Research Article

Formulation, Development and Evaluation of Fast Dissolving Tablet of Salbutamol Sulphate by Using Superdisintegrants of Various Concentrations

Santosh K[1]*, Meenakshi B[2] and Jyoti M[1]

[1]Geetanjali Institute of Pharmacy, Dabok, Udaipur, Rajasthan, India.
[2]B. N. College of Pharmacy, Udaipur, Rajasthan, India.

ABSTRACT

Fast dissolving tablets are highly accepted fast growing drug delivery system. This study was aimed at formulation and development of salbutamol sulphate fast dissolving tablet which can dissolve rapidly in the oral cavity. Asthma is a common chronic inflammatory disease of the airways characterized by variable and recurring symptoms, reversible airflow obstruction, and bronchospasm. Common symptoms include wheezing, coughing, chest tightness, and shortness of breath. Fast dissolving tablets (FDTs) are prepared by several different methods including crystalline transition, phase transition, sublimation, spray drying, and direct compression. Of these approaches, a conventional tablet compression method is used most widely because of its low cost and ease of manufacturing. Fast dissolving Tablets are disintegrating and/or dissolve rapidly in the saliva without the need for water. In the present study, an attempt has been made to prepare fast dissolving tablets of the drug Salbutamol sulphate using superdisintegrants such as Croscarmellose sodium (Ac-Di-Sol), Sodium starch glycolate (Explotab) and Crospovidone(polyplasdone XL) by direct compression technique. The prepared tablets were evaluated for hardness, friability, wetting time, weight variation, *in vitro* disintegration time and *in vitro* dissolution study. In the present study fast dissolving tablets of salbutamol Sulphate was formulated and evaluated. The formulation Polyplasdone XL Showed the maximum dissolution rate of 99.84% drug release in 10 min. Acdisol containing Tablets released more than 94.33 % of the drug in 10 min and Explotab formulations released more than 93.65% of the drug in 10 min. This shows that the effectiveness of super disintegrants was in the order of polyplasdone XL > Acdisol > Explotab. From the overall observations, formulation F9 containing 6% w/w Polyplasdone XL was considered to be the best formulation, which releases up to 99.84% of the drug in 10 min.

Keywords: fast dissolving tablets, salbutamol sulphate, Superdisintegrants, direct compression.

INTRODUCTION

Difficulty in swallowing (Dysphasia) is common among all age groups, especially in elderly, and is also seen in swallowing of conventional tablets and capsules. Geriatric and paediatric patients and travelling patients who may not have ready access to water are most in need of easy swallowing dosage forms. Many patients express difficulty in swallowing tablets and hard gelatin capsules, resulting in noncompliance and ineffective therapy[1]. Recent advances in novel drug delivery systems (NDDS) aim to enhance safety and efficacy of drug molecules by formulating a convenient dosage form for administration and to achieve better patient compliance. One such approach led to development of fast dissolving tablets[2,3,4].

PREPARATION OF FAST DISSOLVING TABLETS

Tablet each containing 4 mg Salbutamol were prepared as per composition given in Table5. The drug and excipients were passed through sieve (#60) to ensure the better mixing. Avicel P^H 102 was used as a direct compressible vehicle. Super disintigrants like Explotab, polyplasdone XL , Acdisol were used in different ratios. Finally talc and magnesium stearate were added and mixed for 5 minutes. The powder was compressed using Rimek compression machine equipped with 6 mm round punch by direct compression technique. A minimum of 50 tablets was prepared for each batch.

EVALUATION PARAMETERS OF THE BLEND OF SALBUTAMOL TABLETS.[5,6]

Blend was characterized with respect to Bulk density, Tapped density, Compressibility index, angle of repose and Hausner ratio.

ANGLE OF REPOSE

Angle of repose (as shown in table 1) was determined using funnel method. The blend was poured through funnel that can be raised vertically until a maximum cone height (h) was obtained. Radius of the heap (r) was measured and angle of repose was calculated using the formula

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

Where, θ is the angle of repose, h is height of pile; r is radius of the base of pile.

BULK DENSITY

Apparent bulk density (ρb) was determined by pouring the blend into a graduated cylinder. The bulk volume (Vb) and weight of powder (M) was determined. The bulk density was calculated using the formula

$$\rho b = M/Vt$$

TAPPED DENSITY

The measuring cylinder containing known mass of blend was tapped for a fixed time. The minimum volume (Vt) occupied in the cylinder and weight (M) of the blend was measured. The tapped density (ρb) was calculated using the following formula

$$\rho t = M/Vt$$

CARR'S COMPRESSIBILITY INDEX

The simplest way of measurement of free flow of powder is compressibility, an indication of the ease with which a material can be induced to flow is given by compressibility. The compressibility index of the granules was determined by Carr's compressibility index (I), which is calculated by using the following formula.

$$I = V0 - Vt \times 100/Vo$$

Limits of Compressibility Index and Hausner ratio are given in table2

HAUSNER RATIO

Hausner ratio5 is an indirect index of ease of powder flow. It is calculated by the following formula

$$\text{Hausner ratio} = \rho t/\rho d$$

Where ρt is tapped density and ρd is bulk density.

COMPRESSION PARAMETERS

Compression was performed on the single rotary compression machine. Hardness of the tablet would be set as much as capable to withstand the transportation after packaging. (As shown in table3)

EVALUATION OF TABLETS

AVERAGE WEIGHT

I.P. procedure for uniformity of weight was followed, twenty tablets were taken and their weight was determined individually and collectively on a digital weighing balance. The average weight of one tablet was determined from the collective. Not more than 2 tablets deviate from the percentage given below from the average weight.[7] (table 4)

The weight variation of the tablets was carried out by taking the average weight of 10 tablets. The acceptable weight variation is ±5%

THICKNESS

The thickness of the tablet was measured by using digital vernier scale. Thickness was expressed in mm.

HARDNESS (TABLET BREAKING FORCE)

Tablets must be able to withstand the rigors of handling and transportation experienced in the manufacturing plant, in the drug distribution system, and in the field at the hands of the end users. Manufacturing processes such as coating packaging and printing can involve considerable stresses,

which the tablet must be withstand. For these reasons, the mechanical strength of tablets is of considerable importance and is routinely measured.
Early measuring devices were typically hand operated. For example, the Monsanto hardness tester was based on compressing tablets between two jaws via a spring gauge and screw. In the Pfizer hardness tester, the breaking load was applied through the action of a small hydraulic pump that was first operated manually but was later motorized. Modern testers employ mechanical drivers, strain gauge-based load cells for force measurements, and electronic signal processing, and therefore are preffered. Hardness of the tablet was measured by using Schleuniger Pharmatron hardness tester. Hardness was expressed in N.

DISINTEGRATION TEST
The test was carried out on 6 tablets using the apparatus specified in I.P.-2007 distilled water at 37˚c ± 2˚c was used as a disintegration media and the time taken for complete disintegration of tablet with no palable mass remaining in the apparatus was measured.

FRIABILITY
For tablets with a unit weight equal to or less than 650 mg, take a sample of whole tablets a sample of corresponding as near as possible to 6.5 gm. For tablets with a unit weight of more than 650 mg, take 10 whole tablets. The tablets should be carefully dedusted prior to testing. Accurately weigh the tablet sample, and place the tablets in the drum. Rotate the drum 100 times, and remove the tablets. Remove any loose dust from the tablets as before, and accurately weigh.
If obviously cracked, cleaved, or broken tablets are present in the tablet sample after tumbling, the sample fails the test. If tablet size or shape causes irregular tumbling, adjust the drum base so that the base forms an angle of about 10˚ with the horizontal and the tablets no longer bind together when lying next to each other, which prevents them from falling freely.[8]

WETTING TIME AND WATER ABSORPTION RATIO[9]
A piece of tissue paper folded twice was placed in a small petridish (i.d. = 6.5 cm) containing 6 ml of distilled water, a tablet was put on the paper, and the time required for complete wetting was measured. The wetted tablet was then weighed. Water absorption ratio, R, was determined using equation –

$$R = 10 \times Wa - Wb/Wb$$

Where, Wb = weight of the tablet before water absorption, Wa = weight of the tablet after water absorption.

IN VITRO DISSOLUTION PROFILE
Determine percent dissolution using U.V. spectrophotometer.
Dissolution parameters of Salbutamol tablets
Media: Phosphate buffer pH 6.8
Apparatus: USP type- II, Paddle
Speed: 75rpm
Volume: 900 ml
Temperature: 37.0˚c ± 0.5˚

MEDIA PREPARATION
27.2gm of potassium dihydrogen phosphate and 8 gm of sodium hydroxide dissolve in 1000ml of distilled water. Adjust pH 6.8 with NaOH.

SAMPLE PREPARATION
In vitro release of Salbutamol Sulphate from tablets was monitored by placing 1 tablet in each dissolution vessel containing 900 ml of phosphate buffer solution pH 6.8 as dissolution medium maintained at 37.0˚c ± 0.5˚ c and run the instrument at 75 rpm. Aliquots were withdrawn at specified regular intervals and were replenished immediately with the same volume of fresh buffer medium. Aliquots, following suitable dilutions, were assayed spectrophotometrically at 276nm.[10]

RESULT AND DISCUSSION
In the present study fast dissolving tablets of salbutamol Sulphate was formulated and evaluated.Bulk densities of various formulations varied 0.445 to 0.449 g/cm^3. The angle of repose and the compressibility values varied from 22° to 24° and 8 to10%, respectively. From these values, it was

evident that these blends had excellent flow properties. Weight variation was found within the specification of the USP limits.. Hardness, thickness and friability of all the tablet formulations were observed in the range of 2.74 to 3.22 kg/cm2 ,2.11 to 2.74 mm and 96.85 to 98.53%, respectively. Wetting time and water absorption ratio was found in the range of 7.11 to 10.94 s and 65.32 to75.92 %, respectively. Drug content of all the formulations was found in the range of 98.89 to 99.32%. The *in vitro* disintegration time was rapid with polyplasdone XL containing batches (8-10 s) and delayed with Explotab containing Batches (20-26 s). The rapid disintegration may be due to the rapid uptake of water from the medium, swelling and bursting effect. (Table 6) *In vitro* dissolution studies of various formulations at different time intervals are reported in (Table 7). The formulation Polyplasdone XL Showed the maximum dissolution rate of 99.84% drug release in 10 min. Acdisol containing Tablets released more than94.33 % of the drug in 10 min and Explotab formulations released more than 93.65% of the drug in 10 min. This shows that the effectiveness of super disintegrants was in the order of polyplasdone XL > Acdisol > Explotab (as shown in table7). From the overall observations, formulation F9 containing 6% w/w Polyplasdone XL was considered to be the best formulation, which releases up to 99.84% of the drug in 10 min.

CONCLUSION

Thus it can be concluded that the fast dissolving tablet of Salbutamol Sulphate with 6% w/w polyplasdone XL as the super disintegrants an alternative to and better than the conventional tablet dosage forms, and the rapid dissolving concept in case of Salbutamol sulphate could be of a great importance in relieving acute asthmatic attack.

Table 1: Angle of Repose

FLOW PROPERTY	ANGLE OF REPOSE (DEGREES)
Excellent	<25˚
Good	25˚–30˚
Fair / Passable	30˚–40˚
Poor	>40˚

Table 2: Compressibility Index and Hausner ratio

COMPRESSIBILITY INDEX (%)	FLOW CHARACTERS	HAUSNER'S RATIO
≤10	Excellent	1.00–1.11
11-15	Good	1.12–1.18
16-20	Fair	1.19–1.25
21-25	Passable	1.26–1.34
26-31	Poor	1.35–1.45
32-37	Very poor	1.46–1.59
≥38	Very-very poor	>1.60

Table 3: Compression process parameters

PUNCH DESCRIPTION	6MM round punch plain on both sides
Weight of tablet	100.0 mg
Hardness	2.3kg/cm^2
Thickness	3.21mm
Number of punches used	Single punch

Table 4: Max. Percentage allow for average weight

S. No.	AVERAGE WEIGHT OF THE TABLETS (MG)	MAXIMUM PERCENTAGE DIFFERENT ALLOWED
1	80 or less	10
2	>80 to 250	7.5
3	>250	5

Table 5: Formulation of Fast dissolving tablets of salbutamol sulphate

Ingredients	F1	F2	F3	F4	F5	F6	F7	F8	F9
Salbutamol sulphate	4	4	4	4	4	4	4	4	4
Explotab (sodiumstarch glycolate)	2	4	6						
Acdisol (crosscarmellose sodium)				2	4	6			
polyplasdoneXL (crosspovidone)							2	4	6
Avicel p^{H}102 (microcrystalline cellulose)	36	34	32	36	34	32	36	34	36
Mannitol	55	55	55	55	55	55	55	55	55
Magnesium stearate	0.4	0.4	0.4	0.4	0.4	0.4	0.4	0.4	0.4
Talc	2	2	2	2	2	2	2	2	2
Aspartame	0.6	0.6	0.6	0.6	0.6	0.6	0.6	0.6	0.6
Total weight	100	100	100	100	100	100	100	100	100

Table 6: Evaluation of the Fast dissolving tablet of salbutamol sulphate

Formulation parameters	F1	F2	F3	F4	F5	F6	F7	F8	F9
Bulk density (g/cm3)	0.448	0.449	0.445	0.446	0.449	0.447	0.448	0.444	0.446
Tapped density	0.512	0.513	0.509	0.510	0.518	0.508	0.515	0.519	0.507
Angle of repose (˚)	24.09	24.12	23.91	22.54	24.11	24.01	23.67	22.95	23.23
Compressibility index (%)	9.64	8.92	10.01	8.45	9.22	8.94	9.21	9.44	10.32
Thickness (mm)	2.56	2.34	2.45	2.65	2.44	2.74	2.11	2.31	2.42
Hardness (kg/cm3)	2.95	2.92	2.99	3.01	3.12	3.22	2.89	2.74	2.84
Friability (%)	98.0	97.9	98.53	96.85	98.12	98.32	98.44	97.91	97.03
Drug content (%)	99.01	99.32	99.12	99.05	99.21	99.10	99.30	99.05	98.89
Wetting time(s)	7.11	7.24	7.54	9.22	9.53	9.21	10.94	10.56	10.85
Water absorption ratio (%)	65.32	68.63	67.44	68.34	69.54	70.33	75.92	75.22	74.54
Disintegration time (s)	20	25	26	13	15	18	08	11	10

Table 7: In vitro dissolution profile of formulation F1-F9

Time(min.)	F1	F2	F3	F4	F5	F6	F7	F8	F9
0	0	0	0	0	0	0	0	0	0
2	75.43	76.24	77.15	76.98	78.21	77.94	76.23	79.54	80.54
4	80.22	82.65	84.44	80.65	82.40	80.55	82.22	80.64	84.62
6	84.43	86.34	88.54	84.22	86.52	85.42	86.32	84.45	90.34
8	90.64	90.26	90.67	92.36	92.58	88.65	95.02	96.41	96.62
10	92.11	92.94	93.65	94.33	96.65	95.34	97.56	98.20	99.84

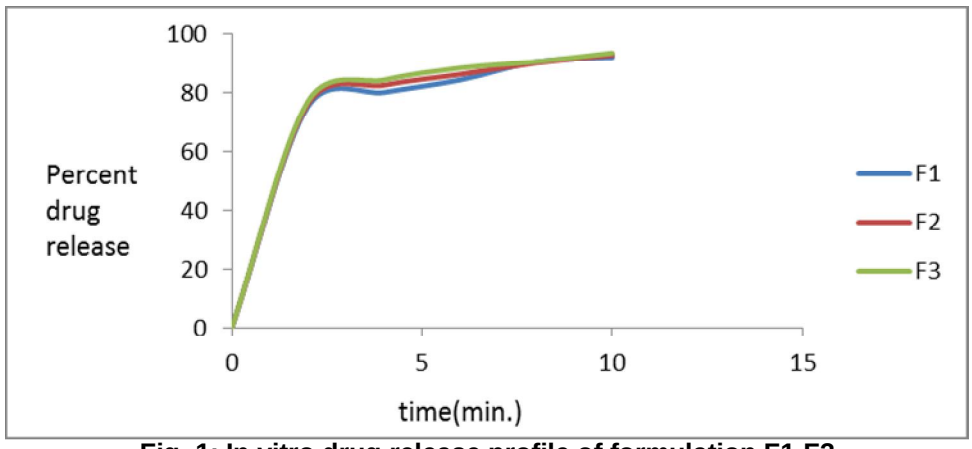

Fig. 1: In vitro drug release profile of formulation F1-F3

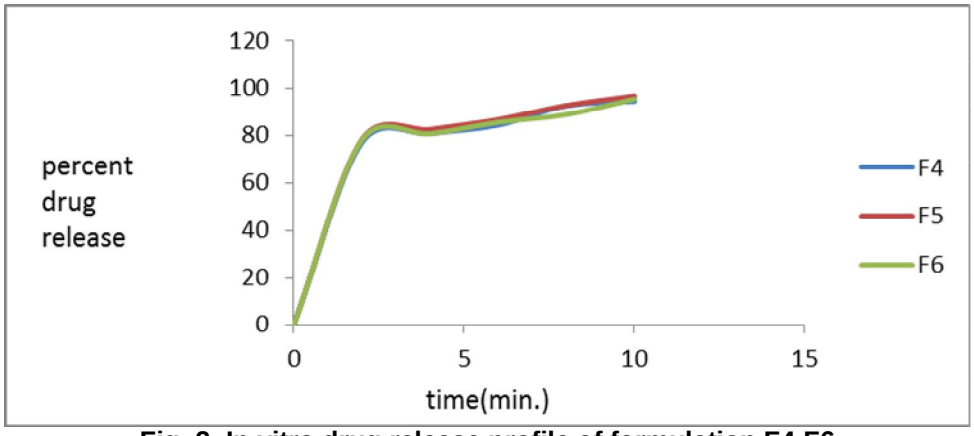

Fig. 2: In vitro drug release profile of formulation F4-F6

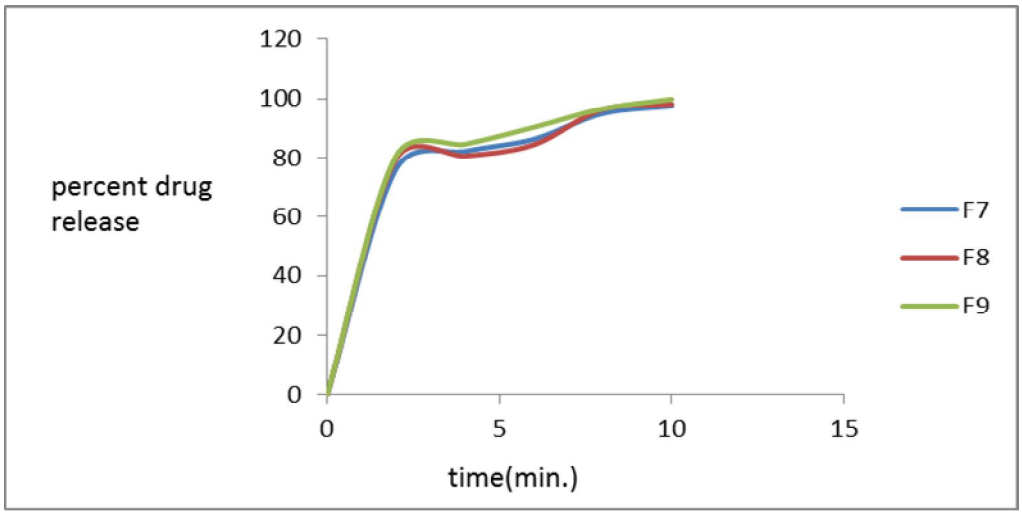

Fig. 3: In vitro drug release profile of formulation F7-F9

REFERENCES

1. Seager H. Drug delivery products and zydis fast dissolving dosage form. J Pharm Pharmacol. 1990;50:375-382.
2. Chang RK, Guo X, Burnside BA and Cough RA. Fast dissolving tablets. PharmTech. 2000;24:52-58.
3. Dobetti L. Fast-melting tablets: Developments and technologies. PharmaTech Suppl. 2001:44-50.
4. Kuchekar BS and Arumugam V. Fast dissolving tablets. Indian J Pharm Educ. 2000;35:150-152.
5. United States of Pharmacopoeia, Rockville.MD, 27th, USP Convention,Inc. 2004:2228-2229.
6. Marshall K, In;Lachman N and Liberman HA. The Theory and Practice of Industrial Pharmacy. 3rd ed. Varghese Publishing House, Mumbai. 1987:66-69.
7. Indian pharmacopeia published by the Indian pharmacopeia commission, Ghaziabad.1996;2:736.
8. United States of Pharmacopoeia, Rockville.MD, 27th, USP Convention, Inc. 2004:2125.
9. Bi Y, Sunada H, Yonezawa Y, Danjo K, Otsuka A and Lida K. Preparation and Evaluation of a Compressed Tablet Rapidly Disintegrating in Oral Cavity. Chem Pharm Bull. 1996;44:2121-2127.
10. United State Pharmacopoeia Convention. NF Asian edition. 2004:74-75.