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Formulation and Evaluation of Montelukast Sodium Lozenges

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ABSTRACT

Montelukast Sodium are formulated as lozenges to provide slow release medicament for the management of chronic asthma and allergic rhinitis. The benefits of prepared lozenges showed increase in bioavailability, reduction in gastric irritation, bypassing of first metabolism and increase in onset of action.The molded lozenges can provide an attractive alternative formulation in allergic conditions. The lozenges are prepared using sucrose, liquid glucose, Hydroxy propyl methyl cellulose K_4M (HPMC K_4M). Sodium Saccharine along with flavors are used to mask the bitter taste of drug. All the formulations prepared are subjected to various physicochemical parameters like weight variation, hardness, thickness, friability, content uniformity, and moisture content etc. The prepared formulations have a hardness of 8-11 kg/cm^2, non-gritty and pleasant mouth feel. Some selected formulations are also tested for drug excipient interactions subjecting to IR Spectral analysis, *In vitro* release rate studies showed that the drug release for lozenges was maximum in formulation F6 (99.3±0.52%) at 30 minutes.

Keywords: Montelukast Sodium, Hard Candy Lozenges, Asthma, HPMC.

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INTRODUCTION

The word “Lozenge” is derived from French word “Lozenge”, which means a diamond shaped geometry having four equal sides (Manasa, 2018). Lozenges are solid preparations that contain one or more medicaments, usually in a flavoured, sweetened base, and are intended to dissolve slowly in the mouth to lubricate and soothe irritated tissues of the throat. They are intended to be dissolved on the back surface of the tongue to provide drug delivery locally to the mouth, tongue, throat, etc., to minimize systematic therapy and to deliver drug multi - directionally into the oral cavity or to the mucosal surface (Dharmajit, 2017).

Asthma and Allergic rhinitis are both chronic heterogeneous disorders. Allergic rhinitis (AR) is an inflammatory disorder of the nasal mucosa, typified by symptoms of nasal itch, sneeze, anterior nasal secretions and nasal blockage. Asthma is a chronic, inflammatory pulmonary disorder characterized by reversible obstruction of the airways, causing recurrent episodes of wheezing, breathlessness, chest tightness and cough. Montelukast Sodium are formulated as lozenges toprovide slow release medicament for the management of chronic asthma and allergic rhinitis. Montelukast Sodium is the orally bioavailable monosodium salt of Montelukast, a selective cysteinyl leukotriene receptor antagonist with anti-inflammatory and bronchodilating activities (Rathod, 2018).

MATERIALS AND METHOD

Materials

Montelukast Sodium was a gift sample from Morepen Laboratories Ltd, Delhi, HPMC K4M was obtained from Sd Fine Chemicals, Mumbai, Sucrose and liquid glucose from HL Agro products Pvt., Ltd, Kanpur and all other chemicals used are of pharmaceutical grade (Madhusudan Rao, 2015).

Methods

Drug excipient compatibility studies

The compatibility between the drugs, polymer and excipients was compared by FTIR spectroscopy. The IR spectra were evaluated for the presence of principal peaks of drug, shifting and masking of the drug peaks due to presence of polymers and other excipients. The FTIR spectra of drugs and optimized formulation of lozenges are shown in figure 1,2 and 3 (Dharmajit, 2018).

Standard graph of montelukast sodium

Standard stock solution of pure drug containing 100 mg of Montelukast Sodium/100 mL is prepared using 6.8 pH phosphate buffer. The working standards were obtained by diluting the

stock solution with corresponding buffer in the range of 2-25µg/mL at the selected wavelength 287.3 nm. Their absorptivity values were used to determine the linearity. Solution was scanned and Beer Lamberts law limit was obeyed in the concentration range of 2, 4, 6, 8, 10 ,12, 20, 25 µg/mL. (Jagadeesh, 2017)

Method of Preparation

Sucrose is accurately weighed and is dissolved in one third amount of water by heating on fire cookers until all sugar granules are dissolved. Liquid glucose is added when cooking temperatures reaches 110^{o}CHeating is continued until final temperature is 141-156^{o}C. Mixture is cooled to 135^{o}C and color is added. Further cooling is carried out mixed until temperature reaches 40^{o}C. Flavor, drug, and polymer is added and mixed for 4-6 minutes and poured in lubricated molds(Nandini, 2018). The composition of hard candy lozenges was given in Table.1

Table 1: Composition of hard candy lozenges

Formulation Code	F1	F2	F3	F4	F5	F6	F7	F8	F9	F10
Montelukast Sodium (drug)(mg)	10	10	10	10	10	10	10	10	10	10
Sucrose (gm)	1.55	0.75	11.125	1.55	1.55	1.55	1.55	1.55	1.55	1.55
Liquid Glucose (gm)	0.75	1.55	11.125	0.75	0.75	0.75	0.75	0.75	0.75	0.75
Sodium Saccharin	qs	qs	qs	qs	qs	qs	qs	qs	qs	qs
HPMC k4 M (gm)	-	-	-	0.4	0.5	0.6	-	-	-	-
Xanthum gum (gm)	-	-	-	-	-	-	0.4	0.5	0.6	0.7
Preservative (Sodium benzoate) (mg)	60	60	60	60	60	60	60	60	60	60
Colour	qs	qs	qs	qs	qs	qs	qs	qs	qs	qs
Flavour	qs	qs	qs	qs	qs	qs	qs	qs	qs	qs

Total weight = 3 gm

Evaluation of the Hard Candy Lozenges (Surbhi Choursiya, 2017)

The prepared Montelukast Sodium lozenges were studied for their physicochemical properties like weight variation, hardness, thickness, friability and drug content.

Weight variation test

Twenty lozenges were taken and their weight was determined individually and collectively on a digital weighing balance. The average weight of one lozenge was determined from the collective weight. The percent deviation was calculated using the following formula.

%Deviation = (Individual weight – Average weight/ Average weight)×100

Lozenge hardness

The hardness of lozenges were determined using Monsanto hardness tester and the average was calculated and presented with standard deviation.

Lozenge thickness

The thickness and diameter of the lozenges was determined using vernier calipers.

Friability

The Roche friability test apparatus was used to determine the friability of the lozenges. The pre-weighed lozenges were placed in the apparatus, which was subjected to 100 revolutions. Then the lozenges were reweighed. The percentage friability calculated was using the formula.

$$\text{Friability (\%)} = \frac{\text{Initial weight of 10 tablets} - \text{Final weight of 10 tablets}}{\text{Initial weight of 10 tablets}} \times 100$$

Determination of drug content

Twenty lozenges were finely powdered quantities of the powder equivalent to 60 mg of Montelukast Sodium (Drug) were accurately weighed, transferred to a 100 mL volumetric flask containing 50 mL of 6.8 phosphate buffer and allowed to stand for 30 minutes with intermittent sonication to ensure complete solubility of the drug. The mixture was made upto volume with distilled water. The solution was suitably diluted and the absorption was determined by UV-Visible spectrophotometer at $\boldsymbol{\lambda}_{max}$ 287.3nm. The drug concentration was calculated from the standard curve.

Moisture Content

It is determined by Gravimetric method, sample was weighed and placed in vacuum oven at 60-70^{o}C for 12-16 hrs.

%Moisture Content = (Initial wt-Final wt/Initial wt) ×100

***In vitro* drug release studies**

Dissolution conditions:

- Apparatus : USP II (Paddle) apparatus
- Dissolution medium : 100 mL of pH 6.8 phosphate buffer
- Temperature : 37$\pm$0.5 ^{o}C
- Rotating speed of the paddle : 50 rpm
- Sample time intervals : 5, 10, 15, 20, 25, 30 minutes
- Detection : UV-Visible spectrophotometer at $\boldsymbol{\lambda}_{max}$ 287.3 nm

The samples were withdrawn at pre-determined time points, diluted appropriately and analyzed spectrophotometrically at 287.3 nm. The cumulative percentage standard deviation were calculated and the results are presented in the table.

***In vivo* Evaluation of Taste and Mouth feel**

Single blind study was designed for the taste masking test in the buccal cavity. Six volunteers participated in the test. They were asked to rate the bitter taste of the formulations. The same human volunteers who participated in taste evaluation test were asked to give their opinion about the feeling of smoothness or grittiness of the lozenge soon after the lozenge got completely dissolved in the oral cavity (Jagadeesh, 2017).

RESULTS AND DISCUSSION

Results

FTIR Drug excipient compatibility studies

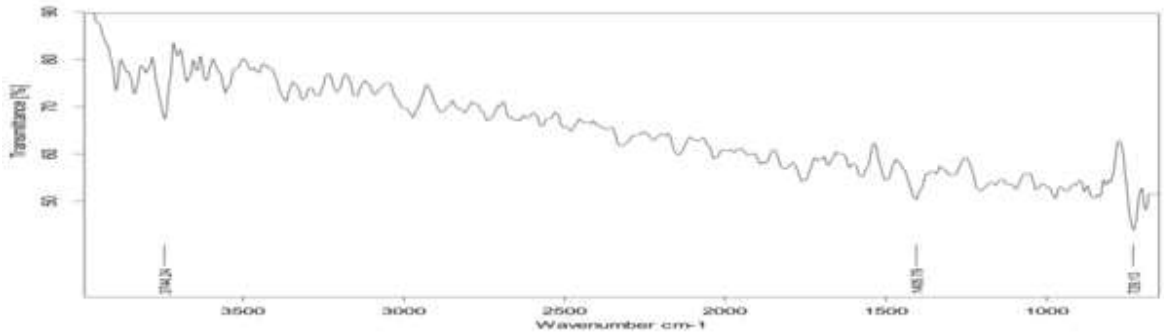

Figure 1: FTIR Spectrum of Montelukast Sodium

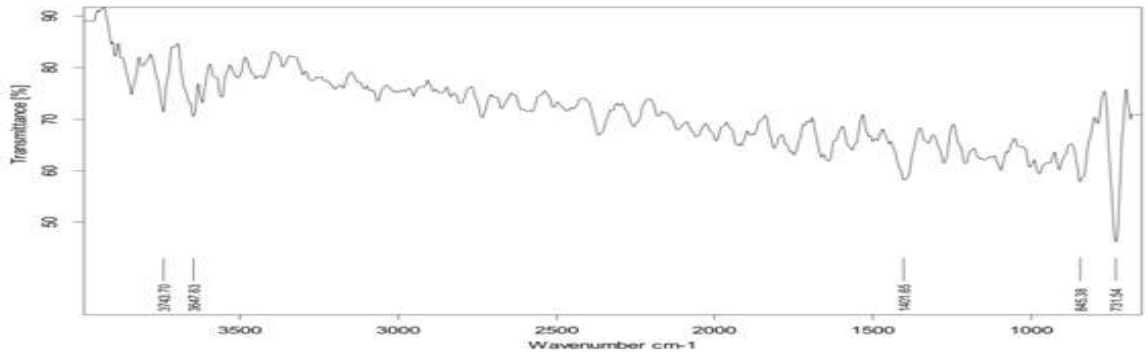

Figure 2: FTIR Spectrum of Montelukast Sodium + HPMC K4 M

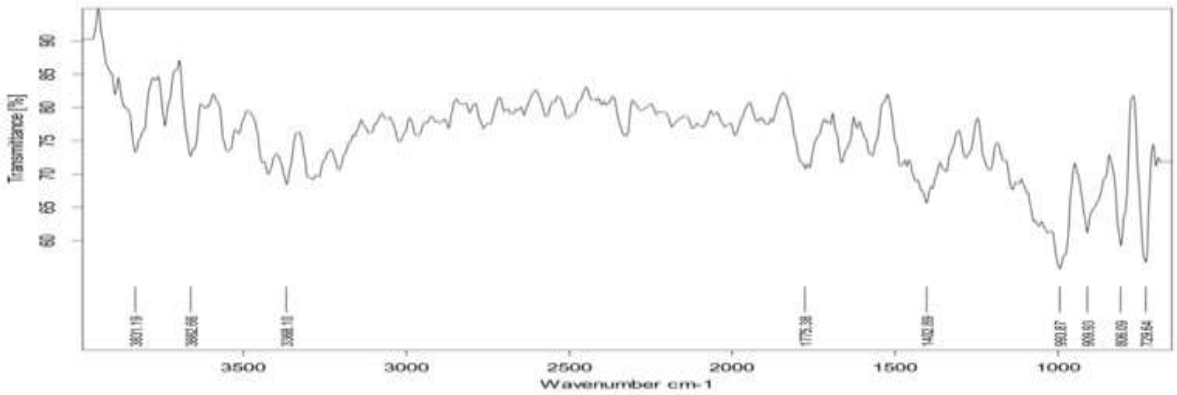

Figure 3: FTIR Spectrum of optimized formulation of lozenge

Table 2: Data for FTIR Spectrum of Montelukast Sodium

IR Spectra	Wave number cm̄¹		
	OH Stretching	C-H Bending	-COOH Bending
Montelukast Sodium	3742.24	1426.79	1000
Optimized Formulation	3662.66	1422.89	993.87

Table 3: Standard graph of Montelukast Sodium at λmax at 287.3 nm

S.No	Concentration (µg/ mL)	Absorbance (nm)
1	0	0
2	2	0.046
3	4	0.083
4	6	0.122
5	8	0.159
6	10	0.263
7	12	0.353
8	20	0.454
9	25	0.541

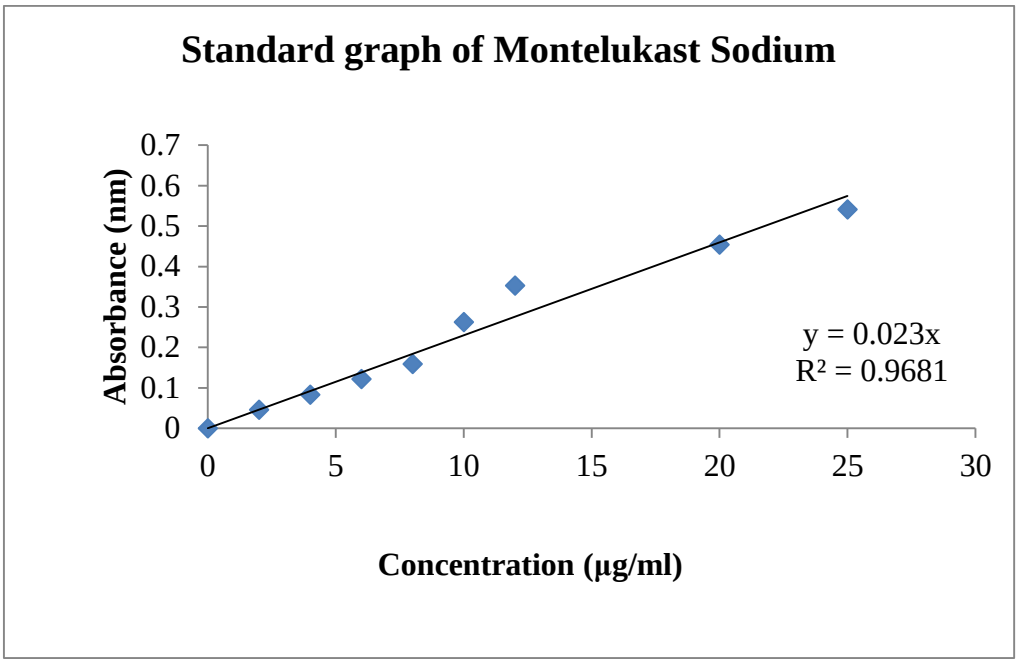

Figure 4: Standard graph of Montelukast Sodium in 6.8 pH phosphate buffer 4

EVALUATION OF PHYSICAL PARAMETERS OF HARD CANDY LOZENGES

Table 4: Characterization of Montelukast Sodium lozenges

Formulation Code	Weight (a) (mg)	Hardness (b) (kg/cm^2)	Thickness (b) (mm)	Friability (b) (%)
F1	2998.1±0.43	10.61±0.34	7.12±0.01	0.42±0.04
F2	2794.8±0.54	9.44±0.91	7.25±0.04	0.79±0.01
F3	2712.4±0.65	9.63±0.73	7.29±0.05	0.63±0.06
F4	2946.9±0.048	10.52±0.49	7.30±0.02	059±0.04
F5	2987.7±0.35	10.56±0.49	7.32±0.04	0.58±0.08
F6	**2950.7±0.68**	**10.59±0.62**	**7.35±0.08**	**0.59±0.10**
F7	2824.4±0.78	10.58±0.25	7.32±0.05	0.51±0.00
F8	2989.8±0.65	10.51±0.36	7.40±0.07	0.58±0.03
F9	2921.5±0.40	10.59±0.66	7.39±0.03	0.56±0.05
F10	2983.7±0.56	10.57±0.47	7.41±0.07	0.55±0.09

a.Results are mean of 20 observations ± SD; b.Results are mean of 10 observations ± SD

Table 5: Characterization of Montelukast Sodium lozenges

Formulation Code	Content uniformity (%)	Moisture content (%)
F1	98.53±1.56	0.85±0.04
F2	99.65±1.69	0.89±0.08
F3	99.78±1.60	0.83±0.05
F4	97.59±2.01	0.91±0.09
F5	98.13±1.87	0.86±0.04
F6	**99.70±1.81**	**0.85±0.07**
F7	99.87±1.85	0.97±0.02
F8	98.33±2.02	0.86±0.03
F9	99.26±1.74	0.90±0.07

F10	97.16±1.91	0.88±0.08

***Result are mean of 3 observation ± SD**

IN VITRO DRUG RELEASE OF MONTELUKAST SODIUM LOZENGES

Table 6: Cumulative percent of Montelukast Sodium release from lozenges (F1-F5)

Time (min)	F1	F2	F3	F4	F5
0	0	0	0	0	0
5	52±0.41	49.3±0.47	50.4±0.64	31.9±0.21	42.3±0.82
10	69.5±0.52	61.4±0.58	65.7±0.56	40.5±0.39	57.4±0.68
15	81.5±0.69	75.3±0.62	76.7±0.34	50.5±0.44	63.3±0.72
20	99.5±0.70	92.3±0.69	98.2±0.94	61.7±0.47	79.8±0.69
25				82.2±0.50	84.9±0.53
30	-	-	-	95.4±0.56	90.8±0.45

***Results mean of 3 observations ± SD**

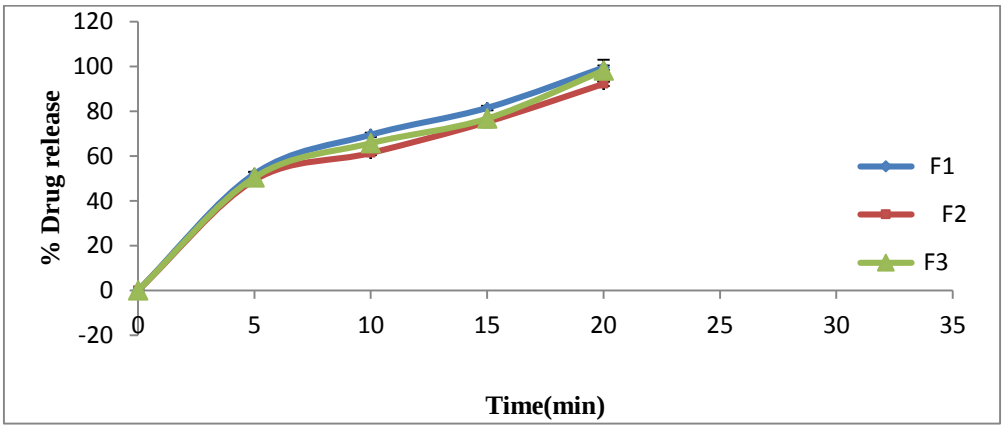

Figure 5: Cumulative percent of Montelukast Sodium release from lozenges(F1 – F3)

Table 7:Cumulative percent of Montelukast Sodium release from lozenges(F6-F10)

Time (min)	F6	F7	F8	F9	F10
0	0	0	0	0	0
5	40.6±0.63	53±0.56	45.1±0.66	43.3±0.68	50.7±0.41
10	58.8±0.57	66.7±0.60	55.3±0.74	62.9±0.43	67.1±0.59
15	63.3±0.72	77.6±0.71	64.7±0.49	73±0.53	74.8±0.62
20	79.6±0.33	88.2±0.65	72.3±0.56	83.2±0.62	80.4±0.72
25	84.3±0.49	99.2±0.58	95.0±0.58	98.1±0.49	97.5±0.64
30	99.3±0.52				

***Results mean of 3 observations ±SD**

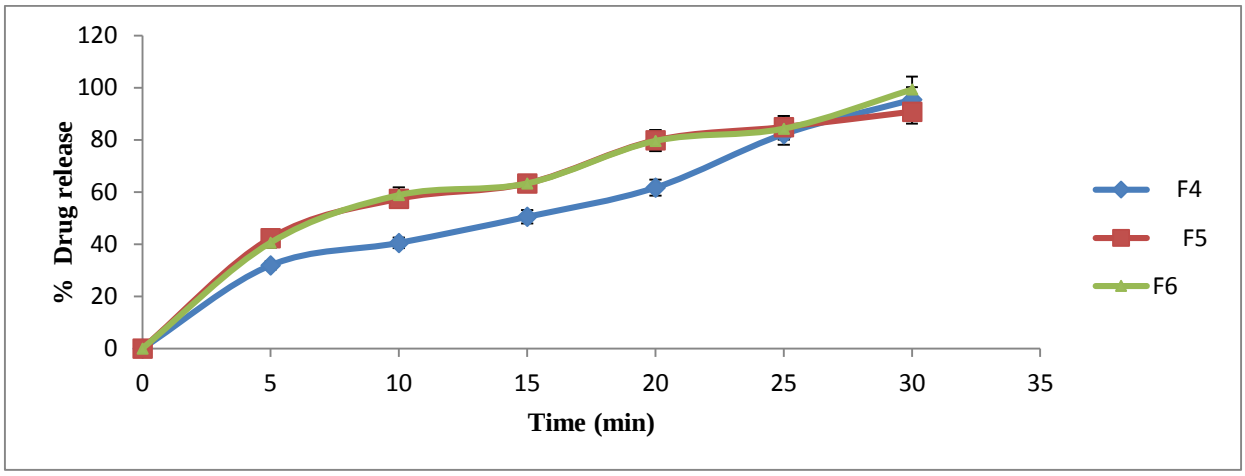

Figure 6 : Cumulative percent of Montelukast Sodium release from lozenges (F4-F6)

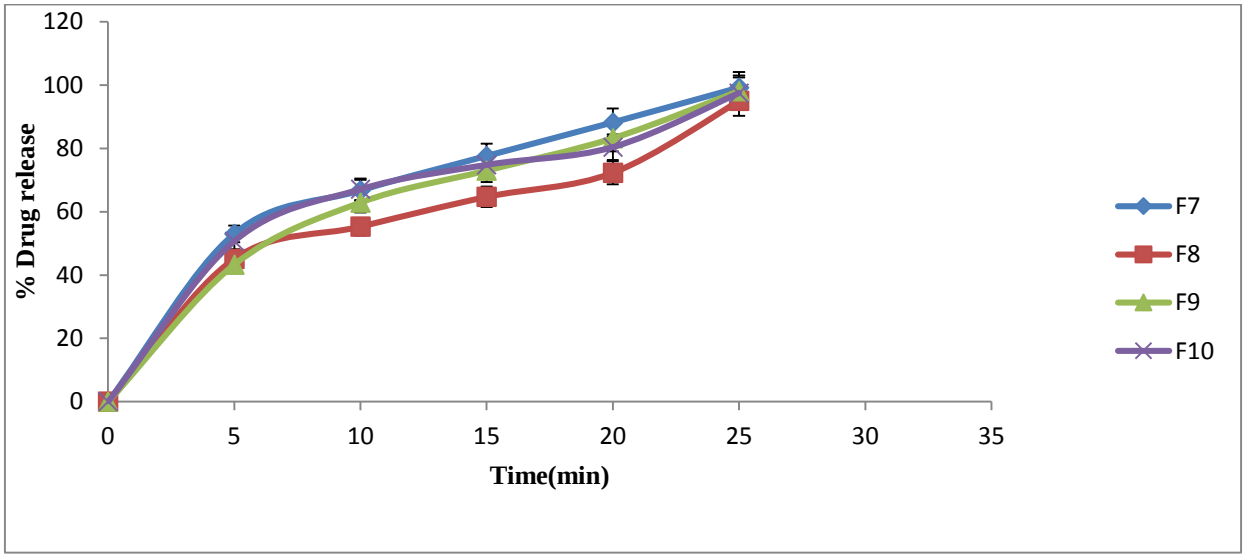

Figure 7: Cumulative percent of Montelukast Sodium release from lozenges (F7-F10)

IN VIVO TASTE EVALUATION OF MONTELUKAST SODIUM

Taste evaluation was performed on six healthy human volunteers and the results were reported in the table.8. The study was approved by Institutional Human Ethics Committee (IHEC)/VGOP/077/2018.

Table 8: Comparative evaluation of taste and mouth feel for optimized formulation

Volunteers	Taste	Mouth feel
1	-	No grittiness, good mouth feel
2	-	
3	+	
4	-	
5	+	
6	-	

= - No bitterness, + = slightly bitter

DISCUSSION

The objective of this study is to formulate and characterize Montelukast Sodium lozenges for leukotriene receptor antagonist activity used for the treatment of asthma and to relieve symptoms of seasonal allergies. All the prepared formulations were tested for physical parameters like weight variation, hardness, thickness, friability, content uniformity, and moisture content found to be within the Pharmacopoeial limits. The results of the tests were tabulated in Table.4.

The lozenges of Montelukast Sodium were prepared by using different polymers of different concentrations by heat congealing method (F1-F10), among all formulations of F6 (HPMC K4M) showed highest percentage of drug release, and drug content. The weight variation in all formulations was found to be in the range of 2712.4±0.65 mg to 2998.1±0.43 mg, which is within the pharmacopoeial limit. Hardness of all lozenges was maintained between 9.44±0.91 and 10.61±0.34 kg/cm^2. The thickness varies between 7.12 and 7.41 mm. Friability of all lozenges was maintained between 0.42±0.04 and 0.79±0.01%. The weight variation, hardness, thickness and friability of optimized formulation (F6) were 2950.7±0.68 mg, 10.59±0.62 kg/cm^2, 7.35±0.08 mm and 0.59±0.10% which was within acceptable limits .Assay was performed and percent content uniformity of all the lozenges was found to be between 97.16±1.91 and 99.87±1.85% of Montelukast Sodium which was within the acceptable limits. Moisture content was found to be between 0.83±0.05and 0.97±0.02 percent which was within the acceptable limits. Content uniformity, and Moisture content of optimized formulation (F6) were 99.70±1.81 and 0.85±0.07.

Formulation F1, F2 and F3 of Montelukast Sodium (Hard candy lozenges without polymer) containing varying concentration of sucrose and liquid glucose recorded the drug release of 99.5±0.70%, 92.3±0.69% and 98.2±0.94 respectively at the end of 20 minutes. Formulation F4, F5 and F6 (Hard candy lozenges with polymer HPMC K4M) recorded the drug release of 95.4±0.56%, 90.8±0.45% and 99.3±0.52% respectively at the end of 30 minutes. Formulation FL7, FL8, FL9 and FL10 (Hard lozenges with Xanthum gum) containing varying concentration recorded the drug release of 99.2±0.58%, 95.0±0.58%, 98.1±0.49% and 97.5±0.64 respectively at the end of 25minutes. The percentage drug release of optimized formulations (FL6) was 99.3±0.52% which showed controlled drug release compared to other formulations.

The stability studies were performed there is no change in drug content, friability, weight variation. FTIR studies were performed and from the FTIR spectra it was evident that there were no interaction between the drug and the excipients being used.

CONCLUSION

Patient compliance is one of the important aspects for administration of drug especially those which are bitter in taste. For, patient compliance, attractive taste masking formulations are the need of hour. In the present study, Montelukast Sodium sweetened hard candy lozenges were designed for the effective treatment of Asthma and other seasonal allergies. The interest was for the development of new dosage form and the effect of different polymers on the *in vitro* release. At the outset, estimation of drug by UV spectrophotometer was carried out. The possible interaction between the drug and excipient was studied by FTIR spectroscopy showed that there was no interaction between the selected drug and polymer. Lozenges could be successfully prepared by fusion method using sucrose, liquid glucose, sodium saccharine, polymers, preservative, flavor and color .*In vitro* release studies showed that the drug release for lozenges was controlled in formulation F6 (99.3±0.52 %) at the end of 30 minutes. *In vivo* studies conformed that the bitter taste of Montelukast Sodium was masked by adding Sucrose, Liquid glucose and Sodium saccharine act as sweetening agents.

REFERENCES

1. Jagadeesh P, Jyothi P, Lokeshwari P. Design and characterization of Tramadol HCI Medicated Hard Candy Lollipops. International Journal of Research in Pharmacy and Chemistry 2017; 7(2): 187-193.
2. MadhusudanRao Y, Srikanth P, Shravan Kumar Y. Formulation and Evaluation of levodropropazine lozenges. World Journal of Pharmaceutical Research 2015; 4: 646-659.
3. MadhusudanRao Y, Shiva kumar R, Praveen G. Fabrication and evaluation of levocetrizine dihydrochloride lozenges. International Journal of Innovative Research in Science Engineering and Technology 2016; 5(1): 664-67.
4. Manasa Advelly, Venu Amma, Rajeshwari Velpula. Formulation and evaluation of Cetrizine lozenges. International Journal of Innovative Pharmaceutical Sciences and Research 2017; 5(10): 93-103.
5. Mandeep W, Rakesh L, Kabra SK. Montelukast in Management of Paediatric Asthma. International Journal of Paediatrics 2006; 73(4): 275-282.
6. Minakshi Rathod, Sachin Poharkar, Yuvaraj Pundhre, Monali Muneshwar, Sandesh Sun.. Medicated lozenges as an easy to use dosage form. World Journal of Pharmaceutical Research 2018; 7(16): 305-322.

7. Nandini Kothagattu, Priyadarshini Arsham, Shravan Kumar Yamsani. Formulation and evaluation of Doxofylline lozenges. Current trends in Biotechnology and Pharmacy 2018; 12(1): 43-52.
8. Renuka Pothu, Aparna A, Rao Y M. Development and *in vitro* Evaluation of Chlorhexidine and Flubiprofen Hard Candy Lozenges. International Journal Pharmaceutical Sciences and Research 2015; 6(8): 3380-3390.
9. Shivaprasad Mujumdar, Vaibav Jogi. Development of Antifungal lozenges for treatment of Oropharyngeal Candidiasis. Indo American Journal of Pharmaceutical Research 2015; 5(1): 370-386
10. Surbhi Choursiya. Formulation and Evaluation of Lozenges for Oral Bacterial Infection. International Journal of Pharmacy and Pharmaceutical Research 2017; 7(1): 606-617.