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Formulation and evaluation of extended release tablets of salbutamol sulphate

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ABSTRACT

The objective of this study was to formulate and evaluate Salbutamol sulphate matrix tablets, extended release dosage form, for the treatment of Chronic Obstructive Pulmonary Disease (COPD). The ER tablets were prepared by direct compression method using two polymers such as hydroxyl propyl methyl cellulose (HPMC K100M) and xanthan gum in varying ratios. Powder blends were evaluated for loose bulk density, tapped bulk density, compressibility index and angle of repose, shows satisfactory results. The compressed tablets were then evaluated for various physical tests like diameter, thickness, uniformity of weight, hardness, friability, and drug content. The results of all these tests were found to be satisfactory. The in vitro dissolution study was carried out for 24 hours using type II dissolution apparatus. Among all the formulation, F7 shows 96.49% of drug release at the end of 12 hours. This finding reveals that above a particular concentration of HPMC K-100M and xanthan gum are capable of providing extended drug release.

Key Words: HPMC K-100, Xanthan gum, Salbutamol sulphate, matrix tablets

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INTRODUCTION

Salbutamol sulphate is a sympathomimetic agent acting on the β_2-adrenergic receptor shows site-specific absorption in the stomach and is used as a bronchodilator in the treatment of reversible bronchospasm.[1] It can be specifically prescribed in case of acute asthma and also for symptom relief during maintenance therapy of asthma and other conditions with reversible airways obstruction (including COPD).[2] The drug has plasma half-life range from 2 - 3 hr and the maximum plasma drug concentration occurs within 2.5 hr. It is given orally at a dose of 2-4 mg, three or four times a day.[3,4,5]

The conventional tablet or capsule provides only a single and a transient burst of drug. A pharmaceutical effect is seen as long as the amount of drug is within therapeutic range. So it is selected to prepare a extended release tablet of the drug.[6]

Extended release drug delivery system achieves a slow release of the drug over an extended period of time or the drug is absorbed over a longer period of time.[7] Extended release dosage form initially releases an adequate amount of drug to bring about the necessary blood concentration (loading dose, D_L) for the desired therapeutic response and therefore, further amount of drug is released at a controlled rate (maintenance dose, D_M) to maintain the said blood levels for some desirable period of time.[8] Extended release drug delivery system (ERDDS) have emerged as an effective mean of enhancing the bioavailability and controlled delivery of many drugs. ERDDS play an important role in reducing the dosing frequency as well as by enhancing the biological half life of specific certain drugs. In recent years, various efforts were made to reduce the dosing frequency of certain patent drugs by this approach.[9]

Present study concerns with the preparation and evaluation of Salbutamol sulphate matrix tablet for prolong drug release leading to minimization of incidences of nocturnal and early morning asthmatic attacks, better patient convenience and a pharmacoeconomic novel drug delivery system, for effective treatment for of COPD.[10]

MATERIALS AND METHODS

Material

The drug Salbutamol sulphate was obtained as a gift sample from Elegant Drugs Pvt. Ltd., Karnataka. Polymers HPMC K100M and Xanthan gum were purchaged from Leon Chem., Banglore, Evonic Degussa and Titan Biotech Ltd., Bhiwadi. All other chemicals and reagents used were obtained from commercial sources and were of analytical grade.

Formulation of Extended Release Tablet of Salbutamol Sulphate

Extended release tablets of Salbutamol sulphate (F1-F7) were prepared by developing the formulae using variable concentrations of different polymers viz. HPMC and Xanthan gum as shown in table 1. The concentration of Salbutamol sulphate was kept constant for all batches of formulations. Salbutamol sulphate and all excipients were weighed accurately except talc and magnesium sterate, after that blended in mortar with the help of pestle for 5-10 min. After the mixing of drug with excipient, required amount of talc and magnesium stearate were added and further mixing was done for 4-5 min. The gross weight of each formulations was kept 200 mg.

Table 1: Different Formulations of Extended Release Tablets of Salbutamol Sulphate

Ingredients (mg)	Formulation Code						
	F1	F2	F3	F4	F5	F6	F7
Salbutamol sulphate	8	8	8	8	8	8	8
HPMC K100M	60	80	100	-	-	-	40
Xanthan gum	-	-	-	60	80	100	60
Lactose	126	106	86	126	106	86	86
Magnesium stearate	2	2	2	2	2	2	2
Talc	4	4	4	4	4	4	4
Total weight	200	200	200	200	200	200	200

Compression of Extended Release Tablets of Salbutamol Sulphate

Extended release tablets of Salbutamol sulphate (F1-F7) were prepared by direct compression method. The powder blends of different batches (F1-F7) has illustrated in table 1 were compressed by using rotary tablet punching machine. The diameter of punches and die was 8 mm and the weight of tablets were kept constant i.e. 200 mg. The compressed tablets were of convex round shaped. 50 tablets of each batch were prepared initially. The prepared tablet were evaluated for different parameters of evaluation.[11]

RESULTS AND DISCUSSION

Evaluation of Tablets

All batches of prepared tablets were evaluated for various parameters like hardness, friability, thickness, weight variation, content uniformity, *in-vitro* dissolution studies.

Tablet Hardness

The crushing strength (Kg/cm^2) of prepared tablets was determined by using Monsanto hardness tester. The hardness tests was performed for each batches of prepared tablets in triplicate manner as shown in Table 2. The average hardness and standard deviation was determined. Tablet hardness indicates the pressure which is needed to break the tablet. Hardness of 4 kg is considered to be minimum for a satisfactory tablet.[11]

Friability

Friability test was done by Roche Friabilator. Twenty tablets were weight (W_o) and were subjected to combined effect of attrition and shock by utilizing a plastic chamber that revolve at 25 rpm dropping the tablets at a distance of 6 inch with each revolution, operated for 100 revolutions. The tablets were dusted and reweighed (W) after completion of 100 revolutions. The percentage friability (Table 2) was calculated using following formula.

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

Friability test is performed to evaluate the ability of the tablet to withstand wear and tear in packing, handling and transporting.[12]

Thickness

Ten tablets from each batch of formulations were selected randomly and thickness of tablets was measured using vernier caliper. The average value of thickness was calculated and illustrated in Table 2.[1]

Weight Variation

For uniformity of weight, twenty tablets from each batch of formulation were selected at random and determined their individual weights by using electronic balance. Then, average weight and standard deviation of the tablets was calculated and shown by Table 2.[12]

Uniformity of Drug Content

Assay of extended release tablets of Salbutamol sulphate was done in distilled water to find out the amount of drug present in one tablet. For this test, 5 tablets were weighed and powdered in a glass mortar and 200 mg of the powder equivalent to 8 mg of drug was placed in a stoppered 100 mL volumetric flask and dissolved in 100 mL water. The resulting solution was filtered and absorbance was measured at λ_{max} 277 nm using UV visible spectrophotometer. The concentration of Salbutamol sulphate in milligram per milliliter (Table 2) was obtained from standard calibration plot of drug.[11]

***In-vitro* Drug Release Studies**

In-vitro release of Salbutamol sulphate from extended release tablets were determined using USP type II dissolution apparatus in 900 mL of phosphate buffer (pH 6.8) at constant temperature of 37° ± 0.5°C at 50 rpm. Aliquots (5 mL) of the solutions were withdrawn from the dissolution apparatus at different time intervals and replaced with fresh dissolution medium to maintain the sink condition. These aliquots were filtered and the absorbance of these solutions were measured by using a double beam ultra-violet spectrophotometer at 277 nm against fresh phosphate buffer solution as blank. All the studies were conducted in triplicate and percent drug release was calculated by using the following formulae and the % drug release shown in Table 3.[13]

% Drug Release = K × Absorbance

Where K can be calculated by using the equation as follows

K = Std. conc. × vol. of dissolution media × dilution factor × 100 / std. abs. × dose × 1000

Table 2: Evaluation of Salbutamol sulphate extended release matrix tablet

Formulation Code	Hardness (Kg/cm^2)	Friability (%)	Weight Variation (mg)	Drug Content(%)	Thickness (nm)
F1	5.5±0.40	0.49±0.068	199.8±3.32	95.57 ± 0.560	4.15 ± 0.11
F2	5.8±0.35	0.46±0.016	200.8±2.25	99.67 ± 1.06	4.27 ± 0.10
F3	5.1±0.21	0.30±0.073	198.3±2.31	97.51 ± 0.66	4.26 ± 0.07
F4	5.7±0.25	0.45±0.065	199.3±2.31	98.02 ± 0.70	4.34 ± 0.05
F5	5.5±0.36	0.55±0.096	199.8±2.57	99.28 ± 1.998	4.23 ± 0.09
F6	5.7±0.32	0.64±0.060	200.3±2.71	97.76 ± 0.872	4.19 ± 0.01
F7	5.6±0.36	0.29±0.065	200.7±1.16	100.29±0.979	4.22±0.05

All values are mean ±SD of three determinations

Table 3: *In vitro* drug release study

Time(h)	F1	F2	F3	F4	F5	F6	F7
0	0	0	0	0	0	0	0
1	22.50 ±0.41	19.32 ±0.32	20.38 ±0.38	20.43±0.35	21.56±0.08	22.67±0.18	20.16±0.19
2	27.50 ±0.27	26.49 ±0.36	28.20±0.39	26.56±0.30	29.56±0.23	27.19±0.03	28.33±0.13
3	31.50 ±0.19	31.42 ±0.21	36.58±0.41	31.21±0.12	35.43±0.77	33.86±0.42	36.45±0.36
4	37.41 ±0.27	36.50 ±0.13	45.69±0.17	38.31±0.18	44.95±0.17	39.60±0.49	45.62±0.37
5	44.34 ±0.29	39.56 ±0.24	53.55±0.21	46.57±0.26	52.12±0.43	47.86±0.27	54.89±0.38
6	49.49 ±0.15	44.24 ±0.13	59.38±0.19	53.86±0.11	59±.0.13	56.78±0.17	61.30±0.36
7	53.56 ±0.17	51.45 ±0.35	65.60±0.33	58.48±0.28	63.76±0.44	62.41±0.20	66.31±0.23
8	57.65 ±0.29	59.50 ±0.36	71.42±0.31	65.77±0.11	68.27±0.34	69.17±0.08	72.79±0.32
9	64.42 ±0.13	65.72 ±0.22	78.31±0.16	71.68±0.21	72.54±0.10	76.33±0.17	79.31±0.29
10	70.43 ±0.34	71.34 ±0.09	81.34±0.32	79.54±0.30	78.45±0.20	81.01±0.39	85.66±0.08
11	76.25 ±0.04	77.29 ±0.09	85.29±0.32	85.43±0.17	89.14±0.30	76.50±0.11	91.31±0.59
12	83.47 ±0.16	81.29±0.15	80.29±0.33	86.38±0.22	92.49±0.33	74.28±0.26	96.49±0.27
16	79.32 ±0.09	78.48±0.36	76.48±0.33	81.61±0.40	87.89±0.26	71.55±0.35	91.39±0.06
20	74.46 ±0.30	73.94±0.24	71.52±0.17	77.36±0.28	81.45±0.31	68.30±0.10	86.47±0.19
24	69.48 ±0.34	68.55±0.33	67.67±0.20	72.62±0.39	76.56±0.30	64.87±0.29	81.55±0.09

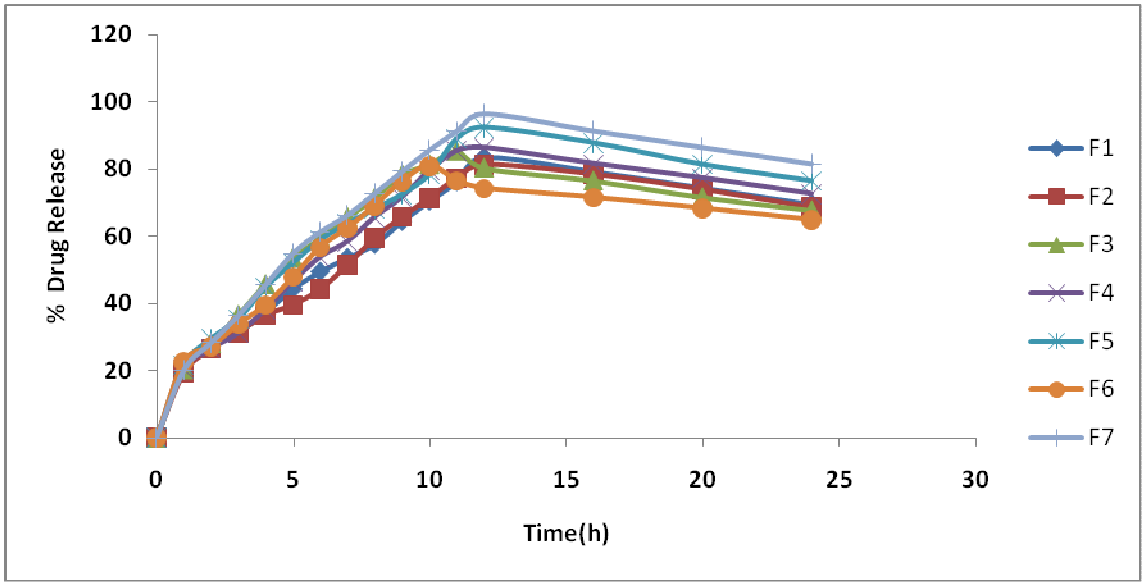

Fig. 1: Dissolution profile of various formulations (F1-F7) of salbutamol sulphate

DISCUSSION

The present investigation was undertaken to formulate and evaluate Salbutamol sulphate matrix tablet for extended release dosage form. All tablet formulations were subjected to various evaluation parameters and the results obtained were within the range. The weight variation test indicates that all the tablets were uniform with low standard deviation values. The tablet mean thickness values ranged from 4.15 ± 0.11 to 4.34 ± 0.05 mm. The hardness of all the tablets was within a range of 5.1±0.21 to 5.8±0.35 kg/cm^2. The loss in total weight in friability test was in a range of 0.29±0.065 to 0.64±0.060 %. The percentage drug content for different tablet formulations varied from 95.57 ± 0.560 to 100.29±0.979 % was found to be within the limit. The % age release of different formulations varied from 81.01±0.39 to 96.49±0.27 %. F-7 containing HPMC K100M and Xanthan gum (2:3 ratio) was selected as the optimum formulation on the basis of the results of in-vitro dissolution studies. It is seen that at the end of 12 hr, 96.49±0.27 % drug was released from the formulation.

CONCLUSION

From the above results, it can be concluded that formulation F-7 has achieved the objectives of prolonged drug release and thus improve the patient convenience by reducing dosing frequency. It was promised a ERT of Salbutamol sulphate and appears to be assessed further by conducting bioavailability studies in human volunteers and long term stability testing

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