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Research paper

FORMULATION DEVELOPMENT AND EVALUATION OF MOUTH DISSOLVING TABLETS OF TERBUTALINE SULPHATE

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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 Mouth Dissolving tablet. In the present study Mouth Dissolving tablets of Terbutaline Sulphate was prepared by using of superdisintegrants. The tablets were prepared by direct compression technique. Eight 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 Dissolving tablets of Terbutaline Sulphate using simple and cost effective technique.

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

INTRODUCTION

Asthma is most 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].

The main problem with the common oral dosage forms is that they have to be swallowed along with water. Many patients find it difficult to swallow tablets, especially in elderly and pediatrics, because of the physiological changes associated with these groups. Due to this dysphagic condition, they donot comply with prescription which results in patient non-compliance. The other causes of patient non-compliance include sudden episodes of allergic attacks, motion sickness, coughing and unavailability of water etc. These problems can be resolved by fast dissolving tablets, which do not require water to aid in swallowing.[3,4]

Mouth dissolving tablets are a new and exciting alternative to traditional tablet and liquid medication dosages. Mouth dissolving tablets are those, which disintegrates or dissolve in the saliva without need of water. Mouth dissolving tablets dissolve on the tongue, with the aid of saliva. Mouth dissolving tablets can dissolve in as little as 1 to 2 seconds or as long as 2 to 3 minutes, depending on the different fast dissolve/disintegration technologies used to manufacture them.[5,6] Orally disintegrating tablets are an appealing dosage form for many reasons. Health professionals find the mouth disintegrating tablets as a good alternative for traditional tablets and liquid forms. Pediatric, geriatric, bedridden, and developmentally disabled patients are especially well suited for this alternative to traditional tablets. Medications used for treating nausea, allergies, migraines, arthritis, depression, and schizophrenia are already available as mouth dissolving tablets form.[7,8]

The aim of the present investigation is to develop Mouth Dissolving tablets taking terbutaline sulphate as a model drug to reduce the lag time and providing faster onset of action to relieve immediately acute asthmatic attack.

MATERIALS AND METHODS

Materials

Terbutaline Sulphate was obtained as a gift sample from CIPLA Pvt. Ltd. Ratlam, India. SSG, Croscarmellose Sodium and Crospovidone were obtained as gift samples from Signet Pharma. Microcrystalline cellulose, Mannitol mag. Stearate and talc, were received from Signet., Mumbai. All other excipient obtained as gift samples from BASF.

Drug-excipient compatibility studies

To study the compatibility of different excipients with Terbutaline Sulphate a mixtures were prepared by mixing the drug with each excipient separately in the ratio of 1:1 and stored in air tight containers. The solid admixtures were characterized using Fourier transform infrared spectroscopy (FTIR)[9]

Solubility profile of Tebutaline Sulphate

An excess quantity of drug was dissolved in 5 ml of solvent definite quantity of each investigated solvents at room temperature (25^0C) in tightly closed glass tubes. The increment of drug was added to each test tube until undissolved particles were seen even after shaking the glass tubes for 1 hour. The solubility of terbutaline sulphate at different solvents is reported in different media.[10]

Preparation of standard curve of Terbutaline Sulphate

10 mg of terbutaline sulphate was accurately weighed and transfer it into 100 ml volumetric flask. The drug was dissolved into distilled water and made up the volume upto 100 ml to obtain 100mcg/ml stock solution. The aliquot of 1, 2, 3, 4, 5, 6, 7, 8, 9, 10 ml of stock solution were transferred to a series of 10 ml volumetric flask and volume was made upto mark with phosphate buffer pH 6.8 to get the solution of different concentrations (µg/ml). The absorbance of these aliquots was measured at 277 nm. Then a graph was

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plotted by taking concentration on X-axis and absorbance on Y-axis which gives a straight line

Formulation design of tablets

Mouth Dissolving tablets of Terbutaline sulphate were prepared by direct compression method using drug, sodium saccharin, flavour, talc, magnesium stearate, mannitol and microcrystalline cellulose. Three different superdisintegrants SSG (sodium starch glycollate), Croscarmellose (Ac-Di-Sol/CCS), and Crospovidone (CCP), were used in different proportions.

The drug and excipients were passed through sieve (#80) to ensure better mixing. The powders were compressed using 8 station tablet punching machine (Model KMP-8, Kambert machinery company pvt. Ltd. Ahmedabad, India) equipped with 8mm concave punches.

Table 1: Composition of tablet of Terbutaline sulphate

Ingredients	Quantity (mg)							
	PF1	PF2	PF3	PF4	PF5	PF6	PF7	PF8
Terbutaline sulphate	5	5	5	5	5	5	5	5
Croscarmellose	2	6	6	2	2	2	6	6
Crospovidone	8	8	4	8	4	4	8	4
SSG	10	10	4	4	10	4	4	10
Mannitol	10.0	10.0	10.0	10.0	10.0	10.0	10.0	10.0
Sod. Saccharin	0.2	0.2	0.2	0.2	0.2	0.2	0.2	0.2
Flavours	2.0	2.0	2.0	2.0	2.0	2.0	2.0	2.0
Magnesium stearate	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0
Talc	2.0	2.0	2.0	2.0	2.0	2.0	2.0	2.0
MCC	q.s. to 100mg	q.s. to 100mg	q.s. to 100mg	q.s. to 100mg	q.s. to 100mg	q.s. to 100mg	q.s. to 100mg	q.s. to 100mg
Total	**100**	**100**	**100**	**100**	**100**	**100**	**100**	**100**

Evaluation parameters of the tablet Physical characterization

Hardness

Hardness indicates the ability of a tablet to withstand mechanical shocks while handling. The hardness of the tablet was determined using Monsanto hardness tester. It is expressed in kg/cm^2. Five tablets were randomly picked and hardness of the tablet was determined.

Weight variation test

The weight variation test is carried out in order to ensure uniformity in the weight of tablets in a batch. Twenty tablets were randomly selected and accurately weighed, in grams on an analytical balance

Friability Test

According to the BP specifications 10 tablets were randomly selected and placed in the drum of a tablet friability test apparatus (Electrolab, India). The drum was adjusted to rotate 100 times in 4 min. the tablets were removed, dedusted and accurately weighed. The percent weight loss was

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calculated.

Wetting time

A piece of tissue paper (12 cm X 10.75 cm) folded twice was placed in a small petridish (ID = 6.5 cm) containing 6 ml of Sorenson's buffer pH 6.8. A tablet was put on the paper, and the time for complete wetting was measured. Three trials for each batch were performed and the standard deviation was also determined.

Water absorption ratio, R was determined using following equation.

$$R = \frac{Wa - Wb}{Wa} \times 100$$

Where, Wa =Weight of tablet after water absorption

Wb = Weight of tablet before water absorption.

Disintegration Time

The test is carried out on the 6 tablets using the apparatus specified in IP distilled water at 37^0 C ± 2^0C was used as a disintegration media and the time in second taken for complete disinigration of the tablet with no palpable mass remaining in the apparatus was measured in seconds.

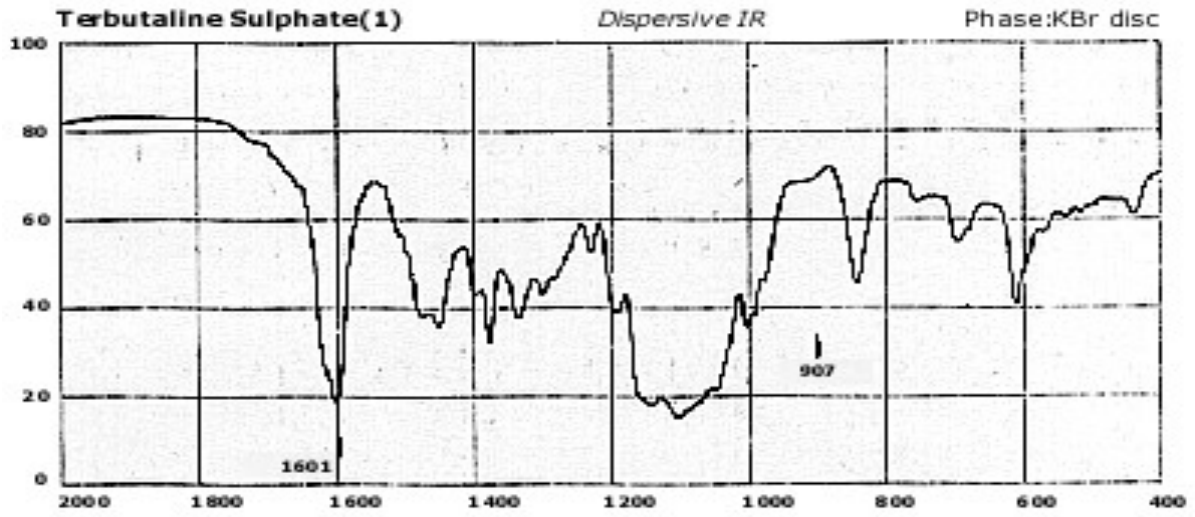
In vitro dissolution studies

In vitro dissolution studies for fabricated Fast Dissolving tablet is carried out by using USP XXIV paddle method at 50 rpm in 900 ml of Sorenson's buffer pH 6.8 as dissolution media, maintained at 37±0.5^{0}C. 10 ml aliquots was withdrawn at the specified time intervals, filtered and assayed spectrophotometrically. An equal volume of fresh medium, which was prewarmed at 37^{0}C is replaced into the dissolution medium after each sampling to maintain the constant volume throughout the test. Dissolution studies are performed in triplicate.

Results and Discussion

Compatibility Study

The Infrared spectra of Terbutalin Sulfate solid admixtures of drug and excipients were recorded between 400 and 4400cm^{-1} on FTIR. From the FTIR studies, no significant change occurred in the characteristics peaks of Terbutalin Sulfate in all the solid admixtures.



Fig, 1. IR spectrum of terbutaline sulphate (Standard), IP (1996)

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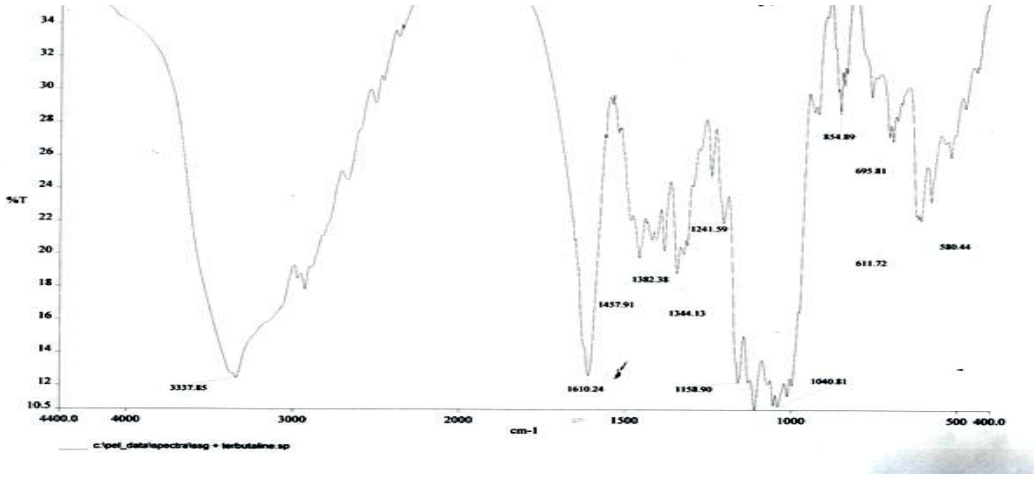

Fig 2 FTIR spectra of terbutaline sulphate with Crospovidone

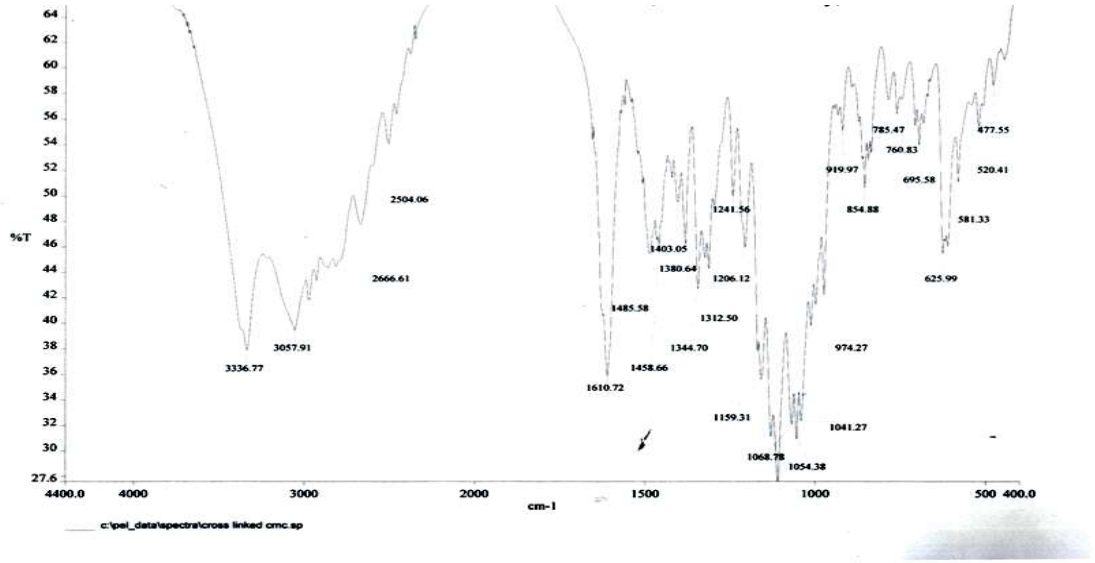

Fig 3.0 **FTIR spectra of terbutaline sulphate with sodium starch Glycolate**

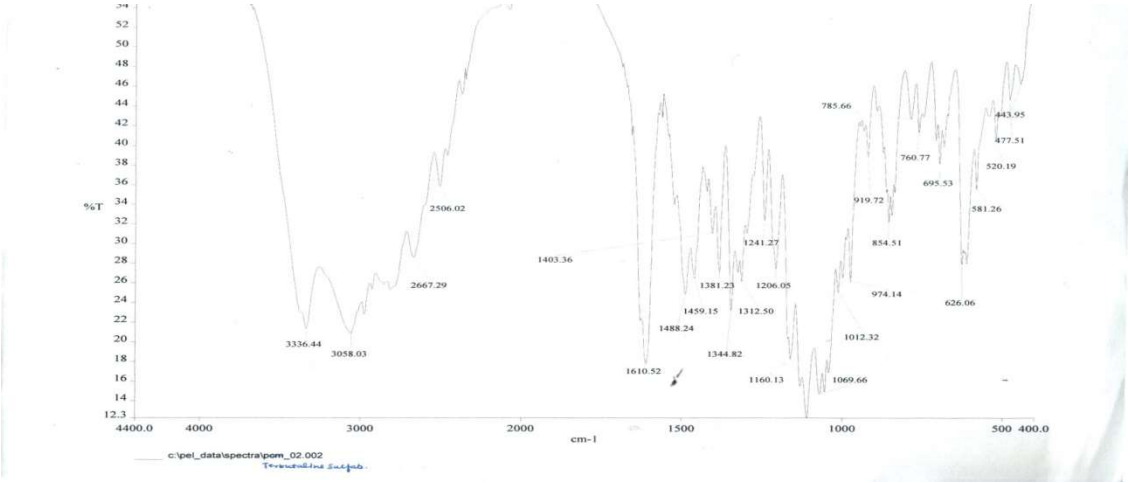

Fig 4.0 FTIR spectra of terbutaline with crosscarmellose

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Table. 2: Evaluations of Mouth dissolving tablets

S.N.	Hardness (kg/cm^2)	Friability (%)	Weight Variation (mg)	Water absorption (%)	Wetting time (sec)	Disintegration time (sec.)	% Drug release in 10 min.
1	2.8	0.63	98.63	75.6	20	150	99.26
2	3.5	0.66	99.31	72.3	22	180	102.26
3	2.9	0.61	97.13	73.5	16	80	97.76
4	2.5	0.62	97.97	72.6	11	120	98
5	3.2	0.62	97.51	74.8	17	124	98.5
6	2.1	0.61	97.32	70.8	10	60	95.55
7	2.4	0.65	98.5	75.4	16	130	98.88
8	3.4	0.64	98.05	80.5	18	150	99.5

Table 3: Solubility of Terbutaline sulphate in different solvents

S.N.	Solvents	SOLUBILITY
1	0.1NHCl	Freely soluble
2	Phosphate buffer 4.8	Freely soluble
3	Phosphate buffer 6.8	Freely soluble
4	Phosphate buffer 7.4	Freely soluble
5	Water	Freely soluble
6	Aq.0.1N HCl	Freely soluble
7	Ethanol	Freely soluble
8	Methanol	Freely soluble

Table 4: Calibration curve data of Terbutaline sulphate in pH 6.8

S. N.	Concentration ((µg/ml))	Absorbance
1	10	0.102
2	20	0.198
3	30	0.311
4	40	0.401
5	50	0.521
6	60	0.612
7	70	0.71
8	80	0.811
9	90	0.909

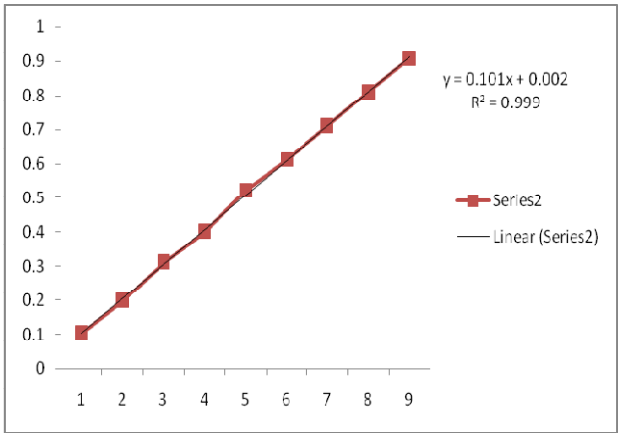

Fig 5: Calibration curve of terbutaline sulphate in pH 6.8

CONCLUSION

The aim of development of Mouth Dissolving 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 all the batches was released completely within 10 minutes of the dissolution study. The tablets disintegrated within 3 min under experimental in vitro

laboratory conditions Results, FTIR indicated that there is no incompatibility, can be used to manufacture the tablet formulation with desired disintegration time.

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