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Formulation and Evaluation of Orally Fast Dispersing Tablets of Terbutaline Sulphate

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ABSTRACT

The present research work was undertaken to develop mouth dissolving tablet of terbutaline sulphate with benefits to the patients. Superdisintegrants such as Crospovidone, Crosscarmellose and Sodium Starch Glycolate were used. A combination of two different diluents in various concentrations was used along with superdisintegrants. The tablets were prepared by direct compression method. The tablets were evaluated for hardness, friability, weight variation, wetting time, disintegration time and the selected formulation was compared with in vitro dissolution test. It was concluded that a mixture of diluents improves disintegrate rapidly and provide rapid onset of action as compare with conventional formulation.

Key-words: Terbutaline Sulphate, Superdisintegrants, mixture of diluents, direct compression.

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Introduction

Mouth dissolving tablets are a new and exciting alternative to traditional tablet and iquid medication dosages. 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. 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[1,2].

Mouth dissolving drug delivery systems (MDDDS) has been widely focused on by a number of researchers, these tablets are expected to dissolve or disintegrate in the oral region without drinking water. Mouth dissolving tablets are also called orally disintegrating tablets (ODTs), melt in-mouth tablets, porous tablets, oro-dispersible, quick dissolving and rapid disintegrating tablets[3,4.] Asthma is a disorder of variable intensity, typified by sentinel symptoms, airway obstruction, inflammation, and hyper responsiveness.[5] About 300 million people worldwide suffer from asthma, with 250,000 annual deaths attributed to the disease. It is estimated that the number of people with asthma will grow by more than 100 million by 2025.[6] Terbutaline Sulphate is used as a fast-acting bronchodilator which relaxes bronchial smooth muscle by selective action on β_2 receptors[7] it is used to prevent and treat wheezing, shortness of breath, and chest tightness caused by asthma, chronic bronchitis, and emphysema. It works by relaxing and opening the airways, making it easier to breathe.[8] Due to sore throat conditions, the patient experiences difficulty in swallowing a tablet type of dosage form. Thus, fast disintegrating tablets would serve as an ideal dosage form pediatric patients who find it difficult to swallow the conventional tablets and capsules.[9] hence an attempt was made for preparation of mouth dissolving tablet of Terbutaline Sulphate with an aim of providing rapid release and faster onset of the drug to relieve the bronchospasm.

Materials and Methods

Terbutaline sulphate was obtained as a gift sample from Medicamen Biotech Ltd, Haridwar. Mannitol, microcrystalline cellulose, sodium starch glycolate, crosspovidone, croscarmelose sodium were procured from CDH, New Delhi used as tablet excipients. Other excipients and chemicals used were of AR grade.

Formulation

Factorial design[6, 8]

To study all the possible combinations of all factors at all levels, a three-factor, two-level factorial design was constructed and conducted in a fully randomized order. The dependent variables measured were uniformity of weight, disintegration time, wetting time, friability and *in-vitro* dissolution study. The composition and responses of the 2^3 design are shown in Table 1. Three independent factors, the concentration of sodium starch glycolate(X_1), the concentration of crosscarmellose (X_2), and the concentration of crospovidone (X_3), were set at two different levels high and low levels of each factor were coded as +1 and -1, respectively. The range of a factor must be chosen in order to adequately measure its effects on the response variables. This design was selected as it provides sufficient degrees of freedom to resolve the main effects as well as the factor interactions. Table 2 represents the High and low concentration of superdisintegrants according to factorial design.

Formulation design
Study Type: Factorial **Runs:** 8
Design Type: 2 Level Factorial **Blocks:** No Blocks

Table. 1. Design of formulation by 2-level factorial design.

S.N	Factor 1	Factor 2	Factor 3
1	-1.00	1.00	1.00
2	1.00	1.00	1.00
3	1.00	-1.00	-1.00
4	-1.00	1.00	-1.00
5	-1.00	-1.00	1.00
6	-1.00	-1.00	-1.00
7	1.00	1.00	-1.00
8	1.00	-1.00	1.00

Formulation design of mouth dissolving tablets.[10]
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), Crosscarmellose (Ac-Di-Sol/CCS), and Crospovidone(CCP), were used in different proportions. The drug and excipients were passed through sieve (#80) to ensure uniform 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 3 represent the list and concentration and ingredients used to formulate the mouth dissolving tablets by direct compression.

Evaluation of compressed Terbutaline Sulphate MDT[11,14]
Twenty tablets were selected in a random and average weight was determined. Then individual tablets were weighed and the individual weight was compared with an average weight.Table 4 representing the observed values of various evaluation parameters.

General Appearance
The general appearance of a tablet, its visual identity and over all "elegance" is essential for consumer acceptance. General appearance includes tablet's size, shape, colour, presence or absence of an odour, taste, surface texture, physical flaws and consistency and legibility of any identifying marking.

Uniformity of weight
IP 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 weight. The weight variation test would be a satisfactory method of determining the drug content uniformity.

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

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 taken and the standard deviation was also determined.

Water absorption ratio, R was determined using following equation.

$$R = (Wa - Wb/Wa) \times 100$$

Where, Wa = Weight of tablet after water absorption

Wb = Weight of tablet before water absorption

In vitro dispersion time

In vitro dispersion time was measured by dropping a tablet in a beaker containing 50 ml of Sorenson's buffer pH 6.8. Tablets from each batch were randomly selected and *In-vitro* dispersion time was measured.

Friability

It is measure of mechanical strength of tablets. Roche friabilator is used to determine the friability by placed the preweighed tablets in the friabalator. Friabilator consist of a plastic chamber that revolves at 25 rpm, dropping those tablets at a distance of 6 inches with each revolution. The tablets were rotated in the friabilator for at least 4 minutes. At the end of test tablets were dusted and weighed, the loss in the weight of tablet is the measure of friability and is expressed in percentage as

% Friability = loss in weight / Initial weight X 100

Tablet hardness

Hardness of tablet is defined as the force applied across the diameter of the tablet until the tablet breaks. The resistance of the tablet to chipping, abrasion or breakage under condition of storage transformation and handling before usage depends on the hardness. Hardness of the tablet of each formulation was determined by Pfizer/Monsanto Hardness tester.

***In-vitro* dissolution studies**

In vitro dissolution studies for the tablets was carried out by 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 of the medium was withdrawn at the specified time intervals, filtered and assayed spectrophotometrically. An equal volume of fresh medium, prewarmed at 37 ^{0}C was added to the dissolution medium after each sampling to maintain the constant volume throughout the test.

The various kinetic treatments were given to the dissolution data. The in vitro dissolution data obtained were subjected to a zero order and first order kinetics, Higuchi model as well as Hixson Crowell Cube Root law to understand the release profile and release mechanism.

Results and Discussion

The present investigation was undertaken to fabricate and evaluate mouth dissolving tablets of Terbutaline Sulphate by the direct compression method using a mixture of diluents and superdisintegrant (Table 1). The results of micromeritic properties of the powder blends of drug and excipients are shown Table 2. The bulk density and tapped density values are within the limit they do not affect the compression of tablets. The angle of repose provides information about the flow properties of the powder blend. The angle of repose of all the formulations was identified between 24 to 28^0 it indicates good flow properties and can be used for direct compression. The results for evaluation of four different formulation batches of Terbutalin Sulphate mouth dissolving tablet prepared by direct compression method are shown in Table 4.

Percentage of weight variation was identified which were well in acceptable limit for uncoated tablets as per USP. Faster disintegration and rapid dissolution are the basic requirements of immediate release tablet hardness of the tablet is deciding factor of those two requirements. The tablets with more hardness show longer disintegration time and dissolution. The hardness of Terbutalin Sulphate mouth dissolving tablet was found to be in the range of 2.5-3.5 kg/cm^2. Friability of the tablet was found between 0.61-0.63%, the hardness and friability data indicates good mechanical resistance of tablets. *In vitro* disintegration time for different formulations of MDT tablets of Terbutaline Sulphate was identified. The formulation containing 1% concentration of super disintegrant (X_1-X_2) alone showed higher values of (82-84) seconds for *in-vitro* disintegration time. Formulations containing mixture of excipients including super disintegrant (X_3-X_4) the *in vitro* disintegration time was found to be (35 – 45) seconds. Both the formulations disintegration time is within the limit as per the US Pharmacopeia.

Table. 2. High and low concentration of superdisintegrants according to factorial designs.

List of Superdisintegrants	Higher level (+1) (in mg)	Lower level (-1) (in mg)
Sodiumstarchglycolate(X_1)	10	4
Crosscarmellose (X_2)	6	2
Crospovidone (X_3)	8	4

Table.3Formulation composition for mouth dissolving tablets prepared by direct compression: Batch 1 to Batch 8

Ingredients	Quantity in mg							
	B1	B2	B3	B4	B5	B6	B7	B8
Terbutaline sulphate	5	5	5	5	5	5	5	5
Mannitol	10	10.0	10	10.0	10	10.0	10	10.0
Sod. Saccharin	0.2	0.2	0.2	0.2	0.2	0.2	0.2	0.2
Flavours	2	2.0	2	2.0	2	2.0	2	2.0
Magnesium stearate	1	1.0	1	1.0	1	1.0	1	1.0
Talc	2	2.0	2	2.0	2	2.0	2	2.0
Sodium starch glycolate	4	10	10	4	4	4	10	10
Crosscarmellose	6	6	2	6	2	2	6	2
Crospovidone	8	8	4	4	8	4	4	8
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**

Table. 4.Evaluations of mouth dissolving tablets

S.No	Hardness (kg/cm^2)	Friability (%)	Weight Variation (mg)	Water absorption (%)	Wetting time (sec)	Disintegration time (sec.)	% Drug release in 10 min.
B_1	2.8	0.63	98.63	75.6	20	150	99.26
B_2	3.5	0.66	99.31	72.3	22	180	102.26
B_3	2.9	0.61	97.13	73.5	16	80	97.76
B_4	2.5	0.62	97.97	72.6	11	120	98
B_5	3.2	0.62	97.51	74.8	17	124	98.5

B_6	2.1	0.61	97.32	70.8	10	60	95.55
B_7	2.4	0.65	98.5	75.4	16	130	98.88
B_8	3.4	0.64	98.05	80.5	18	150	99.5

Eight batches of mouth dissolving tablets were prepared and evaluated for weight variation test, hardness, friability, water absorption ratio, in-vitro disintegration test & dissolution test. It was observed that all the tablets pass the test for weight variation and content uniformity. Hardness of all tablets was between 2.5 to 3.5 kg/cm^3, while the friability below 1%, all they have good mechanical strength. Water absorption ratio, & disintegration time of all batches were observed within 22 sec and 180 seconds respectively. It was found that as the concentration of sodium starch glycolate, and croscarmellose decreases, the disintegration time also decreases ,but when the concentration of sodium starch glycolate increase the disintegration time also increases, which may be because of gel formation. Tablets containing combination of sodium starch glycolate, croscarmellose & crospovidone showed 100% drug release within 10 minutes. It was observed that with the increase in concentration of superdisintegrants, the disintegration time decreased in following order: - Crospovidone > crosscarmellose > sodium starch glycolate.Faster dissolution was obtained when combination of superdisintegrants was used. Dissolution studies indicated, that tablets prepared by combination of three superdisintegrants showed rapid dissolution

Conclusion:

It can be concluded that the mouth dissolving tablets formulated by using higher concentration of the 3 superdisintegrants viz. sodium starch glycolate, crosscarmellose & Crospovidone at higher concentrations showed 100% drug release within 10 minutes. On the other hand at lower concentration of the superdisintegrants, disintegration time decreased.In comparision to the conventional tablets mouth dissolving tablets of terbutaline sulphate showed quick disintegration and dissolution and may have higher bioavailability. Such formulation may avoid first pass metabolism, enzyme degradation in GI tract and increase patient compliance. The present study reports successful formulation of mouth dissolving tablet of terbutaline sulphate.

References:

1. Abdelbary, G., Eouani, C., et al.Determination of the in vitro disintegration profile of rapidly disintegrating tablets and correlation with oral disintegration. Int. J. Pharm. 2005; 292, 29-41.
2. Avachat, A., Ahire, V. J. Characterization and evaluation of spray dried co-processed excipients and their application in solid dosage forms. Indian J. Pharm. Sci., 69(1), 2007; 85-90.
3. Ansel, H.C., Allen, L.V. Pharmaceutical dosage form and drug delivery systems. Eight edition, 2005; 166.
4. Banker, G.S., Rhodes, C.T., Modern pharmaceutics, fourth edition, 2002, vol-121 Marcel Dekker Inc. ,667.
5. Chakraborty, S., Khandai, M., Singh, S. P., Patra, N. C., Comparative study on effect of natural and synthetic superdisintegrants in the formulation of fast dissolving tablets. Int. J. Green Pharmacy. 2008; 2(1), 22-25.
6. Fini, A., Bergamante, V., Ceschel, G. C., Ronchi, C., Moraes, C. A. F. Fast dispersible/slow releasing ibuprofen tablets. European J. Pharm. and Biopharm. 2008; 69, 335-341.
7. Gohel, M., Patel, M., Amin, A., Agrawal, R., Dave, R., Bariya, N.,. Formulation design and optimization of mouth dissolve tablets of nimesulide using vacuum drying technique. AAPS PharmSciTech. 2004; 5(3), 1-6.

8. Gohel, M. C., Parikh, R. K., Brahmbhatt, B.K., Shah, A. R., Preparation and assessment of novel coprocessed superdisintegrant consisting of crosspovidone and sodium starch glycolate. AAPS PharmSciTech. 2007; 8(1), 1-7.
9. Gattani, S.G., Shiyani, B.G., Kakade, K. N., Patil, A.B., Surana, S.J., Formulation and evaluation of mouth dissolving tablet of ondansetron hydrochloride by using superdisintegrants. Indian Drugs. 2009; 46(1), 44-50.
10. Ghosh, T.K., Pfister, W.R., Drug delivery to the oral cavity, Drugs and the pharmaceutical sciences, Taylor & Francis. 2005; 18-68.
11. Jacob, S., Shirwaikar, A. A., Joseph, A., Srinivasan, K. K. Novel coprocessed excipients of mannitol and microcrystalline cellulose for preparing fast dissolving tablets of glipizide. Indian J. Pharm. Sci. 2007; 69(5), 633-639.
12. Kaushik, D., Saini, T. R., Dureja, H. Development of melt in mouth tablets by sublimation technique. J. Pharm. Research. 2004; 3(2), 35-37.
13. Kuno, Y., Kojima, M., Nakagami, H., Yonemochi, E., Terada, K. Effect of the type of lubricant on the characterstics of orally disintegrating tablets manufactured using the phase transition of sugar alcohol. European J. Pharm. and Biopharm. 2008; 69, 986-992.
14. Khan, S., Kataria, P., Nakhat, P., Yeole, P. Taste masking of ondansetron hydrochloride by polymer carrier systemand formulation of rapid disintegrating tablets. AAPS PharmSciTech. 2007; 8(2), 1-7.