

IMMEDIATE RELEASE SOLID ORAL DOSAGE FORM OF SALBUTAMOL SULPHATE: DESIGN, OPTIMIZATION AND EVALUATION

MD SARFARAZ^{1,2} AND V.G.JOSHI^{1,3}

¹Jawaharlal Nehru Technological University, Hyderabad, Kukatpally, Hyderabad- 500085, A.P, ²N.E.T Pharmacy College, mantralayam road, Raichur- 584103. Karnataka, ³Government College of Pharmacy, Subbaiah circle, Bengaluru-560027, Karnataka. India.
Email: sarfindia@gmail.com

Received: 07 Aug 2013, Revised and Accepted: 08 Sep 2013

ABSTRACT

Objective: In the present investigation an attempt was made to develop immediate release solid dosage form of salbutamol sulphate. Salbutamol sulphate a selective β_2 receptor agonist is widely used in initial therapy for chronic as well as acute asthma, an inflammatory disorder characterized by obstruction of air pathways and difficulty in breathing. The currently available conventional oral dosage forms are associated with lag time and delayed onset of action while aerosols and parenterals in spite of rapid onset of action strongly affect the patient compliance. Immediate release tablets are highly accepted fast growing drug delivery systems and thus, an attempt was made to improve the onset of action of drug.

Methods: To achieve this goal, selective superdisintegrants croscarmellose sodium, crospovidone and sodium starch glycolate in different concentrations (2.5 – 7.5%w/w), were evaluated for their effect on the disintegration behavior of tablets, while microcrystalline cellulose and lactose were used as diluents. The tablets were prepared by direct compression method and were evaluated for various physicochemical properties, FTIR, in vitro disintegration and in vitro drug release studies.

Results: Out of nine formulations prepared tablet F3 containing 7.5% w/w of Croscarmellose sodium disintegrated in 89 ± 2.08 seconds and released 99.26% and 99.75% of drug in 12 minutes in pH 6.8 and pH 7.4 phosphate buffer respectively and thereby selected as best formula. FTIR studies revealed no chemical interaction between the drug and excipients used.

Conclusion: The tablets gave fast release of salbutamol sulfate which produces fast action in asthmatic attacks and may serve as a successful strategy for enhancing the bioavailability of drug.

Keywords: Superdisintegrants, Immediate release tablets, Salbutamol sulphate, Direct compression.

INTRODUCTION

In the present scenario, a variety of pharmaceutical research has been come in to focus to develop new dosage forms for effective therapy with increased safety. Considering value of life, most of these endeavors have been focused on patient compliance [1]. Tablet manufacturing by direct compression has increased steadily over the years. It offers advantages over the other manufacturing processes for tablets, such as wet granulation and provides high efficiency [2]. As direct compression is more economic, reducing the cycle time and straight forward in terms of good manufacturing practice requirements. On the other hand wet granulation not only increases the cycle time, but also has certain limits imposed by thermolability and moisture sensitivity of the active ingredients. So pharmaceutical industry is now focusing increasingly on this process [3, 4]. The unnecessary exposure of any drug to moisture and heat can never be justified [5]. Tablets produced by direct compression method give lower microbial levels than those prepared by the wet granulation method. The compaction process exerts lethal effect on the survival of microorganisms [6]. The tablets prepared by direct compression disintegrate into API particles instead of granules that directly come into contact with the dissolution fluid and exhibit a comparatively faster dissolution [7]. Bioavailability of a poorly soluble drug from a solid oral dosage form depends on the release of the drug substance from the dosage form, i.e., disintegration of the solid oral dosage form which will increase the wettability of the drug by increasing the surface area of the drug particles [8]. Immediate release tablets are one of the tablets prepared by direct compression method. Immediate release tablets have received ever increasing demand during the last decade and the field has become a rapidly growing area in the pharmaceutical industry because of such tablets readily dissolve or disintegrate in generally less than 60 seconds. As disintegration plays a crucial role, so for development of solid orals, formulators are fascinating towards selection of proper disintegrants / superdisintegrants in dosage systems. Disintegrants are substances or mixture of substances added to the drug formulations, which assist dispersion or breakup of tablets and contents of capsules into smaller particles

for dissolution. Superdisintegrants are those substances, which improves disintegration compared to disintegrants [9].

Asthma is a common respiratory disease among both adults and children whose prevalence is increasing worldwide; affecting 15-20 million Indians. It is characterized by airway narrowing, airway dysfunction, inflammation and symptoms such as dyspnea, wheeze, chest tightness, and cough. If not treated in time Asthma leads to significant degrees of morbidity and mortality. Salbutamol sulphate is β_2 receptor agonist widely used as bronchodilator to relieve acute as well as chronic attacks of asthma. Salbutamol sulphate dilates or enlarges the airways by relaxing the muscles surrounding the airways and thereby opens airways [10]. The aim of this study was to develop an immediate release solid dosage form of salbutamol sulphate by simple and cost effective direct compression technique using superdisintegrants.

MATERIALS AND METHODS

Materials

Salbutamol sulphate was a gift sample from S.M. Pharmaceuticals, Bengaluru. Croscarmellose sodium, crospovidone and sodium starch glycolate were gifted from Gland Pharma Ltd., Mumbai. Magnesium stearate, microcrystalline cellulose and Aerosil were procured from S. D. Fine chemicals Pvt. Ltd, Mumbai. All other reagents used were of analytical grade.

Methods

Drug-excipients compatibility study

In order to establish any possible incompatibility between drug and superdisintegrants used FTIR spectrum of pure drug and its physical mixtures were recorded in the stretching frequency range of 400 – 4000 cm^{-1} . Samples were prepared by KBr press pellet technique.

Evaluation of mixed powder blends of drug and excipients

The mixed powder blend of drug and excipients was evaluated by angle of repose, bulk density, tapped density and Carr's index. Each analysis was carried out in triplicate.

Angle of repose: The flow characteristics of the powder blend were measured by angle of repose. It is determined by using funnel method. Powder was poured from a funnel that can be raised vertically until a maximum cone height 'h' was obtained. Radius 'r' of heap is obtained by measuring the diameter of heap of powder formed. The repose angle was calculated by using the formula; $\tan \theta = h/r$.

Bulk density: is defined mathematically as

Bulk density = mass of powder/ bulk volume of powder

Apparent bulk density was determined by pouring pre-sieved (40 sieve) powder blend of drug and excipients into a graduated cylinder via a large funnel and measuring the volume and weight "as it is".

Tapped density: is the ratio of mass of powder to the tapped volume. Tapped volume is the volume occupied by the same mass of powder after a standard tapping of a measure.

Carr's index: To know the relative flow rate, cohesiveness and compressibility properties of the drug and excipient blend Carr's index was determined and is given by

$$\text{Carr's consolidation index} = \frac{\text{tapped density} - \text{fluff density} \times 100}{\text{tapped density}}$$

Fluff density is the ratio of mass of powder to the fluff volume. Fluff volume is the volume occupied by a certain mass, when gently poured into a measuring cylinder.

Hausner's Ratio

Hausner's ratio is an indirect index of ease of powder flow. If the Hausner's ratio of the powder is near to 1.25 indicates better powder flow. It is calculated by the following formula [11- 13]:

Hausner's ratio = tapped density/bulk density

< 1.25 - good flow. > 1.25 - poor flow.

Preparation of tablets: Tablets containing 4 mg of salbutamol sulphate were prepared by direct compression method. Superdisintegrants such as Croscarmellose sodium, crospovidone and sodium starch glycolate were used in varying concentrations (2.5 - 7.5% w/w) to get the optimized formula. The drug, diluents and superdisintegrants were passed through sieve no.40 and mixed together in a plastic container. Magnesium stearate and aerosil passed through sieve no.80 were mixed and blended with above mixture. The mixed blend of excipients was compressed into tablets using 7 mm flat punches on a 10 stationed rotary compression machine. The tablet formula is given in Table 1.

Table 1: Composition of Salbutamol sulphate immediate release tablets

Ingredients (mg)	Formulation code								
	F1	F2	F3	F4	F5	F6	F7	F8	F9
Salbutamol sulphate	5	5	5	5	5	5	5	5	5
Croscarmellose sodium	5	10	15	---	---	---	---	---	---
Crospovidone	---	---	---	5	10	15	---	---	---
Sodium starch glycolate	---	---	---	---	---	---	5	10	15
Lactose	70	70	70	70	70	70	70	70	70
Microcrystalline cellulose	115	110	105	115	110	105	115	110	105
Magnesium stearate	3	3	3	3	3	3	3	3	3
Aerosil	2	2	2	2	2	2	2	2	2
Total weight (mg)	200	200	200	200	200	200	200	200	200

Evaluation of Salbutamol sulphate immediate release tablets

The compressed tablets were evaluated for shape, appearance, uniformity of thickness, diameter, hardness test, friability test, weight variation, drug content, in-vitro disintegration and in-vitro drug release studies.

Shape and appearance

The tablets prepared were randomly picked from each batch and examined under lens for shape and in presence of light for color.

Thickness and diameter

Thickness and diameter of prepared tablets were tested using verniercalipers. The test was done in triplicates and average was determined.

Hardness and Friability

Using Monsanto tablet hardness tester, hardness of the tablet was checked. Using Roche Friabilator friability of the tablet was checked. This device subjected tablets to the combined effect of abrasions and shock by utilizing a plastic chamber that revolved at 25 rpm dropping the tablets at distance of 6 inches with each revolution. Pre weighed sample of 10 tablets was placed in the friabilator, which was then operated for 100 revolutions. Tablets were dusted and weighed again. The friability was determined using following formula:

$$\text{Friability} = \frac{[(\text{Initial weight} - \text{Final weight}) / (\text{Initial weight})] \times 100}{\%}$$

Weight variation test

The weight variation test was done by (Shimadzu digital balance) weighing 20 tablets individually, calculating the average weight and

comparing the individual tablet weights to the average. The percentage difference in the weight variation should be within the permissible limits. The percent deviation was calculated and the limits followed as per the limits mentioned in united state pharmacopoeia (USP) [14].

Drug Content Uniformity

Ten tablets were weighed individually and powdered. The powder equivalent to 4 mg of salbutamol sulphate was weighed and extracted in phosphate buffer pH 6.8 (100 ml) and the concentration of drug was determined by measuring absorbance at 276 nm by spectrophotometer.

Wetting time

Wetting time is closely related to the inner structure of the tablets and to the hydrophilicity of the excipient. According to the following equation proposed by Washburn E.W (1921), the water penetration rate into the powder bed is proportional to the pore radius and is affected by the hydrophilicity of the powders.

$$dl/dt = r \gamma \cos \theta / (4 \eta l)$$

Where l is the length of penetration, r is the capillary radius, γ is the surface tension, η is the liquid viscosity, t is the time, and θ is the contact angle. It is obvious that pores size becomes smaller and wetting time increases with an increase in compression force or a decrease in porosity. A linear relationship exists between wetting time and disintegration time. Thus wetting is the important step for disintegration process to take place.

The wetting time of tablet was measured by the method described by Bi et al. (1996). The method is as follows. A piece of tissue paper folded twice was placed in a small culture dish (72.39 cm²)

containing 6 ml of purified water. A tablet was placed in the centre and a small amount of amaranth powder was placed on top of it. The time required for development of red colour at 25°C on the tablet

surface was considered as time for complete wetting [15, 16]. Figure 1 shows the tablet before and after wetting studies. The test was done in triplicate.

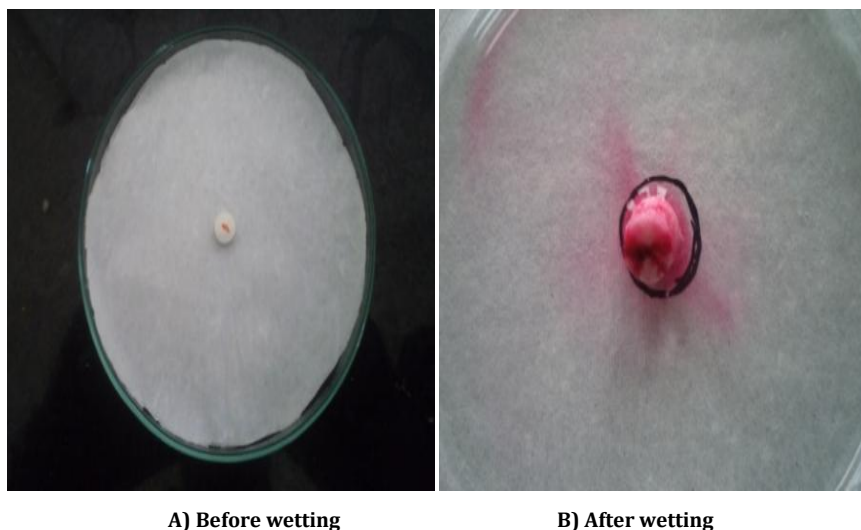


Fig. 1: Wetting time study of salbutamol sulphate immediate release tablets.

Water absorption ratio (R)

A piece of tissue paper folded twice was placed in a small petri dish (72.39 cm²) containing 6 ml of water. A weighed tablet (W_b) was put on the tissue paper at the centre and allowed to completely wet, then the tablet was weighed again to get weight of tablet after water absorption (W_a). Then water absorption ratio, R was determined according to the following equation:

$$R = (W_a - W_b) / W_b$$

Where, W_a and W_b are the weight after and before water absorption, respectively [15]. The test was done in triplicate.

In-vitro disintegration test

Six tablets from each batch along with disc were introduced in each tube of basket of USP disintegration test apparatus (Lab care instruments). The basket was positioned into a beaker containing 900 ml of distilled water and operated at $37 \pm 0.5^\circ\text{C}$. The time of disintegration of tablet was recorded. The average time and standard deviation were calculated [17].

In-vitro drug release study

Dissolution rate was studied by using USP type-II apparatus at 50 rpm (USP XXIII Dissolution Test Apparatus) using 500 ml of phosphate buffer pH 6.8 as dissolution medium. Temperature of the dissolution medium was maintained at $37 \pm 0.5^\circ\text{C}$, 5 ml aliquot of dissolution medium was withdrawn at every 1 minute interval and the absorbance was checked by UV spectrophotometric method at 276 nm and concentration of the drug was determined from standard calibration curve. Dissolution rate was studied for all designed formulations. Dissolution study was carried out in triplicate for all formulations.

RESULTS AND DISCUSSION

Drug-excipients compatibility study

The FTIR spectrum of pure drug Salbutamol sulphate (in KBr) and the physical mixture of formulations F3, F6, F9 showed the characteristic absorption peaks in the IR region with negligible variation in the band position of different functional groups and various bonds in comparison to FTIR of pure drug. As there was no much variation in the nature of IR spectrum, it was concluded that there was no interaction of the drug with the excipients used for the study and the drug retained its identity without undergoing any type of interaction with the excipients. The FTIR spectrums are given in Figure 2 - 5.

Evaluation of mixed powder blends of drug and excipients

The flow properties and compression properties of the mixed powder blend of drug and excipients was carried out by measuring various parameters. The Angle of repose for powder blend was in the range of 23.31 to 29.28°. The Carr's index was in the range of 15.28 and 20.37% and Hausner's Ratio in the range of 1.18 to 1.25. The results indicated that the powder blend possessed considerable flow and compaction properties for all the formulations. The results of precompression analysis of powder blend for Angle of repose, Carr's index and Hausner's ratio are presented in Table 2.

Table 2: Precompression analysis of mixed powder blends of drug and excipients.

Formulation	Angle of Repose(θ)	Carr's index (%)	Hausner's ratio
F1	27.78	20.00	1.25
F2	23.31	20.00	1.25
F3	28.51	20.37	1.25
F4	28.15	18.09	1.22
F5	24.48	17.10	1.20
F6	26.81	16.36	1.19
F7	25.11	15.28	1.18
F8	27.16	19.14	1.23
F9	29.28	18.99	1.23

Evaluation of Salbutamol sulphate immediate release tablets

The present investigation was undertaken to fabricate and evaluate salbutamol sulphate immediate release tablets by the direct compression method. All the formulations were round, white in colour, odorless, with smooth surface and sharp edges. Thickness and diameter of all formulations were found to be uniform.

Hardness and friability of all formulations was within acceptable limits. Hardness of tablets prepared by direct compression was 3.8 ± 0.35 to 4.2 ± 0.28 kg/cm². The friability of all formulations was found to be less than 1.0% and hence the tablets with lower friability may not break during handling on machines and or shipping. Weight variation was found within the specification of the USP limits. Average weight of all formulations was found in the range of 198.2 ± 0.26 - 200.9 ± 0.21 mg. The drug content uniformity of all the formulations was found in the range of 4.04 ± 0.14 - 4.31 ± 0.11 mg. The drug content was uniform and within limits indicating the

method followed to prepare the powder blend and tablets distributed the drug uniformly through the blend. The results of

post compression analysis of salbutamol sulphate immediate release tablets is given in Table 3.

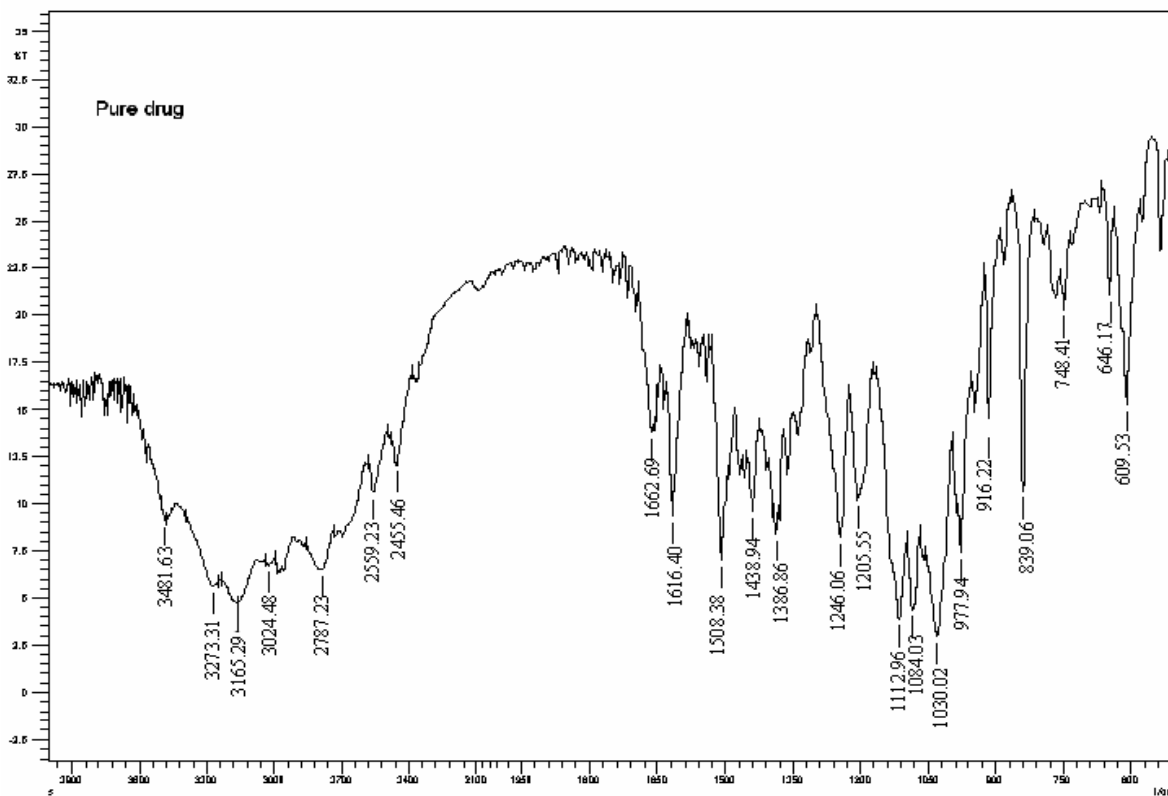


Fig. 2: FT-IR Spectra of pure drug Salbutamol sulphate

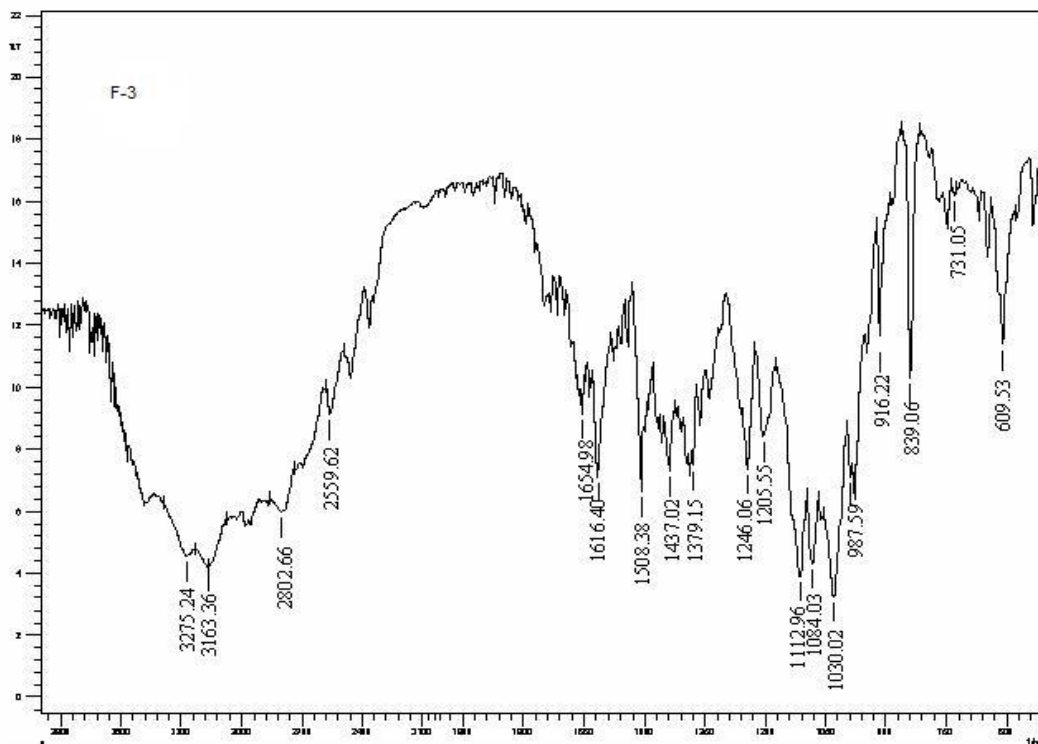


Fig. 3: FT-IR Spectra of physical mixture of drug and Croscarmellose sodium

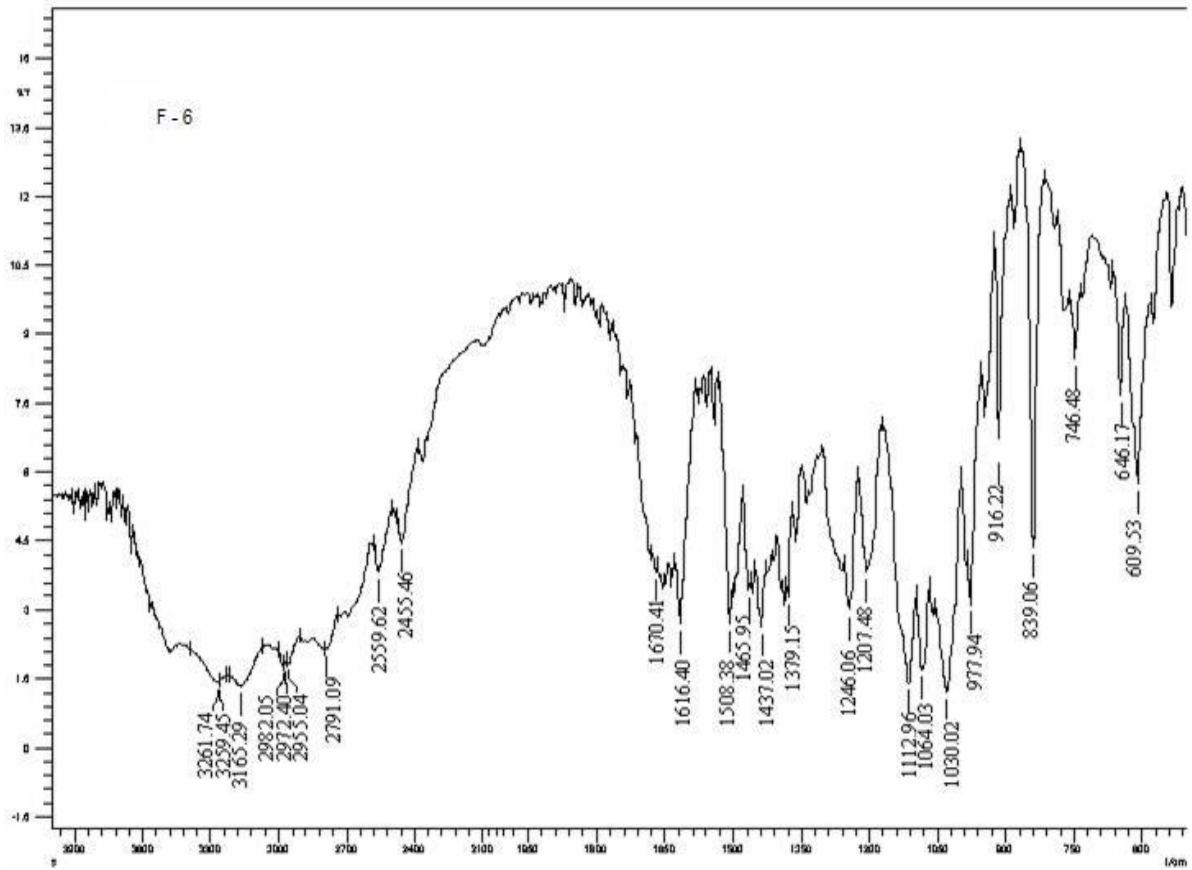


Fig. 4: FT-IR Spectra of physical mixture of drug and Crospovidone

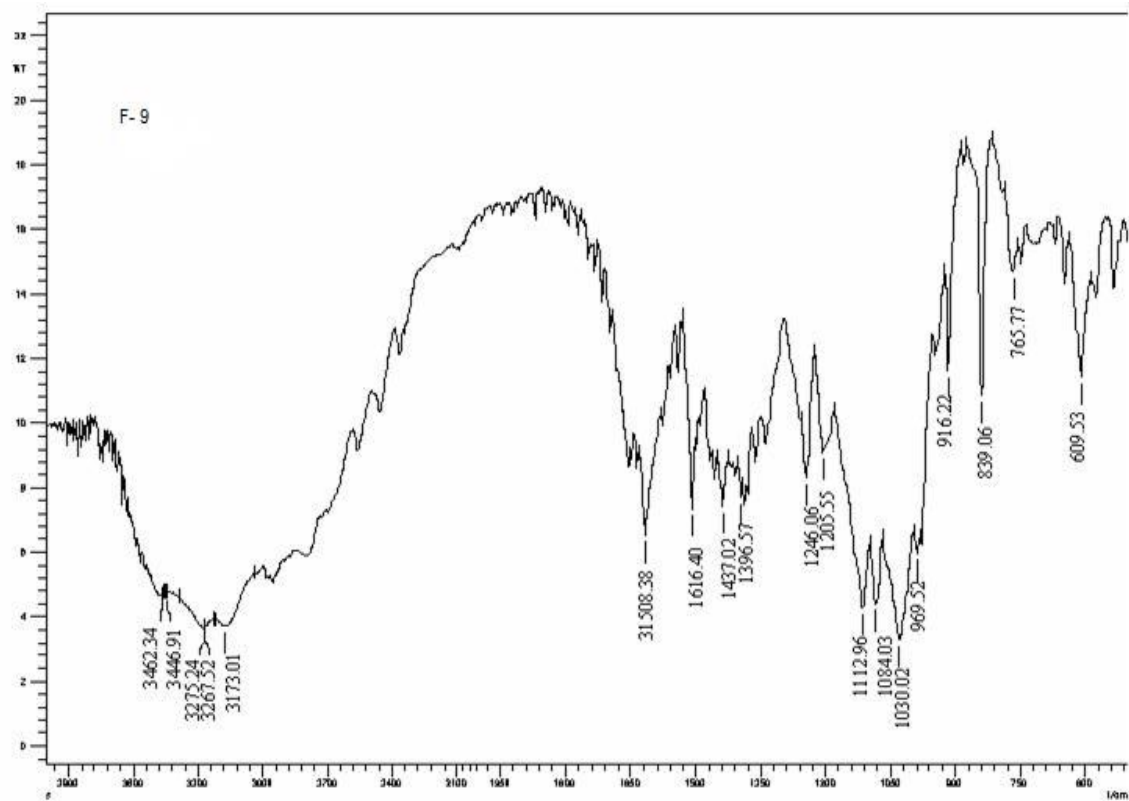


Fig. 5: FT-IR Spectra of physical mixture of drug and Sodium starch glycolate

Table 3: Post compression analysis of salbutamol sulphate immediate release tablets

Formulation	Thickness (mm)	Diameter (mm)	Hardness (kg/cm ²)	Weight variation (%)	Friability (%)	Drug content (mg)
F1	4.84±0.38	7.0	4.0±0.55	199.8±0.05	0.34±0.03	4.13±0.09
F2	5.08±0.06	7.0	3.8±0.35	200.3±0.06	0.36±0.01	4.08±0.03
F3	5.63±0.13	7.1	4.1±0.43	200.9±0.21	0.42±0.04	4.05±0.11
F4	5.61±0.15	7.0	4.2±0.28	199.5±0.93	0.33±0.01	4.16±0.19
F5	5.64±0.08	7.0	4.0±0.34	198.7±0.11	0.41±0.02	4.31±0.11
F6	6.06±0.09	7.0	3.9±0.30	199.3±1.09	0.74±0.01	4.17±0.26
F7	5.52±0.10	7.0	4.1±0.24	199.7±0.72	0.32±0.03	4.21±0.03
F8	5.49±0.09	7.0	4.2±0.28	198.2±0.26	0.65±0.01	4.04±0.14
F9	5.53±0.09	7.2	4.0±0.38	198.8±0.16	0.46±0.02	4.08±0.01

Wetting time

Wetting time is closely related to the inner structure of the tablet and to the hydrophilicity of the excipients. Wetting time for all the tablets was found in the range of 18.33 ± 0.58 (F6) - 44.17 ± 1.04 (F7) sec. The results are shown in Figure 6. The wetting time was rapid with tablets prepared using Crospovidone as superdisintegrant and was minimum with formulations having Sodium starch glycolate as disintegrant. The wetting time for different superdisintegrants was in the order Crospovidone > Croscarmellose sodium > Sodium starch glycolate. Crospovidone rapidly exhibits swelling due high capillary activity and pronounced hydration capacity, with little tendency to form gels which can be observed by intact nature of tablets F4 - F6, even after swelling during the wetting studies [18]. The wetting time of Tablets F1 - F3, prepared with Croscarmellose sodium is more than Crospovidone because the wicking and swelling process takes more time. Tablets F7 - F9 compressed with Sodium starch glycolate showed maximum wetting time as water uptake and swelling is slowed down because of its high degree of cross linking [19]. It was also observed that as the concentration of disintegrants was increased from 2.5% to 7.5%, the time taken for wetting was reduced in all the nine formulations, Whereas in case of Sodium starch glycolate with increase in concentration of disintegrant from 5 (F8) - 7.5 (F9) % not much difference in wetting time was observed.

Water absorption ratio (R)

Water absorption ratio was in the range of 0.34 ± 0.01 (F9) - 1.03 ± 0.04 (F6) for all the tablets prepared and is presented in Figure 7. Salbutamol sulphate immediate release tablet F6 containing Crospovidone (7.5% w/w) showed the highest 'R' value of 1.03 ± 0.04 because of its swelling behavior and had lowest wetting time of 18.33 ± 0.58 sec. The least amount of water absorption was by formulations containing Sodium starch glycolate. The water absorption study was found to be directly related to wetting studies of the tablets. Here also the water absorption ratio for different superdisintegrants was in the order Crospovidone > Croscarmellosesodium > Sodium starch glycolate. The water absorption ratio was also found to increase with increase in the concentration of the superdisintegrants from 2.5% to 7.5%w/w in case of Croscarmellose sodium and Crospovidone. Interestingly in case of Sodium starch glycolate i.e., tablets F7 - F8, initial rise in R value was observed when concentration was increased from 2.5 - 5.0 %w/w, but at 7.5%w/w concentration (F9) the R value was lowered indicating the decrease in water absorbing property at higher concentration. This is also supported by similar observation in wetting studies. The reason behind this may be attributed to the swelling behavior of Sodium starch glycolate accompanied by gelling, which could possibly occlude the pores in the tablet preventing further penetration of water into the tablet matrix [20].

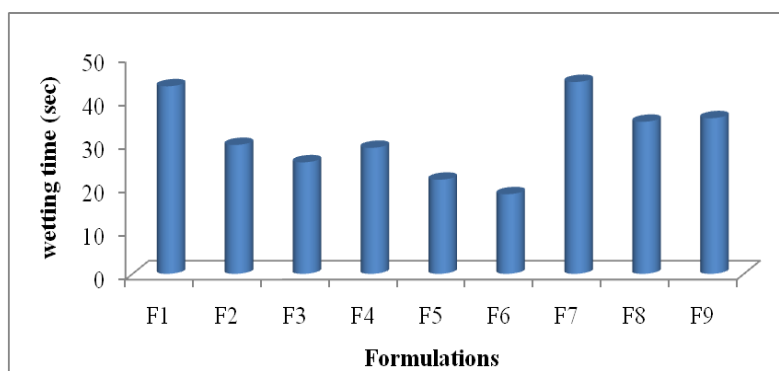


Fig. 6: Wetting time studies of salbutamol sulphate immediate release tablets

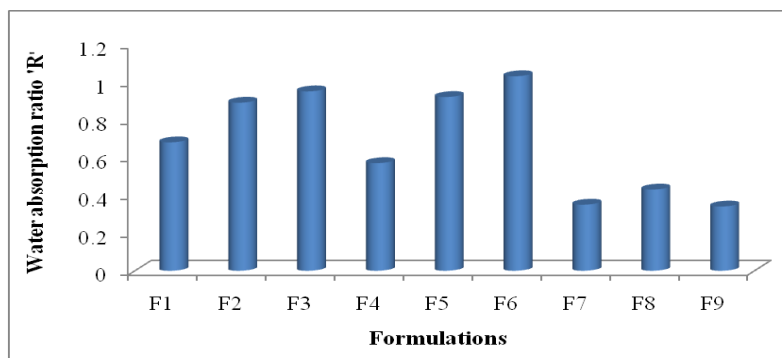


Fig. 7: Water absorption ratio (R) of salbutamol sulphate immediate release tablets

In-vitro disintegration test

Superdisintegrants at different concentration levels (2.5, 5 and 7.5% w/w) were used to assist disintegration. In-vitro disintegration time is very important for immediate release tablets, which is desired to be less than 60 sec. The rapid disintegration may be due to the rapid uptake of water from the medium, swelling, burst effect and thereby promoting bioavailability of the drug. The in-vitro disintegration time of Salbutamol sulphate immediate release tablet was rapid with Crospovidone (F6) i.e. 16.17 ± 1.04 sec and delayed with Sodium starch glycolate (F9) i.e. 137.47 ± 1.67 sec. The order of disintegration time for different superdisintegrants was Crospovidone < Croscarmellose sodium < Sodium starch glycolate. Crospovidone and Croscarmellose sodium perform their disintegrating action by wicking through capillary action and fibrous structure, respectively with minimum gelling and thereby the disintegration time is minimum. As the concentration of

superdisintegrants in the formulations is increased, the disintegration time was found to decrease. This finding is in agreement with results obtained from wetting time studies. Tablets with Croscarmellose sodium exhibit a visible 'breakdown' of the tablet matrix during disintegration which is less with crospovidone and sodium starch glycolate. In case of formulations with sodium starch glycolate disintegration time was found to be extended. The significantly longer wetting time and lower water absorption ratio were related to its disintegration mechanism which is by swelling and formation of gel on contact with aqueous medium. As the swelling is accompanied by gelling, this possibly occludes the pores in the tablet preventing further penetration of water into the tablet matrix and hence the delay observed in the disintegration time of these tablets [21]. In-vitro disintegration studies of tablets F7 - F9 show that increasing sodium starch glycolate concentration from 2.5 - 7.5% w/w, actually leads to longer disintegration time. In-vitro disintegration studies of various formulations at different time intervals are reported in Figure 8.

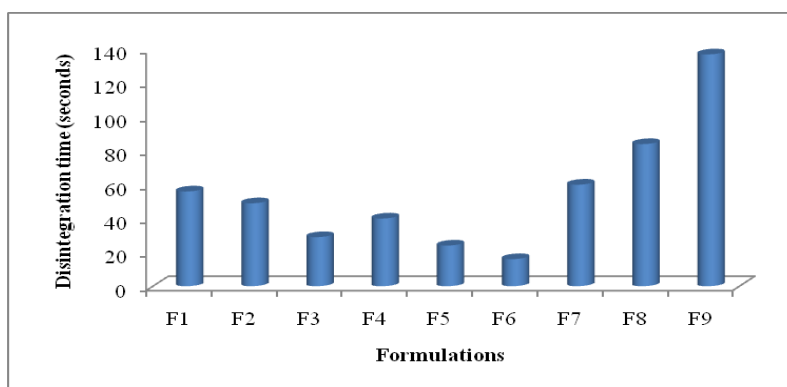


Fig. 8: In-vitro disintegration studies of salbutamol sulphate immediate release tablets

In-vitro dissolution test

The In-vitro drug release profile of salbutamol sulphate immediate release tablets revealed that formulation F-3 containing 15 mg of cross carmellose sodium (7.5% of tablet weight) released 98.58% of drug in 12 minutes in pH 6.8 phosphate buffer. The in-vitro drug release for all the formulations was in the range of 61.15 - 98.58% at the end of 12 minutes. All the tablets produced rapid release of drug from the disintegrated tablets. The release behavior of the tablets largely depended on the type of disintegrant present in the formulation. Out

of the three superdisintegrants used interestingly Croscarmellose sodium gave the maximum drug release of 98.58% (F3), even when its disintegration time, wetting time was considerably less than crospovidone. Also the water absorption ratio of crospovidone was highest compared to Croscarmellose sodium. The reason behind this behavior of Croscarmellose sodium is the visible 'breakdown' of the tablet matrix in to smaller granules during dissolution which is less with crospovidone and sodium starch glycolate. Despite the closeness of their disintegration times the tablets with Croscarmellose sodium released comparatively more drug than Crospovidone.

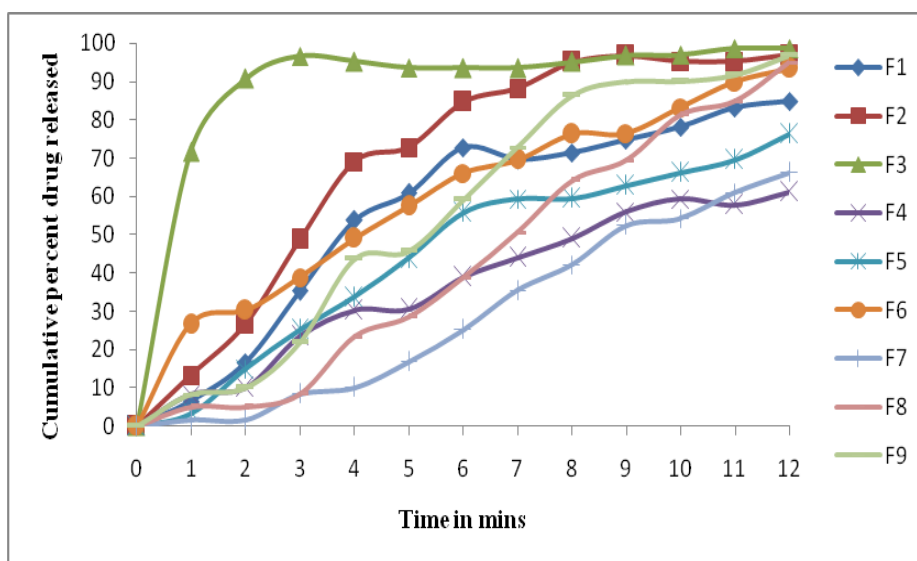


Fig. 9: In-vitro release behavior of salbutamol sulphate immediate release tablets.

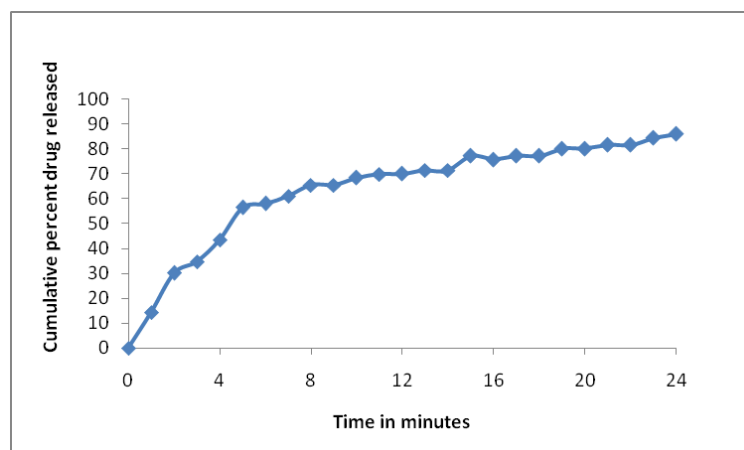


Fig. 10: In-vitro release behavior of salbutamol sulphate marketed conventional tablet.

The weakly held fragments of porous tablets of Croscarmellose sodium disaggregate into relatively fine particles under the rotating movement of the paddle. As a result the total water contact area with drug is enhanced and thereby maximum dissolution is achieved. Tablets with crospovidone released drug from 61.15 (F4) – 93.36% (F6) in 12 minutes. Crospovidone had the high water uptake potential and lowest disintegration rate, but its drug release is less because of its swelling nature which restricts the movement of drug due to diffusion. Moreover the tablets prepared with Crospovidone were observed to remain intact structurally without considerable breakage even at the end of dissolution. This behavior of Crospovidone is responsible for the lower release of drug compared to Croscarmellose sodium. In case of tablets F7 – F9, prepared with Sodium starch glycolate, the tablets initially swelled and disintegrated slowly toward the end of dissolution into large irregularly shaped fragments. It can be observed that the disintegration time of these formulations increased with increase in disintegrant level which was possibly due to its gelling action. This property contributes to binding of the tablet matrix and hence limiting tablet disintegration. The swelling of Sodium starch glycolate accompanied by its gelling property in the dissolution medium possibly occludes the pores in the tablet and prevents further penetration of water into the tablet matrix. Hence the tablets remain intact initially for a certain period and later disintegrate. The dissolution rate of drug or the in-vitro release of drug was found to be directly related to concentration of disintegrants used. For all the disintegrants used in the study, when concentration was increased from 2.5 – 7.5%w/w, the release rate also enhanced considerably. The order of in-vitro release of drug for the superdisintegrants used was Croscarmellose sodium > Sodium starch glycolate > Crospovidone. The results are summarized in Fig. 9. The in-vitro release was compared with a marketed conventional dosage form available. Salbetol – 4 (FDC Ltd, Goa) released 85.91% of salbutamol in 24 mins in phosphate buffer pH 6.8 (Figure 10). It was clear that the immediate release tablet F3 was better than the marketed product in terms of in-vitro release studies.

CONCLUSION

The most important parameter that needs to be optimized in the development of immediate release tablets is disintegration time of tablets. The disintegration time of the tablets prepared by using superdisintegrants was well within the limits. Croscarmellose sodium provided the immediate and highest release compared to other disintegrants. It was concluded that salbutamol sulphate immediate release tablets could be successfully prepared by direct compression technique with a view of obtaining immediate action of the drug and is advantageous in comparison to the currently available conventional form of tablet. Salbutamol sulphate being a water-soluble drug would be readily available in a dissolved form for rapid oral uptake resulting in enhanced bioavailability. The immediate release concept in case of salbutamol sulphate could be

of great importance in relieving acute asthmatic attacks. The applied method was found to be economically and industrially feasible.

ACKNOWLEDGEMENTS

The authors are grateful to S.M. Pharmaceuticals, Bengaluru and Glenmark Pharmaceuticals, Mumbai, for providing gift samples of drug and superdisintegrants respectively. The author wishes to thank Sri H.Doddappa, Sri Dhananjay and Ch. Suryanarayana for their help in carrying out the research work.

REFERENCES

- Jadon SR, Nayak S, Amlan S, Vaidya DV, Khemariya P, Subhate S et al. Taste Masking of Lornoxicam by Polymer Carrier System and Formulation of Oral Disintegrating Tablets. *Int J Drug Deliv* 2009; 1:27-31.
- Zhang Y, Law Y, Chakrabarti S. Physical Properties and Compact Analysis of Commonly used Direct Compression Binders. *AAPS Pharm Sci Tech* 2003; 4(4):1-11.
- Yasmeen R, Shoaib MH, Khalid H. Comparative Study of Different Formulations of Atenolol. *Pak J Pharm Sci* 2005; 18(1):47-51.
- Beyer T, Day GM, Price SL. The Prediction, Morphology and Mechanical Properties of the Polymorphs of Paracetamol. *J Am Chem Soc* 2001; 123:5086-5094.
- Shangraw RF. In: Liberman HA, Lachman L and Schwartz JB, editors. *Pharmaceutical Dosage Forms: Tablets*. Vol. 01, New York: Merck Dekker, Inc; 1989. p. 109-64.
- Ibrahim, Olurinola. Comparative Microbial Contamination Levels in Wet Granulation and Direct Compression Methods of Tablet Production. *Pharm Acta Helv* 1991; 66:293-301.
- Gohel MC. A Review of Co-processed Directly Compressible Excipients. *J Pharm Sci* 2005; 8(1):76-93.
- Mallick S, Pattnaik S, Swain K, De PK. Current Prospectives of Solubilization: Potential for Improved Bioavailability. *Drug Dev Ind Pharm* 2007; 33: 865-73.
- Himanshu Deshmukh, Chandrashekhara S, Nagesh C, Amol Murade and Shridhar Usgaunkar. Superdisintegrants: A Recent Investigation and Current Approach. *Asian J Pharm Tech* 2012; 2(1): 19-25.
- <http://www.medicinenet.com/asthma/page3.htm>
- Subrahmanyam CVS. *Textbook of Physical Pharmaceutics*. 2nd ed. New Delhi: Vallabh Prakashan; 2000. p. 180-228.
- Aulton ME. *Pharmaceutics -The Science of Dosage Form Design*. 2nd ed. Leicester: Churchill Livingstone; 2002. p. 200-206.
- Ameer SS, Abdul Rassol A, Shaimaa NAAH. Preparation and Evaluation of Phenobarbital Orodispersible Tablets. *Int J Pharm Pharm Sci* 2013; 5(1): 193-197.
- Lachman L. *Theory and Practice of Industrial Pharmacy*. 3rd ed. Mumbai: Varghese Publishing House; 1987. p. 297.
- Biljana Govedarica, Rade Injac, Rok Dreu, Stane Srcic. Formulation and Evaluation of Immediate Release Tablets with Different Types of Paracetamol Powders Prepared by Direct

- Compression. African Journal of Pharmacy and Pharmacology 2011; 5(1): 31-41.
16. Sivakranth M, Abdul SA, Rajasekhar S. Formulation and Evaluation of Oral Fast Dissolving Tablets of Sildenafil Citrate. *Int J Pharm Pharm Sci* 2011; 3(2): 112-121.
 17. Aly A, Sermen M, Qato M. Rapidly Disintegrating Tenoxicam Tablets via Camphor Sublimation. *Pharm Technol* 2005; 68-78.
 18. Schiermeier S, Schmidt PC. Fast Dispersible Ibuprofen Tablets. *Eur J Phar Sci* 2002; 15(3): 295 – 305.
 19. Wan LSC, Prasad KPP. Uptake of Water by Excipients in Tablets. *Int J Pharm* 1989; 50: 147 – 153.
 20. Zhao N, Augsburg LL. The Influence of Swelling Capacity of Superdisintegrants in Different pH Media on the Dissolution of Hydrochlorothiazide from Directly Compressed Tablets. *AAPS PharmSciTech* 2005;6:120-6.
 21. Gissinger D, Stamm AA. Comparative Evaluation of the Properties of Some Tablet Disintegrants. *Drug Dev Ind Pharm* 1980; 6:511-36.