Original Article

FORMULATION AND EVALUATION OF ORAL DISINTEGRATING TABLETS OF SALBUTAMOL SULPHATE

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Abstract

The purpose of the present research was to compare the effect of superdisintegrants on the mouth dissolving property of salbutamol sulphate tablets. Orodispersible tablets of salbutamol sulphate of prepared using sodium starch glycollate, crosscarmellose sodium as superdisintegrants. The results revealed that the tablets containing subliming agent had a good dissolution profile. The optimized formulation showed good release profile with maximum drug being released at all time intervals. This work helped us in understanding the effect of formulation processing variables especially the super disintegrants on the drug release profile. The present study demonstrated potentials for rapid absorption improved bioavailability effective therapy and patient compliance.

Keywords: Mouth dissolving tablet, salbutamol sulphate, Super disintegrant, β2 adrengic agonist.

Introduction

The tablet is the most widely used dosage form because of its convenience in terms of self- administration, compactness, and ease in manufacturing. However, geriatric and pediatric patients experience difficulty in swallowing conventional tablets, which leads to poor patient compliance. To overcome this weakness, scientists also have developed innovative drug delivery systems known as melt in mouth or mouth dissolve (MD) tablets. These are novel types of tablets that disintegrate/dissolve/disperse in saliva. Their characteristic advantages such as administration with out water, anywhere, anytime lead to their suitability to geriatric and pediatric patients. They are also suitable for the mentally ill, the bedridden, and patients who do not have easy access to water. The benefits, in terms of patient compliance, rapid onset of action, increased bioavailability, and good stability make these tablets poplar as a dosage form of choice in the current market[1-4] Salbutamol sulphate is a β_2 receptor agonist widely used as bronchodilator to relieve acute as well as chronic attacks of asthma[5]. Asthma is a complex genetic disorder involving the interplay between various environmental and genetic factors. Salbutamol sulphate was selected as drug candidate as it is not available in such a dosage form. Their growing importance was underlined recently when European Pharmacopoeia adopted the term "Oral Disintegrating Tablets" as a tablet that to be placed in the mouth where it disperses rapidly before swallowing. It is one of the fastest growing segments in the pharmaceutical market.

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Material and Methods

Materials

The materials used for preparing the orodispersible tablets were Crosscarmellose Sodium (CCS) and Sodium starch Glycollate (SSG) Micro crystalline cellulose powder (MCC) The model drug was Salbutamol sulphate. All other ingredients used were of analytical grade[6].

Methods

Preparation of mixed blend of drug and excipients
Blend of drug, SSG, CCS and MCC for direct compression

All the ingredients were passed through mesh no. 60. Required quantity of ingredients were weighed as given in table I and coground in mortar and pestle. The powder blend was evaluated for flow property and compressibility behavior.

Evaluation of Powder Blend and Granules
Angle of Repose[7]

Angle of Repose (θ) was measured by using funnel method. The blend was poured through funnel that can be raised vertically until a maximum cone height (h) was obtained. The radius of heap (r) was measured and angle of repose was calculated.

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

Bulk Density, Tapped Density, Hausner Ratio and Compressibility Index[8]

Weighed quantity of powder blend was taken in a graduated cylinder and the bulk volume (V_b) was measured, and weight of the blend (M) was determined. The measuring cylinder containing known mass of powder blend was tapped for a fixed time and the tapped volume (Vt) occupied in the cylinder and the weight of the blend (M) was measured. From that bulk density, tapped density, Hausner ratio and Compressibility index were calculated,

Bulk density (ρ_b) = M/V_b
Tapped density (ρ_t) = M/V_t
Hausner ratio = ρ_t / ρ_b
Compressibility index (I) = ρ_b-ρ_t/ρ_t x 100

Compression of Tablets
The composition of melt in mouth of Salbutamol Sulphate was shown in Table I Weighed quantities of Salbutamol Sulphate along with appropriate concentrations of superdisintegrants along with colloidal silicon dioxide, saccharin sodium were weighed and mixed in geometric progression in a dry and clean mortar. Then the blend was passed through sieve no 60 for direct compression.

The powder blend for direct compression and granules were then compressed into tablets using 8 mm convex faced punches in a 10 Station Rotary Tablet Machine (Cadmach, India). These Fabricated tablets were evaluated for weight variation, hardness, friability, wetting time, water adsorption ratio, drug content uniformity, *in vitro* dispersion time, *in vitro* disintegration time and *in-vitro* dissolution studies respectively.

Evaluation of Tablets
Weight variation Test[9]
Twenty tablets were selected at random, individually weighed and the average weight was calculated. The uniformity of weight was determined according to I.P. Specification. As per I.P. not more than two of individual weights would deviate from average weight by more than 5% and none deviates by more than twice that percentage.

Hardness Test[10]
Tablets require a certain amount of strength or hardness and resistance to Friability to with stand mechanical shocks. The hardness of tablet was measured by Monsanto hardness tester and results were expressed in Kg/cm^2

Friability Test[11]
The friability of the tablet was determined using Roche friabilator. It is expressed in percentage (%). Tables were initially weighed (W_0) and transferred in to the Friabilator. The Friabilator was operated at 25 rpm for 4 minutes in which tablets are subjected to combined effect of shock and abrasion in a plastic chamber dropping the tablets at a height of 6 inch in each revolution. The tablets were dedusted and weighed again (W). The % Friability was then calculated by

$$\% \text{ Friability} = \frac{W_0 - W}{W} \times 100$$

Drug-Excipients Interaction Study
There is always a possibility of drug-excipients interaction in any formulation due to their intimate contact. The technique employed in this study is IR spectroscopy. IR spectroscopy is one of the most powerful analytical techniques which offer the possibility of chemical identification.The I.R. spectroscopy of Salbutamol sulphate was obtained by KBr pellet method.

***In Vitro* Dispersion Time[9]**
In vitro dispersion time was measured by dropping a tablet in a measuring cylinder containing 6 ml of phosphate buffer pH 6.8 (simulated saliva fluid). The time for the tablet to completely disintegrate into fine particles was noted. Six tablets from each batch were randomly selected and ***in vitro*** dispersion time was performed.

***In Vitro* Disintegration Time[9, 12]**
The disintegration time of the tablets was determined as per Indian Pharmacopoeia monograph. The time required for disintegration of six tablets from each batch placed in each tube of disintegration test apparatus were measured at 37 $\pm$ 0.5°C using 900 ml of distilled water. The time required to obtain complete disintegration of all the six tablets was noted.

***In Vitro* Dissolution Studies[9, 12]**
In vitro drug release studies for the Melt-in- Mouth Tablets of Salbutamol sulphate was studied using dissolution test apparatus II USP XXVII model [Paddle type] for the fabricated batches with the rotation speed 50rpm using phosphate buffer pH 6.8 as the dissolution medium maintained at a temperature of 37 $\pm$ 0.5°C. Samples were withdrawn at predetermined time interval and filtered through Whatman filter paper, diluted suitably and analyzed at 285nm for cumulative drug release using Schimadzu UV-Visible spectrophotometer. The dissolution experiments were conducted in triplicate.

Results and Discussion
Formulations were prepared by direct compression techniques are shown in Table I. The data obtained for precompressional parameters such as bulk density, tapped density, Hausner's ratio, Carr's index and angle of repose are shown in Table II found within acceptable pharmacopoeia limits. While post-compressional parameters like hardness, friability, weight variation, drug content, wetting time, ratio, *in vitro* dispersion time, *in vitro* disintegration time are mentioned in Table III. The tablets measured hardness was found to be in the range of 3 to 3.5 kg/cm^2. The percentage friability was less than 1% for all formulation ensuring mechanical stability of the formulated tablets. All formulations then evaluated for variation in weight and results indicated that for all formulations exhibit very low weight variation which lies within the pharmacopoeia limits i.e. $\pm$ 7.5%. The percentage drug content in all the formulations were found in the range of 90 to 99.5 indicating the compliance with the pharmacopoeia limits. According to the pharmacopoeia standards the dispersible tablet must disintegrate within 3 min but all formulated batches have shown very low disintegration time indicating suitability of formulation for fast dissolving tablet. Also evaluated for wetting time, *in vitro* dispersion time and ratio and found to be faster for the formulation CP-12 compared to other formulations. Disintegration time of various formulations is mentioned in Fig. I. and drug excipient interaction indicated in Figure II & III. And found that there is no interaction between drug and excipients.

Table I
Composition of Oral Disintegrating Tablets of Salbutamol sulphate

Sl.No.	Ingredients	C.P-8%	C.P-10%	C.P-12%	S.S.G-8%	S.S.G-10%	S.S.G-12%	C.C.S-8%	C.C.S-10%	C.C.S-12%
1	Salbutamol sulphate(mg)	4	4	4	4	4	4	4	4	4
2	Crospovidone(%)	16	20	24	-	-	-	-	-	-
3	Sodium starch glycolate(%)	-	-	-	16	20	24	-	-	-
4	Croscarmellose sodium(%)	-	-	-	-	-	-	16	20	24
5	Mannitol(mg)	154	150	146	154	150	146	154	150	146
6	Aspartame(mg)	2	2	2	2	2	2	2	2	2
7	Avicel(mg)	20	20	20	20	20	20	20	20	20
8	Orange flavour (mg)	2	2	2	2	2	2	2	2	2
9	Magnesium stearate(mg)	2	2	2	2	2	2	2	2	2
	Total wt.(mg)	200	200	200	200	200	200	200	200	200

Table II
Physical Characteristics of Powder Blends/Granules

Parameters	CP-8%	CP-10%	CP-12%	SSG-8%	SSG-10%	SSG-12%	CCS-8%	CCS-10%	CCS-12%
Angle of repose(˚c)	25.3	23.6	21.7	28.4	26.3	24.7	26.6	25.2	24.8
Bulk density(g/ml)	0.467	0.458	0.441	0.497	0.487	0.476	0.507	0.492	0.483
Tapped density(g/ml)	0.667	0.654	0.642	0.682	0.654	0.675	0.703	0.684	0.681
Carr's index (%)	19.34	17.88	15.34	22.12	18.34	19.22	20.87	21.23	17.78
Haunsers ratio	1.428	1.427	1.455	1.372	1.342	1.418	1.386	1.39	1.409

Table III
Evaluation of Oral Disintegrating Tablets

Formulation No.	Wt. variation in mg	Hardness Kg/cm²	Thickness in mm.	Wetting time	Disintegration time in sec.	% friability	Drug content	% drug release in 5 min
CP-8%	199.95±0.13	3	2.85	60	21	0.88	95.4	91
CP-10%	200.1±0.98	3.2	2.71	57	17	0.72	97.4	94.5
CP-12%	200.05±0.89	3.1	2.81	50	13	0.61	99.5	99.5
SSG-8%	200.10±0.62	3.5	2.93	78	38	0.54	99.7	90
SSG-10%	200.15±1.08	3.1	2.78	70	35	0.46	96.8	92.5
SSG-12%	200.05±0.48	3.2	2.81	65	28	0.34	95.2	98
CCS-8%	200.15±0.98	3.5	2.95	66	29	0.44	98.4	91
CCS-10%	199.8±0.47	3.1	2.76	62	23	0.42	97.3	99
CCS-12%	200.3±0.65	3	2.75	58	20	0.38	98.4	96.5

*Note: C.P – Crospovidone, S.S.G - Sodium starch glycollate & CCS - Croscarmellose sodium.

Figure 1
In vitro Disintegration Time of various formulations

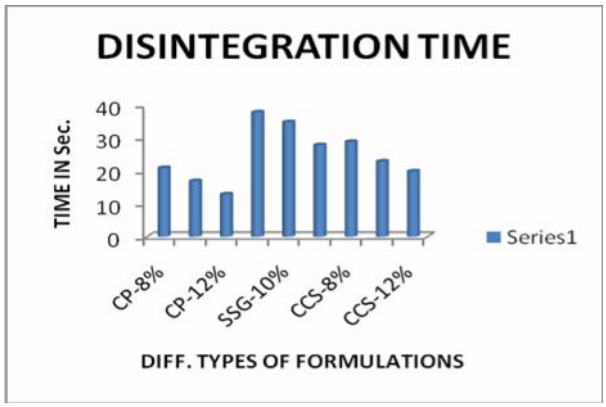


Figure-II
I.R. Studies of salbutamol sulphate

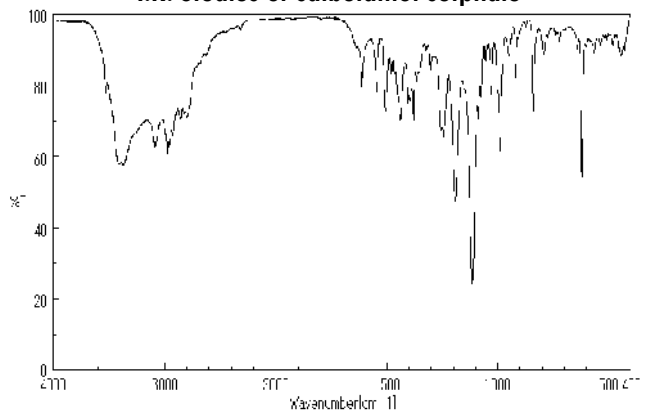
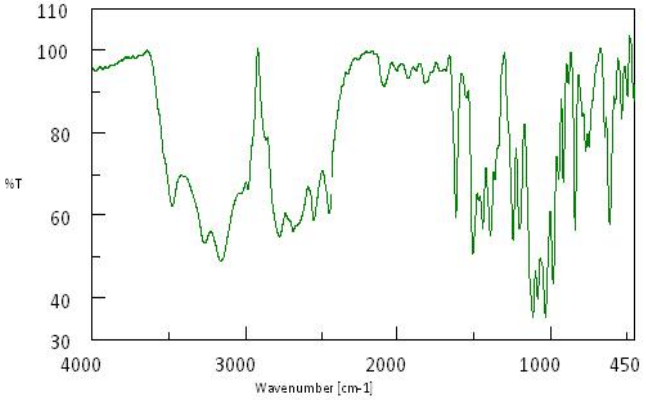


Figure-III
I.R. Studies of salbutamol sulphate along with excipients



Conclusion

Overall, the results suggest that suitably formulated mouth-dissolving tablets of salbutamol sulphate containing crospovidone 12% can be achieved. The tablets exhibited good in *vitro* dispersion, wetting properties and there is no interaction between drug and excipients. Prepared tablets disintegrate within few seconds without need of water; thereby enhance absorption leading to increased bioavailability. Thus the present study demonstrated potentials for rapid absorption, improved bioavailability, effective therapy and increased patient compliance.

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