Indian Journal of Novel Drug Delivery

IJNDD

An Official Publication of Karnataka Education and Scientific Society

Research Article

Formulation and Characterization of Rapidly Dissolving Buccal Films of Montelukast Sodium

ANKITA B HOGALE, JAMEEL AHMED S MULLA*

Department of Pharmaceutics, Shree Santkrupa College of Pharmacy, Ghogaon, Karad, Maharashtra, India - 415111

ARTICLE DETAILS

Article history:
Received on 20 July 2021
Modified on 21 August 2021
Accepted on 25 August 2021

Keywords:
Rapidly Dissolving Film,
Montelukast Sodium,
Solvent Casting Method,
Buccal Film.

ABSTRACT

In the event of chronic illnesses, fast-dissolving drug delivery systems have been created as an alternative to traditional dosage forms as an oral mode of drug delivery. Fast dissolving films are now favoured over traditional tablets and capsules for disguising the taste of bitter medications and increasing patient compliance. In this study, montelukast sodium-loaded fast dissolving oral films were made using HPMC K-100 and the solvent casting method. Disintegration time, thickness, tensile strength, percent elongation, folding endurance, moisture content, surface pH, content uniformity, swelling index, FTIR Spectroscopy, Differential Scanning Calorimetry, and an *in-vitro* dissolution investigation were all used to describe the prepared films. The chemical structure of montelukast sodium was preserved in the formulation, according to FTIR analysis. At the end of 5 minutes, the drug release was found to be between 90.75 and 99.14 percent.

INTRODUCTION

In the late 1970s, rapid-dissolving drug-delivery systems were developed as an alternative to tablets, capsules, and syrups for juvenile, geriatric, bedridden, nauseated, or noncompliant patients who had difficulty ingesting typical oral solid-dosage forms. The technique, which was based on the technology of transdermal patches, is also known as oral thin films, fast dissolving films, mouth dissolving films, oro-dispersible films, quick disintegrating films, and melt in mouth dosage form [1, 2]. Drug administration via rapidly dissolving buccal films has developed as a cutting-edge alternative to the usual pills, capsules, and liquids commonly used in prescription and over-the-counter drugs. Thin film strips are primarily designed for oral administration, with the user placing the strip on or under the tongue or along the inside of the cheek, and are similar in size, shape, and thickness to a postage stamp. When a film is placed on the tongue or buccal cavity, it dissolves quickly, sending the medication to the systemic circulation via breakdown [3, 4]. Montelukast sodium is an anti-asthmatic medicine that works as a leukotriene receptor antagonist, highlighting the importance, optimal qualities, and many aspects of mouth dissolving film formulation as a superior dosage form for treating asthma and improving patient compliance [5].

The primary goal of this study is to develop a fast dissolving film of montelukast sodium, an anti-asthmatic medicine, which will aid in the rapid beginning of action and increase the performance of the active pharmaceutical ingredient.

Author for Correspondence:
Email: jameelahmed5@rediffmail.com

MATERIALS AND METHODS

Materials

Aarti Pharma in Mumbai provided the Montelukast Sodium. Loba Chemie, Mumbai, provided HPMC K100, PEG 600, and sodium lauryl sulhate. All of the other chemicals, excipients, and solvents utilized were obtained from reputable sources and are of laboratory and analytical quality.

Formulation of Fast Dissolving Films of Montelukast Sodium

Solvent casting was used to make the quickly dissolving films, with HPMC K-100 as the film former. With constant stirring on a magnetic stirrer, the calculated amount of polymer, HPMC K-100, was dissolved in one fourth amount of distilled water. The montelukast sodium was adequately dissolved in a suitable amount of ethanol and then added to the polymeric solution

Table 1: Formulations of montelukast sodium loaded buccal films

Ingradients	F1	F2	F3	F4	F5	F6	F7	F8	F9
Montelukast sodium (mg)	50.62	50.62	50.62	50.62	50.62	50.62	50.62	50.62	50.62
HPMC K-100 (mg)	910	910	910	1000	1000	1000	1100	1100	1100
PEG-600 (mg)	20	30	40	20	30	40	20	30	40
Citric acid (mg)	100	100	100	100	100	100	100	100	100
Sorbitol (mg)	100	100	100	100	100	100	100	100	100
Tween 20 (ml)	0.2	0.2	0.2	0.2	0.2	0.2	0.2	0.2	0.2
lemon oil (ml)	1	1	1	1	1	1	1	1	1
Color (ml)	1	1	1	1	1	1	1	1	1

described above. Later, the plasticizer PEG-600 was added to the aforementioned solution, along with other excipients such as sweeteners (sorbitol), surfactant (tween-20), and taste (vanila), and the mixture was well mixed until all of the constituents were dissolved in the polymeric solution. This solution was poured into a clean Petri dish and placed in a 400°C hot air oven. The films were sliced into 2 cm^2 pieces after drying, each containing 5mg montelukast sodium [6, 7].

Weight Variation of the Film

The caste film was cut at five separate locations with a 2x2 cm^2 film. The weight of each film/strip was measured using a digital analytical balance, and the weight variation was determined, as shown in Table 2 [8, 9].

Disintegration Time

In this approach, 2 mL of distilled water was poured in a Petri dish, one film was placed on the water's surface, and the time it took for the oral film to completely dissolve was measured. Both methods were used to investigate drug-loaded films. Strips disintegrate every 5–30 seconds on average [9, 10].

Thickness of Film

At various points on the film, the thickness of the patch was measured using digital Vernier Calipers with a least count of 0.01 mm. The patch's thickness was measured at three distinct locations, with an average and SD determined [11].

Tensile Strength

The greatest stress applied to a point where the strip specimen breaks is known as tensile strength. It's computed by dividing the applied load at rupture by the strip's cross-sectional area, as shown in the equation below [8, 9].

$$\text{Tensile strength} = \frac{\text{Load at Failure}}{\text{Strip Thickness} \times \text{width}}$$

It was determined with the help of a Universal testing device. The film, which was 2×2 cm^2 in size and free of physical flaws, was clamped between two clamps spaced 10 mm apart. Clamping was used to draw the film at a rate of 5mm/min. The entire experiment was repeated three times. It was decided to take the average of three readings.

Percent Elongation

When a strip sample is stressed, it stretches, which is referred to as strain. Strain is defined as the distortion of a strip divided by the sample's initial dimension. Strip elongation rises in general when the plasticizer content rises. The chosen films were cut into 2x2 cm^2 dimensions and pulled from both sides by two clamps set above a scale until it cracked. The elongation was calculated by noting the increase in film length and applying the calculation below [11].

$$\text{Percentage elongation} = \frac{[L_f - L_o]}{L_o} \times 100$$

Where,

L_f = Final length, and L_o= initial length.

Folding Endurance

A sharp blade is used to cut three films of each formulation to the necessary size. Folding endurance is measured by folding the film repeatedly in the same spot until it breaks. The value of folding endurance is determined by the number of times the film could be folded at the same location without breaking [12].

Moisture Content

The produced films must be weighed separately and maintained at room temperature for 24 hours in desiccators with calciumchloride. After a predetermined interval, the films must be weighed again until they exhibit a steady weight. The following formula should be used to compute the % moisture content [8, 9].

$$\% \text{ Moisture content } = \frac{\text{Initial weight} - \text{Final weight}}{\text{Final weight}} \times 100$$

Surface pH

The film to be tested was moistened with 0.5 mL of distilled water and left in a petri dish for 1 hour. After bringing the electrode of the pH meter in touch with the surface of the formulation for 1 minute to allow for equilibrium, the pH was recorded [13].

Content Uniformity

Any standard test method provided for the particular API in any of the standard pharmacopoeias determines this. The API content in each strip is estimated to determine content consistency. The content homogeneity limit is set at 98–102 percent. A 2x2 cm^2 size film was cut and placed in a beaker with 50mL of 0.5% SLS solutions. To dissolve the film, the contents were agitated in a magnetic stirrer and then transferred to a 50mL volumetric flask. At 342 nm, the absorbance of the solution was compared to that of a blank solution [8, 9].

Swelling Index

The examinations of the film's swelling index are carried out in simulated salivary fluid. The film sample is weighed and placed in a stainless steel wire sieve that has been pre-weighed. In a mortar, the mesh containing the film is submerged in 50mL of simulated salivary medium. At each interval, the weight of the film is measured until it reaches a consistent weight. The following formula is used to determine the degree of swelling [14].

$$\text{Swelling index } = \frac{W_t - W_0}{W_0}$$

Where,

W_t is the film's weight at time "t" and W_0 is weight of the film at time = 0

Fourier Transform Infrared Spectroscopy

FTIR spectra are typically recorded in the middle infrared [4000 cm^{-1} to 650 cm^{-1}] for 8 to 128 scans at room temperature in the absorbance mode with a resolution of 4 cm^{-1}. The samples for FTIR analysis are made by mixing dry mixed powders with powdered KBr in a 1:5 ratio [Sample: KBr] and compressing them into discs. Spectra are occasionally measured on films using an IR spectrometer [15].

Differential Scanning Calorimetry (DSC)

Differential Scanning Calorimetry allows the fast evaluation of possible incompatibilities, because it shows changes in the appearance, shift of melting endotherms and exotherms, and variations in corresponding enthalpies of reaction. The differential scanning colourimetric thermograms of pure drug montelukast sodium and are optimized fast dissolving buccal film formulation were recorded on the thermal analyzer of equipped with an intercooler. The thermal analysis was performed at a heating rate of 10°C/min over temperature range of 30°C to 275 °C in a nitrogen atmosphere [11].

***In-Vitro* Dissolution Studies**

In-vitro dissolution experiments of the produced films were carried out in 0.5 percent SLS for 30 minutes at 50rpm using a USP type II (paddle) dissolution device. The dissolution tests were done in triplicate for 30 minutes using a 0.5% SLS solution as the dissolution medium. The dissolving media was kept at a constant temperature of 37±0.5°C. At 30 second intervals, 5mL samples were withdrawn and replaced with 5mL of fresh dissolving media through (filtered whatmann filter paper 0.45µ). Using a UV Win3000+double beam UV-Visible spectrophotometer, the drug concentration was determined spectrophotometrically at 342nm. The dissolution rate of all developed formulations was investigated, and dissolution parameters were calculated [16].

RESULTS AND DISCUSSION

The solvent casting approach, which used HPMC K-100 as a film forming, was successful in producing rapidly dissolving buccal films of montelukast sodium. Following parameters were used to evaluate montelukast sodium-loaded buccal films.

Weight of Film

The weights of the films were determined to be in the 32.2mg to 33.4mg range. The weight of each film varied due to differences in the concentration of excipient in each film. It was discovered that as the concentration of polymer increases, so does the weight of the film.

Disintegration Time

All batches' disintegration times were found to be between 122 and 127 seconds.

Thickness of the Film

All batches were found to have thicknesses ranging from 0.28mm to 0.34mm. The difference in film thickness was caused by the excipient concentration utilized in the formulation.

Tensile Strength

All batches' tensile strength was found to be between 1.78 and 2.18 N/m^2. The difference in tensile strength is caused by the concentration of polymer having a film-forming property.

Table 2: Evaluation of montelukast sodium buccal films

F* code	Visual appearance	Weight (mg)	Disintegration time (sec.)	Thickness (mm)	Tensile strength (N/m^2)	Percent elongation (%)	Folding endurance	Moisture content (%)	Surface pH	Drug content (%)	Swelling index (%)
F1	Opaque	32.3	122	0.28	1.78	140	299	2.52	6.8	94.79	36
F2	Opaque	32.4	124	0.30	2.0	160	302	2.20	6.7	93.43	29
F3	Opaque	33.00	125	0.32	2.03	120	298	2.40	7.1	98.43	33
F4	Opaque	32.4	122	0.31	1.93	130	302	2.20	6.9	95.83	34
F5	Opaque	33.4	123	0.32	2.18	140	299	2.76	7.2	95.31	28
F6	Opaque	32.3	126	0.28	2.17	160	310	3.52	7.0	96.87	36
F7	Opaque	32.3	123	0.29	2.06	130	302	2.53	6.8	94.27	37
F8	Opaque	32.2	124	0.32	2.09	140	299	3.28	7.2	97.91	36
F9	Opaque	33.00	127	0.34	1.98	160	300	2.48	7.0	96.35	33

F*=Formulation

Percent Elongation

All batches' % elongation was found to be between 120 and 160 percent. Because all batches have the same elongation, the plasticizer content in percent elongation is the same.

Folding Endurance

The film will not break or crack after folding at the same location; the folding endurance was in the range of 298 to 310. PEG 600, which was utilized as a plasticizer, increased the folding endurance of the film as the concentration of PEG 600 rose. Film's folding durability has also improved, giving it more flexibility and plasticity.

Moisture Content

All of the batches had moisture content ranging from 2.20 to 3.52 percent.

Surface pH

All batches' surface pH was found to be in the range of 6.7 to 7.2. The pH of the surface is measured with a digital pH meter, and the pH ranges are identical to those of saliva.

Drug Content

The drug content was determined to be in the range of 93.43 % to 98.43 %. *In vitro* dissolving tests were carried out based on this medication content.

Swelling Index

The prepared buccal film's swelling index was found to be between 28 and 37 %.

FTIR Study

Fig. 1a and 1b show the FT-IR spectra of the pure drug and formulation, respectively. Montelukast sodium displays COOH stretching at 3370 cm^{-1}, aromatic C–H stretching at 3055 cm^{-1}, aliphatic C–H stretching at 2920 cm^{-1}, and C–O stretching at 1710 cm^{-1}. These drug's distinctive peaks were present in the formulation with no significant changes. As a result, it has been established that the chemical structure of montelukast sodium has been preserved.

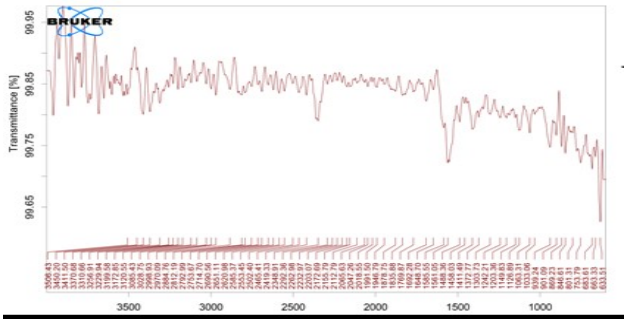

Figure 1a: FTIR of pure Drug, Montelukast Sodium

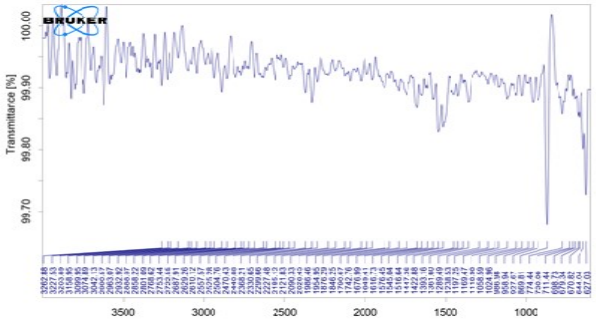

Figure 1b: FTIR of Montelukast Sodium-loaded film

DSC Study

Fig. 2 shows the DSC thermograms of montelukast sodium-loaded quickly dissolving buccal films and their components. The thermal peaks of montelukast sodium and HPMC K-100 were 109°C and 173°C, respectively. A slightly broad peak of montelukast sodium was visible on the thermogram of montelukast sodium-loaded quickly dissolving buccal films. This will reduce the amount of drugs that are ejected from the films.

In-Vitro Dissolution Studies

It was discovered after the dissolution study that the medication might be released in as little as 5

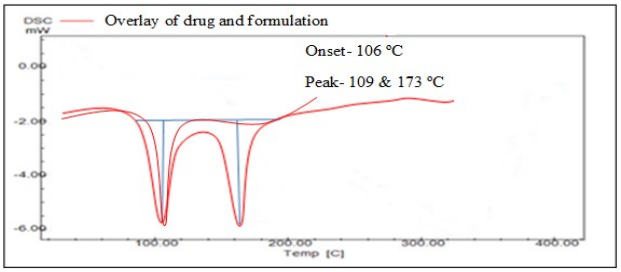

Figure 2: Overlay of DSC of Pure drug, Montelukast and Formulation.

minutes. This could be owing to the presence of HPMC K 100, which absorbed the surrounding fluid and released the drug. The drug release was determined to be between 90.75 and 99.14 percent at the end of 5 minutes in the drug release trials of formulations F1 to F9. Fig. 3 depicts the medication release profile for these formulations.

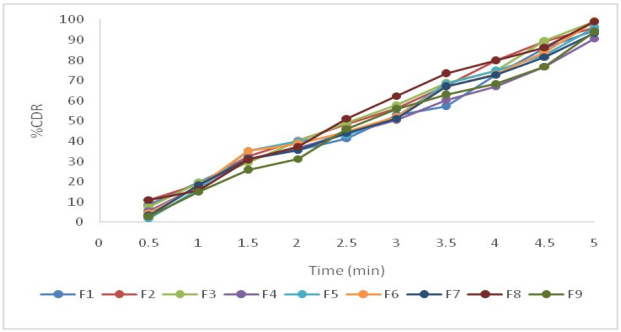

Figure 3: *In-vitro* dissolution studies

CONCLUSION

The solvent casting approach was used to successfully manufacture Montelukast sodium-loaded quickly dissolving oral films using HPMC K-100. All batches' disintegration times were found to be between 122 and 126 seconds. The chemical structure of montelukast sodium was preserved in the formulation, according to FTIR analysis. At the end of 5 minutes, the drug release was found to be between 90.75 and 99.14 percent.

REFERENCES

[1] Siddeshwar SS, Dattaprasad NV, Waghmare GA, Wadghule PB, Varpe PS. Fast Dissolving Oral Films: Easy way of Oral Delivery. Int J Curr Trends Pharmaceut. Res.2014; 2(3): 483-490.

[2] Satam MN, Bhuruk MD, Pawar YD. Fast Dissolving Oral Thin Films. Int J Uni Pharm Bio-Sci. 2013; 2(4):27-39.

[3] Parul Saini, Anoop Kumar, Pankaj Sharma, Sharad Visht, Fast Disintegrating Oral Films: A Recent Trend of Drug Delivery International Journal of Drug Development & Research, October-December 2012;4(4):80-94.

[4] Banker. G.S.,"Film coating theory and practice", J. Pharm. Sci.1966;55:81- 89.

[5] Naziyakhatoon, N.G. Raghvendra Rao, B. Mahipal Reddy. Formulation and evaluation of fast dissolving film of montelukast sodium, International Journal of Pharmaceutical Science and Research, 2014;5(5).

[6] Ali MS, Vijendar C, Sudheer Kumar D, Krishnaveni J. Formulation and Evaluation of Fast Dissolving Buccal Film Of Diazepam, J. Pharmacovigilance, 2016; 4(3):1-5

[7] K. Pallavi, P. Srinivasa Babu "Validated UV Spectroscopic Method for Estimation of Montelukast Sodium From Bulk and Tablet Formulations. International Journal of Advances in Pharmacy, Biology and Chemistry. 2012;1(4):1-4.

[8] M. Sri Rekha, S. K. Shahida. Formulation and Evaluation of Fast dissolving buccal film containing Isradipine solid dispersion. American Journal of Pharmatech and Research, 201; 5(2).

[9] Jadhav, SD, Kalambe RN, Jadha CM, Tekade BW, Patil VR. Formulation and evaluation of fast dissolving oral film of levocetirizine dihydrochlorid. Int J Pharm PharmSci 2012; 4(1): 337-341.

[10] A.Deepthi, B.Venkateshwara Reddy, K. Navaneetha. Formulation and Evaluation of fast dissolving oral film of Zolmitriptan. Americam Journal of Advanced Drug Delivery, 2014;2 (1):153-163.

[11] Vidhidesai, Nihar Shah, Formulation and Evaluation Of OlmesartanMidoxomil Mouth Dissolving Film. J. Pharm. Sci. Bioscientific Res. 2014;4(3):201-206.

[12] Apoorva Mahajan. Formulation and evaluation of Fast Dissolving Buccal Film of Sertraline. Int. J. Drug Develop. Res. 2012;14 (1):220-226.

[13] Apoorva Mahajan, Neha Chabra, Geeta Agrawal. Formulation and Characterization of Fast Dissolving Buccal film: A review. Scholar Research library, 2011;3(1):152-165.

[14] Sravanthi R.R., Rajlaxmi R, Krishna Moorthy S B. Mucoadhesive Buccal Films: An Innovative Drug delivery system. International Journal Of Pharmatech and research, 2014;6(5):1665-1678.

[15] Trupti Pednekar, Subash. S. Pillai, A. R. Shabaraya, Mohd Azharuddin, Design and Evaluation of Buccal Films of an Antihypertensive Drug, Am. J. PharmTech Res. 2012; 2(5):711- 722.

[16] Raghvendrarao N.G., Development of Mucoadhesive films for buccal administration of montelukast, International journal of pharmacy and technology, March 2010;2,(1).