Research Article ISSN: 2349-2678

Contents lists available at www.ijpba.in

International Journal of Pharmaceutical and Biological Science Archive

NLM (National Library of Medicine ID: 101738825)

Index Copernicus Value 2019: 71.05

Volume 11 Issue 3; May-June; 2023; Page No. 01-05

Formulation and Evaluation of Mouth Dissolving Tablets of Montelukast Sodium

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Article Info: Received: 20-02-2023 / Revised: 02-03-2023 / Accepted: 15-03-2023

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Conflict of interest statement: No conflict of interest

Abstract

Mouth dissolving tablets provide patient convenience as it does not require water as well as offer faster onset of action as compared to conventional oral tablets. The objective of the present study is to formulate mouth dissolving tablet of Montelukast sodium for improved patient compliance, faster onset of action and better management of Asthma. The prepared MDT were evaluated for various parameters i.e. shape and size, weight variation, thickness, hardness, friability, wetting time, disintegration time, drug content, dissolution test, accelerated stability studies etc. The prepared tablet passed all the evaluation tests. After comparing the results , it was concluded that formulation MT9 was selected as the best formulation among all. Finally, it can be concluded that mouth dissolving tablet of Montelukast sodium can be formulated using above excipients and method that disintegrate rapidly for improved patient compliance, faster onset of action and better management of Asthma.

Key Words: Patient compliance, Asthma, Accelerated stability studies.

Introduction

Mouth dissolving tablets are solid dosage forms containing drugs that disintegrate in the oral cavity within less than one minute leaving. The convenience of administration and improved patient compliance are important in the design of oral drug delivery system which remains the preferred route of drug delivery inspite of various disadvantages. One such problem can be solved in the novel drug delivery system by formulating “mouth dissolving tablets” (MDTs) which disintegrates or dissolves rapidly without water within few seconds in the mouth due to the action of superdisintegrant or maximizing pore structure in the formulation. These dosage forms are placed in the mouth, allowed to disperse or dissolve in the saliva. The release the drug as soon as they come in contact with the saliva, thus obviating the need for water during administration.[1,2]

Montelukast Sodium

Its molecular formula is $C_{35}H_{35}ClNNaO_3S$. Montelukast sodium is a leukotriene receptor antagonist (LTRA) used in maintenance treatment of asthma and to relieve symptoms ofseasonal allergies. It is usually administered orally. Montelukast blocks the action of leukotriene D4 on the cysteinyl leukotriene receptor CysLT1 in lungs and bronchial tubes by binding to it. This reduces the bronchoconstriction otherwise caused by the leukotriene, and results in less inflammation. Montelukast sodium bioavailability is 63%. It has extensive first-pass metabolism and show a very poor dissolution rate.[3]

Material and Method

Montelukast sodium, Cross-povidone, Sodium starch glycolate, Microcrystalline cellulose, Mannitol, Magnesium Stearate,Talc and Aspartame are the ingredients which were

utilized in the formulation of mouth dissolving tablets of montelukast sodium.

Evaluation of Mouth Dissolving Tablets

Shape and Size [4]

Diameter and thickness of prepared MDTs were determined using Vernier callipers. Three tablets from each formulation were taken and average was calculated.

Weight variation

This test is performed to check the uniformity of weight of the prepared tablets, as drug content is directly related to the weight of tablet. In this process, 20 tablets were weighed individually. The average weight of one tablet was calculated by taking average mean. As per IP, not more than two tablets deviate by more than the limit prescribed and none tablets deviate by more than twice of the limit prescribed in individual monograph.

Thickness variation [5]

Thickness of prepared MDTs was determined using Vernier callipers. Three tablets from each formulation were taken and average was calculated.

Hardness

Hardness of tablets is the amount of force needed to split them. Monsanto's hardness tester, Pfizer's hardness tester, and others are used to determine the tablet hardness. Hardness is measured in kilogrammes or pounds.

Both Monsanto and Pfizer hardness tester were used to determine the hardness of the formulated tablets. The hardness was calculated as kg/cm2. Three tablets from each formulation were taken and average was calculated.

Friability [6]

The friability of the tablet is determined using the friability test instrument. Friability is used to determine the amount to which tablets break during physical stress situations such as packaging, handling, transportation, and so on. The % weight reduction is estimated by comparing the pre- and post-operative weight of 20 tablets.

The Roche friabilator was used to measure friability of the formulated tablets. Weight of 20 tablets was measured and placed in the friabilator chamber. The friabilator was rotated at speed of 25 rpm for 4 min. After completion of 100 revolutions, the tablets were weighted again and % weight loss is calculated, which corresponds to friability.

$$\% \, Friability = \frac{Initial\ weight - Final\ weight}{Initial\ weight} \times 100$$

Wetting time [7]

The wetting time was calculated by placing the tablets in Petri dish containing wet tissue paper. Wet tissue was placed in a petri dish and the tablet was placed over it. The time required for complete wetting of tablets was noted.

Disintegration time [8]

Disintegration time of mouth dissolving tablets was determined using the disintegration test apparatus. One tablet was kept in each tube of the disintegration test apparatus. Phosphate buffer pH 6.8 was used to determine disintegration time at 37°C. The time taken to disintegrate all six tablets was noted as disintegration time.

Drug content [9]

The drug content was calculated by triturating ten tablets in a mortar with pestle to get fine powder. Powder equivalent to weight of one tablet was taken and was dissolved in distilled water. Measure the absorbance of diluted sample of MS at 283 nm using UV-Visible Spectrophotometer. The drug content was calculated by using standard calibration curve.

Dissolution Test

Dissolution testing measures the extent and rate of solution formation from a dosage form. The dissolution of a drug is important for its bioavailability and therapeutic effectiveness. Dissolution of prepared mouth dissolving tablets was determined in phosphate buffer ph 6.8 using paddle apparatus, 50 RPM at 370C.

Accelerated Stability Studies [10]

Short term accelerated stability studies of the selected formulations were carried out at400C/75%RH over a period of 3 months. The MDTs were wrapped with aluminium foil, and stored in humidity controlled oven for 3 months. Samples were analysed for residual drug contents at time interval of

30days.Disintegration time of mouth dissolving tablets was determined using the disintegration test apparatus. One tablet was kept in each tube of the disintegration test apparatus. Phosphate buffer pH 6.8 was used to determine disintegration time at 37°C.The time taken to disintegrate all six tablets was noted as disintegration time.

Results and Discussion:

Evaluation parameters: shape, diameter, and thickness, average Weight:

All the tablets prepared and evaluated parameters like shape, diameter, thickness, average weight. They were round in shape. Diameter was found to be 8.00±0.01 mm to 8.05±0.05 mm and thickness was found to be 3.20±0.01mm to 3.23±0.02 mm for all the formulations. None of the tablet deviated by the limit prescribed (5%). Therefore, the prepared tablets pass the test for weight variation.

Table No. 1: Evaluation parameters: shape, diameter, thickness, average weight.

Formulation	Shape	Diameter(mm)	Thickness(mm)	Average weight (mg) (Mean±S.D.*)
MT1	Round	8.01±0.03	3.21±0.02	152.70±1.30
MT2	Round	8.05±0.05	3.20±0.02	149.40±1.60
MT3	Round	8.02±0.02	3.22±0.03	155.10±1.90
MT4	Round	8.04±0.03	3.23±0.02	152.80±1.59
MT5	Round	8.02±0.04	3.21±0.01	151.60±1.68
MT6	Round	8.01±0.02	3.20±0.04	148.20±1.85
MT7	Round	8.02±0.02	3.22±0.02	154.20±1.75
MT8	Round	8.03±0.04	3.21±0.04	151.90±1.65
MT9	Round	8.00±0.01	3.20±0.01	150.60±1.32

Table No. 2: Evaluation parameters: Average hardness, friability, wetting time, disintegration time, percentage drug content.

Formulation	Average hardness (kg/cm^2) (Mean±S.D.*)		Friability (%)	Wetting time (second)	Disintegration time (Sec.)	% Drug Content (Mean±S.D.*)
	Monsanto type	Pfizer type				
MT1	4.5±0.1	4.3±0.2	0.56±0.07	89	110±6	97.35±1.53
MT2	4.7±0.2	4.5±0.1	0.46±0.02	75	92±7	96.70±2.41
MT3	4.6±0.3	4.7±0.6	0.34±0.05	63	78±4	96.80±2.24
MT4	4.5±0.2	4.6±0.4	0.56±0.04	66	84±5	96.48±1.20
MT5	4.8±0.3	4.9±0.5	0.45±0.06	72	76±4	96.40±2.80
MT6	4.6±0.3	4.5±0.5	0.34±0.02	81	52±3	96.90±1.64
MT7	4.7±0.4	4.6±0.4	0.45±0.03	65	74±5	95.25±3.42
MT8	4.6±0.6	4.5±0.3	0.38±0.05	53	46±6	96.40±2.14
MT9	4.4±0.7	4.4±0.5	0.23±0.02	45	30±2	98.90±1.01

The average hardness of prepared tablets was found to be 4.4 – 4.9 kg/cm2, which are within the standard limits. It may be inferred that hardness is optimum for mouth dissolving tablets.The friability of prepared tablets was found to be 0.23±0.02 to 0.56±0.07%, which are less than the standard limits (1%). It may be concluded that the prepared mouth dissolving tablets pass the friability test.The wetting time of prepared tablets was found to be 45 - 89 second, which are optimum for mouth dissolving tablets. Formulation MT9 showed minimum wetting time(43 second) among all the formulations.The Disintegration time of prepared tablets was found to be 30 seconds – 110 seconds, which is optimum for mouth dissolving tablets. Formulation MT9 showed minimum Disintegration time 30 Seconds among all the formulations.The % drug content of prepared tablets was found to be 95.25±3.42 to 98.90±1.01%, which is within the prescribed limits. The acceptable limit of Montelukast

content as per I.P is 90 to 110%. The results revealed that the content of Montelukast sodium was within the acceptable limits in all the formulations.

Dissolution Test

Table No. 3: Dissolution profile of formulations

Time (Min.)	Cumulative % drug release of formulations								
	MT1	**MT2**	**MT3**	**MT4**	**MT5**	**MT6**	**MT7**	**MT8**	**MT9**
0	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
1	7.56	8.28	14.40	9.00	14.76	18.36	16.20	19.44	26.64
3	19.09	20.53	29.18	21.61	29.54	31.70	30.26	32.42	43.59
5	29.91	31.71	38.93	32.43	39.65	41.46	40.73	42.54	51.56
7	36.42	37.51	45.81	38.23	46.17	47.98	47.26	50.86	62.78
9	44.74	45.83	55.58	46.91	55.94	57.75	56.67	62.80	73.28
11	56.31	57.76	63.20	58.84	63.57	65.38	64.29	71.51	81.65
13	61.42	65.74	68.67	66.11	69.04	77.69	70.12	80.59	92.90
15	65.80	73.02	77.75	73.74	78.47	84.62	79.56	88.60	99.84

Dissolution of Montelukast sodium starts immediately when the tablet is added to the dissolution media. The drug release of formulation MT1 to MT9 was found to be 65.80 to 99.84% at 15 minutes. The acceptable in vitro dissolution limit for Montelukast sodium as per IP is NLT 80% of drug release at 30 minutes. Among the all formulations, formulation MT9 containing high concentration of superdisintegrants showed highest dissolution rates at the end of 15 minutes.

Accelerated Stability Studies:

Table No. 4: Drug content of prepared MDT at accelerated conditions

Storage Conditions: (40^0 C ± 2^0 C at 75% RH ± 5% RH)				
Parameters	**Initial Period**	**1st Month**	**2nd Month**	**3rd Month**
Physical appearance	Off white, round	Off white, round	Off white, round	Off white, round
Weight variation (mg)	150.60±1.32	150.60±1.11	150.10±1.26	150.00±2.13
Thickness (mm)	3.20±0.01	3.20±0.01	3.20±0.01	3.20±0.01
Hardness (Kg/cm^2)	4.4±0.56.15	4.4±0.2	4.3±0.2	4.3±0.4
Friability (%)	0.23±0.02	0.23±0.05	0.24±0.06	0.25±0.06
Wetting time (Sec.)	45	45	46	47
Disintegration time (Sec.)	30±2	32±2	34±3	39±1
Drug content %	98.90±1.01	98.90±1.01	98.78±0.12	98.70±0.20
In vitro drug release (%)	99.84	99.64	98.56	98.13

After 3 months of stability studies at 40°C ± 2°C / 75% RH ± 5%, the results in the above table given that the optimized formulation MT9 had shown satisfactory stability. Only there were minimal deviations which are acceptable.

Conclusion

The objective of the present study is to formulate mouth dissolving tablet of Montelukast sodium for improved patient compliance, faster onset of action and better management of Asthma. All the prepared mouth dissolving tablets were found suitable for various evaluation parameters of mouth dissolving tables. After comparing the results (particularly disintegration time and dissolution profile), it was concluded that formulation MT9 was selected as the best formulation among all. Finally, it can be concluded that mouth dissolving tablet of Montelukast sodium can be formulated using above excipients and method that disintegrate rapidly for improved patient

compliance, faster onset of action and better management of Asthma.

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