodium bicarbonate as gas generating agent. The formulations were evaluated for their physicochemical properties, buoyancy lag time, total floating time, swelling index and in-vitro drug release. All ten formulations possessed good floating properties with total floating time >12 hrs.

Keywords: gastroretentive drug delivery, ethyl cellulose, HPMC, effervescent, sustained release

1. INTRODUCTION

Oral administration is the most convenient and preferred means of any drug delivery to the systematic circulation. Oral sustained release drug delivery have recently been of increasing interest in pharmaceutical field to achieve improved therapeutic advantages, such as ease of dosing administration, patient compliance and flexibility in formulation. This route has high patient acceptability, primarily due to ease of administration. Over the years, oral dosage forms have become increasingly sophisticated with major role being played by sustained release drug delivery system (SRDDS). SRDDS release drug at a predetermined rate, as determined by drug's pharmacokinetics and desired therapeutic concentration. This help in achieving predictable drug plasma concentration required for therapeutic effect.[1]

Novel oral controlled dosage form that is retained in the stomach for prolonged and predictable period is of major interest among academic and industrial research groups. One of the most feasible approaches for achieving prolonged and predictable drug delivery profile in the GI tract is to control gastric residence time (GRT). Dosage form with prolonged GRT or gastro-retentive dosage form (GRDF) provides an important therapeutic option.[2]

Various approaches for preparation of gastroretentive drug delivery system include floating systems, swellable and expandable systems, high density systems, bioadhesive systems, altered shape systems, gel forming solution or suspension system and sachet systems. Among these, the floating dosage form has been used most commonly. The floating systems include gas-generating systems, non-effervescent systems and raft forming systems.[2]

Rabeprazole is a proton pump inhibitor with actions and uses similar to those of omeprazole. Rabeprazole is rapidly absorbed and peak plasma concentrations are reached about 3.5 hours after an oral dose. The oral bioavailability is about 52% with the enteric-coated tablet formulation, because of first-pass metabolism, and does not appear to vary after single or repeated doses. Rabeprazole is about 97% bound to plasma proteins.[3]

This study was an attempt to formulate Rabeprazole as sustained release matrix tablet for extending its release rate for prolong period of time thus increasing the bioavailability.

2. MATERIALS AND METHODS

Rabeprazole was received as a gift sample from Aristo Pharmaceuticals Pvt Ltd, Mumbai (India). All the other chemicals/excipients used were of analytical grade and used as such.

2.1 Fabrication of floating tablets

Effervescent Floating tablets containing Rabeprazole were prepared by direct compression technique using varying concentrations of different grades of polymers with Sodium bicarbonate and citric acid. All the ingredients were accurately weighed and passed through different mesh sieves accordingly. Then, except Magnesium stearate all other ingredients were blended uniformly in glass mortar After sufficient mixing of drug as well as other components, Magnesium stearate was added, as post lubricant, and further mixed for additional 2-3 minutes. The tablets were compressed using rotary tablet machine. The weights of the tablets were kept constant for all formulation. The compositions of different formulations are given in Table 1.

2.2 Evaluation of prepared floating matrix tablets

2.2.1 Hardness test

Monsanto hardness tester was used for the determination of hardness of tablets.[4]

2.2.2 Friability

Twenty tablets were accurately weighed and placed in the friabilator (Jyoti Scientific Industries) and operated for 100 revolutions. The tablets were dedusted and reweighed. The tablets that loose less than 1% weight were considered to be compliant.[4]

2.2.3 Weight variation

10 tablets were selected randomly from the lot and weighed individually to check for weight variation.[4]

2.2.4 Bulk density

It is the ratio of total mass of powder blend to the bulk volume of powder blend. It was measured by pouring the weighed powder blend into a graduated cylinder and the volume was noted. It is expressed in gm/mL and is determined by following formula.[5]

Bulk density = mass of powder blend / bulk volume

2.2.5 Tapped density

Tapped density was determined by using graduated cylinder. An accurately weighed sample of powder blend was carefully added to the graduated cylinder with the aid of funnel. The initial volume was noted and the sample was tapped on a horizontal base. Tapping was continued until no further reduction in sample volume was observed. Volume was noted and tapped density is calculated by using the following formula.[5]

Tapped density = mass of powder blend / tapped volume

It is expressed in gm/ml.

2.2.6 Compressibility index %

It indicates the ease with which a material can be induced to flow and powder compressibility. It is expressed in percentage and is given by the following formula.[5]

$$I = (D_t - D_b / D_t) \times 100$$

Where, D_t is the tapped density of the powder, D_b is the bulk density of the powder.

2.2.7 Angle of repose

The angle of repose was determined by funnel method suggested by Newman. Angle of repose is determined by following formula

$$\theta = \tan^{-1}(h/r)$$

Where, θ = angle of repose, h = height of the cone, r = radius of heap.

A funnel was fixed at a height of approximately of 2-4 cm over the platform. The sample was slowly passed along the wall of funnel, till the cone of the powder formed. Angle of repose was determined by measuring the height of the cone of powder and radius of the heap of the powder.[5]

2.3 Drug Content Estimation

The drug content in each formulation was determined by triturating 20 tablets and powder equivalent to average weight was added in 100ml of 0.1N hydrochloric acid. The solution was filtered through a 0.45µ membrane filter, diluted suitably and the absorbance of resultant solution was measured spectrophotometricaly at 275 nm using 0.1N hydrochloric acid as blank.[6]

2.3.1 Determination of Swelling Index[4]

The swelling index of tablets was determined in 0.1N HCl (pH 1.2) at room temperature. The swollen weight of the tablet was determined at predefined time intervals over a period of 8 h. The swelling index (SI), expressed as a percentage, and was calculated from the following equation,

$$SI = \frac{\text{Weight of tablet at time } (t) - \text{Initial weight of tablet}}{\text{Initial weight of tablet}} \times 100$$

2.3.2 In vitro buoyancy studies

In vitro buoyancy studies were performed for all the twelve formulations as per following procedure. Randomly selected tablets from each formulation were kept in a 100ml beaker containing simulated gastric fluid, pH 1.2 as per USP. The time taken for the tablet to rise to the surface and float was taken as floating lag time (FLT). The duration of time the dosage form constantly remained on the surface of medium was determined as the total floating time (TFT).[6]

2.3.3 In vitro dissolution study

In vitro release studies were carried out by using United States Pharmacopoeia (USP) 23 Dissolution Testing Apparatus II (Paddle method). The dissolution test was performed using 900 ml of 0.1N HCl (pH 1.2) at 37±0.5°C at 50 rpm. 5 ml of sample was withdrawn at predetermined time intervals for 24 hours and the same volume of the fresh medium was replaced. The absorbance of the withdrawn sample was measured spectrophotometricaly at 275 nm.[4]

3. RESULTS AND DISCUSSION

3.1 Hardness, Friability and Weight variation

All formulations were subjected for hardness, friability and weight variation. Results are presented in Table 2.

3.2 Bulk density, Tapped density, Compressibility index and Angle of repose

To get an idea about the flow properties of granules, they were subjected to various tests. All the results were in the acceptable range. Results are presented in Table 3.

3.3 Drug Content Estimation

The drug content estimations exhibited values in the range of 97.12 to 102.02% which reflects good uniformity in drug content among different formulations. Results are presented in Table 4.

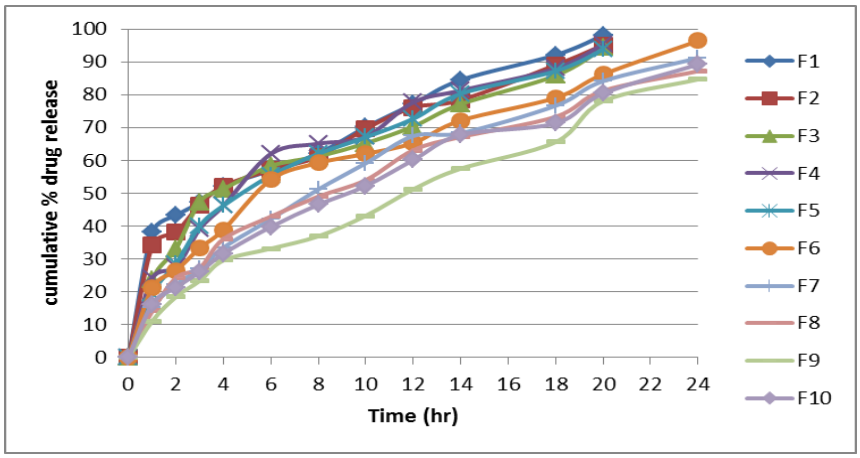

Figure 1: *In vitro* drug release from floating tablet formulations

Table 1: Composition of formulations of floating tablets

Formulation code	Drug (mg)	HPMC K100M (mg)	HPMC K15M (mg)	Ethyl cellulose (mg)	$NaHCO_3$ (mg)	Citric acid (mg)	Mg stearate (mg)	Talc (mg)	Lactose (mg)
F1	200	50	-	-	50	25	3	2	55
F2	200	75	-	-	50	25	3	2	30
F3	200	100	-	-	50	25	3	2	5
F4	200	-	50	-	50	25	3	2	55
F5	200	-	75	-	50	25	3	2	30
F6	200	-	100	-	50	25	3	2	5
F7	200	-	-	50	50	25	3	2	55
F8	200	-	-	75	50	25	3	2	30
F9	200	-	-	100	50	25	3	2	5
F10	200	25	25	25	50	25	3	2	30

Table 2: Hardness, friability and weight variation of prepared tablets

Formulation code	Hardness (Kg/cm^2)	Friability (%)	Weight variation (mg)
F1	5	0.57	386 ± 1.92
F2	6	0.40	390 ± 1.58
F3	4.5	0.57	387 ± 2.70
F4	6	0.89	385 ± 0.70
F5	5	0.48	388 ± 1.48
F6	6	0.74	384 ± 2.06
F7	4	0.32	391 ± 4.08
F8	5	0.36	389 ± 2.86
F9	6	0.16	386 ± 0.44
F10	5	0.30	386 ± 1.56

Table 3: Results of Bulk density, Tapped density, Compressibility index and Angle of repose studies

Formulation code	Bulk density	Tapped density	Compressibility index (%)	Angle of repose
F1	0.42	0.54	22.22	28
F2	0.39	0.48	18.75	26
F3	0.41	0.52	21.15	29
F4	0.45	0.56	19.64	24
F5	0.34	0.45	24.44	27
F6	0.46	0.54	14.81	26
F7	0.44	0.55	20.00	30
F8	0.41	0.50	18.00	31
F9	0.35	0.43	18.60	26
F10	0.37	0.46	19.56	29

Table 4: Drug Content, Floating lag time and In-vitro buoyancy of prepared floating tablets

Formulation code	Floating lag time (Sec.)	In-vitro buoyancy time (hour)	Drug Content (%)
F1	60	>12	97.12
F2	50	>12	99.13
F3	52	>12	98.60
F4	103	>12	99.62
F5	75	>12	99.60
F6	40	>12	100.53
F7	44	>12	99.68
F8	39	>12	99.68
F9	60	>12	97.13
F10	35	>12	102.02

Table 5: Swelling Index of prepared floating tablets

Time (hour)	Swelling index (%)									
	F1	**F2**	**F3**	**F4**	**F5**	**F6**	**F7**	**F8**	**F9**	**F10**
1	32	29	38	31	39	36	41	39	45	35
2	40	38	49	42	46	45	54	53	59	46
3	51	48	57	54	52	54	66	64	68	54
4	68	67	76	70	67	66	74	71	75	64
5	80	81	88	84	81	84	91	89	94	83
6	96	94	101	98	92	97	107	102	106	94
7	111	106	116	105	109	115	121	114	120	111
8	121	118	129	119	122	129	130	124	138	126

3.4 Swelling Index and *in vitro* buoyancy

All the tablets were prepared by effervescent approach. Sodium bicarbonate was added as a gas-generating agent. Sodium bicarbonate induced carbon dioxide generation in presence of dissolution medium (0.1 N hydrochloric acid). The combination of sodium bicarbonate and citric acid provided desired floating ability and therefore this combination was selected for the formulation of the floating tablets. It was observed that the gas generated is trapped and protected within the gel, formed by hydration of polymer, thus decreasing the density of the tablet below 1 and tablet becomes buoyant. The tablet swelled radially and axially during in-vitro buoyancy studies. All the batches of tablets were found to exhibit short floating lag times due to presence of sodium bicarbonate and citric acid. Results are presented in Table 4 and 5.

3.5 *In vitro* dissolution study

All the formulations were subjected to In-vitro dissolution study**.** All the formulations exhibited sustained release over a period of >20 hour. Results are presented in figure 1.

4. CONCLUSION

In our study, our observation shows that the Rabeprazole matrix tablet extends the release rate of drug for a prolong period of time at least 10 hrs and shows to increase the bioavailability and simultaneously decrease the dosing interval as well as dosing amount. The formulation minimizes the blood level oscillations, dose related adverse effects and cost and ultimately improve the patient compliance and drug efficiency.

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