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FORMULATION AND EVALUATION OF ORODISPERSIBLE TABLETS OF SALBUTAMOL SULPHATE

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ABSTRACT

Objective of the present work is to develop orodispersible tablets of Salbutamol sulphate to improve bioavailability, disintegration time, dissolution efficacy and patient compliance. Orodispersible tablets are the fast growing and highly accepted drug delivery system in now days mainly to improve patient compliance. Orodispersible tablets have number of advantages over conventional dosage forms, because of that Orodispersible tablets have emerged as an alternative to conventional dosage forms. Orodispersible tablets dissolve or disintegrates instantly on the patient tongue or buccal mucosa. Orodispersible tablets of solbutamol sulphate were prepared using superdisintegrants, ac di sol, sod.cmc, alginic acid, chitosan, mcc, as diluents by direct compression method. Twelve formulations were prepared using the superdisintegrants at lower, intermediate & higher concentration. Mannitol is used to enhance the organoleptic properties of tablets. Tablets were evaluated for uniformity of weight, hardness, friability, water absorption ratio, dispersion time, disintegration time and in vitro drug release. All the formulations showed disintegration time less than 33mins and drug release by dissolution (100% at the end of 10 mins).

INTRODUCTION: The tablet is the most widely used dosage form because of its convenience in terms of self- administration, compactness, and ease in manufacturing. However, geriatric and pediatric patients experience difficulty in swallowing conventional tablets, which leads to poor patient compliance.

To overcome this weakness, scientists also have developed innovative drug delivery systems known as melt in mouth or mouth dissolve (MD) tablets. These are novel types of tablets that disintegrate/ dissolve/ disperse in saliva. Their characteristic advantages such as administration without water, anywhere, anytime lead to their suitability to geriatric and pediatric patients. They are also suitable for the mentally ill, the bedridden, and patients who do not have easy access to water. The benefits, in terms of patient compliance, rapid onset of action, increased bioavailability, and good stability make these tablets poplar as a dosage form of choice in the current market. Drinking water plays an important role in the swallowing of oral dosage forms.

Often times people experience inconvenience in swallowing conventional dosage forms such as when water is not available. For these reasons tablets that can easily dissolve or disintegrate in the oral cavity have attracted a great deal of attention. Orodispersible tablets are not only indicated for people who have swallowing difficulties, Salbutamol sulphate is a Beta 2 receptor agonist widely used as bronchodilator to relieve acute as well as chronic attacks of asthma.

Asthma is a complex genetic disorder involving the interplay between various environmental and genetic factors. Objective of present study was to develop such as novel drug delivery systems for Salbutamol sulphate by simple & cost effective direct compression method. An attempt was made in the present work to formulate and evaluate Orodispersible tablets of Salbutamol sulphate.

The percentage of drug release was enhanced for the formulation containing Ac-Di- Sol (F11-F12), when compared with the other super disintegrants. The % of drug released in the case of Ac-Di-Sol (F10) was more when compared with the other two concentrations (F11 & F12).

MATERIALS & METHODS:

Materials: The materials used for preparing the orodispersible tablets were *ac di sol*, sod.cmc, alginic acid; chitosan was purchased from CDH chemicals from Bengluru. The model drug was Salbutamol sulphate obtained as a gift sample from Akums drugs Pvt. Ltd. Haridwar. All other ingredients used were of analytical grade.

Formulation of Orodispersible tablets: Tablets, each containing 20 mg Solbutamol sulphate were prepared as per composition given in Table1. The drug and excipients were passed through sieve (#80) to ensure the better mixing. Microcrystalline Cellulose was used as a direct compressible vehicle. Superdisintegrants like ac di sol, sod.cmc, alginic acid, chitosan. The powder was compressed using Rimek compression machine equipped with 8 mm round punch by direct compression technique. A minimum of 50 tablets was prepared for each batch.

Formulation designing: Four super-disintegrating agents are used at lower, medium & higher concentration. Twelve formulations were designed. Sodium Cmc used in concentration of 2.5%, 5%, 7.5%, Alginic Acid 2.5%, 5%, 7.5%, Chitosan 2.5%, 5%, 7.5%, Ac Di Sol 2.5%, 5%, 7.5%. Microcrystalline cellulose was used as diluent,which is also a superdisintegrants. Each formulation was composed of drug and excipients in various proportions. This design technique was used to optimized and obtain a better formulation with respect to in-vitro dispersion time.

Table 1:

Tablet Ingredients (mg)	F1	F2	F3	F4	F5	F6	F7	F8	F9	F10	F11	12
DRUG	5	5	5	5	5	5	5	5	5	5	5	5
CHITOSAN	5	10	15	-	-	-	-	--	-	-	-	-
SOD.CMC	-	-	-	5	10	15	-	-	-	-	-	-
Ac-Di-Sol	-	-	-	-	-	-	5	10	15	-	-	-
ALGINIC ACID	-	-	-	-	-	-	-	-	-	5	10	15
MCC	54.4	53.0	51.3	54.4	53.0	51.3	54.4	53.0	51.3	54.4	53.0	51.3
MANNITOL	127.2	123.8	120.1	127.2	123.8	120.1	127.2	123.8	120.1	127.2	123.8	120.1
MG.STEARAE	2	2	2	2	2	2	2	2	2	2	2	2
TALC	2	2	2	2	2	2	2	2	2	2	2	2
MENTHOL	4	4	4	4	4	4	4	4	4	4	4	4

Evaluation of Tablets: (Table 2 & 3)

1. **Weight variation Test:** Twenty tablets were selected at random, individually weighed and the average weight was calculated. The uniformity of weight was determined according to I.P. Specification. As per I.P. not more than two of individual weights would deviate from average weight by more than 5% and none deviates by more than twice that percentage [1].

2. **Hardness Test:** Tablets require a certain amount of strength or hardness and resistance to Friability to with stand mechanical shocks. The hardness of tablet was measured by Monsanto hardness tester and results were expressed in Kg/cm^2 [2].

3. **Friability Test:** The friability of the tablet was determined using Roche friabilator. It is expressed in percentage (%). Tables were initially weighed (W0) and transferred in to the Friabilator. The Friabilator was operated at 25 rpm for 4 minutes in which tablets are subjected to combined effect of shock and abrasion in a plastic chamber dropping the tablets at a height of 6 inch in each revolution [3].

The tablets were dedusted and weighed again (W). The % Friability was then calculated by;

$$\% \text{ Friability} = (W0 - W)/W \times 100$$

4. ***In-vitro*** **Dispersion Time:** *In vitro* dispersion time was measured by dropping a tablet in a measuring cylinder containing 6 ml of phosphate buffer pH 6.8 (simulated saliva fluid). The time for the tablet to completely disintegrate into fine particles was noted. Six tablets from each batch were randomly selected and *in vitro* dispersion time was performed [4].

5. ***In-vitro*** **Disintegration Time:** The disintegration time of the tablets was determined as per Indian Pharmacopoeia monograph. The time required for disintegration of six tablets from each batch placed in each tube of disintegration test apparatus were measured at 37±0.5°C using 900 ml of distilled water. The time required to obtain complete disintegration of all the six tablets was noted [4, 5].

6. ***In-vitro*** **Dissolution Studies:** *In vitro* drug release studies for the Melt-in- Mouth Tablets of Salbutamol sulphate was studied using dissolution test apparatus II USP XXVII model [Paddle type] for the fabricated batches with the rotation speed 50rpm using phosphate buffer pH 6.8 as the dissolution medium maintained at a temperature of 37±0.5°C. Samples were withdrawn at predetermined time interval and filtered through Whatman filter paper, diluted suitably and analyzed at 285nm for cumulative drug release using Schimadzu UV-Visible spectrophotometer. The dissolution experiments were conducted in triplicate [3, 4].

7. **Water Absorption Ratio:** A piece of tissue paper folded twice was placed in a small Petri dish containing 6 ml of water. A tablet was put on the paper & the time required for complete wetting was measured. The wetted tablet was then weighed [6].

TABLE 2: EVALUATION RESULTS OF TABLETS

Formulations	Weight variation (in mg)	Thickness (in mm)	Hardness (in Kg/cm^2)	Friability (%)	*In Vitro* Disintegration Time (sec.)	*In Vitro* Dispersion Time (sec.)	Water Absorption Ratio
F1	PASS	2.96	2.2	0.42	27	30	73.21
F2	PASS	3.0	2.6	0.32	23	27	74.43
F3	PASS	2.94	2.1	0.41	21	24	72.41
F4	PASS	2.89	2.3	0.23	24	27	72.51
F5	PASS	2.98	2.5	0.33	21	31	73.90
F6	PASS	2.91	2.0	0.37	19	30	77.67
F7	PASS	3.01	2.4	0.26	17	27	75.54
F8	PASS	3.02	2.6	0.29	19	23	78.88
F9	PASS	2.92	2.5	0.31	16	27	74.42
F10	PASS	2.88	2.1	0.21	14	18	80.12
F11	PASS	2.96	2.3	0.27	16	23	79.12
F12	PASS	2.99	2.3	0.31	15	19	75.62

TABLE 3: *IN VITRO* DRUG RELEASE OF FORMULATIONS

Formulations → / Time. ↓ (mins)	F1	F2	F3	F4	F5	F6	F7	F8	F9	F10	F11	F12
2	47.4	48.2	52.1	50.12	51	50.45	54.34	55.12	54.66	57.11	58.12	57.24
4	62	64.9	67.2	65.43	64.11	65.11	64.54	65.68	67.83	70.10	71.55	69.16
6	70.22	74.6	84.8	74	77	76.6	76.66	81.14	76.88	81.22	83.34	82.10
8	87.5	89.5	93.6	91.12	91.8	93.12	89.55	91.64	88.86	92.11	91.87	91.26
10	97.9	98.2	97.77	98.11	98.68	98.92	99.65	99.88	99.32	100.10	99.91	100.02

RESULT & DISCUSSION: Four super-disintegrating agents are used at lower concentration, medium & higher concentration. Twelve formulations were designed. SODIUM CMC used in concentration of 2.5%, 5%, 7.5%, Alginic Acid 2.5%, 5%, 7.5%, CHITOSAN 2.5%, 5%, 7.5%, Ac Di Sol 2.5%, 5%, 7.5%. Microcrystalline cellulose was used as diluent, which is also a superdisintegrants. The flow properties of the powdered blend for all the batches were found to be good and free flowing.

The weight variation, hardness and friability of all the formulated tablets were within the specified requirements. The disintegration times for the formulated tablets are less than (30secs). The in vitro dispersion times for all formulations were found to be within (33 secs). *In vitro* dissolution studies showed higher percentage of drug release for all the formulated batches (F1-F12). Formulation containing Ac-Di-Sol showed excellent in vitro disintegration time (14secs) and *in vitro* dispersion time (18 secs) as compared to other formulations. The optimum formula F10 released (100.10%) with in 10 mins.

Hence, the percentage of drug release was enhanced and reduced the time when compared with marketed product. The percentage of drug release was enhanced for the formulation containing *Ac-Di-Sol* (F11- F12), when compared with the other superdisintegrants. The % of drug released in the case of *Ac-Di-Sol* (F10) was more when compared with the other two concentrations (F11 & F12). Hence, Ac-Di- Sol (F10) was found to be better superdisintegrants for the formulation of Salbutamol sulphate orodispersible tablets when compare to other superdisintegrants used in the study.

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