

Visible spectrophotometric methods for estimation of *Montelukast* sodium in bulk dosage forms and formulations

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ABSTRACT

Sophisticated analytical methods viz. HPLC and HPTLC which are being employed for analysis are relatively expensive and hence need for simple analytical methods arises, that are suggested in the proposed methods for routine determination of *Montelukast* sodium (MTK)^{1,2} in pharmaceutical formulations and bulk dosage forms. These methods are based on the formation of colored species on binding of *Montelukast* Sodium (MTK) with ferric chloride and Concentrated. Hydrochloric acid reagents to produce a yellowish green colored chromogen (λ_{max} at 440 nm) for method A and orcinol in Conc. HCl to produce a green colored chromogen (λ_{max} at 420 nm) for Method B. Results of analysis were validated statistically and by recovery studies. Assay and recovery studies were also performed. The percent Relative Standard Deviation of these methods were found to be 1.32 for Method A and 0.35 for Method B. Based on these values these methods could be treated as simple, sensitive and reproducible based on the principle of absorption visible spectrophotometry for the determination of *Montelukast* Sodium (MTK) in bulk and pharmaceutical formulations.

Key words: *Montelukast* Sodium (MTK) , Analysis, Spectroscopy, Molar absorptivity, Beer's Law.

INTRODUCTION

Montelukast Sodium^{1,2}

Montelukast sodium is [R-(E)-1-[[[1-[3-[2-(7-chloro-2-quinolinyl) ethenyl] phenyl]-3-[2-(1-hydroxy-1-methylethyl)phenyl]propyl]thio]methyl]cyclopropaneacetic acid, sodium salt (mono).which is a leukotriene receptor antagonist used as an alternative to anti-inflammatory medications in the management and chronic treatment of asthma and exercise-induced bronchospasm (EIB)drug that is marketed under trade names such as Singulair[®] and Montair is usually administered orally. *Montelukast* blocks the

action of leukotriene D4 on the cysteinyl leukotriene receptor Cys LT1 in the lungs and bronchial tubes by binding to it. This reduces the bronchoconstriction otherwise caused by the leukotriene, and results in less inflammation. Because of its method of operation, it is not useful for the treatment of acute asthma attacks. Again because of its very specific locus of operation, it does not interact with other allergy medications such as theophylline.

Only a few methods viz, HPLC^{3, 4, 6, 9, 11}, Spectrofluorimetry⁵, Electrophoresis¹⁰, Spectrophotometry^{7, 8} and LC-ESI-MS¹² appeared in the literature for the determination of MTK in bulk and

pharmaceutical formulations. As the drug has recently come into existence, the number of available procedures that could be of utility to a small-scale industry are less and hence the author has presented these methods described below for the routine quality control analysis of Montelukast sodium in dosage forms.

MATERIAL AND METHODS

Instrumentation

After due calibration of the instrument, spectral and absorbance measurements are made using Genesys 10 UV Spectrophotometer procured from Thermo Scientific company marketed by Merck.

Reagents

All the chemicals used were of analytical grade. All the solutions were freshly prepared with double distilled water. Freshly prepared solutions were always used for analysis. In the proposed methods aqueous solutions of ferric chloride (0.5% w/v) and conc. HCl for Method A and orcinol (0.5% w/v in conc. HCl) for Method B were used.

Standard and Sample solution of Montelukast Sodium

About 100 mg of Montelukast Sodium (formulation for method A) and (Bulk sample for Method B) was accurately weighed on a digital single pan balance and dissolved in 100 ml of water in a volumetric flask to prepare a solution that has a concentration equal to 1 mg/ml standard solution and further dilutions are made with the same solvent (100 μ g/ml) for Method A and Method B.

Assay Procedure

Method A

Aliquots 0.2-1.0 ml of standard MTK solution (100 μ g/ml) was transferred to a series of 10 ml graduated tubes. To each tube 2 ml of ferric chloride (0.5%) was added followed by 0.5 ml of conc HCl. The absorbance of the yellowish green colored chromogen was measured at 440 nm against reagent blank.

Method B

Aliquots 0.4-2.0 ml of standard MTK solution (100 μ g/ml) was transferred to a series of 10 ml graduated tubes. To each tube 2 ml of orcinol

Table 1: Optical characteristics, precision and accuracy of the proposed method

Parameter	Method A	Method B
λ_{\max} (nm)	440	420
Beer's law limit (μ g/ml)	2-10	4-20
Sandell's Sensitivity (μ g/cm ² /0.001 abs. unit)	0.0185	0.0209
Molar absorptivity (litre.mole ⁻¹ .cm ⁻¹)	3.2841x10 ⁴	2.8964 x 10 ⁴
Correlation coefficient (r)	0.9998	0.9999
Regression Equation (Y)		
Slope a	0.1397	0.0377
Intercept b	0.002855	0.0043625
% RSD	1.32	0.35
%Range of errors (95%Confidence limit)		
0.05 level of Significance	\pm 1.103	\pm 0.2926
0.01 level of Significance	\pm 1.632	\pm 0.4329

* Y= a + bx, where 'Y' is the absorbance and x is the concentration of Montelukast Sodium in μ g/ml.

** For six replicates.

(0.5% in conc HCl) solution was added. The absorbance of the resulting green colored chromogen was measured at 420 nm against reagent blank. The amount of MTK was computed from the calibration curve.

RESULTS

The results of analysis for methods A and B were validated through systematic statistical analysis and the results are tabulated. The statistical analysis values are reported in Table-1 and assay and recovery results for these methods are tabulated in Table-II.

Table 2: Estimation of Motelukast Sodium (MTK) in Pharmaceutical formulations

Labeled amount Formulations	Bulk / Tablet	% Recovery by proposed methods	
		Method A	Method B
Tablet 1	10 mg	98.68	99.65
Tablet 2	10 mg	98.7	99.85
Tablet 3	10 mg	99.1	99.9
Tablet 4	10 mg	99.5	100.1

which is capable of reaction with orcinol in HCl to undergo a dehydration reaction resulting in the formation of a green colored complex. This method is a simple example of dehydration under acidic conditions involving the hydroxyl group of the drug and hydroxyl group of orcinol.

For these methods the optical characteristics such as absorption maxima, Beer's law limits, molar absorptivity and sandell's sensitivity, regression analysis using the methods of least squares, slope (a), intercept (b) and correlation coefficient (r) obtained from different concentrations are summarized in Table-1. The precision and accuracy were found by analyzing six replicate samples containing known amounts of the drug and the results are summarized in Table-1. The accuracy of these methods in the case of formulations was thoroughly studied by recovery experiments and the results were presented in Table-2. Additional checks on the accuracy of these methods were analyzed by adding known amounts of pure drug to pre-

DISCUSSION

Method A

The proposed method is based on oxidation of the drug in the presence of ferric chloride under acidic conditions to form a yellowish green colored complex. This method is a simple example of oxidation reaction under acidic conditions, i.e., oxidation in the presence of ferric chloride.

Method B

Exploitation of the functional groups in the drug exhibited the involvement of the hydroxyl group,

analyzed formulations.

CONCLUSION

Performance recovery experiments and percent recovery values obtained indicated the absence of interferences from the commonly encountered pharmaceutical additives and excipients. Thus the proposed methods are simple and sensitive with reasonable precision and accuracy and can be used as a standard method for the routine determination of *Montelukast Sodium* in quality control analysis.

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