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FORMULATION AND EVALUATION OF ORAL FAST DISSOLVING TABLET FOR ANTI-ASTHMATIC DRUG

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ABSTRACT

Objective: This research was aimed at to formulate and evaluate oral fast dissolving tablets of montelukast sodium using superdisintegrants at variable concentrations. **Methods:** In the present study, the oral fast dissolving tablets of *Montelukast Sodium* were formulated using direct compression method incorporating microcrystalline cellulose (MCC) as direct compressible diluents after finding encouraging results of prefomulation studies. Sodium starch glycol ate (SSG) and Crosprovidone were selected as superdisintegrants seeing their minimum dissolution time. Six formulations were prepared using varied concentrations of superdisintegrants. The investigations of these formulations were aimed to look into their influence on the disintegration time and dissolution rate of these tablets and other evaluation parameters were also evaluated. **Results:** Fast dissolving tablets of montelukast sodium were prepared with crosprovidone and SSG had a shorter disintegration time or dissolution time and gives the best pharmaceutical performance. The evaluation of formulations reflected good pre and post-compressive characteristics.

1) INTRODUCTION

Oral routes of drug administration have wide acceptance up to 50-60% of total dosage forms. Solid dosage forms are popular because of ease of administration, accurate dosage, self-medication, pain avoidance and most importantly the patient compliance.

United States Food and Drug Administration (USFDA) defined fast dissolving tablet (FDT) as "a solid dosage form containing a medicinal substance or active ingredient which disintegrate rapidly usually within a matter of seconds when placed upon the tongue". Fast dissolving drug delivery systems were first developed in the late 1970s as an alternative to conventional dosage forms for the pediatric and geriatric patient. These tablets are designed to dissolve or disintegrate rapidly in the saliva generally less than 60 seconds. To fulfill these medical needs, pharmaceutical technologists have developed a novel oral dosage forms known as orally disintegrating (dispersible) tablets (ODTs) or Fast disintegrating (dissolving) tablets (FDTs) or mouth melting tablets (MMTs) or mouth dissolving tablets(MDTs), immediate release tablets which disintegrate rapidly in saliva, usually in a matter of seconds, without the need to take water.[1]

Montelukast inhibits broncho-constriction due to antigen challenge. Montelukast Sodium is the selective leukotriene receptor antagonist of the cysteinyl leukotriene CysLT 1 receptor. The cysteinyl leukotriene's (LTC 4, LTD 4, and LTE 4) are products of arachidonic acid metabolism that are released from various cells, including mast cells and eosinophil's.[2] Drug bind to cysteinyl leukotriene receptors (CysLT) found in the human airway. Binding of cysteinyl leukotriene's to leukotriene receptors has been correlated with the pathophysiology of asthma, including airway edema, smooth muscle contraction, and altered cellular activity associated with the inflammatory process, factors that contribute to the signs and symptoms of asthma. Montelukast sodium binding to the CysLT 1 receptor is high-affinity and selective, preferring the CysLT 1 receptor to other pharmacologically important airway receptors, such as the prostanoid, cholinergic, or beta-adrenergic receptor. Montelukast inhibits physiological actions of LTD 4 at the CysLT 1 receptors, without any agonist activity.[3] Montelukast Sodium is a drug which was chosen as the best drug candidate for fast dissolving formulation because it fulfills all the required ideal characteristics for FDT's. Montelukast Sodium has various characteristics which are required for the FDT formulation like good stability & solubility in water, having low dose then 50 mg, having smaller molecular weight & having a shorter half-life. In this study, our main goal was to achieve the fast onset of action in the asthmatic attack. Montelukast Sodium is desired to depict the quick onset of action in the serious asthmatic attack. My work aims to determine the right superdisintegrant and also their optimum concentration which gives the maximum release of the drug.

2. MATERIALS AND METHODS

Materials:-Montelukast sodium was procured from Leben Pharma Ltd, Akola, India. Sodium starch glycol ate, Talc, and MCC were purchased from Concept Pharma, Aurangabad India. Crosprovidone was received from Leben Pharma Akola, India. Sodium saccharin was obtained from Zim Laboratories Ltd; Nagpur magnesium stearate was procured from, India. Zim Laboratories Ltd, Nagpur.

Formulation of fast dissolving tablets of montelukast sodium

Different formulations (F1 to F6) were prepared by direct compression technique (table-1). In this technique all the ingredients were weighed as specified in the formula (table-1). Drug, diluent, lubricant and disintegrates were passed through sieve # 40. Required quantities of Montelucast sodium and polymers such as Crospovidone, and Sodium starch glycol ate were mixed thoroughly Magnesium stearate was added as lubricant. Microcrystalline cellulose was used as diluent and talc was used as gliedent. Finally the powder mix was subjected to compression after mixing uniformly in a polybag. Prior to compression, the blends were evaluated for several tests. In all formulations, the amount of the Active ingredient is equivalent to 5 mg of montelukast sodium to made up to 100mg of tablet.

Table 1: Composition of oral fast dissolving tablets of montelukast sodium.

Name of Ingredients	Formulation Code With Their Quantity					
	F1	F2	F3	F4	F5	F6
Sodium Montelucast	5	5	5	5	5	5
Crosprovidone	5	10	15	-	-	-
Sodium Starch glycol ate	-	-	-	5	10	15
Microcrystalline Cellulose	81.4	76.4	71.4	81.4	76.4	71.4
Magnesium stearate	5	5	5	5	5	5
Sodium Saccharin	0.6	0.6	0.6	0.6	0.6	0.6
Talc	3	3	3	3	3	3

3. Pre compression Parameters

Prior to the compression, the powder blends are evaluated for their bulk and tapped density. From these values the compressibility was calculated. While the flow Properties of powder blend was access from the angle of repose. The evaluation Parameters was studied before and after addition of lubricant to check and compare the inherent flow properties of powders. 3

A. Bulk density

Calculated amount of the model drug was introduced in a 100ml graduated Cylinder. Powder level was noted without compacting Bulk Density was calculated using the following equation:[3]

Bulk density = M/Vo

M =Mass of the test sample

Vo =Unsettled apparent volume

It is expected in gm./ ml.

B. Tapped Density (Dr)

It is the ratio of total mass of powder to the tapped volume of powder. The tapped Volume was measured by tapping the powder to constant volume. It is expressed in gm. /ml and is given by

Dr= M\V1

Where, M is the mass of powder

V1 is the tapped volume of powder

C. Hausner Ratio

The Hausner ratio is a number that is used to correlate the flow ability of drug Substance.

$$\text{Hausner ratio} = \frac{\text{Tapped density}}{\text{Bulk density}}$$

D. Compressibility Index (Carr's index)

This parameter is the measure of propensity of powder to be compressed and reflect the relative importance of interparticulate interaction

Carr's Index= 100(TD-BD)/TD

- **Carr's index limit table:-table no.2.**

Carr's Index	Types of flow
5-15	Excellent
12-18	Good
18-23	Fair to Passable
23-35	Poor
35-38	Very poor
>40	Extremely poor

E. Angle of Repose:- Angle of repose is defined as the maximum angle possible between the Surface of a pile of the powder and horizontal plane. The frictional force in a loose Powder or granules can be measured by angle of repose.

Tan Ø = h / r,

Ø= tan-1(h/r)

Where, Ø is the angle of repose,

h is height of pile

R is radius of the base of pile

Different ranges of flow ability in terms of angle of repose are given in table no 3.

Angle of Repose	Flowability
<20	Excellent
20-30	Good
30-34	Passable
33-38	Poor
>40	Extremely poor

4. Post compression parameters

1. Hardness Test

The Hardness of the tablets was determined using Monsanto Hardness tester. It is expressed in Kg/cm2 three tablets were randomly picked from each formulation and the mean and Standard deviation values were calculated.[4]

2. Friability test

It is the phenomenon whereby tablet surfaces are damaged and/or show evidence of lamination or breakage when subjected to mechanical shock or attrition. The friability of tablets was determined by using Roche Friabilator. It is expressed in percentage (%). tablets were initially weighed (Initial) and transferred into friabilator. The friabilator was operated at 25 rpm for 4 minutes or run up to 100 revolutions. The tablets were weighed (Final). The percentage friability was then calculated by,[5]

$$F = \frac{W(\text{initial}) - w(\text{final})}{W(\text{initial})} \times 100 \text{ again}$$

% Friability of tablets less than 1% is considered acceptable.

3. Weight variation test

The tablets were selected randomly from each formulation and weighed individually To check for weight variation. The U.S Pharmacopoeia allows a little variation in the Weight of a tablet. The percentage deviation in weight variation is shown in table.[6]

Percentage deviation in weight variation; table no. 4.

Average Weight of tablet(mg)	Percentage deviation
80mg or less	10
80-250	7.5
More than 250	5

In all the formulations the tablet weight was more than130mg and less than 324 Mg, hence 7.5% maximum difference allowed.

4. Thickness and Diameter

Thickness of the 10 tablets was measure by using vernier caliper. It was expressed in mm,

5. Disintegration Time

In vitro disintegration time was determined using tablet disintegration tester, at 37c°+_2°containing 500ml of distilled water. A tablet was placed in each of the six tubes of the apparatus and one disc was added to each tube. The time in seconds taken for complete disintegration of the tablet with no palpable mass remaining in the mass was measured in seconds.[7]

6. In vitro dissolution studies

Dissolution was taken by using type-II apparatus of USP, by using 500ml of 0.1N HCI medium, the temperature of dissolution media was maintained at 37 +_0.5° C. The paddle rotation speed was kept at 50 rpm. Tablets was placed in the baskets containing 0.1N HCl and 5 ml samples were withdrawn predetermined time intervals and replaced with same dissolution media. This sample were withdrawn and analyzed by using UV spectrophotometer (Shimadzu 1800, Japan W 216 nm.[7]

Table no. 5: Parameters of In -Vitro dissolution Test for tablet.

Sr.No	Parameter	Detail
1	Apparatus	USP type II
2	Volume of medium	500ML
3	Temperature	37-+0.5C
4	Paddle speed	50rpm
5	Dissolution medium	0.1N HCl
6	Aliquot withdrawn	5ml

5) Pre-compression Evaluation

The angle of repose values varied from 25.95 to 29.39 degree°. Bulk densities of various formulations varied from 0.253 to 0.293 gm. /ml. The values obtained from Tapped density, Compressibility index and Hausner's Ratio was 12.85 to 2.633, 1.14 to 0.426 and 1.18 to 0.266 respectively and found be in range for the preparation of tablets, From these values, it was evident that these blends had good flow properties and excellent compressibility.

Formulation Code	Bulk Density (gm./cm3)	Tapped Density (gm./cm3)	Compressibility Index(%) ±S.D	Hauser's Ratio ± S.D	Angle Of Repose± S.D
F1	0.339± 0.0020	0.389± 0.0030	12.85±2.633	1.14±0.426	22.91±1.403
F2	0.321± 0.0020	0.381± 0.0045	15.74±2.829	1.18±0.266	26.62±0.528
F3	0.347± 0.0105	0.398± 0.0051	12.81±1.5354	1.14±1.311	27.05±0.959
F4	0.327± 0.0050	0.380± 0.0072	13.94±1.3345	1.16±1.535	28.45±0.720
F5	0.338± 0.0070	0.389± 0.0117	13.11±1.374	1.15±1.512	23.58±2.059
F6	0.348± 0.0050	0.402± 0.0062	15.51±2.338	1.15±1.447	22.52±0.371

6) Post Compression Parameters

The Hardness, thickness and friability of all the tablet formulations were observed in the range of 4.01 to 4.07 gm. /cm² 2.50 to 2.02 mm and 0.90 to 0.01 % w/w respectively. Weight variation was found within the specification of the I.P.11 limits of 7.5%. Average weight of 20 tablets of all six formulations was found in the range of 198.97 to 203.05 mg. Drug content of all the formulations was found in the range of 98.48 to 100.42% as per limits of I.P.

Evaluation of Post Compression Parameters

Formulation Code	Hardness (gm/cm3) ±S.D	Friability (%) ±S.D	Weight Variation(mg) ±S.D	Thickness of Tablets (mm) ±S.D
F1	4.1±0.1	0.95±0.011	0.10±0.7	2.50±0.01
F2	4.05± 0.4	0.45±0.010	0.102±0.7	2.40±0.02
F3	4.05±0.3	0.53±0.018	0.108±1.0	2.46±0.03
F4	4.2±0.1	0.40±0.016	0.110±0.4	2.29±0.02
F5	3.8±0.5	0.12±0.026	0.107±0.2	2.10±0.04
F6	4.7±0.4	0.80±0.167	0.103±1.2	2.81±0.01

Formulation Code	Drug Content ±S.D	Disintegration Time (sec)± S.D	Diameter(mm) ±S.D
F1	97.1±0.06	76.74±0.78	2.0±0.49
F2	98.3±0.07	68.00±2.44	2.0±0.20
F3	99.8±0.01	55.00±5.00	2.02±0.40
F4	86.2±0.79	90.0±2.62	2.0±0.52
F5	87.3±0.61	85.0±2.57	2.0±0.70
F6	99.4±0.11	60.0±2.05	2.20±0.56

7. In vitro Dissolution Study of Oral Fast Dissolution Tablet

Batch Time	% Drug Release at Different Time Interval					
	F1	**F2**	**F3**	**F4**	**F5**	**F6**
0	0	0	0	0	0	0
10	55.70±0.098	68.04±0.45	75.4±0.48	55.76±0.99	48.03±2.5	54.66±0.60
20	59.11±0.65	75.20±0.43	87.37±0.59	60.11±0.61	55.80±0.66	64.67±0.31
30	69.10±0.92	88.29±0.59	100.01±0.57	65.52±0.13	65.66±0.13	79.28±0.052
45	81.25±0.37	100.01±0.45		72.90±0.47	78.90±0.47	88.78±0.54
60	100.0±0.01			80.3±0.015	89.3±0.041	100.0±0.27
90				100.3±0.73	100.01±073	
120						

RESULT

It was observed that, their dissolution criteria is depends upon polymers. It was conclude that as the concentration of polymer increases then % drug release time of formulation decreases. In this formulation batch the concentration of crosprovidone is high then has given the fast drug release.

DISCUSSION

Cumulative % drug release of fast dissolving tablets (F1-F6) was found to be range (89.3±0.041 to 100.0±0.27). It was observed that Cumulative % drug release of dissolving tables depend on concentration of polymer (crosprovidone, SSG), Maximum cumulative %drug release was found 100.0±0.01to be for F3and prolong cumulative % drug release was F4.

CONCLUSION

The result obtained in this research work clearly shows that a promising potential of oral fast dissolving tablets of montelukast sodium containing crosprovidone, sodium starch glycol ate as a result of faster dissolution leading to possibilities of faster onset of action in asthma attack may be beneficial.

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