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Formulation and Evaluation of Floating Tablet of Bambuterol Hydrochloride

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ABSTRACT

The objective of this present study is to formulate and evaluate the floating drug delivery system of Bambuterol HCl prepared by using synthetic polymers. Formulations were prepared by direct compression technique and sodium bicarbonate was incorporated as gas generating agent. Using different polymers of hydroxyl propyl methylcellulose (HPMC) such as, HPMC K100M, HPMC K4M and HPMC K100M for their gel-forming properties. The compressed Bambuterol HCl floating tablets were evaluated for physical parameters like Tablet Thickness, Hardness, % Friability, Weight variation, Content uniformity, In vitro buoyancy, Swelling index and In vitro dissolution study. Its bioavailability was reported about 20%. As the concentration of the polymers in the formulations increased the drug release decreased. Hence it was considered suitable candidate for formulation as gastro-retentive floating drug delivery system. Floating tablets has been accepted as a process to achieve controlled drug delivery by prolonging the residence time of the dosage form at the site of absorption, thereby improving and enhancing the bioavailability of drug.

Keywords: Bambuterol HCl, Floating drug delivery system, Hydroxyl propyl methylcellulose.

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INTRODUCTION

Gastro retentive dosage forms containing suitable drug candidates which would remain in the stomach and/or upper part of gastrointestinal tract for a prolonged period of time there by maximizing the drug release at desired site within the time before gastro retentive dosage forms left the stomach and upper part of the gastrointestinal tract, has provoked a great deal of increase interest in the formulation of such drugs as floating drug delivery system.[1]

Floating systems or hydro dynamically controlled systems are low-density systems that have sufficient buoyancy to float over the gastric contents and remain buoyant in the stomach without affecting the gastric emptying rate for a prolonged period of time. While the system is floating on the gastric contents, the drug is released slowly at the desired rate from the system. After release of drug, the residual system is emptied from the stomach. This results in an increased GRT and a better control of the fluctuations in plasma drug concentration. However, besides a minimal gastric content needed to allow the proper achievement of the buoyancy retention principle, a minimal level of floating force (F) is also required to keep the dosage form reliably buoyant on the surface of the meal. Many buoyant systems have been developed based on granules, powders, capsules, tablets, laminated films and hollow microspheres.[2]

Bambuterol HCl is a sympathomimetics, bronchodilator agent, adrenergic beta-agonists rapidly well absorbed from the gastrointestinal tract. Half life of Bambuterol HCl is 13 hours and is used in the treatment of asthma.[3]

MATERIALS AND METHODS

Materials

Bambuterol HCl, HPMC K4M, HPMC K100M, was purchased from Shubam pharma chem., Mumbai, India. All other ingredients were used from Elcon drug and formulation Ltd & those were the laboratory grade.

Method

Preparation Method of Bambuterol HCl Floating Tablets

Drug, polymer, sodium bicarbonate and microcrystalline cellulose were weighed and passed through an 80 mesh sieve (180 micrometer size). Then, except Aerosil all other ingredients were blended uniformly in glass mortar. After sufficient mixing of drug as well as other components, Aerosil was added, as post lubricant, and further mixed for additional 2-3 minutes. The blend was compressed in to tablets having average weight of 100 mg using a single punch tableting machine fitted with a 6mm round flat punches (Table 1).

Table 1. Formula for preparation of Bambuterol HCl floating tablets

Ingredients* (mg)	Batch No.					
	D01	**D02**	**D03**	**D04**	**D05**	**D06**
Bambuterol HCl	10	10	10	10	10	10
HPMC K4M	25	32	45	-	-	-
HPMC K100M	-	-	-	25	32	45
Sodium Bicarbonate	30	30	30	30	30	30
Aerosil	1	1	1	1	1	1
Talc	1	1	1	1	1	1
Micro crystalline cellulose	q.s.	q.s.	q.s.	q.s.	q.s.	q.s.
Total wt.	100	100	100	100	100	100

*All the ingredients are in mg. per tablet

EVALUATION OF FLOATING TABLET

Thickness

Thickness of tablets was determined using Vernier caliper. Three tablets from each batch were used, and average values were calculated.[4,5]

Weight variation

To study weight variation, 20 tablets of each formulation were weighed using an electronic balance, and the test was performed according to the official method.[4,5]

Hardness

The resistance of tablets to shipping or breakage, under conditions of storage, transportation and handling before usage depends on its hardness. The hardness of tablet of each formulation was measured by Monsanto hardness tester.[5]

Friability

Friability is the measure of tablet strength. Roche type friabilator was used for testing the friability using the following procedure. Twenty tablets were weighed accurately and placed in the tumbling apparatus that revolves at 25 rpm dropping the tablets through a distance of six inches with each revolution. After 4 min., the tablets were weighed and the percentage loss in tablet weight was determined.[6]

$$\%\ loss\ = \frac{Intial\ wt.of\ tablets - Final\ wt.of\ tablets}{Intial\ wt.of\ tablets} \times 100$$

Determination of Swelling Index

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 24 hrs. The swelling index (SI), expressed as a percentage, and was calculated from the following equation. The percentage weight gain by the tablet was calculated by the formula.[7,8]

$$Swelling\ \ index\ (S.I.) = \{\frac{Wt - Wo}{Wo}\} \times 100$$

Where, S.I. = Swelling index

Wt = Weight of tablet at time t

Wo = Weight of tablet before immersion

***In vitro* buoyancy studies**

The randomly selected tablets from each formulation were kept in a 100 ml 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).[7,9]

Drug content uniformity

10 tablets were weighed and triturated. The tablet triturate equivalent to 100 mg of the drug was weighed accurately, dissolved in pH 1.2 buffers and diluted to 100 ml with the same. Further dilutions were done suitably to get a concentration of 10 mcg/ml with simulated gastric fluid pH 1.2. Absorbance was read at 266 nm against the reagent blank, and the concentrations of Bambuterol HCl in mcg / ml was determined.[10,11]

***In-vitro* dissolution studies**

The *In-vitro* dissolution study was carried out in USP Dissolution Test Apparatus, Type 2 (paddle type). 900ml of simulated gastric fluid pH 1.2 was used as dissolution medium. The temperature of dissolution media was maintained at 37±0.5°C. The paddle rotation speed was kept at 50 rpm. One tablet at a time was weighed and taken for study. 5ml of the sample was withdrawn at every 1-hour interval for 12 hours and the same volume was replaced with pre warmed fresh dissolution media. The sample withdrawn was diluted to suitable volume with simulated gastric fluid and the absorbance was recorded at 266 nm using UV-VIS spectrophotometer.[11]

RESULTS AND DISCUSSION

Thickness

The thickness of floating tablets' were measured by Vernier caliper of formulation D01 to D06 and were range between 2.8±0.108 to 2.8±0.191 mm (Table 2).

Weight variation

All the formulation tablet D01 to D06 passed the weight variation test as the percent weight variation was within the pharmacopeia limit of 7.5% of average weight (Table 2).

Hardness

The hardness of the floating tablet was measured by the Monsanto tester of formulation D01 to

D06 and were controlled between 3.7 to 4.1 kg/cm^2. The standard hardness of the tablet is 4 kg/cm^2 (Table 2).

Friability

The friability of the floating tablet was measured by The Roche Friabilator of formulation D01 to D06 and were controlled between 0.35 to 0.63%. The standard friability of the tablet is below 0.8% according to IP and 1% according to USP (Table 2).

Table 2. Evaluation of floating tablets

Formulation	Thickness (mm)	Hardness Kg/cm^2	Average weight mg	Friability % loss	Drug content %
D01	2.8±0.129	3.8±0.14	100.1±0.118	0.63±0.37	90.1±0.10
D02	2.8±0.108	3.9±0.18	99.5±0.148	0.51±0.31	91.1±0.12
D03	2.8±0.191	4.0±0.18	101.7±0.274	0.48±0.56	92.1±0.19
D04	2.8±0.177	3.7±0.15	102.4±0.097	0.47±0.82	97.4±0.15
D05	2.8±0.172	4.0±0.13	101.4±0.093	0.46±0.35	96.5±0.22
D06	2.8±0.169	4.1±0.16	100.4±0.054	0.35±0.33	99.3±0.17

Drug content uniformity

The percent drug content of formulation D01 to D06 was found to be 90.1 to 99.3% of Bambuterol HCl in which was within the acceptable limit, the standard drug content uniformity 100±10% (Table 2).

***In-vitro* buoyancy studies**

On immersion of tablets of different formulations from D01 to D06 in 0.1N HCl solution at 37±5°C, the tablets floated, and remained buoyant without disintegration, the results of the buoyancy lag time (BLT) and total floating time (TFT) were shown in Table. Buoyancy lag time (BLT) and total floating time (TFT) of different formulation were noted. With reference to buoyancy studies results it can be concluded that as the amount of HPMC polymers increase, the formulation showed good buoyancy lag time (BLT) and total floating time (TFT). The formulation of D01 to D06 buoyancy lag time (sec.) between 10.34 to 13.72 sec. and total floating time (hrs) 13 to 24 hrs. or more (Table 3).

Table 3. Evaluation of floating tablets

Formulation	Buoyancy lag time (sec.)	Total floating time (hrs.)
D01	10.57	13
D02	12.53	14
D03	13.72	16
D04	10.36	18
D05	10.37	20
D06	10.34	24

Swelling index study

The Swelling Index for different formulations was shown in table. formulation D06 shows max swelling index comparing to other formulation. while formulation D01 shows less swelling index as concentration of HPMC K100M increases may be due to high viscosity and hydrophilic nature **(**Table 4).

Table 4. Swelling Index of floating tablets

Time (hrs)	Swelling Index %					
	D01	**D02**	**D03**	**D04**	**D05**	**D06**
1	34	41	77.2	59	81	97.03
2	43	54	101.9	65	94	134.29
3	51	65	114.8	75	117	149.9
4	58	73	116.8	81	125	163.7
5	67	81	145.5	92	138	175.47
6	77	84	156.4	101	145	186.25
7	80	88	158.4	112	151	197.03

***In-vitro* dissolution study**

In-vitro drug release studies exhibited a decrease drug release with an increase in polymer concentration which may be due to increase in viscosity of the gel as well as the gel layer with longer diffusion path. Formulations containing high viscosity grade HPMC showed slower drug release compared to formulations containing low viscosity polymers. There was no considerable effect of gas generating agents on the release of the drug.

Drug release profile of batches of Bambuterol HCl floating tablet D01-D06 was found 98.11%, 97.81%, 97.01%, 97.021%, 96.24%, 95.185% respectively after 12 hrs. D01 formulation of Bambuterol HCl floating tablet shows highest release of drug among the all batches (Table 5 & Figure 1).

Table 5. *In-vitro* dissolution floating tablet of Bambuterol HCl

Time (hrs.)	% CDR					
	D01	**D02**	**D03**	**D04**	**D05**	**D06**
1	19.82	16.82	13.82	14.879	13.37	12.24
2	39.19	32.19	29.19	35.656	32.12	30.893
3	54.66	47.66	46.66	48.77	46.13	39.22
4	70.82	63.12	57.12	65.578	57.732	47.32
6	78.92	72.92	69.92	74.639	68.63	60.03
8	81.1	77.1	78.12	78.56	79.578	70.591
10	89.61	87.21	86.81	85.87	84.13	82.843
12	98.11	97.81	97.01	97.021	96.24	95.185

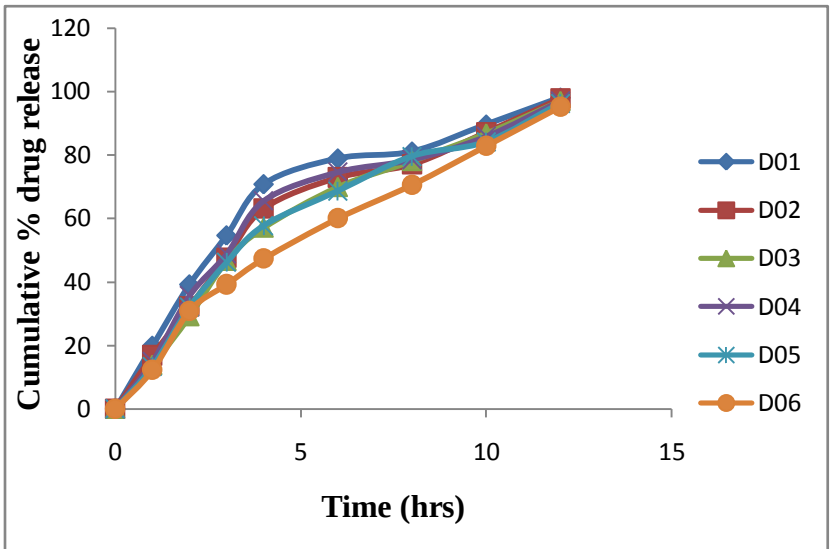

Figure 1: % cumulative drug release of Bambuterol HCl floating tablets

CONCLUSION

The objective of the study was to formulate and evaluate Bambuterol HCl floating tablets. The tablets were formulated using direct compression method using varying quantities of the excipients. The formulated tablets were tested for the parameters such as weight variation, hardness, thickness, friability and drug content and were found to be within the limits. The floating lag time and the floating duration of the tablets are the most important parameters. Hence, diffusion controlled Bambuterol HCl gastro retentive tablets were formulated and evaluated and formulation D01 was concluded as the best formulation for the manufacture of Bambuterol HCl gastro retentive tablets which can assure 100% bioavailability. Floating drug delivery tablets of Bambuterol HCl were developed to enhance gastric residence time and there by eradication of Helicobacter pylori infection. The optimized formula D01 showed better sustained drug release and which also had good floating properties.

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