INTERNATIONAL RESEARCH JOURNAL OF PHARMACY
www.irjponline.com
ISSN 2230 – 8407

Research Article

DEVELOPMENT AND VALIDATION OF A SIMPLE UV SPECTROPHOTOMETRIC METHOD FOR THE DETERMINATION OF MONTELUKAST SODIUM BOTH IN BULK AND MARKETED DOSAGE FORMULATIONS

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Article Received on: 14/03/14 Revised on: 25/03/14 Approved for publication: 02/04/14

DOI: 10.7897/2230-8407.050467

ABSTRACT
In the present study a rapid, specific and economic UV spectrophotometric method has been developed using a solvent composed of methanol : water (80 : 20) to determine the montelukast sodium content in bulk and pharmaceutical dosage formulations. A pre-determined λ_{max} at 344 nm, it was proved linear in the range of 5 to 30 µg/ml, and exhibited good correlation coefficient (R^2 = 0.999). This method was successfully applied to the determination of montelukast sodium content in five marketed brand the results were in good agreement with the label claims. The method was validated statistically and studies for linearity, precision, repeatability and reproducibility. The obtained results proved the method can be employed for the routine analysis of montelukast sodium in bulk as well as in the commercial formulations.
Keywords: Montelukast sodium; UV spectrophotometric method; Validation

INTRODUCTION

Montelukast sodium is described chemically as [R-(E)]-1-[[[1-[3-[2-(7-chloro-2quinolinyl) ethenyl]phenyl]-3-[2-(1-hydroxy-1-methylethyl)phenyl]propyl]thio]methyl] cyclopropaneacetic acid, monosodium salt. It is used primarily for the treatment of Asthma in children and adult, it is freely soluble in ethanol, methanol, and water.[1,2] Montelukast (sodium salt) is potent, selective CysLT1 receptor antagonist. It is indicated for the prophylaxis and chronic treatment of asthma in adults and paediatric patients. The drug is commercially available in various forms of oral dosage formulations including oral granules.[1,3] Montelukast is a CysLT1 antagonist it blocks the action of leukotriene D4 (and secondary ligands LTC4 and LTE4) on the cysteinyl leukotriene receptor CysLT CysLT1 in the lungs and bronchial tubes by binding to it. This reduces the broncho constriction caused by the leukotriene and results in less inflammation.[4] It is particularly effective in treating children with both mild persistent asthma and frequent episodic asthma and individuals with aspirin-sensitive asthma.[5]

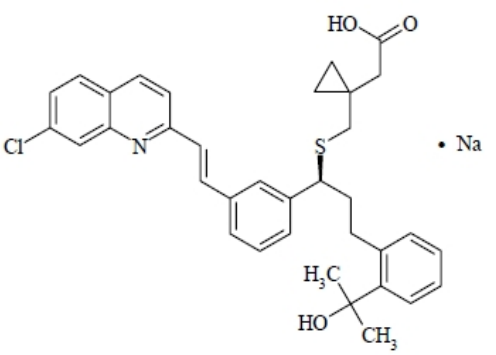

Figure 1: Chemical structure of Montelukast sodium[6]

Development of a spectrophotometric method is based on the knowledge of the chromatographic process. A good method development strategy require only as many experimental runs as are necessary to achieve the desired final result. The scope of developing and validating analytical method is to ensure a suitable method for a particular analyte more specific, accurate and precise the main objective for that is to improve the condition and parameter, which should be followed in the development and validation.[7] The objective of validation of an analytical procedure is to demonstrate that it is suitable for its intended purpose. The objective of the analytical procedure should be clearly understood since this will govern the validation characteristics which need to be evaluated. Typical validation characteristics which should be considered are listed as: Accuracy Precision Repeatability Intermediate Precision Specificity Detection Limit Quantitation Limit Linearity Range.[8] In this study, efforts were made to develop a simple, easy and economic UV spectrophotometric method using diluents composed of methanol : water (80:20) for the determination of montelukast sodium in the raw materials as well as in the marketed dosage formulations. The developed method was optimized and validated as per the guidelines of International Conference on Harmonization (ICH) and demonstrated excellent specificity, linearity, precision and accuracy for montelukast sodium.

MATERIALS AND METHODS

Apparatus

A Shimadzu UV–visible spectrophotometer (UV1800, Shimadzu Corporation, Kyoto, Japan) was used for all absorbance measurements with matched quartz cells.

Materials

All chemicals and reagents were of analytical grade montelukast sodium in the form of powder with certificate of analysis was provided by Alkem Research Centre, Mumbai, India which was used as the reference standard.

Determination of wavelength of maximum absorption

Standard stock solution montelukast sodium (0.1 mg/ml) was prepared. A stock solution was prepared by 10 mg drug dissolved in 100 ml methanol (100 µg/ml stock solution). An UV spectroscopic scanning (200–400 nm) was carried out with to determine the λ_{max} for the detection of montelukast sodium using diluents as blank.

Linearity and range

For linearity study, six solutions at different concentrations (5, 10, 15, 20, 25, and 30 µg/ml) were prepared using six different aliquots of montelukast sodium, and the obtained data were used for the linearity calibration plot.

Intra-day precision (repeatability) and inter-day precision study (intermediate precision)

Prepare the standard stock solution of montelukast sodium drug. Prepare the three concentration of (5, 15, and 30 µg/ml), by using combination of methanol : water (80:20). Take λ_{max} at the intraday and inter day. Calculate the % RSD

Stability study

Samples prepared for repeatability study were preserved for 24 hour at room temperature and analyzed on the following day to test for short-term stability.

Accuracy study

This study was carried out using the stock solution (100 µg/ml). Take three concentrations 5 µg/ml, 15 µg/ml, and 30 µg/ml. And take six reading of these concentrations. Calculate the % RSD of each concentration.

Assay of content of montelukast sodium selected marketed brands

Brought the marketed 4 and 8 mg tablet strips of montelukast sodium. Take the total weight of tablet. Then individually take 10 tablet weights. Crush the tablet. Calculated weight to be taken then prepare the 100 µg/ml stock solution. Prepare the 5 µg/ml solution and take the absorbance at 344 nm. Compare with the standard. Calculate the percentage purity.

Table 1: Data for calibration curve

Concentration µg/ml	Absorbance
5	0.239
10	0.446
15	0.689
20	0.908
25	1.156
30	1.387

Table 2: Linear regression data for calibration curve

Parameters	Data
Range	5-30 µg/ml
Correlation coefficient	0.999
Slop	0.231
Intercept	0.004

Table 3: Intra-day and inter day precision determined for three different concentrations of Montelukast sodium

Concentration (µg/ml)	Intra-day precision		Inter-day precision	
	Absorbance Measured (Mean ± SD)	RSD (%)	Absorbance Measured (Mean ± SD)	RSD (%)
5	0.239 ± 0.000894	0.37	0.241 ± 0.000816	0.33
15	0.660 ± 0.00216	0.22	0.662 ± 0.00894	0.13
30	1.382 ± 0.00216	0.15	1.380 ± 0.002898	0.21

Table 4: Short term stability determined by the proposed method

Concentration declared (µg/ml)	Concentration found (µg/ml)	RSD (%)
5	4.93	0.92
15	14.85	0.59
30	29.80	0.26

Table 5: Accuracy for three different concentrations of Montelukast sodium by the proposed method

Concentration (µg/ml)	Absorbance Measured (Mean ± SD)	RSD (%)
5	0.240 ± 0.000753	0.31
15	0.653 ± 0.001941	0.29
30	1.386 ± 0.002608	0.18

Table 6: Content of Montelukast sodium five marketed products determined by the proposed method

Brand	Label claim (mg)	Amount found	RSD (%)
Brand 1	4	3.98	0.47
Brand 2	4	3.85	0.28
Brand 3	4	3.85	0.44
Brand 4	8	3.80	0.37
Brand 5	8	7.81	0.49

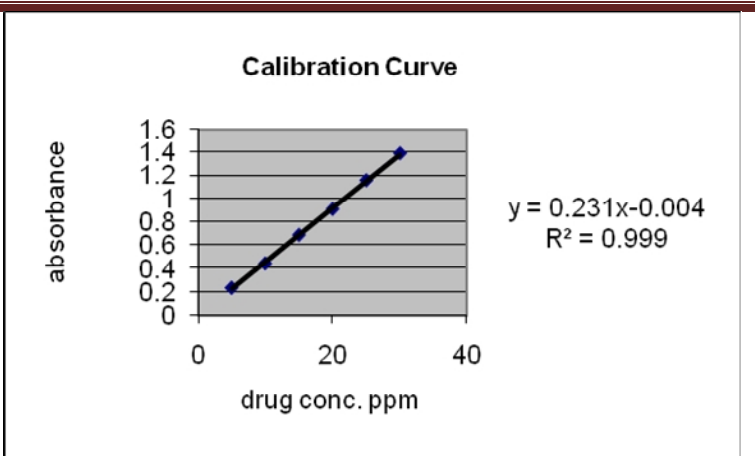

Figure 2: Calibration curve

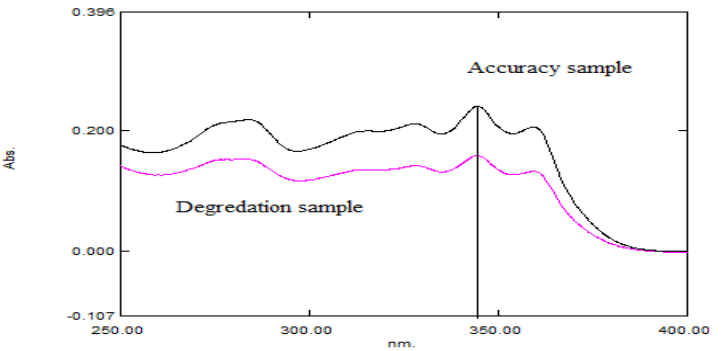

Figure 3: UV Spectra for Specificity

RESULTS AND DISCUSSION

Montelukast sodium is practically insoluble in acetonitrile and soluble in methanol. During the development phase, the use of a methanol with water as the diluents resulted in preferable outcome in UV analysis. The solvent composition was optimized Methanol (80 %) and Water (20 %). The pre-determined wavelength of maximum absorption (λ_{max}) was 344 nm.

Method Validation

Linearity and range

The calibration curve (Figure 2) obtained was evaluated by its correlation coefficient. The absorbance of the samples in the range of 5 to 30 mg/ml (Table 1 and 2) was linear with a correlation coefficient (R2) 0.999.

Intra-day and inter-day precision

The intra-day and inter-day precision study (Table 3) of the developed method confirmed adequate sample stability and method reliability.

Stability

Stability study's results were within the acceptance range (Table 4) and indicated the samples stability over 24 h (short-term).

Accuracy

Results within the range of ensure an accurate method (Table 5) as well as indicate non-interference with the excipients of formulation.

Specificity in the presence of excipients degradation product, the specificity of the analytical method was proved by comparing the spectra of degradation product of sample solution with that of accuracy sample (Figure 3).

Content of Montelukast sodium in marketed brands

Montelukast sodium content of five marketed products determined by the proposed method was in good agreement with the label claims (Table 6)

CONCLUSION

The results and the statistical parameters demonstrate that the proposed UV spectrophotometric method is simple, rapid, specific, accurate and precise. Therefore, this method can be used for the determination of Montelukast sodium either in bulk or in the dosage formulations without interference with commonly used excipients and related substances.

ACKNOWLEDGMENT

The authors thanks to Mr. Amol Kulkarni and Mr. Arun Pandey, Vice President-R and D, Alkem Research Centre for providing gift sample. Also thank to Dr. Sanjay Thonte, Principal for providing research facilities in the college.

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Cite this article as:
Sachin Gholve, Riyaj Shaikh, Sayali Budhwant and Omprakash Bhusnure. Development and validation of a simple UV spectrophotometric method for the determination of Montelukast sodium both in bulk and marketed dosage formulations. Int. Res. J. Pharm. 2014; 5(4):317-320 http://dx.doi.org/10.7897/2230-8407.050467

Source of support: Nil, Conflict of interest: None Declared