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A simple spectrophotometric assay of Montelukast in Pharmaceutical formulations

G. Srihari[1*], K. Nagaraja Setty[2], N. Rami Reddy[1] and I.E. Chakravarth[3]

[1]*Department of Chemistry, S.B.S.Y.M. Degree College, Kurnool AP, India*
[2]*Department of Chemistry, Government Degree College for Men, Kurnool, AP, India*
[3]*Department of Chemistry, Rayalaseema University, Kurnool AP, India*

ABSTRACT

A simple and sensitive spectrophotometric method for the estimation of montelukast is developed by the formation of ion pair complexe with wool fast blue. The ion pair complex is formed by the interaction of drug with wool fast blue. Wool fast blue is insoluble in water and soluble in chloroform. The organic layer is extracted from chloroform and the absorbance of organic layer is measured at 585 nm against chloroform blank.

Key words: Wool fast blue, Montelukast, spectrophotometric.

INTRODUCTION

Montelukast is a specific cysteinyl leukotriene receptor antagonist belonging to a styryl quinolines series with the chemical name 2-[1-[1(R)-[3-[2(E)-(7-chloroquinolin-2-yl) vinyl] phenyl]-3[2-(1-hydroxy-1-methylethyl) phenyl] propylsulfanylmethyl] cyclo-propyl] acetic acid sodium salt. It is developed as a therapeutic agent for the treatment of bronchial asthma by Merck and Co. Some method available for the determination of montelukast sodium include Spectrophotometric method[1], HPLC[2], protein precipitation,[3]liquid chromatography/tandem mass spectrometry(LC-MS/MS),[4] liquid-liquid extraction using HPLC with the fluorescence detector,[5] its *S*-enantiomer in human plasma by stereo selective high performance liquid chromatography (HPLC) using column-switching[6] and its determination in human plasma by the column-switching HPLC method,[7] derivative spectroscopy, HPLC,[8] microwave-assisted extraction (MAE) technique,[9] method for the application of pressurized liquid extraction technology for

pharmaceutical solid dosage form[10] Residual acetate analysis in bulk drug.[11] Voltammetric determination[12] and Spectrofluorometric determination[13]. Various combinations of montelukast sodium is reported in the literature for simultaneous determination by spectroscopy method [14-16]. It would therefore be beneficial to provide accurate, precise, and reliable method for determination of montelukast in pharmaceutical dosage forms. In the present work, the ion pair complex is formed by the interaction of montelukast sodium with Wool fast blue. Wool fast blue is insoluble in water and soluble in chloroform. The organic layer is extracted from chloroform and the absorbance of organic layer is measured at 585 nm against chloroform blank.

In developing the proposed methods a systematic study of the effects of various relevant parameters in the methods concerned, concentration of reagents, order of addition, time and temperature required for reaction, p^H of buffer, nature of solvents for final dilution, stability of reagents of the coloured species are undertaken by varying one parameter at a time and controlling all other parameters to get a maximum colours development and minimum black colours, reproducibility and the reasonable period of stability of final coloured species formed.

After systematic and detailed study of the various parameters mentioned above, the following procedures are recommended for the determination of montelukast in bulk samples and pharmaceutical formulations.

EXPERIMENTAL SECTION

Instrumentation

A Milton Roy 1001 plus spectrophotometer with 1 cm quartz cells was used for all measurements. An Eutech p^H meter model: cyber scan ECPH 1000 is used for p^H measurements.

Chemicals and reagents

All the chemicals and reagents used were of AR grade. Double distilled water was used throughout the investigation. .

Buffer solution (p^H 1.5)

Buffer solution is prepared by mixing 289 ml of glycine solution (37.52 gm of glycine and 29.24 gm of Nacl are dissolved in 500ml of distilled water) with 711ml of 0.1 M Hcl.

Wool fast blue solution: (0.2% W/V)

Wool fast blue solution is prepared by dissolving 200mg of wool fast blue (Flaka) in 100 ml of distilled water.

Standard solution

Pure montelukast (50 mg) was dissolving in 50 ml methanol. This stock solution was further diluted with methanol to get desired concentration

Assay procedure

Into a series of 10ml volumetric flasks, aliquot samples of montelukast ranging from 0.2 to 2.0 ml (1ml containing 100mg) were transferred. To each flask, 2 ml buffer solution and 2 ml dye were added. The final volume was brought to 10ml with distilled water. The solution in each

flask is shaken well with 5ml chloroform and allowed to separate two layers. The absorbance of the organic layer was measured at 585 nm against chloroform as bulk. The amount of montelukast present in the sample was read from calibration curve was shown in fig.2.

Pharmaceutical formulations

Twenty tablets of montelukast were weighed and powdered. The powdered equivalent to 50 mg of montelukast was transferred into 50 ml volumetric flask, shaken thoroughly with 30 ml methanol and filtered. The filtrate was diluted to 50 ml with methanol. This stock solution is further diluted to obtain the working concentration of 100 µg/ml. Different aliquots of solutions were taken and analyzed by using the procedure described earlier and the amount of montelukast present in sample was read from calibration graph. The results are tabulated in Table 1.

RESULTS AND DISCUSSION

In the present work montelukast and wool fast blue was treated with chloroform in the p^H 1.5 to form ion pair complex. The ion pair complex is soluble in chloroform and the complex is extracted from the chloroform layer. The absorption spectral analysis (fig.1) shows that the maximum of absorbance of montelukast was found to be 585 nm. The absorbance of blue chloroform layer is measured at 585 nm against reagent blank. The results shown in Table 2 are in good agreement with label claim. The optimum conditions were established by varying one parameter and keeping others fixed and observing the effect of produced on the absorbance of the solution. The effect of buffer solution concentration and reagent concentration were studied through controlled experiments and optimum conditions were incorporated in the procedure. The common excipients employed do not interfere in the estimation of montelukast. Beer's law is obeyed in the concentration range of 50-250 µg/ml of montelukast**.** The optical characteristics of the proposed method such as absorption maxima, Beer´s law limits, molar absorptivity and Sandell´s sensitivity are presented in Table 1. The molar absorptivity and Sandell´s sensitivity values shows sensitivity of the method. The regression analysis using method of least squares was made for the slope (b), intercept (a) and correlation (r) obtained from different concentrations and results are summarized in the Table 1. The value of correlation coefficient was 0.999, which indicated the good linearity of calibration lines. The values of standard deviation are low, indicates high accuracy and reproducibility of the method. In the student's 't' tests, no significant differences were found between the calculated and theoretical values of both the proposed methods at 95% confidence level. This indicated similar precision and accuracy in the analysis of montelukast in its tablets

Table 1: Optical characteristics, precision and accuracy of montelukast

parameters	Proposed method
λmax (nm)	585
Beer's law limit (µg/ml)	50-250
Molar absorptivity (l $mole^{-1}$ cm^{-1})	$1.9x10^{-3}$
Sandell's sensitivity (µg cm^{-2} / 0.001 absorbance unit)	0.191
Regression equation (Y = a + bC)	Y=0.005X+0.014
Slope (b)	0.005
Intercept (a)	0.014
Correlation coefficient (r)	0.999

**Y = a+bX, where Y is the absorbance and X concentration in µg / ml*

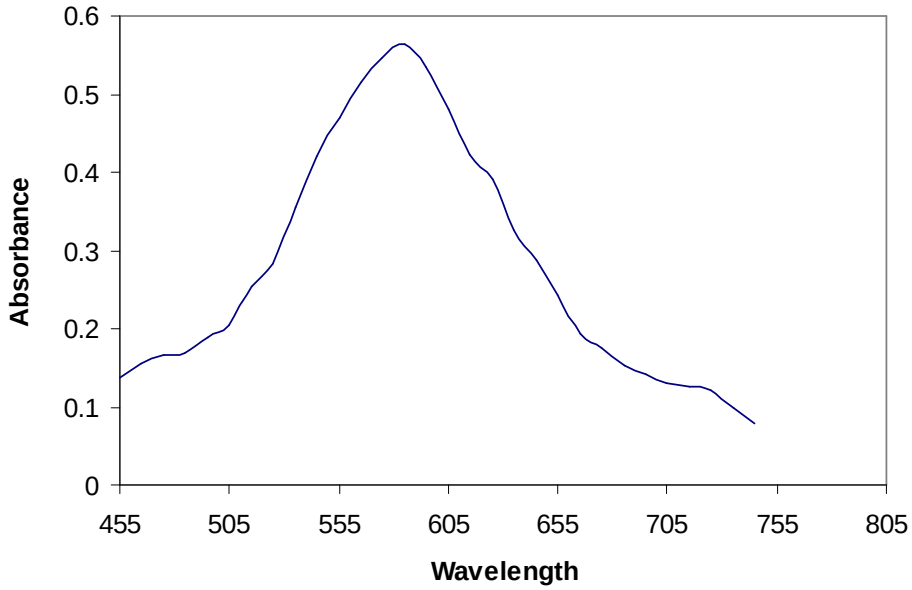

Fig 1. Absorption spectrum of montelukast with wool fast blue at 585 nm

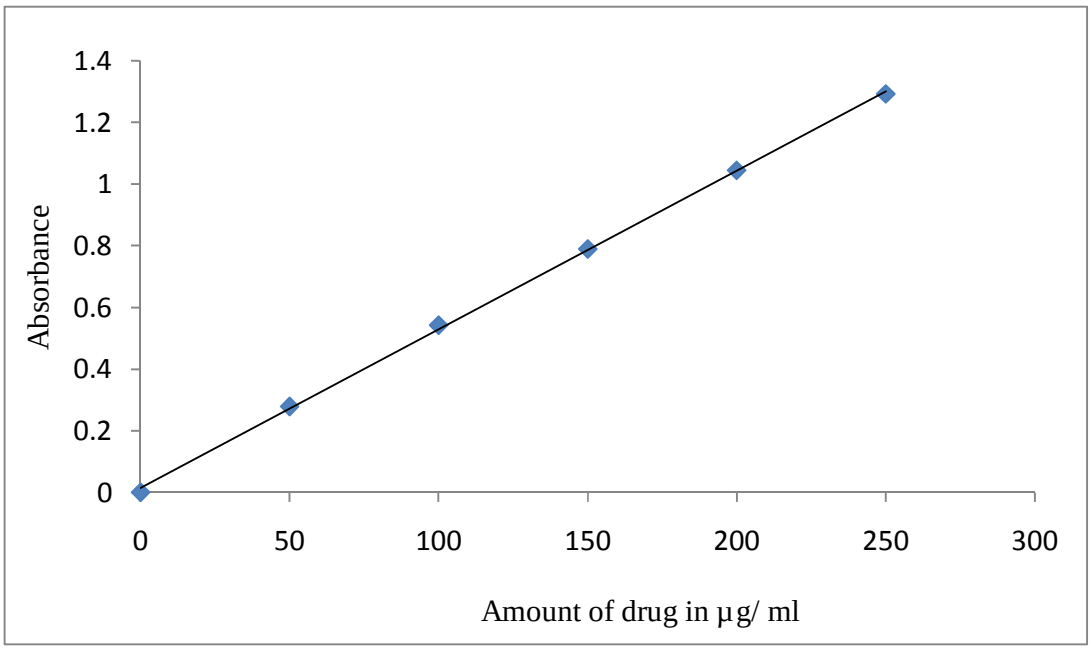

Fig 2. Calibration curve of montelukast

The developed visible spectrophotometric method was simple, sensitive, accurate, precise, and reproducible and can be successfully applied for the routine estimation of montelukast in bulk and pharmaceutical dosage forms.

Table2: Assay of montelukast in tablets

Sample	Labelled Amount (mg)	*Amount found by Proposed method ±S.D*	Percentage of Label claim	$^{*}t_{cal}$
Tablet 1	10	10.01 ±0.11	100.1	0.1968
Tablet 2	10	9.99 ±0.15	99.9	0.1412
Tablet 3	10	9.95 ±0.15	99.5	0.7321
Tablet 4	10	10.03 ±0.17	100.3	0.3567

**Average of five determinations based on label claim*

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