

FORMULATION DEVELOPMENT AND EVALUATION OF MOUTH DISSOLVING TABLET OF BAMBUTEROL HYDROCHLORIDE

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ABSTRACT

The aim of the present study was to prepare mouth dissolving tablets of Bambuterol hydrochloride by using pertinent disintegrants. The tablets were prepared using mannitol and lactose along with two levels of disintegrant by direct compression method. The superdisintegrants used in this study were croscarmellose sodium (CCS) and sodium starch glycolate (SSG). The tablets were evaluated for uniformity of weight, thickness, hardness, friability, wetting time, water absorption ratio, disintegration time and dissolution study. Using the same excipients, the tablets were prepared, without disintegrants and were evaluated in the similar way. From the result obtained, it can be concluded that the tablet formulation (batch B4) showed disintegration time of 25 ± 2.0 seconds in vitro. The hardness, friability and dissolution rate of prepared tablet (batch B4) were found to be acceptable according to standard limits.

Keyword: Bambuterol hydrochloride, direct compression, superdisintegrants.

INTRODUCTION

Asthma is caused by inflammation in the airways. When an asthma attack occurs, the muscles surrounding the airways become tight and the lining of the air passages swells. This reduces the amount of air that can pass by. For the past one decade, there has been an enhanced demand for more patient-friendly and compliant dosage forms. Thus an attempt was made to improve onset of action by preparing bronchodilator used commonly in treatment of asthma.

Bambuterol hydrochloride (RS)-5-(2-tert-butylamino-1-hydroxyethyl)-m-phenylene bis (dimethylcarbamate) hydrochloride is a direct acting sympathomimetic with predominantly adrenergic activity (β_2 agonist). It is an ester pro-drug of β_2 adrenergic agonist terbutaline. In these research study, an attempt was made to develop mouth dissolving tablets of Bambuterol hydrochloride with enhance dissolution rate and improved patient compliance.¹⁻⁴

MATERIALS AND METHODS

Bambuterol HCl was procured from market, Croscarmellose sodium (CCS) used was analytical reagent (AR) grade procured from Loba Chemie, Mumbai and Sodium Starch Glycolate (SSG) used was procured from Merck Limited, Mumbai. All other reagents and chemicals used were of analytical grade.

Preparation of mouth dissolving tablets of Bambuterol HCl

All the materials were passed through 60 # screens prior to mixing. Bambuterol HCl, croscarmellose sodium (CCS), Sodium Starch Glycolate (SSG), and Mannitol were mixed using a glass mortar and pestle. All the materials were directly compressible so this uniformly mixed blend was compressed into tablets using concave face round tooling on a Rimek-rotary tablet machine⁵. The composition of the batches is shown in Table 1.

EVALUATION OF MOUTH DISSOLVING TABLETS

The formulations were evaluated for weight variation, thickness, content uniformity, drug content (assay) and in vitro dissolution studies.

Weight variation

Weight variation was done by selecting 20 tablets randomly and weighing individually. Average weight was calculated and the weight of individual tablet was compared with it⁶. All results are given in table 2.

Thickness

The thickness was measured using vernier caliper and expressed in mm. All results are given in table 2.

Friability

Friability test was performed using a Roche Friability testing apparatus. It is performed to access the effect of

friction and shocks which may often cause tablet to chip, cap or break. This device subjects a number of tablets to the combine effect of abrasion and shock by utilizing a plastic chamber that revolves at 25 rpm, dropping the tablets at the distance of 6 inches with each revolution. Pre-weighed tablet sample is placed in friabilator which is then operated for 100 revolutions. The tablets are then dusted and re-weighed. The % friability was measured using following formula⁶:

$$\% F = [(W - W_0) / W_0] * 100$$

Where, % F = Friability in percentage, W = initial weight of tablet, W₀ = Weight of tablets after test. All results are given in table 2.

Hardness

The strength of tablet is expressed as tensile strength (Kg/cm²). The tablet crushing load, which is the force required to break a tablet into halves by compression. It was measured using tablet hardness tester (Monsanto hardness tester)⁶. All results are given in table 2.

Water absorption ratio

A piece of tissue paper folded twice was placed in a small petridish (internal diameter =5.8 cm) containing 5.5 ml of water. A tablet was placed on the paper and the time required for complete wetting was then measured. The water absorption ratio (R) was determined using the following Equation⁶

$$\text{Water absorption ratio (R)} = [(W_a - W_b) / W_b] * 100$$

Where, W_b is the weight of tablet before water absorption and W_a is the weight of tablet after water absorption. All results are given in table 2.

Disintegration time

One tablet was placed in each of six tubes of disintegration test apparatus. The test was carried out at 37±2°C according to USP XXII. Disintegration test apparatus was used without disc. Time required for complete disintegration of tablet fragments through sieve (#10) was considered as a disintegration time of tablet⁶. All results are given in table 2.

In vitro Dissolution studies

The in vitro dissolution study was carried out in USP dissolution test apparatus Type II (Electrolab, India). The dissolution medium consisted of phosphate buffer (pH 6.8). An amount of 900 ml of dissolution fluid was used at 37±0.5°C with stirring speed of 50 rpm. Aliquot was withdrawn at interval of 2, 4, 6, 8, 10 minutes, at the time interval of 2 minute by replacing with same dissolution medium and samples were analyzed by measuring the absorbance at 265 nm by UV spectrophotometer⁶ (Shimadzu 1700). All results are given in table 2.

RESULT AND DISCUSSION

The use of superdisintegrants for preparation of mouth dissolving tablets is highly effective and commercially feasible. The results of tablets were evaluated for uniformity of weight, wetting time, water absorption ratio, disintegration time and dissolution as show in Table 2.

Using the same excipients, the tablets were prepared, without these superdisintegrants accelerate disintegration of tablets by virtue of their ability to absorb a large amount of water when exposed to an aqueous environment. The absorption of water results in breaking of tablets and therefore faster disintegration. This disintegration is reported to have an effect on dissolution characteristics as well. Prepared mouth dissolving tablet gets dispersed in the mouth quickly and releases the drug early as compared to its formulated conventional tablet. Figure 1 show the cumulative percentage of Bambuterol HCl released from formulated tablet with different concentration of CCS and SSG.

It is clear that the dissolution of Bambuterol HCl has improved considerably in formulation B4 as compared to formulation B1, B2, B3 and B5 .The table of batch B4 shows good dissolution efficiency and rapid dissolution. The study shows dissolution of Bambuterol HCl can be enhanced to great extend by direct compression technique with the addition of superdisintegrants, which give quick relief from asthma.

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Table 1: Formulation of Bambuterol HCl mouth dissolving tablet

Ingredients	B1	B2	B3	B4	B5
Bambuterol Hydrochloride	10	10	10	10	10
Lactose DCL11	70	60	80	80	100
Pearlitol SD200	130	130	130	130	180
Croscarmellose sodium	40	50	40	30	-
Sodium starch glycolate	40	40	30	40	-
Magnesium stearate	5	5	5	5	5
Talc	5	5	5	5	5
Total (mg)	300	300	300	300	300

Table 2: Evaluation of Bambuterol HCl mouth dissolving tablet

Batch	Weight variation	Thickness (mm)	Hardness n=10 (Kg/cm ²)	Friability (%)	Wetting time (sec.)	Water absorption ratio (%)	Disintegration time (sec.)
B1	299±3.09	4.2	3.2±0.12	0.32	32	78.45	30±2.5
B2	300±2.98	4.4	3.6±0.15	0.35	37	73.57	31±2.9
B3	301±1.45	4.3	3.7±0.21	0.29	31	80.12	33±2.1
B4	298±1.33	4.3	3.5±0.32	0.36	34	90.89	29±2.0
B5	299±2.06	4.2	3.0±0.27	0.27	61	61.99	58±2.1

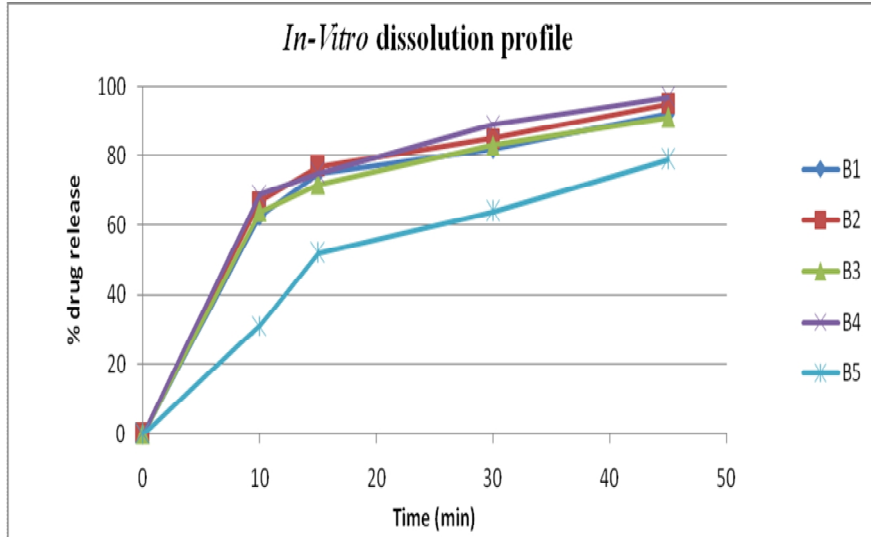


Fig 1: Drug release profile of Bambuterol HCl mouth dissolving tablets of various batch

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