# Design and development of fast Melting Tablets of Terbutaline Sulphate

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*Available online at*: **www.isca.in**
**(Received 5th April 2011, revised 7th April 2011, accepted 9th April 2011)**

**Abstract**

*Difficulty in swallowing leads to non-compliance and subsequently leading to ineffective therapy. Terbutaline Sulphate is a beta-2 agonist and has action similar to that of Isoproterenol. The basic aim of this formulation was to decrease the onset time of the drug by decreasing the disintegration time of the tablet by formulating fast melting tablet. In the present study fast melting tablets of Terbutaline Sulphate was prepared by using of superdisintegrants. The tablets were prepared by direct compression technique. Six formulations of tablets were prepared containing drug. Prepared tablets were evaluated on different parameters. Evaluation results shows tablet to be within the official limits. Wetting time and disintegration were in limits that are prescribed for mouth dissolving tablets. Dissolution profile of the tablet shows that the excipients used in the tablet had no negative influence on the release pattern of the drug. It was thus possible to formulate mouth melting tablets of Terbutaline Sulphate using simple and cost effective technique.*

**Key words:** Terbutaline Sulphate, direct compression, super disintegrant.

## Introduction

In today's world when air pollution is rampant people of all ages and classes are vulnerable to diseases related to respiratory system. Asthma is one such common disease of the respiratory system to have a big influence on human race. This disease affects people of all age; young or old all alike. This disease is caused by the constriction of the airways particularly bronchi. Terbutaline Sulphate is a selective beta -2 adrenoreceptor agonist and used in acute treatment of bronchial asthma since it help in dilating the constricted bronchi, Terbutaline sulphate is used in various other forms of chronic obstructive pulmonary diseases. Terbutaline sulphate is a short acting bronchorelaxant and is given in all the major routes of administration. The peak plasma concentration of Terbutaline sulphate is 1.2µg/ml for every milligram of oral dose. A lesser amount than that of oral administration reaches the systemic circulation via inhalation route, since it is difficult to coordinate the breathing when the pump is pressed; this creates problems in the treatment of the patient. Also pumps are expensive as compared to solid oral dosage form[1,2].

In-spite of innumerable advancement in the dosage form technology solid oral dosage remains among the most favoured option by patients due to reasons like easy to handle, cost effective, no dose variation associated with solid orals, ease of storage[3]. Although solid orals come with these advantages but there is a drawback associated with them. Many patients particularly paediatric and geriatric find it difficult to swallow solid oral dosage form like tablets and capsules[4], owing to which patients do not stick to the dosage regimen prescribed by the physician resulting in incomplete dose reaching the systemic circulation and leads to resistance development in case of antibiotics and similar disadvantages with other classes of active moieties.

Recent advancement in novel drug delivery systems aims to enhance the safety and efficacy of the drug molecule and decrease the problems associated to the conventional dosage form. One such novel dosage form for drug delivery is fast melting tablets which are more commonly known as oral disintegrating tablets. The proper choice of disintegrants and the optimum concentration of the same is critical factor in the design and development of fast melting tablets. These super

disintegrants are polymers which are cross linked and have the capability to swell in contact with aqueous medium. As the superdisintegrants swell they increase the diameter of the tablet and help in overcoming the binding force of the binder and the compaction force used in the formulation of the tablet which held together the granules.

In this work we have tried to formulate a mouth melting dosage form of Terbutaline Sulphate by varying the concentration of superdisintegrants [Crospovidone (CP) and Croscarmellose Sodium (CCS)] so as to know at which concentration it is most effective.

**Materials and Methods**

Terbutaline Sulphate was obtained as a gift sample from IPCA laboratories Pvt. Ltd. Ratlam, India. Croscarmellose Sodium and Crospovidone were obtained as gift samples from Syncom labs. Pvt. Ltd. All other chemicals were of analytical grade.

**Optimisation of Superdisintegrant concentration:** Before the formulation of Fast melting tablet the amount of CP and CCS was optimised. Various batches of tablets were prepared containing blend of Mannitol and CP or CCS in varying concentration. The weight of tablet was fixed at 150 mg. All the tablets were prepared using direct compression method. All the formulation variables were held constant in order to optimise the amount of CP and CCS. The data displayed in table 1.

**Preparation of fast melting tablets:** Fast melting tablets of batch size five hundred (500) was prepared by direct compression process using different proportions of Mannitol and CP or CCS. Mannitol, CP or CCS to be used in each batch and Terbutaline Sulphate were mixed thoroughly for 15 minutes in a porcelain mortar and passed through sieve # 60. This blend was mixed with aerosil, pre-gelatinised starch, and magnesium separate (magnesium separate was added in last as it is hydrophobic in nature and affects tablet disintegration) for five minutes and again the entire blend was passed through sieve # 80. Powder blend was evaluated for bulk density, tapped density, Carr's index and Hauser's ratio. Compression of tablets was done on single punch machine (Scientech) using 7 mm flat punch. Compression force was kept constant for all formulations.

**Evaluation of powder blend**

**Angle of repose:** The angle of repose of powder blend was determined by the funnel method[5]. Results are shown in table 3.

**Bulk density and Tapped density:** Powder bulk density and tapped density were determined using the usual process [5]. Results are displayed in table 3

**Carr's Index:** Carr's Index was determined by using the under mentioned formula[5].

Carr's Index (%) = [(TD-BD) x100]/TD

Where
TD- tapped density
BD- bulk density
table 3 shows results

**Hausner's Ratio:** Hausner's ratio was determined by the underlying formula[5].

$$H = P_T/P_B$$

Where

H denotes Hausner's ratio
$P_T$ denotes tapped density
and $P_B$ denotes bulk density
Results are shown in table 3
Evaluation of Tablet Characteristics

**Hardness test and Friability:** Hardness of tablet was evaluated using Monsanto hardness tester [6]. Friability of tablets was tested by Roche's friabilator[6].

**Drug Content:** Drug content of prepared tablet of each batch of the formulation was determined[8]. From each batch 20 tablets were taken, weighted and finely grounded. An amount of powder equivalent to 5 mg of powder was accurately weighted and dissolved in 6.8 phosphate buffer. The resulting solution was suitably diluted and analysed on UV spectrophotometer Shimadzu 1601 at 284 nm.

**Weight Variation:** Weight variation[6] was determined by taking 20 tablets using electronic balance (Contech).

**Wetting time:** A double folded absorbent paper[7] was kept on petridish and thoroughly wetted with distilled water. Excess distilled water was drained out of the petridish. Tablet was placed at the centre of the wet absorbent paper. The time required for the water to diffuse from the absorbent paper throughout the entire tablet was recorded using stopwatch. This test was performed thrice (n = 3). This method will duplicate the in-vivo disintegration of tablet kept on tongue. Lesser is the disintegration time more porous is the tablet.

**Disintegration test:** Disintegration test was measured using disintegration test apparatus. One tablet was placed in each of the six tubes of disintegration test apparatus. I.P. method was followed without using disc[8]. The time required for complete disintegration of tablet in each tube was determined using stop watch.

**In *–vitro* Dissolution rate study:** Dissolution test of Terbutaline Sulphate was performed in 6.8 phosphate buffer at 50 rpm using USP dissolution test apparatus type II (paddle type) [9,10]. Five ml aliquots were withdrawn with a pipette and replaced with 5 ml fresh dissolution medium at an interval of 1 minute. The aliquots were passed through Whatman filter paper number 41 to remove any suspended impurity which may interfere during spectroscopic estimation. The absorbance of samples was taken on UV spectrophotometer (Shimadzu 1601) at 284 nm against blank and correspondingly concentration of the drug was determined at various time intervals.

## Result and Discussion

The pre-compression parameters of the powder blend were evaluated and batch F4 was found to have angle of repose value 24°.36' indicating excellent flow. Formulation F3 had the highest value of angle of repose suggesting comparatively poor flow. The other evaluation parameters of powder blend namely Carr's index for all the formulations showed values in range of 7.70% to 13.53% indicating good flow property; similarly Hausner's ratio values for all the formulations lied in the range of 1.086 to 1.156. The values obtained for Hausner's ratio indicate good flowability. Table3 shows the results for powder blend characterisation.

The additives used in the formulation did not interfered with the UV absorption of Terbutaline sulphate and there was no interaction between drug and the excipients as per the physical observation of the mixture of drug and excipients in 1:1 ratio.

From the data obtained from the optimisation of the formulation the amount of superdisintegrants were varied from 2.66%w/w to 6.66% w/w keeping in mind the optimisation between the disintegration time and final cost of the tablet. Correspondingly amount of mannitol was varied to maintain the final weight of the tablet. The amount of CP and CCS containing 6.66% w/w of superdisintegrants produced optimum result

Fast melting tablet of Terbutaline sulphate was being formulated successfully by use of direct compression technique. Formulation F4 was found to have best disintegration time of 52 seconds under experimental conditions at room temperature. Concentration dependent disintegration of the tablet was seen in the results. As the amount of disintegrant was increased the time required for the disintegration of tablets were reduced. The water uptake by the polymers (CP and CCS) and corresponding swelling resulted in the bursting of the tablet structure. The swelling force acted against the binding force in order to break apart the tablet.

Wetting time of the various different formulations was found to be in the range of 49-70 seconds. Formulation F4 containing CP had lowest wetting time of 49 sec; this may be due to the better wicking action produced by the polymer.

## Conclusion

The aim of development of fast melting tablets of Terbutaline sulphate by direct compression technique was achieved. This formulation is more cost effective than aerosol inhalation pumps available. It was found that the total amount of drug from the optimised batch was released in first 4 minutes of the dissolution study. The tablets disintegrated within 50 sec under experimental in vitro laboratory conditions.

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**Table-1: Formula for different batches of Fast melting tablets of Terbutaline sulphate**

| Batch | Superdisintegrant | Superdisintegrant (%w/w) | Disintegration Time (Sec) |
|---|---|---|---|
| **A1** | CCS | 1.33 | 138 |
| **A2** | CCS | 2.66 | 80 |
| **A3** | CCS | 5.33 | 76 |
| **A4** | CCS | 6.66 | 60 |
| **A5** | CCS | 8.00 | 55 |
| **A6** | CP | 1.33 | 125 |
| **A7** | CP | 2.66 | 76 |
| **A8** | CP | 5.33 | 69 |
| **A9** | CP | 6.66 | 56 |
| **A10** | CP | 8.00 | 50 |

CP- Crospovidone; CCS- Croscarmellose Sodium

**Table-2: Formula for different batches of Fast melting tablets of Terbutaline sulphate**

| Ingredients | F1 | F2 | F3 | F4 | F5 | F6 |
|---|---|---|---|---|---|---|
| Terbutaline Sulphate | 5 | 5 | 5 | 5 | 5 | 5 |
| Mannitol | 127.0 | 130.0 | 133.0 | 127.0 | 130.0 | 133.0 |
| Croscarmellose sodium | 10.0 | 7.0 | 4.0 | - | - | - |
| Crospovidone | - | - | - | 10.0 | 7.0 | 4.0 |
| Aerosil | 3.0 | 3.0 | 3.0 | 3.0 | 3.0 | 3.0 |
| Pre-gelatinised Starch | 2.0 | 2.0 | 2.0 | 2.0 | 2.0 | 2.0 |
| Menthol | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 |
| Magnesium stearate | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 |

**Table-3: Pre compressed parameter of powder blend for Fast melting tablets of Terbutaline Sulphate**

| Powder blend | Angle of Repose ($^0$) (n=3) | Bulk Density (g/cm$^3$) (n=3) | Tapped Density (g/cm$^3$) (n=3) | Carr's Index (%) | Hausner's ratio |
|---|---|---|---|---|---|
| F1 | 27°.30' | 0.527 | 0.571 | 7.70 | 1.083 |
| F2 | 27°.54' | 0. 523 | 0.575 | 9.04 | 1.099 |
| F3 | 27°.64' | 0. 520 | 0.573 | 9.24 | 1.101 |
| F4 | 24°.36' | 0. 516 | 0.583 | 11.49 | 1.129 |
| F5 | 24°. 43 ' | 0. 514 | 0.588 | 12.58 | 1.143 |
| F6 | 24°.45' | 0. 511 | 0.591 | 13.53 | 1.156 |

**Table-4: Physical parameters of Fast melting tablets of Terbutaline Sulphate**

| Batches | Thickness (mm) n = 3 | Hardness ($Kg/cm^2$) n = 3 | Friability (%) n = 3 | Weight Variation (mg) n = 3 | Wetting time (sec) | Disintegration time (sec) | Drug content uniformity (%) |
|---|---|---|---|---|---|---|---|
| F1 | 2.7 ±0.1 | 2.43 | 0.51 ± 0.1 | 150.15 | 52 | 59 | 98.97 |
| F2 | 2.8 ±0.1 | 2.45 | 0.56 ± 0.1 | 151.5 | 59 | 68 | 98.95 |
| F3 | 2.7±0.1 | 2.41 | 0.54 ± 0.1 | 151.1 | 70 | 75 | 98.76 |
| F4 | 2.9±0.1 | 2.42 | 0.51 ± 0.1 | 149.5 | 49 | 52 | 99.81 |
| F5 | 3.0±0.1 | 2.45 | 0.51 ± 0.1 | 152.0 | 55 | 64 | 98.69 |
| F6 | 3.5±0.1 | 2.50 | 0.50 ± 0.1 | 155.11 | 56 | 63 | 98.95 |

**Figure-1: Drug release profile of Fast melting tablet of Terbutaline Sulphate**