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NEW RP- HPLC METHOD FOR THE ANALYSIS OF MONTELUKAST SODIUM IN PHARMACEUTICAL DOSAGE FORMS

N.Kanakadurga devi*, A.Prameela rani, B.R. Madhavi, B.S.Mrudula

Kvsr Siddhartha college of pharmaceutical sciences,Vijayawada-520010.

***Corres.author: nellurik@rediffmail.com**

ABSTRACT: A simple and sensitive RP-HPLC method has been developed for the estimation of Montelukast sodium in pharmaceutical formulations. The separation of analyte was carried on inert sil ODS 3r column (250mm×4.6mm×5µm) and mobile phase having a fixed composition of methanol and trifluoro acetic acid in the ratio of 90:10 v/v. The analyte was monitored with UV detector at 350nm. The developed method has linearity in the concentration range of 2 – 20 µg/ml. The proposed method was validated for precision, accuracy and linearity. The method was applied for quality control of Montelukast sodium in tablets as well as in pure drug form.
KEYWORDS: Montelukast sodium, RP-HPLC.

INTRODUCTION

Montelukast sodium[1-3] is chemically 1-[[[(1R)-1-[3-[(1E)-2-(7-chloro-2-quinolinyl)ethenyl]phenyl]-3-[2-(1-hydroxy-1-methylethyl)phenyl]propyl]thio]methyl]cyclopropane acetic acid **(Fig 1)**. It is for prophylaxis and chronic asthma. Literature survey reveals the availability of only a few analytical methods such as HPLC[4-8], LC-MS[9-10],for determination of Montelukast sodium in pharmaceutical formulations and in biological fluids. We developed a simple and accurate RP-HPLC method for the estimation of Montelukast sodium in pure form and in pharmaceutical dosage forms.

EXPERIMENTAL DETAILS

INSTRUMENTATION:

Shimadzu prominence HPLC was employed for RP-HPLC method development. Inert sil ODS 3r column (250mm×4.6mm×5µm) was used for drug separation.A sample volume of 20µl was used throughout the analysis. The analyte was monitored with UV detector at 350 nm .The data was acquired and analyzed by LC solution software.

CHEMICALS USED:

Pure drug sample of Montelukast sodium was procured as a gift sample from Cadila Pharmaceuticals, Ahmedabad . HPLC grade methanol and acetonitrile were obtained from Merck, Mumbai.All other chemicals used were of analytical reagent grade.

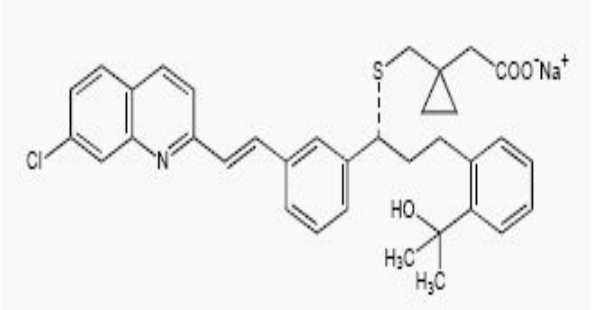

Fig.1 : Chemical Structure of Montelukast sodium

MOBILE PHASE PREPARATION:
Methanol and trifluro acetic acid were mixed in a proportion of 90:10 v/v. The above prepared mobile was filtered through 0.45µm nylon membrane filter and degassed with ultrasonicator.

STANDARD PREPARATION:
About 100 mg of pure Montelukast sodium was taken and dissolved in 100 ml of acetonitrile to get a stock solution of concentration 1000 µg/ml. The stock solution was further diluted with the mobile phase to get standard solutions in the concentration range of 2 – 20 µg/ml.

SAMPLE PREPARATION:
Twenty tablets were taken and crushed to a fine powder in a mortar. Tablet powder equivalent to 10 mg of Montelukast sodium was taken and transferred to 100 ml volumetric flask. About 70 ml of acetonitrile was added and sonicated for 20 min.The resulting mixture was filtered through a 0.45µm membrane filter in to another 100 ml volumetric flask. The volume was made up to the mark with same solvent. This sample solution was further suitably diluted with the mobile phase for chromatography. Similarly placebo solution was prepared by using the tablet exciepients omitting the drug.

PROCEDURE FOR ESTIMATION OF DRUG:
The HPLC system consisting of intersil column was stabilized with the mobile phase at a flow rate of 1.0 ml/min for 30 min. The standard solutions in the concentration range of 2 to 20 µg/ml were injected five times in to the system followed by one placebo injection. The calibration curve was constructed by taking concentration on X-axis and correspondig mean peak area on Y-axis. The sample prepared above was injected twice in to the system and average peak area from the chromatograms was determined. The concentration of the drug in the sample was calculated from regression equation.

RESULTS AND DISCUSSION:
After performing some systematic trials, methanol and trifluoro acetic acid in a proportion of 90:10 v/v was fixed as a mobile phase and inert sil ODS 3r column as a stationary phase. Montelukast sodium elutes at a retention time of 7.904 minutes. The blank chromatogram and the typical chromatogram showing the separation of Montelukast sodium were shown in the **fig.2 and 3** respectively.
The placebo prepared from tablet excipients was injected into system and no interfering substances were found at retention time corresponding to analyte peak, indicating the specificity of the method. The proposed method is having good linear response over the concentration range of 2 to 20
µg/ml with a correlation coefficient of 0.9998 the limit of detection and limit of quantification were found to be 0.0332 µg/ml and 0.1005 µg/ml respectively. The linearity graph was presented in **fig.4**
Intra-day and inter-day precision was performed with 5 µg/ml and 10 µg/ml of Montelukast sodium solution to study the day to day variations which may effect chromatographic performance. The intra-day and inter-day precision data were presented in **Table.1**.Low percent RSD values indicates that developed method is precise.

TABLE 1 : Intra-day and Inter-day precision

Montelukast sodium conc(µg/ml)	Montelukast sodium conc(µg/ml) found			
	Intra-day		Inter-day	
	Mean(n=5)	%RSD	Mean(n=5)	%RSD
5	5.01	0.98	5.03	1.12
10	10.03	0.84	9.99	0.98

TABLE 2 : Analysis of Montelukast sodium in pharmaceutical formulations

Formulations Labelled amount(mg/tab)		Mean amount found(mg)*		Mean% recovery found	
		Proposed method(n=6)	Reference method(n=6)	Proposed method	Reference method
Tablet1	4	4.03±0.03 t=1.33 F=2.12	4.01±0.06 t=1.21 F=1.15	101.52±0.28	100.33±0.41
Tablet2	5	5.01±0.06 t=0.98 F=2.39	5.02±0.04 t=0.74 F=2.48	99.99±0.43	99.97±0.71
Tablet3	10	10.04±0.11 t=1.05 F=3.13	10.06±0.12 t=1.23 F=1.88	100.83±0.15	101.27±0.51

*The 't' and 'F' values refer to the comparision of test HPLC method with the reference HPLC method.Theoritical values of 't' and 'F" at 95% level of significance are 2.57 and 5.05 respectively.

The accuracy of the method was established by recovery studies. High percent recovery values indicate that the proposed method is accurate. Some of the commercially available formulations as well as formulation developed by us were analysed by the proposed method and the reference method. The percent recovery and analysis results were incorporated in **Table 2.**

As the developed method is simple, sensitive and accurate it can be adapted for routine quality control of Montelukast sodium in pure form and in pharmaceutical formulations.

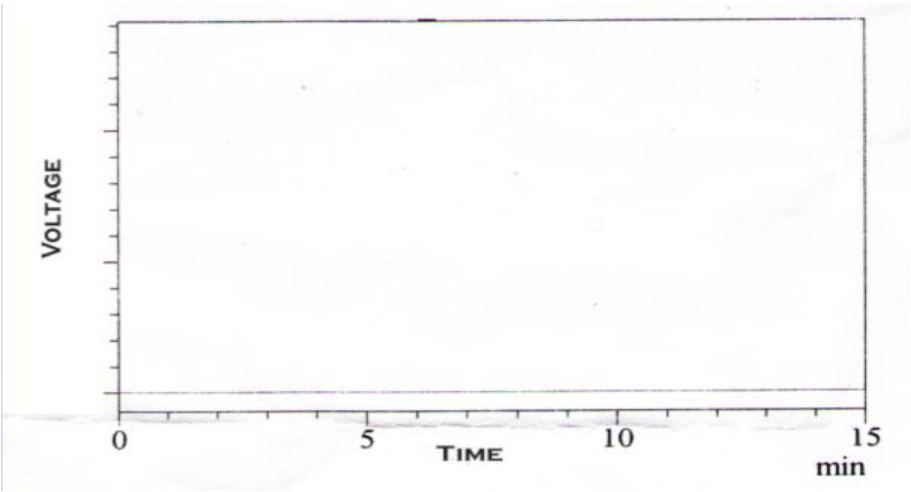

Fig.2 : Blank chromatogram

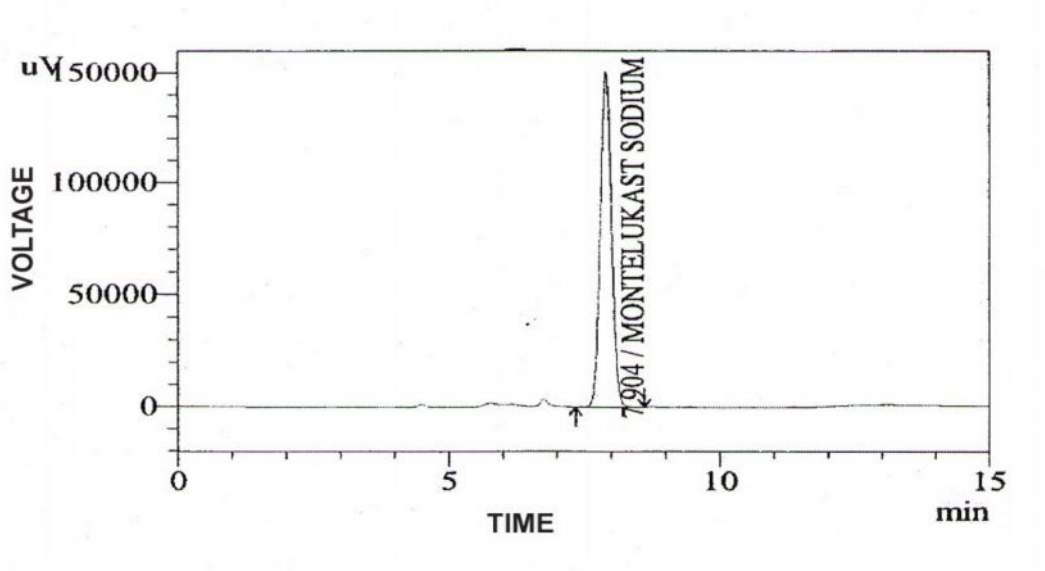

Fig.3 :Typical test chromatogram.

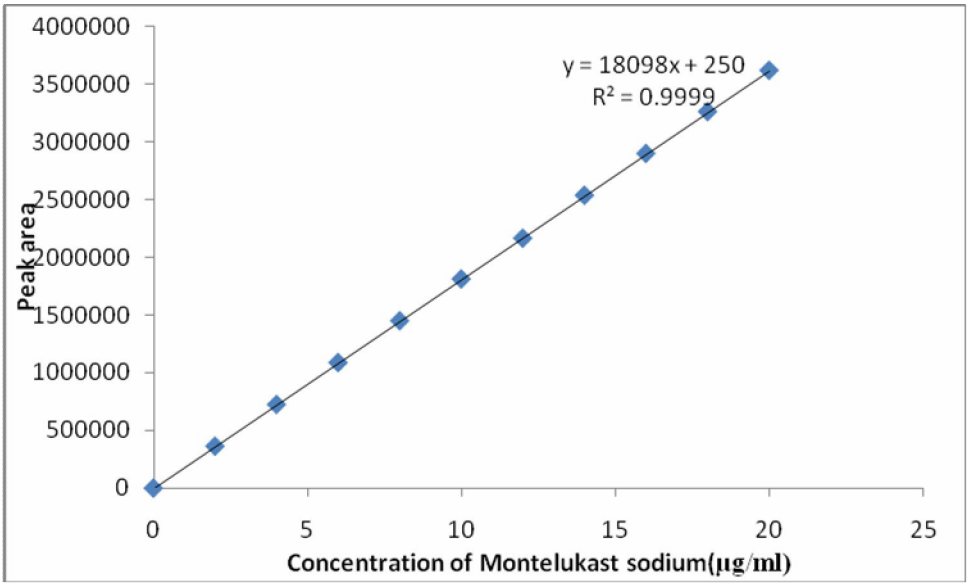

Fig.4 : Linearity graph of Montelukast sodium

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