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Research Article

Formulation and *In-vitro* Evaluation of Chewable Tablets of Montelukast Sodium

Laxman Devkota, Bhupendra Kumar Poudel*, Junu Khatri Silwal

Institute of Medicine (IOM), Tribhuvan University, Nepal.

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ABSTRACT

The objective of the present study is to develop chewable tablets containing different pharmaceutical compositions with simple manufacturing procedures using different excipients. Mannitols, L-HPC 11, Aspartame, Crospovidone, Crospovidone, Aerosil, and Magnesium Stearate are used as excipients for effective formulation of anti-asthmatic drug Montelukast. Montelukast is a selective, orally acting leukotriene receptor antagonist that is used for the treatment of asthma and seasonal allergic rhinitis. Montelukast chewable tablets were prepared by Direct Compression methods using suitable excipients. The chewable tablets were better presented using artificial sweetener Aspartame as flavouring agent. A total of forteen formulations were prepared and the granules were evaluated for pre-compression parameters. The formulated tablets were evaluated for post-compression parameters .The results showed that all the physical parameters were within the acceptable limits. The *in vitro* release study of all the formulations showed good release. The study concludes that aforementioned excipients can be used to design chewable montelukast sodium tablets.

Key Words: Chewable Tablets, Mannitol, Crospovidone, Aerosil, Magnesium Stearate.

INTRODUCTION

Today in the world of pharmacy around 90% of the tablets manufactured are ingested orally[8]. Administration of drugs through oral route is the most common and the easiest way to administer a drug. However, pediatric, geriatric and bedridden patient shows inconvenience swallowing conventional tablets or capsules due to difficulties in swallowing with lesser amounts of water with the medication, unable to tolerate the taste of many drugs when formulated as liquid dosage forms, resulting in poor patient compliance. The rationalized approach in case of medication leads to the development of chewable tablets. These are formulated and manufactured so that they may be chewed in the mouth producing a pleasant tasting residue in the oral cavity that is easily swallowed and does not leave a bitter a unpleasant taste. Chewable tablets are the tablets which are required to be broken and chewed in between the teeth before ingestion. These tablets are given to the children who have difficulty in swallowing and to the adults who dislike swallowing. Successfully tablet formulation development involves the careful selection of ingredients in order to manufacture a robust solid dosage form. Choosing the appropriate excipients to perform a specific function in a tablet formulation, such as disintegration or lubrication can be critical to achieving acceptable manufacturing performance. Sweeteners, both naturally occurring and synthetic, are one type of functional excipients commonly used in chewable tablet formulations to mask unpleasant tastes and facilitate pediatric dosing[1]. Ideally chewable formulations should have smooth texture upon disintegration, pleasant taste and no bitter or unpleasant after taste. Upon chewing, they are broken down in the mouth and release their ingredients in the process and therefore, do not have much lag time as required for the disintegration of tablets before absorption from stomach[2]. Montelukast is an oral leukotriene receptor antagonist that is used for the treatment of asthma and seasonal allergic rhinitis. Leukotrienes are a group of naturally occurring chemicals in the body that promote inflammation in asthma and seasonal allergic rhinitis. It is used for the treatment of asthma, seasonal allergic rhinitis, and prevention of exercise induced bronchospasm and begins working after 3 to 14 days of therapy. It should not be used for the treatment of an acute asthmatic attack. The recommended dose of montelukast in adults is 10 mg daily for treating asthma and allergic rhinitis and 10 mg two hours before exercising for prevention of exercise induced bronchospasm. Montelukast should be taken in the evening with or without food when used for asthma or allergic rhinitis. The 4 and 5 mg tablets are used in children**6**. Children find it difficult to swallow the normal tablets of Montelukast. So in order to avoid this problem, chewable tablets are most preferable. Hence it was decided to formulate montelukast chewable tablet to improve the compliance in children. Additionally, chewable tablets facilitate more rapid release and hence more rapid absorption of active ingredients and provide quick onset of action[3].

MATERIALS AND METHODS

**Author for Correspondence*

Table 1:Formulations prepared by direct compression method

SN	Ingredients	F1 mg	F2 mg	F3 mg	F4 mg	F5 mg	F6 mg	F7 mg	F8 mg	F9 mg	F10 mg	F11 mg	F12 mg	F13 mg	F14 mg
Intergranular excipients															
1	Montelukast	5	5	5	5	5	5	5	5	5	5	5	5	5	5
2	Mannitol	219	214	209 .5	205	200	198	194 .5	189 .75	185 .5	181. 5	178. 5	175	172. 5	
3	Cellulose, Microcrystalline (ph 101)	42	45. 5	48. 5	51. 5	55	55. 5	57. 5	60. 75	63. 5	66	67.5	69.5	71.5	
4	Cross carmilose sodium	1.7 5	2.5	3.2 5	4	4.7 5	5.5	6.2 5	7	7.7 5	8.5	9.25	10	10.7 5	11.5
Granulating fluid															
5	HPMC	6	6	6	6	6	6	6	6	6	6	6	6	6	6
6	Purified water	qs	qs	qs	qs	qs	qs	qs	qs	qs	qs	qs	qs	qs	qs
Extragranular Excipients															
7	Cellulose, Microcrystalline (ph 101)	20	20	20	20	20	20	20	20	20	20	20	20	20	20
8	Cross carmilose sodium	1.7 5	2.5	3.2 5	4	4.7 5	5.5	6.2 5	7	7.7 5	8.5	9.25	10	10.7 5	11.5
9	Aspartame	1.5	1.5	1.5	1.5	1.5	1.5	1.5	1.5	1.5	1.5	1.5	1.5	1.5	1.5
10	Magnesium stearate	3	3	3	3	3	3	3	3	3	3	3	3	3	3
	Total	300	300	300	300	300	300	300	300	300	300	300	300	300	300

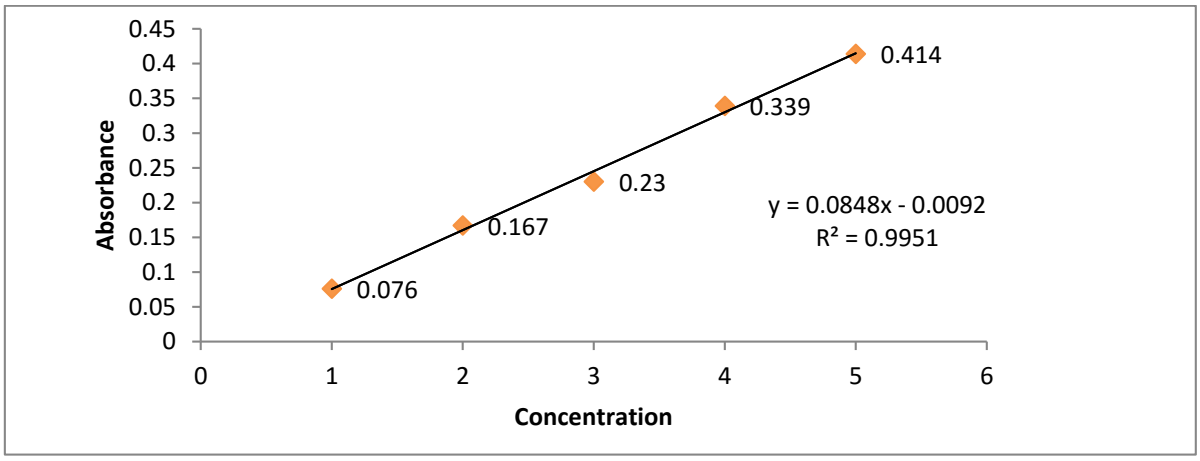

Figure. 1: Calibration curve of Montelukast sodium

Montelukast sodium API and standard were obtained as a gift sample from Lomus Pharmaceutical Pvt. Ltd. All other reagents and chemicals were of analytical grade obtained from the university laboratory.

Chewable tablets containing 10mg of Montelukast were prepared with a total tablet weight of 150 mg by Direct Compression Method. Exactly Weighed quantities of Mannitol (intragranular), Montelukast, L-HPC 11 and aspartame were weighed and were pass through #30 mesh. Diluents were weighed according to ratio and sifted through #30mesh and added to the above and mixed for 5 m in a poly bag. Shift the dried granules through #30 mesh along with the remaining quantity of Mannitol (extra granular) Superdisintegrant crospovidone weighed was also added. The final blend was mixed thoroughly for 2-3 minutes in polybag; tablets were compressed in 7 mm round flat punches. The formulation is:

Evaluation of Tablets[4]

The tablets were evaluated for their physicochemical parameters such as weight variation, thickness, friability, drug content, and in-vitro dissolution.

Weight Variation

For the determination of weight variation of each batch, tablets were randomly sampled and individual weight of 20 tablets was taken in analytical balance. Mean ± standard deviation (SD) was calculated.

Thickness

From randomly sampled tablets, thickness of 10 tablets was measured individually using digital vernier caliper. Then mean ± SD was calculated

The study of precompressional parameters: Angle of repose, Bulk density, Tapped density, Compressibility Index and Hausner's ratio is as:

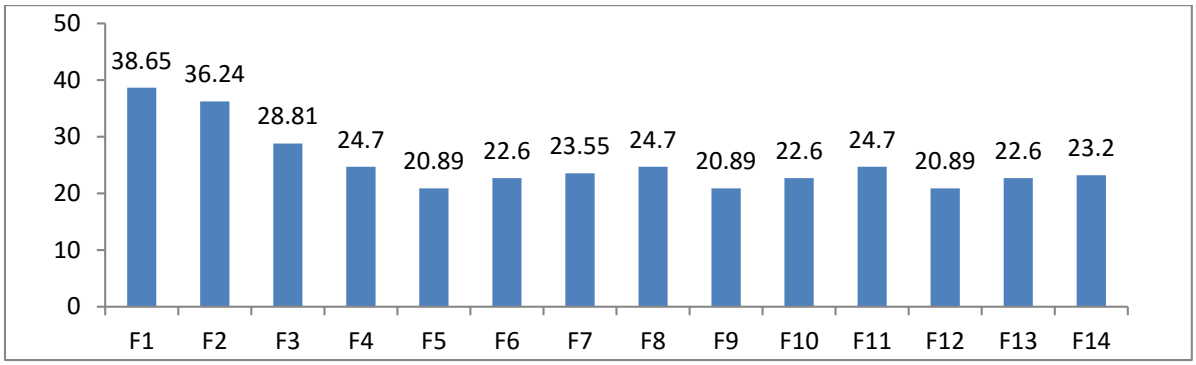

Figure 2: Angle of repose of formulations

As shown above, the maximum angle of repose was of formulation F1 with 38.65 and least of F5 with 20.89.

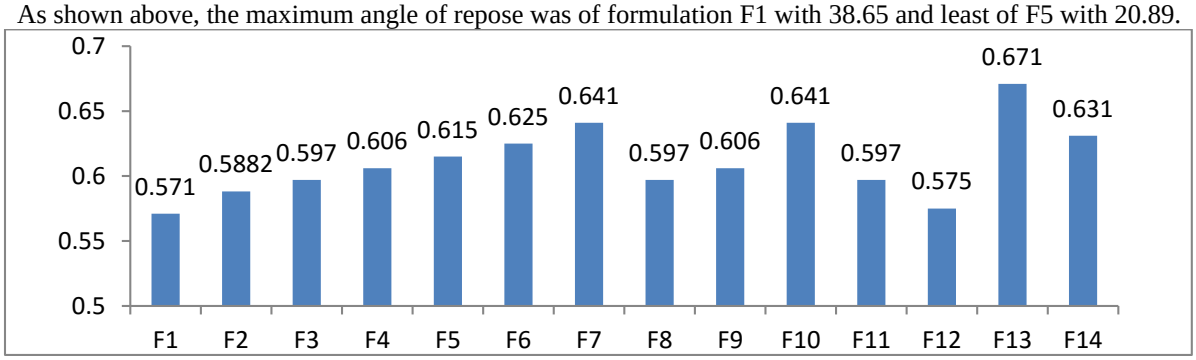

Figure 3: Bulk density of formulations

As shown above, the maximum bulk density was of formulation F13 with 0.671 and least of F1 with 0.571.

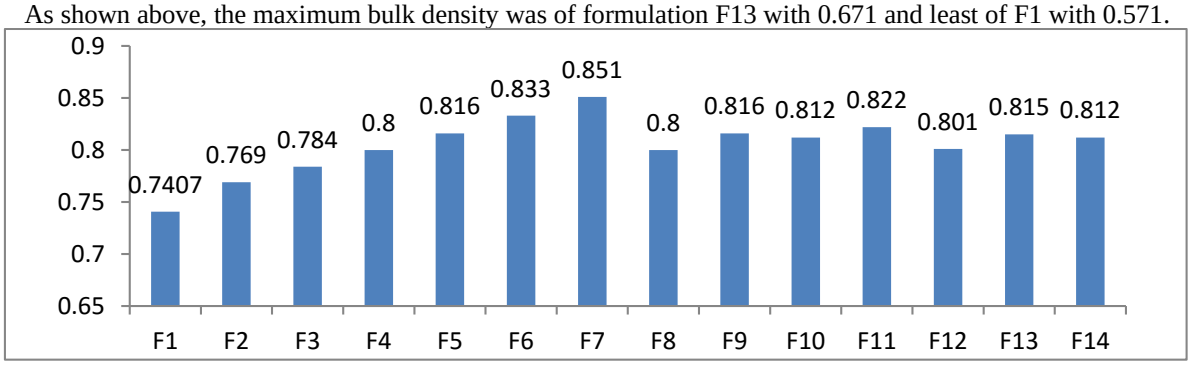

Figure 4: Tapped density of formulations

As shown above, the maximum tapped density was of formulation F7 with 0.851 and least of F1with 0.7407.

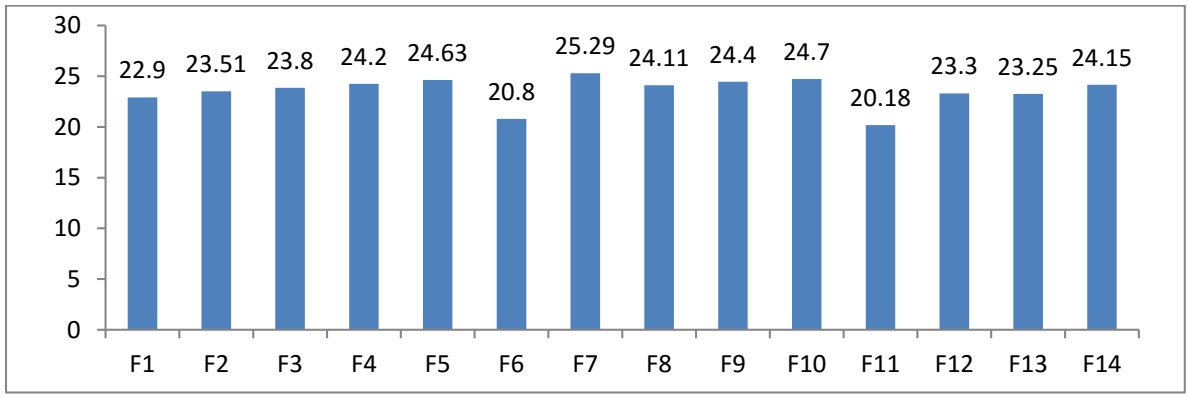

Figure 5: Compressibility index of formulations

As shown above, the maximum compressibility index was of formulation F7 with 25.29 and least of F11 with 20.18

Hardness

Hardness of 10 tablets was measured individually using pre-calibrated digital hardness tester. Then mean ± SD was calculated.

Friability

Twenty tablets were weighed in a balance having readability of 1 mg. These tablets were transformed into a friabilator set 100 revolutions. After the completion of revolution dust was removed completely, weighted again in the same balance and percentage loss was calculated.

Preparation of Calibration Curves

Various dilute solution of Montelukast sodium concentration ranging in ppm was prepared in water. The response of individual solution was measured at the maximum absorbance wavelength in UV Visible spectrophotometer. Calibration curve were prepared by

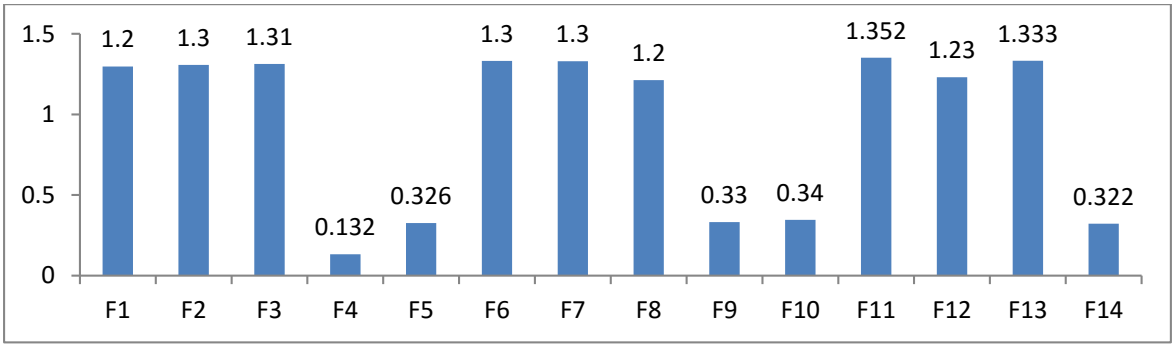

Figure 6: Hausner's ratio of formulations

As shown above, the maximum Hausner's ratio was of formulation F11 with 1.352 and least of F4 with 0.132

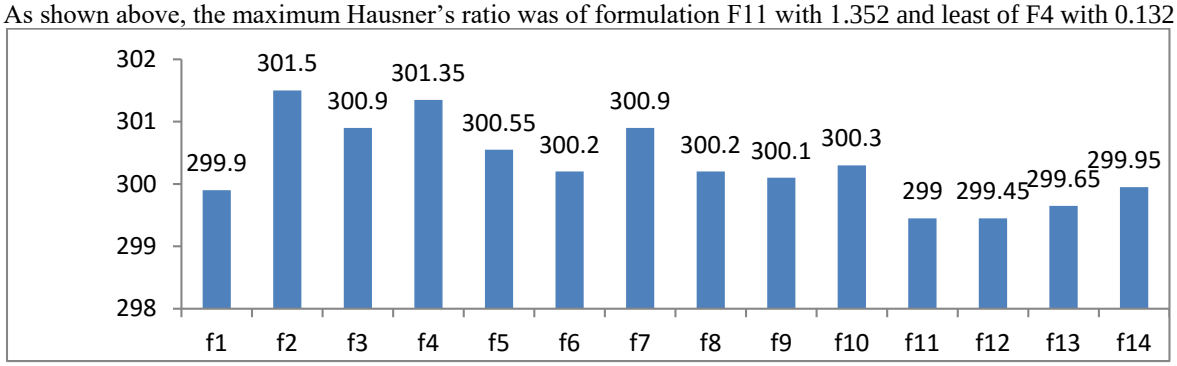

Figure 7: Average weight of all the tablets.

Maximum weight was of F2 301.5 and minimum of F1 299.9.

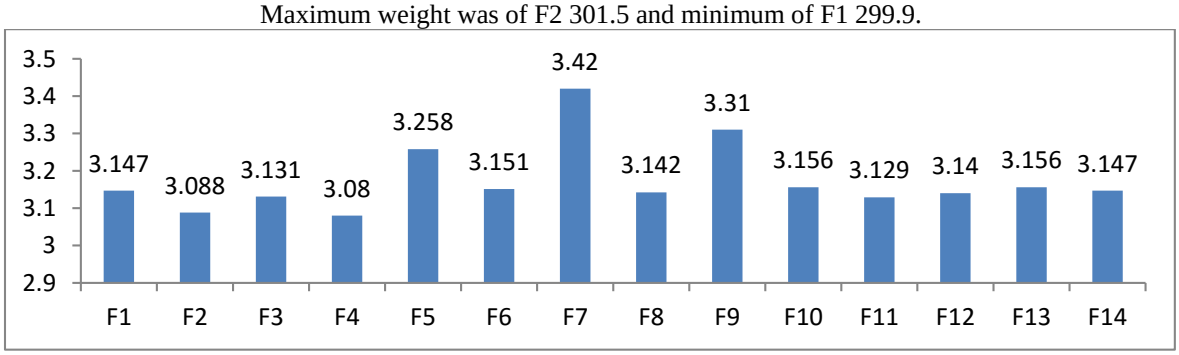

Figure 8: Thickness of all tablets formulated

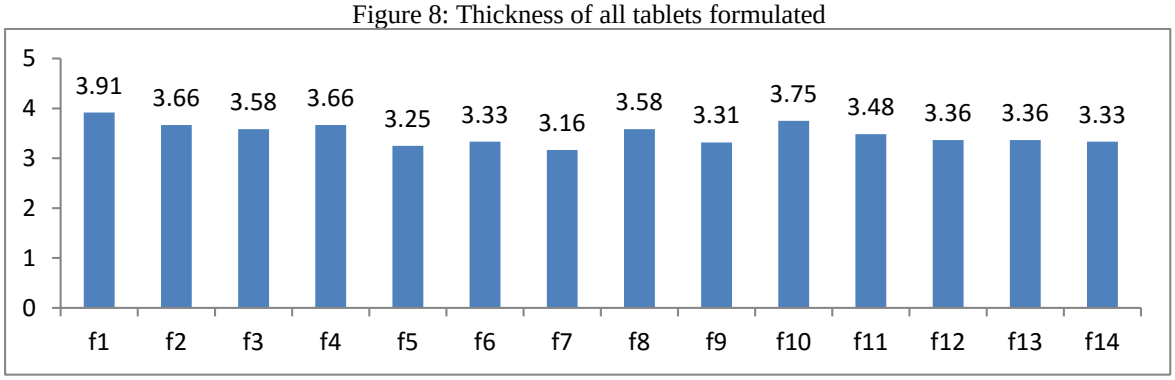

Figure 9: Average Hardness of all tablets formulated

It showed maximum hardness of F1 3.91 and lowest of F5 3.27.

plotting the absorbance versus concentration of the montelukast sodium.

Determination of Drug Content[5]

Drug content in all formulations was estimated by U.V Spectrophotometric method. A tablet from each batch was taken into 0.5% SLS containing in 100ml Volumetric Flask. Finally the volume was made upto 100ml with 0.5% SLS. It was filtered through whatman filter paper no: 41. First10ml was discarded. The clear filtrate was collected and diluted suitably with 0.5% SLS and measured at 350nm.

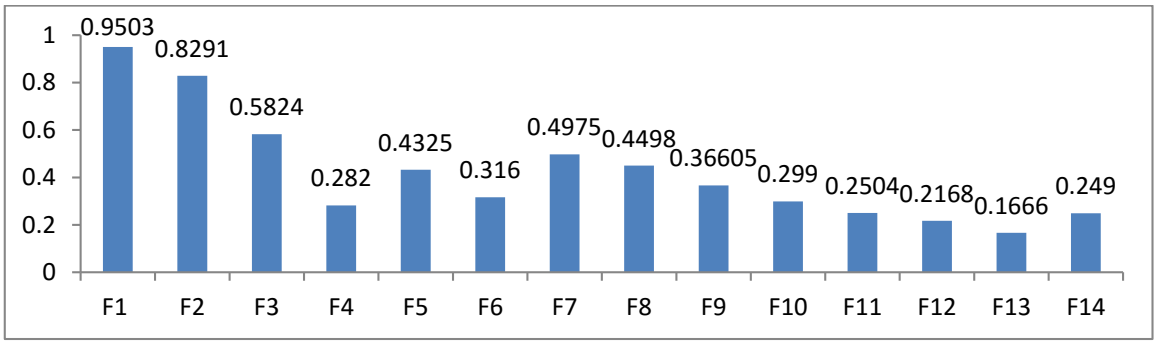

Figure 10: Friability Percent of all the formulations

It showed maximum friability was of F1 0.9503 and minimum of F13 0.1666.

Study on wetting time

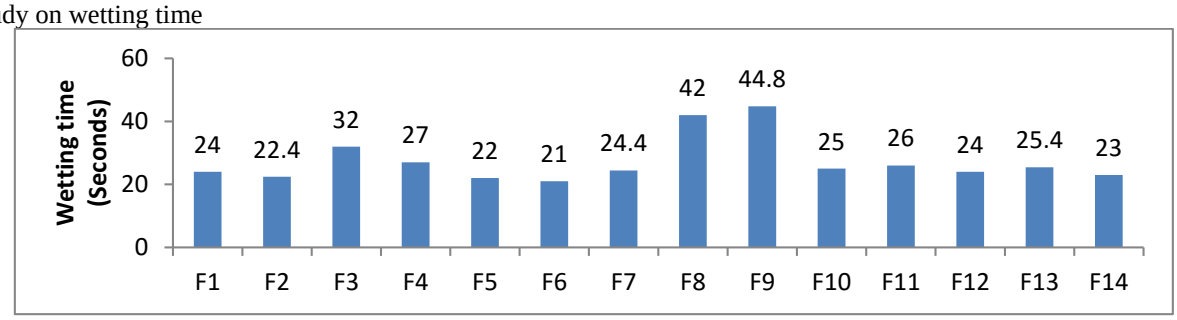

Figure 11: Wetting time of all the formulations

Maximum wetting time was of F9 44.8 seconds and minimum of F6 21 seconds

Dissolution Study

Table 2: Study of drug release of all the formulations carried at 10, 15, 20 and 30 minutes

Formulation	10 mins	15 mins	20 mins	30 mins
F1	82.53%	85.12%	86.94%	89.96%
F2	82.951%	85.823%	88.24%	91.43%
F3	80.37%	85.59333	88.945	92.60333
F4	80.95%	86.89%	88.26%	91.00%
F5	88.14%	91.686%	96.06%	98.983%
F6	86.24%	88.92%	91.59%	94.11%
F7	85.75%	89.48%	90.10%	92.17%
F8	85.77%	87.86%	89.24%	91.36%
F9	84.42%	87.83%	90.65%	92.25%
F10	86.18%	88.48%	90.01%	92.24%
F11	84.78%	90.56%	91.64%	94.10%
F12	83.95%	87.01%	90.19%	93.52%
F13	84.61%	88.79%	91.84%	93.27%
F14	84.61%	89.17%	94.21%	95.58%

Content Unifomity

Table 3: Content Uniformity of Formulations

F1	F2	F3	F4	F5	F6	F7
97±2.12	98±1.21	97±2.10	99±1.21	97±1.21	98±1.14	98±2.3
F8	F9	F10	F11	F12	F13	F14
98±1.13	96±2.36	99±2.54	99±1.32	96±1.32	98±1.04	97±2.05

In-Vitro dissolution study[5]

Dissolution test has been performed by using dissolution apparatus USP Type II with a paddle. The dissolution fluid was 900ml of distilled water with 0.5% SLS and a speed of 50 rpm and a temperature of 37±0.5˚C. The samples of dissolution medium (5ml) were withdrawn through a filter of 0.45µm at different time intervals, suitably diluted and assayed for Montelukast by measuring absorbents at 350nm. Samples withdrawn were analyzed for the percentage of drug released.

RESULTS AND DISCUSSION

Calibration curve

Formulation Development

Total of 14 formulations were prepared varying MCC PH-101, Mannitol and CCS.

Study of post compression parameters

The study of post compression parameters was done by studying hardness, weight variation, thickness, friability, wetting time, dissolution and content uniformity as:

CONCLUSION

It can be concluded that montelukast sodium chewable tablets with aforementioned excipients can be prepared for asthmatic patients.

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