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Formulation and Evaluation of Fast Dissolving Tablet of Montelukast Sodium: Effect of Superdisintegrants

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Abstract **Original Research Article**

Montelukast sodium is a selective, orally active leukotriene receptor antagonist drug used in the treatment of asthma in adults and children. It is rapidly absorbed after administration with a mean bioavailability of 73%. There is a need to develop formulations which overcomes problems of Tablet as a dosage form, such as difficulty in swallowing, inconvenience in administration while travelling and dyspghagia. Hence in the present study an attempt has been made to prepare fast dissolving tablets of Montelukast sodium with enhanced dissolution rate. The tablets were prepared by direct compression method using with superdisintegrants. Direct compression is the most simple and economical method used in tableting. The simplicity of the direct compression process is apparent from a few steps involved in the manufacture of tablets as compared to wet granulation. The tablets were evaluated for hardness, drug content, friability and were found as per the specification. Drug content estimation showed that more than 95% of the drugs was present. The highest drug release was obtained with the formulation F9 containing higher concentration of super disintegrants such as Sodiun starch glycolate and Crosspovidone.

Keywords: Montelukast sodium, Fast dissolving tablet, superdisintigrants, direct compression.

INTRODUCTION

Montelukast sodium is a selective, orally active leukotriene receptor antagonist drug used in the treatment of asthma in adults and children. It is rapidly absorbed after administration with a mean bioavailability of 73% [1]. Convenience of administration and patient compliance are the important factor in the designing of dosage forms. Fast dissolving drug delivery systems generally dissolve or disintegrate within a minute, without water or chewing and include various dosage forms such as, tablets, logenzes, films/strips and microspheres etc [2]. Amongst the other dosage form, tablets are popular oral solid dosage forms due to its patient convienence, easy administration, stability, and compactness .Mouth dissolving drug delivery systems are suitable for the geriatric, pediatric, psychotic and for the patient suffering from dysphagia [3, 4]. Significance of this system includes accuracy of dosage forms, administration without water, easy handling and rapid onset of action [5]. Direct compression is the most simple and economical method used in tableting. The simplicity of the direct compression process is apparent from a few steps involved in the manufacture of tablets as compared to wet granulation [6].

The objective of the present study was to prepare rapidly disintegrating tablets of Montelukast sodium by direct compression process with the aim to enhanced dissolution rate and improved patient compliance. The basic approach used in the development of mouth dissolving tablets is the use of super disintegrants.

EXPERIMENTAL

MATERIALS AND METHODS

Montelukast sodium (obtained assample fromSnehal Pharmaceuticals Pvt. Ltd, Nagpur) Sodium Starch Glycolate, Crosspovidone, Talc, Magnesium Stearate, Microcrystalline Cellulose used were of Pharmacopeial grade.

Preparation of Montelucast Fast Dissolving Tablets

Fast dissolving tablets of Montelukast were prepared by direct compression method using 3^2 factorial design (Table-1). All the ingredients (as shown in Table-2) were powdered weight separately and passed through sieve no. 40 separately. Microcrystalline cellulose was used as diluent, talc as an antiadherent, and magnesium stearate as a lubricant. All the

ingredients were blended together to get uniform mixture. Then the blend was compressed to get tablets of 100 mg weight using rotary tablet machine [7].

Table-1: Factorial Design

Batch	Crosspovidone	Sodium Starch Glycolate
F1	-1	-1
F2	0	-1
F3	+1	-1
F4	-1	0
F5	0	0
F6	+1	0
F7	-1	+1
F8	0	+1
F9	+1	+1

Table-2: Composition of Fast Dissolving Tablet

Name of ingredient	Formulation Batches (Quantity in mg)								
	F1	F2	F3	F4	F5	F6	F7	F8	F9
Montelukast sodium	4	4	4	4	4	4	4	4	4
Crosspovidone	2	4	6	2	4	6	2	4	6
Sodium Starch Glycolate	2	2	2	4	4	4	6	6	6
Micro crystalline cellulose	77	75	73	75	73	71	73	71	69
Sodium Saccharine	10	10	10	10	10	10	10	10	10
Magnesium Stearate	2	2	2	2	2	2	2	2	2
Talc	3	3	3	3	3	3	3	3	3

Preformulation Studies

Preformulation studies were carried out to determine the purity of the drug and any evaluation could also help to known if there is any detoriation of drug. It involve the determination of melting point, ג max determination and determination of standard calibration curve of Montelukast.

Melting Point of Drug

Melting point determination of Montelukast by use in capillary tube method. Pure drug was placed in capillary tube which is fuse at one end and it is attached to the thermometer and dipped in capillary tube in liquid paraffin is added in Thiel's tube and heat the Thiel's tube above the burner and the temperature at which drug starts melting was noted.

Evaluation of Oral Fast Dissolving Tablets

Compressed tablets were then evaluated for hardness, Weight variation, disintegration, friability, and drug content.

Weight Variation

The Weight variation was determined by weighing 20 tablets using an electronic balance (Mettler Toledo) individually and collectively and calculating the average weight, and comparing the individual tablet weight to the average [8].

Tablet Hardness

The hardness of prepared tablets was determined by using Monsanto hardness tester. Three tablets from each formulation batch were tested randomly, and the average reading was noted. The hardness is measured in kg/cm^2 [9].

Tablet Friability

The friability of the tablets was measured in a Roche friabilator by using 10 tablets. The percentage friability of the tablets was measured as per the following formula [10, 11]:

$$\text{Percentage friability} = W_1 - W_2 / W_1 \times 100$$

Where,

W_1 = Intital weight of tablet.

W_2 = Final weight of tablet.

Drug Content Uniformity

Ten tablets were powdered and 10mg drug equivalent powder dispersed in phosphate buffer pH 6.8 and analyzed in UV. The absorbance of the sample preparations was measured at λmax 283 nm for Montelukast sodium [12].

Disintegration Test

The in-vitro disintegration test was performed by using disintegration test apparatus. The test is carried out for total 6 tablets and distilled water at 37°C ± 2°C was used as a disintegration media. The time taken for the complete disintegration of the tablets was noted [13, 14].

Dissolution Rate Study

In vitro dissolution studies were performed for the tablets (n = 6) using USP dissolution apparatus II ((LABINDIA, DISSO 8000) paddle type), at 50 rpm,

thermostatically maintained at temperature 37 ± 0.5^{0}C. Samples of dissolution fluid (1 ml) were withdrawn through a filter at different time intervals and assayed for Montelukastat 283nm [15].

RESULTS AND DISCUSSION

Physicochemical Properties

Melting point of montelukast sodium by capillary tube method was found to be 148°c. All the formulations were evaluated for weight variation, hardness, friability, thickness, disintegration and assay and their results are shown in Table-3.

Evaluation of Fast Dissolving Tablet

Uniformity of thickness

The Thickness of tablet ranged from 1.80±0.05-3.03±0.1 mm, all the batches of tablets showed less deviation in thickness.

Weight Variation Test

The Average percentage deviation in weight of 20 tablet of each batch was less than ±10. The tablets passed the USP limits.

Hardness and Friability test

Hardness of all formulations was between 3.7±0.6-5.2±0.1 kg/cm and this was found satisfactory and within desired specification. Percentage Friability of all batches range from 0.13- 0.96 % (within the limit <1%). The Hardness and Percent Friability indicates good mechanical strength of tablets.

Drug content uniformity:

Drug content of FDT of Montelukast was found to be between 86.3±0.50 and 99.8±0.01% as shown in Table-3.

Disintegration Time

The *in vitro* disintegration time for all the compressed tablets was determined and results of all formulations are given in Table-3. Formulations F9, show good disintegration and drug release at 20sec. All tablets disintegrated in less than 2 min.

Table-3: Post Compression Studies for Formulation of Fast Dissolving Tablets of Montelukast

Formulation code	Avg. Wt.(g) (n=10)	Thickness (mm) (n=3)	Hardness (kg/ cm²)	%Friability	% Drug content	Disintegration time (sec)	Dispersion time (min)
F1	0.107 ±0.7	2.50±0.01	5.2±0.1	0.96	98.1±0.07	82	1.15
F2	0.103 ±0.8	2.50±0.01	4.07±0.5	0.47	98.2±0.08	72	0.50
F3	0.109 ±1.0	2.47±0.03	4.05±0.4	0.54	99.8±0.01	52	1.25
F4	0.110 ±0.5	2.99±0.01	4.2±0.2	0.41	86.3±0.80	60	1.52
F5	0.107 ±0.4	1.80±0.05	3.9±0.6	0.13	88.3±0.71	48	1.36
F6	0.104 ±1.2	2.83±0.01	4.7±0.5	0.80	86.3±0.50	44	1.13
F7	0.107 ±0.9	3.03±0.1	4.8±0.3	0.81	94.4±0.12	42	1.29
F8	0.105 ±0.7	2.79±0.02	4.8±0.2	0.50	96.5±0.06	33	1.38
F9	0.103 ±0.8	2.4±0.05	3.7±0.6	0.87	99.8±0.01	20	1.27

In –vitro dissolution studies of Montelukast tablets in 6.8 pH Phosphate Buffer solution

It was observed from *in vitro* dissolution data, that an average of more than 75 % of montelukast, released from all the formulations within 20 min indicates that the tablet complies as per pharmacopoeial specifications as shown in Figure-1. This indicates quick delivery of drug for systemic absorption. The highest concentration of disintegrant showed faster dissolution rate. The highest drug release was obtained with the formulation F8 and F9 containing higher concentration of super disintegrants Sodiun starch glycolate and Crosspovidone.

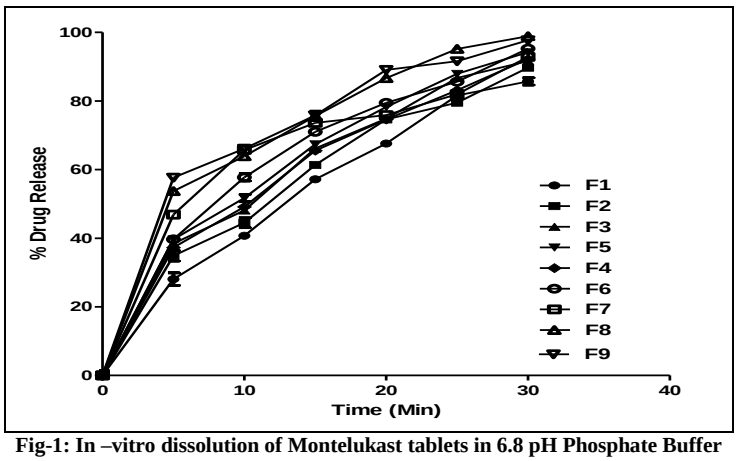

Fig-1: In –vitro dissolution of Montelukast tablets in 6.8 pH Phosphate Buffer

CONCLUSION

The aim of the research study was to design and develop a new formulation of orally disintegrating montelukast 4 mg tablet by using direct compression method and by choosing the various types of superdisintigrants. Montelukast sodium tablets containing superdisintegrants exhibit quick disintegration and improved drug dissolution. It can be concluded from the present work that the type and concentration of SSG and Crosspovidon as superdisintegrants affects the disintigration and dissolution parameter of the tablets. The highest drug release was obtained with the formulation F8 and F9 containing higher concentration of super disintegrants Sodiun starch glycolate and Crosspovidone.

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