Research Article

DEVELOPMENT AND VALIDATION OF UV SPECTROPHOTOMETRIC METHODS FOR ESTIMATION OF MONTELUKAST SODIUM IN BULK AND PHARMACEUTICAL FORMULATION

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ABSTRACT

Three simple, economical, precise and Accurate UV Spectrophotometric methods have been developed for the estimation of Montelukast sodium in bulk and pharmaceutical formulations. Method A involves measurement of absorbance of solution at 344.30 nm in methanol. Method B involves integrating area under curve in the wavelength range of 342.93 nm – 343.75 nm and is used to construct calibration curve. Method C is first order derivative spectroscopy method, in which first derivative amplitude at 347.91 nm is measured. Linearity for detector response was observed in the concentration range of 5 - 25 µg/ml for all the three methods in methanol. The results of analysis have been validated as per ICH analytical method validation guidelines. Accuracy, precision and recovery studies were carried and confirmed the validity of the proposed methods.

Keywords: Montelukast Sodium, UV Spectrophotometric methods, Area under curve.

INTRODUCTION

Montelukast Sodium [2-[1-[[1-[3-[2-[(7-Chloro-2-quinolyl)] vinyl] phenyl]-3-[2-(1-hydroxy-1-methyl-ethyl) phenyl]-propyl] sulfanylmethyl] cyclopropyl] acetic acid sodium salt] is particularly effective in treating children with both mild persistent asthma and frequent episodic asthma and individuals with aspirin-sensitive asthma.

Several analytical methods that have been reported for the individual determination of Montelukast Sodium in biological fluids and pharmaceutical formulation which includes stability-indicating HPLC method[1], RP-HPLC Method[2], HPLC method[3], RP-HPLC Method Development and Validation for Simultaneous Estimation of Montelukast Sodium and Levocetirizine Dihydrochloride[4], montelukast sodium in oral granules dosage forms by a simple and accurate UV spectrophotometric methods[5]. Therefore aim of the study was to develop and validate simple UV absorbance, area under curve and derivative spectrophotometric methods for estimation of montelukast Sodium in bulk and formulations.

MATERIALS AND METHODS

Instrumentation

An UV-Visible double beam spectrophotometer of makes Varian Cary 100 with 10MM matched quartz cells were used for spectrophotometric method. All weighing were done on electronic balance (Model Shimadzu AUW-220D).

Reagents and chemicals

Pure drug sample of Montelukast Sodium (% purity- 99.8) was kindly supplied as a gift sample by Cipla Ltd. Malpur, Dist. Solan, India. Tablet used for analysis was Montair (Batch no: D00495, Formulation T1) each tablet containing montelukast sodium equivalent to 10 mg of Montelukast. Spectroscopic grade methanol was used throughout the study.

Preparation of standard stock solution and calibration graph

An accurately weighed quantity of about 100 mg of montelukast sodium was transferred into 100 ml volumetric flask; it was dissolved in sufficient quantity of methanol to get standard stock solution. Standard stock solution was suitably diluted with methanol to get concentration in the range 5-25 µg/ml, solutions were scanned and instrument response was measured by applying the proposed methods. Linearity was studied by using zero absorbance method (method A) at 344.30 nm, area under curve method (method B) at 342.93-343.75 nm and first derivative amplitude at 347.91 nm (method C).

Formulation analysis

Quantity of tablet Powder, form 20 tablets, equivalent to 10 mg was weighed and transferred to 10 ml volumetric flask and dissolved in 8 ml of methanol. This solution was then filtered through Whatmann filter paper no. 41 and volume was made up to 10 ml with methanol.

METHOD DEVELOPMENT [6-10]

Absorbance method (method A)

The method involves measurement of absorbance of solutions in the concentration range of 5-25 µg/ml at 344.30 nm (Fig. I).

Area under curve method (method B)

The AUC (Area under Curve) method involves the calculation of integrated value of absorbance with respect to the wavelength between two selected wavelength 342.93 nm and 343.75 nm (Fig. 2).

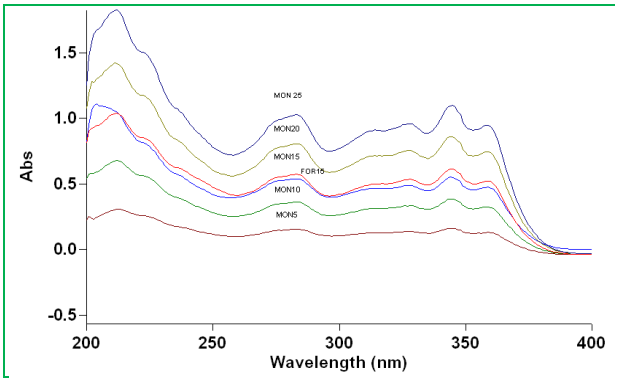

Figure 1: Overlay spectra of montelukast sodium standard (5 – 25 µg/ml) and formulation (15 µg/ml) in methanol

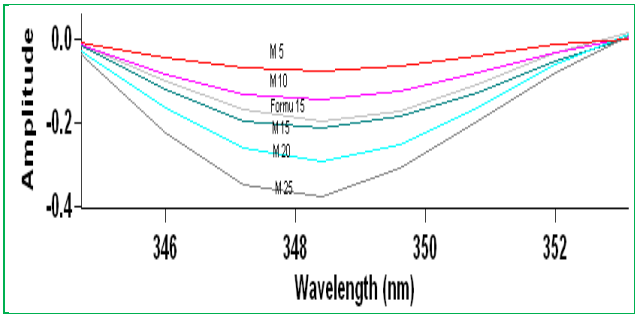

Figure 2: First order spectra of montelukast sodium (5 – 25 µg/ml) in methanol

The first order derivative method (method C)

The first order derivative spectra of montelukast sodium solution show a sharp peak and linearity at 347.91 nm (Fig. 2).

Precision

The precision of the assay was determined by repeatability and intermediate precision (intraday and inter-day) and reported as % RSD. For this 5 µg/ml, 15 µg/ml and 25 µg/ml concentration of solution was analysed three times in day and similarly it was analysed on three days and the % RSD values were calculated. (Table 1)

Recovery

The accuracy of the method was evaluated through standard addition method. In this known amount of standard montelukast sodium was added in pre-analyzed sample. This was done for 5 µg/ml, 10 µg/ml, and 15 µg/ml and in triplicate. (Table 2)

Table 1: Optical Characteristics and Validation Data of montelukast sodium

Parameter		Method A	Method B	Method C
λ (nm)		344.30 nm	342.93 – 343.75 nm	347.91 nm
Beer's law limit (µg/ml)		5 -25 µg/ml	5 – 25µg/ml	5 – 25µg/ml
Regression Equation (y = mx + c)	Slope (m)	0.036806	0.0379	0.0144
	Intercept (c)	0.006806	0.02640	0.0044
	Correlation coefficient	0.999	0.9998	0.9996
Precision (% R.S.D.)	Intra-day*	0.62	0.66	0.58
	Inter-day*	0.59	0.60	0.79
Tablet Assay (%), % RSD(Formulation T1)		99.44, 0.89	99.76, 0.74	100.54, 0.98
LOD (µg/ml)		0.75	0.45	0.99
LOQ (µg/ml)		2.26	1.49	2.97

Table 2: Recovery study of montelukast sodium by using proposed methods

Recovery Level	Amount Spiked (µg/mL)	% Mean Recovery, % RSD by (n=6)		
		Method A	Method B	Method C
50%	5	98.95%, 0.58	99.86%, 0.76	98.87%, 0.54
100%	10	99.94%, 0.59	100.3%, 0.91	98.98%, 0.94
150%	15	99.88%, 1.22	99.846% ,0.77	101.60%, 0.83

RESULTS AND DISCUSSION

Using appropriate dilutions of standard stock solution, the solutions were scanned. The zero order overlain spectra are shown in Fig 1. A critical evaluation of proposed method was performed by statistical analysis of data where slope, intercept, correlation coefficient is shown in Table - 1. As per the ICH guidelines, the method validation parameters checked were linearity, accuracy, and precision and method sensitivity.

Beer's law obeyed in the concentration range (5-25 µg/ml) and with correlation coefficient > 0.999 for the proposed methods. The proposed method was also evaluated by the assay of commercially available tablets containing montelukast sodium.

The % assay was found to be in the range of 99.44% - 100.54% for the formulation (T1) by all the three proposed methods as shown in Table 1. Results of recovery studies are presented in Table 2. For montelukast sodium, the recovery study results ranged

from 98.87% to 101.60% with RSD values raging from 0.54 to 1.22%. The accuracy and reproducibility is evident from the data as results are close to 100% and standard deviation is low. Result of precision and recovery shows that the methods are precise and accurate.

CONCLUSION

The proposed UV Spectrophotometric methods for the determination of montelukast sodium in bulk and pharmaceutical formulation are very simple, as it needs methanol as solvent.

The validated spectrophotometric methods employed here proved to be simple, fast, accurate and precise and sensitive thus can be used for routine analysis of montelukast sodium.

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