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METHOD DEVELOPMENT AND VALIDATION OF MONTELUKAST SODIUM IN BULK AND PHARMACEUTICAL DOSAGE FORMS BY RP-HPLC

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ABSTRACT

A rapid and precise reverse phase High performance liquid chromatographic method has been developed for the estimation of Montelukast sodium in its pure form as well as in pharmaceutical dosage forms. Chromatography was carried out on a C_{18} Column(150 x 4.6mm) using a mixture of Ammonium acetate buffer(pH 4.0+0.05) ,water and Methanol in a ratio of (15:25:60 v/v) as the mobile phase at a flow rate of 1.0mL/min the detection was done at 257nm. The retention time of the drug was 4.2 min. The method produced linear responses in the concentration range of 40-120 µg/ml of Montelukast. The method was found to be reproducible for analysis of the drug in tablet dosage forms.

KEY WORDS: Montelukast, Estimation, RP-HPLC.

1.INTRODUCTION

Montelukast sodium, r-(E)-1-[[(1-(3-(2-(7-chloro-2-quinolinyl) Ethyl) phenyl)-(3-(2-(1-hydroxy-1-methyl ethyl)phenyl)propyl)thio) methyl) cyclo propaneacetic acid, monosodium salt. It is a anti asthmatic drug it inhibits the broncho constriction due to antigen challenge. It is a selective leukotriene receptor antagonist of the cysteinyl CysLT1 receptor. A literature survey revealed that only a few HPLC (Chauhan,2006; Sameer2001; Sripalkit,2008) methods are available for the estimation of Montelukast sodium. The authors now propose a new validated, sensitive and reproducible HPLC method for the determination of Montelukastsodium and the dosage forms was also observed.

2.EXPERIMENTAL

Chromatographic conditions : A prominence isocratic HPLC system (waters) C_{18}ODS column (150x4.6mm, 5µ) with a UV-visible detector was employed in the study. A 20µL Hamitton injection syringe was used for sample injection.HPLC grade Ammonium acetate buffer, water and methanol andwere used for the preparing the mobile phase. A freshly prepared (15:25:60 v/v) mixture of buffer, water and methanol was used as the mobile phase. The solvents was filtered through a 0.45µ membrane filter and sonicated before use.The flow rate of the mobile phase was maintained at 1.0mL/min. the column temperature was maintained at room temperature, the detection of the drug was carried out at 257nm.

Preparation of Standard Solutions: Weigh accurately Montelukast working standard equivalent to about 20mg of Montelukast in to 20mL of volumetric flask, add 15mL of diluents and sonicate to dissolve for about 10min, further make up the volume with diluents. And dilute 1mL to 10mL with methanol. Subsequent dilutions of this solution ranging from 40-120µg/mL were made in 10mL volumetric flask to each dilution. Each dilution was injected 5 times in to the column (20mL) and the corresponding chromatographs were obtained, fromthese chromatograms the ratio of the area under the peak of the drug was calculated. The regression of the drug concentrations over the ratios was computed. This regression equation obtained was used to estimate the amount of Montelukast sodium in pharmaceutical dosage forms.

Solutions containing 40-120µg/mL of montelukast were subjected to the proposed HPLC analysis to check the inter day and intra day variation of the method by adding known amounts of montelukast sodium to the pre-analyzed samples and then analyzing samples and then analyzing them by the proposed method.

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Estimation of Montelukast in tablets: Two commercial samples of the tablets containing the drug were chosen for testing the suitability of the proposed method to estimate montelukast in tablets. For this, Weigh accurately quantity of the powdered tablets equivalent to about 10mg of montelukast in to 100mL volumetric flask, add about 60mL of diluents, Sonicate for about 30min and dilute to 100ml with water and methanol. Filter through 0.45 micron filter.The contents of the flaskswere made up to the volume with the mobile phase and mixed well. Twenty micro liters of each of these solutions was then injected five times in to the column. The mean peak area ratios of the drug to the five such determinations were calculated and the drug content in the tablets was quantified using the regression equation obtained for the pure sample.

3.RESULTS AND DISCUSSION

The aim of this study was to develop a rapid and precise reverse phase high performance liquid chromatographic method has been developed for the estimation of Montelukast sodium in its pure form as well as in pharmaceutical dosage forms. Chromatography was carried out on a C_{18}column (150 x 4.6mm) using a mixture of Ammonium acetate buffer (pH 4.0+0.05),water and Methanol in a ratio of (15:25:60(v/v)) as the mobile phases at a flow rate of 1.0mL/min the detection was done at 257nm. The retention time of the drug was 4.2 min. The method produced linear responses in the concentration range of 40-120 µg/ml of montelukast. The method was found to be reproducible for analysis of the drug in tablet dosage forms. The chromatogram is shown in Fig.1.

Each of the samples was injected 5 times and the same retention time was observed in all the cases. The ratio of the peak areas of Montelukast for the different concentrations taken up was calculated and the average value for 5 such determinations are shown in Table.1. The peak area of Montelukast was reproducible as indicated by low coefficient of variation. A good linear relationship (r=0.9991) was observed between the concentration of Montelukast and the respective ratios of peak areas in the concentration range of 40 to 120µg/mL of the drug. The linearitycurve was constructed and it's regression coefficient is Y=21977X+32398, when Montelukast solutions containing 40 to120 µg/mL were analyzed by the proposed method for finding out the intra & inter day variations in the recoveries, A low coefficient of variation in the results was observed as shown in Table.2. This shows that the present HPLC method is highly precise. The amount of Montelukast obtained from the preanalyzed samples containing known amounts of added drug are shown in Table.3. About 99.12% of Montelukast could be recovered from the Pre-analyzed samples indicating high accuracy of the proposed method.

The drug content in the tablet was quantified by using the proposed analytical method. The tablets were found to contain an average of 99.12% of the labeled amount of the drug. The low coefficient of variation indicates the reproducibility of the assay of Montelukast in dosage forms. It canbe concluded that the proposed HPLC method is sufficiently sensitive and reproducible for the analysis of Montelukast in pharmaceutical dosage forms with in a short analysis time. The method was validated by the evaluation of the validated parameters.

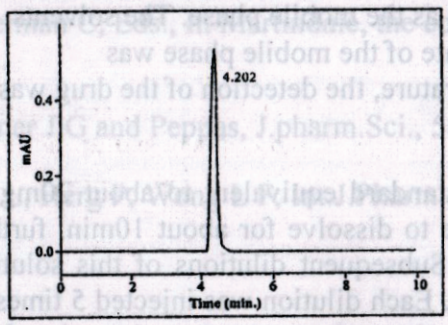

Fig: 1 A typical chromatogram of Montelukast

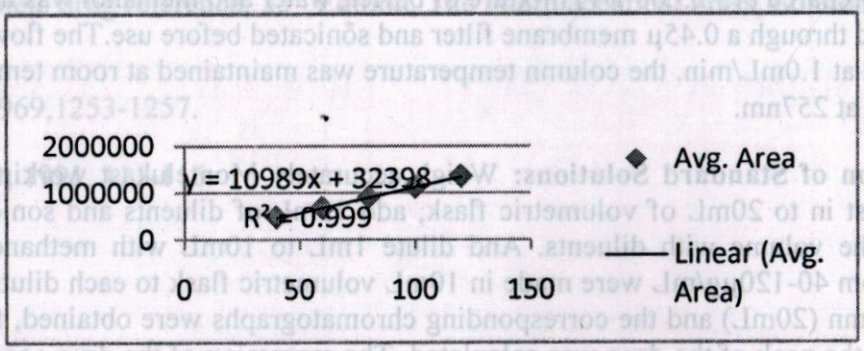

Fig.2: Linearity graph of Montelukast

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S.No.	Concentration (mcg\ml)	Avg. Area	SD	%RSD
1	40	485449	1024.7	0.18
2	60	678359	305.5	0.05
3	80	904209	238.3	0.03
4	100	1131854	603.2	0.05
5	120	1357563	232.6	0.02

Table: 1-Calibration of the proposed method

Sample No.	Area	Amount%
1	970418	98.5
2	1111109	99.2
3	1014665	98.9
4	1077323	100.0
5	1063352	98.7
	Mean	99.06
	SD	0.63
	% RSD	0.64

Table: 2 – Precision of proposed method

S.No.	Concentration %	Area	Amountadded mcg/ml	Amountfound mcg/ml	%Recovery	Mean
1	40	561737	49.9	49.4	99.6	99.5
2	40	561224	49.6	49.4	99.5	
3	40	561004	49.6	49.4	99.5	
4	60	838272	74.4	73.8	99.1	99.1
5	60	838947	74.4	73.8	99.2	
6	60	838103	74.4	73.8	99.1	
7	80	1117585	99.3	98.4	99.1	99.1
8	80	1118630	99.3	98.4	99.2	
9	80	1116306	99.3	98.2	99.0	
10	100	1395847	124.1	122.8	99.0	99.0
11	100	1395118	124.1	122.8	99.0	
12	100	1394733	124.1	122.7	98.9	
13	120	1672141	148.9	147.2	98.8	98.9
14	120	1672964	148.9	147.2	98.9	
15	120	1671676	148.9	147.1	98.8	

Table: 3: Recovery data of Montelukast

REFERENCES

Chauhan B, Shuba Rani, Niviskar M, Padh H, Developed and validated RP-HPLC method for the estimation of Montelukast in human plasma, I.J.P.S., 68(4), 2006, 517-520.

Sameer Alrawithi, Gazlan SAL, Ahmadi WA, Ibrahim A, Alshowaler, Ahmed Yusuf & Raines DA, Developed and validated RP-HPLC method for the estimation of Montelukast in human plasma, Jour. of chromatogr B: biomed scie and applications, 754(2), 2001, 527-531.

Sripalakit P, Kongthong B, Witthava A.S.C, Developed and validated RP-HPLC method for the estimation of Montelukast in human plasma, Journal of Chromatogr B Analyt.technol.Biomed Life sci., 2008.