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Formulation and evaluation of mouth dissolving tablets of montelukast sodium

Ajaykumar Patil*, Taqiuddin Aman, Nithin Bhargava B, Abhilash P, Madhuri Turaga, Supriya Kulkarni

Department of Pharmaceutics, Karnataka College of Pharmacy, Manhalli Road, Bidar – 585403, Karnataka, India.

ABSTRACT

Montelukast sodium is an anti-asthmatic, it mainly prevents leukotriene mediated effect associated with asthma and allergic arthritis. Mouth dissolving tablets of montelukast sodium was prepared by direct compression method using superdisintegrants such as croscarmellose sodium and crospovidone. The compatibility of the drug in the formulations was confirmed by IR studies. The formulations were subjected to precompression and postcompression parameters and the results were found to be within acceptable limits. The formulated tablets disintegrated in less than 26.33 sec fulfilling the official requirements for dispersible tablets. The rapid drug dissolution was observed in the formulations containing croscarmellose sodium and followed first order release kinetics. Finally, it can be concluded that mouth dissolving tablets of montelukast sodium can be prepared by direct compression method using croscarmellose sodium as superdisintegrant.

Key words: Mouth dissolving tablets, Montelukast sodium, Croscarmellose sodium, Crospovidone.

Corresponding author

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INTRODUCTION

Fast dissolving drug delivery is rapidly gaining acceptance as an important new drug delivery technology [1,2]. Not all fast dissolving technologies actually dissolve; some use different disintegration mechanisms such as high levels of disintegrants [3,4] and/or effervescent agents that cause the dosage form to disintegrate rapidly in the patient's mouth within a minute and can be gulped easily without the need of water. Thus, it offers increased patient compliance and convenience. The present work was aimed to formulate and evaluate efficacy of croscarmellose sodium and crospovidone in mouth dissolving tablets. Mouth dissolving tablets are dosage forms, which when placed in the mouth, disintegrate or dissolve in the saliva within a minute without the aid of water or chewing [5]. Montelukast sodium is chemically designated as [R-(E)]-1-[[[1-[3-[2-(7-chloro-2-quinolinyl) ethenyl] phenyl]-3-[2-(1-hydroxy-1-methylethyl) phenyl] propyl] thio] methyl] cyclopropaneacetic acid, monosodium salt, an orally administered drug of choice in the treatment of asthma in adults and children. Other problems like hand tremors, dysphagia in case of geriatric and non co-operative patients and the problem of swallowing is common phenomenon which leads to poor patient compliance. To overcome these drawbacks mouth dissolving tablets or orally disintegrating tablets or fast dissolving tablets has emerged as an alternative oral dosage form [6].

In the present study an attempt had been made to prepare mouth dissolving tablets of montelukast sodium in the oral cavity with enhanced dissolution rate and hence improved patient compliance. The basic approach used in the development of mouth dissolving tablets is the use of superdisintegrants like croscarmellose sodium and crosspovidone, which provide instantaneous disintegration of tablet after putting on tongue, thereby releasing the drug in saliva. These systems may offer superior profile with potential mucosal absorption, thus increase the drug bioavailability.

MATERIALS AND METHODS

Materials

Montelukast sodium was obtained as a gift sample from Matrix India (P) Ltd, Hyderabad. Microcrystalline cellulose (directly compressible), Croscarmellose sodium (Ac-di-sol) and Crospovidone (polyplasdone XL) were obtained as a gift samples from Signet Chemicals Corporation, Mumbai. All other chemicals and solvents used were of analytical reagent grade.

Methods

Preparation of Mouth dissolving tablets

Mouth dissolving tablets of montelukast sodium were prepared by direct compression method using croscarmellose sodium and crospovidone as superdisintegrants. The composition of formulation is shown in the table 1. The drug, diluents, superdisintegrants and sweetener

were screened through 40 mesh and properly mixed together. Talc and magnesium stearate were screened through 80 mesh and blended with initial mixture. Powder thus obtained was compressed into tablets on a 10 station single punch rotary tablet compression machine (Rimek). A biconvex punch 8 mm in diameter was used for tableting. Compression force of the machine was adjusted to obtain the hardness of 3-4 kg/cm^2.

Table 1: Composition of mouth dissolving tablets of Montelukast Sodium

Ingredients (mg/tab)	F_0	F_1	F_2	F_3	F_4	F_5	F_6
Montelukast sod.	5	5	5	5	5	5	5
Croscarmellose sod	-	3	6	9	-	-	-
Crospovidone	-	-	-	-	3	6	9
Aspartame	4	4	4	4	4	4	4
Magnesium stearate	1.5	1.5	1.5	1.5	1.5	1.5	1.5
Cherry flavor	3	3	3	3	3	3	3
Talc	3	3	3	3	3	3	3
MCC	127.5	124.5	121.5	118.5	124.5	121.5	118.5
Total weight	150	150	150	150	150	150	150

Evaluation of Mouth dissolving tablets

Tablets were evaluated for precompression parameters like angle of repose and compressibility index and for postcompression parameters like dimensions, weight variation, hardness, friability, *in vitro* dispersion time, wetting time, water absorption ratio, *in vitro* drug release. Drug content was analysed using Shimadzu 1700 UV- Visible spectrophotometer at 342 nm in 0.5% Sodium Lauryl Sulphate [7].

For *in vitro* dispersion time, tablet was added to 10ml of 0.5% Sodium Lauryl Sulphate solution, time required to complete dispersion was measured. To measure wetting time [8] of tablet, a piece of tissue paper was folded twice and placed in small Petri dish (Internal diameter 5.5 cm) containing 6 ml of amaranth solution. A tablet was put on the paper and time required for complete wetting or development of red colour on the tablet surface was measured. The wetted tablet was then weighed. Water absorption ratio R, was determined using the following equation: $R=100 \times W_a - W_b / W_b$ where W_a and W_b are the weights after and before water absorption respectively.

Compatibility studies

The stability of the drug in the formulation was confirmed by FTIR spectral analysis. FTIR spectra of the pure drug and all the formulations were determined by using Shimadzu FTIR spectrophotometer by KBr pellet method.

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Dissolution study

In vitro release of montelukast sodium from tablets was determined by using USP XXIV paddle dissolution apparatus (Electrolab TDT-06P) at 50 rpm using 900 ml of 0.5%SLS and temperature was maintained at 37±1° C throughout the study. 5 ml sample was collected at regular intervals for 30 min and the same volume of fresh medium was replaced. The samples withdrawn were filtered and drug content in each sample was analysed after suitable dilution by Shimadzu 1700 UV-Visible spectrophotometer at 342 nm [7].

RESULTS AND DISCUSSION

In this present study, mouth dissolving tablets of montelukast sodium has prepared by direct compression method, total 10 formulations were prepared by using croscarmellose sodium and crosspovidone as superdisintegrants while microcrystalline cellulose was used as diluent, which is also a superdisintegrant.

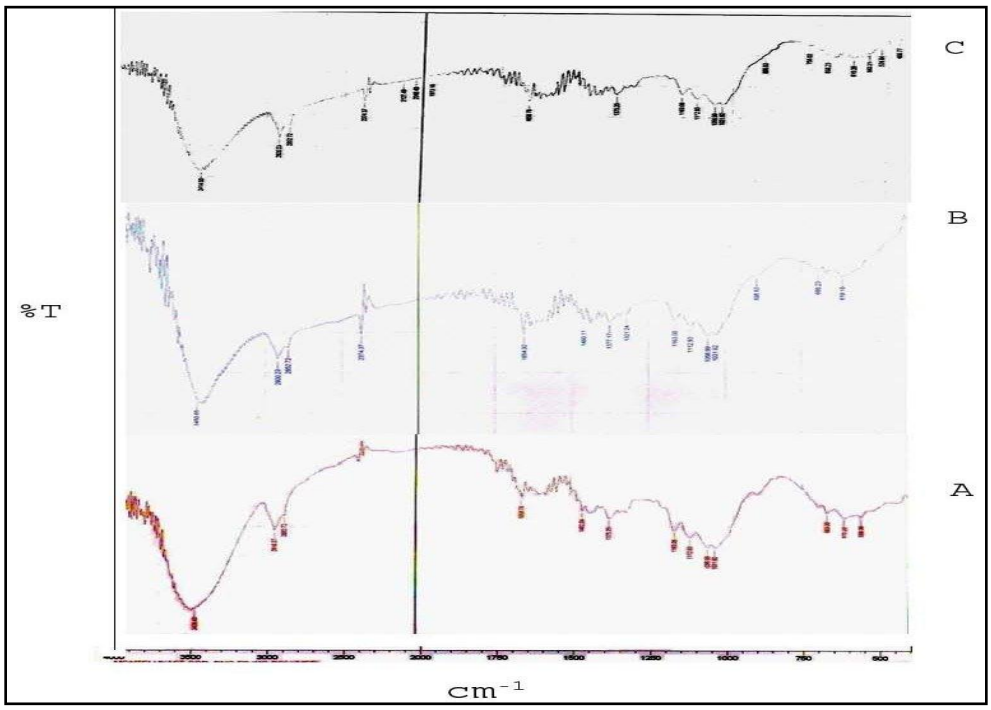

Figure 1: FTIR Spectra of Montelukast sodium (A), Montelukast sodium + Croscarmellose sodium (B) and Montelukast sodium + Crospovidone (C).

IR spectra analytical reports shown in fig 1 indicating that there was no interaction between drug and excipients used. The flow of the powder mixture was analysed before compression to tablets. Low compressibility index (≤15.96) and angle of repose (≤29.75) values indicated a fairly good flow ability of powder mixture. As the tablet powder mixture was free flowing, tablets produced were of uniform weight with acceptable weight variation (≤3.54%) due to uniform die fill. Hardness (3.00-3.34kg/cm^2) and friability loss (0.19-0.63%) indicated

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that tablets had a good mechanical resistance. Drug content was found to be high (≥95.45%) in all the tablet formulations, all the tablets disintegrated in (≤26.33sec) fulfilling the official requirements (<3 min) for dispersible tablets [9]. Fig 2 shows the tablet before and after wetting where as fig 3 depicts the disintegration behavior, wetting time and water absorption ratio of the tablets. It is observed that the disintegration time of the tablets decreased (from 26.33 to 17sec) with increase in the concentration of croscarmellose sodium, the disintegration time of the tablets decreased (from 11.33 to 8.39sec) with increase in the concentration of crospovidone. The disintegration times of crospovidone containing tablets are comparatively lower than those containing croscarmellose sodium. The faster disintegration of crospovidone tablets may be attributed to its rapid capillary activity and pronounced hydration with little tendency to gel formation [10]. Thus, these results suggest that the disintegration times can be decreased by using wicking type of disintegrants (crospovidone).

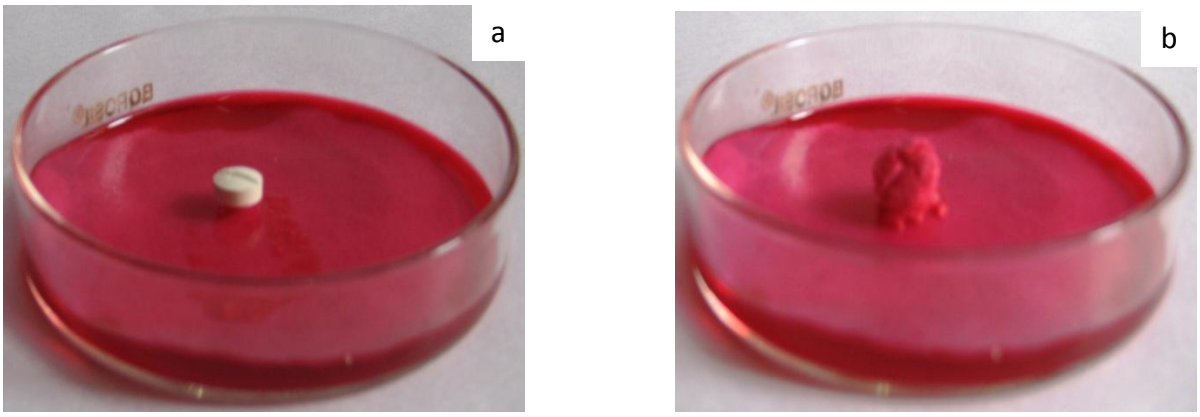

Figure 2: Mouth Dissolving Tablet a) before wetting, b) after wetting

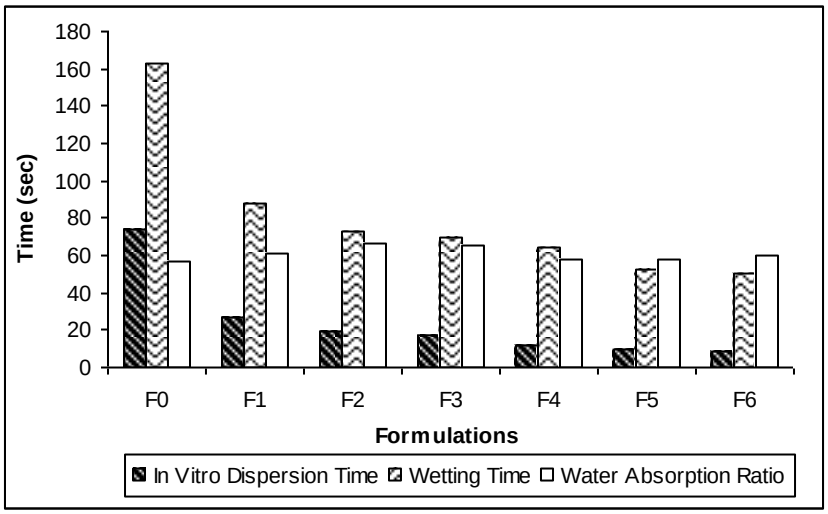

Figure 3: Comparison of *in vitro* dispersion time, wetting time and water absorption ratio of the formulations

Since the dissolution process of a tablet depends upon the wetting followed by

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disintegration of the tablet, the measurement of wetting time may be used as another confirmative test for the evaluation of dispersable tablets. Wetting time of the tablets decreased(from 88.3 to 69.33 sec)with increase in concentration of croscarmellose sodium, wetting time of the tablets decreased (from 64.3 to 50sec)with increase in concentration of crospovidone, the wetting times of crospovidone containing tablets are comparatively lower than those containing croscarmellose sodium. The results are in consistent with disintegration test results. Water absorption ratio increased with decrease in wetting time.

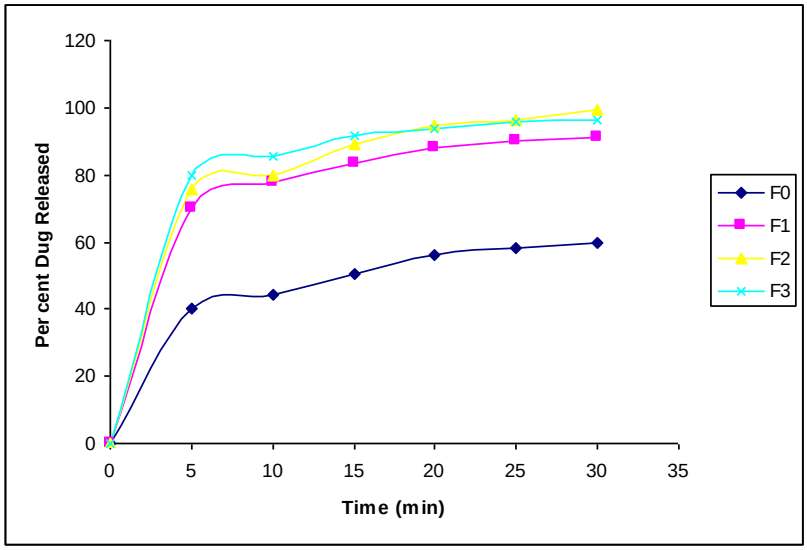

Figure 4: *In vitro* drug release of formulations containing croscarmellose sodium

Formulations F_0, F_1, F_2 and F_3 (Fig.4) releases 60%, 90.93%, 99.3% and 96.56% respectively at the end of 30 min. Formulations F_0, F_4, F_5 and F_6 (Fig.5) releases 60%, 90.93%, 97.5% and 95.62% respectively at the end of 30 min. The rapid drug dissolution was observed in the formulations containing croscarmellose sodium, this may be attributed to rapid swelling and disintegration [10] of tablet in to apparently primary particles [11]. The slow drug dissolution was observed in formulations containing crosspovidone when compared to croscarmellose sodium, this may be attributed to high capillary activity and pronounced hydration with a little tendency to gel formation [10] and disintegrates the tablet rapidly but into larger masses of aggregated particles [11]. Thus the differences in the size distribution generated and the differences in surface area exposed to the dissolution medium with different superdisintegrants rather than speed of disintegration of tablets may be attributed to the differences in drug dissolution with the same amount of super disintegrants in the tablets. To know the order of drug release, the dissolution data were subjected to different kinetic models i.e., zero order and first order. The correlation coefficient values obtained were found to be linear for first order release.

CONCLUSION

Finally, it can be concluded that mouth dissolving tablets of montelukast sodium can be prepared by direct compression method using croscarmellose sodium as superdisintegrant.

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