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VALIDATED UV SPECTROSCOPIC METHOD FOR ESTIMATION OF MONTELUKAST SODIUM

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ABSTRACT: Montelukast sodium is a leukotriene receptor antagonist (LTRA) used for the maintenance treatment of asthma and to relieve symptoms of seasonal allergies[1-2]. Montelukast comes as a tablet, a chewable tablet, and granules to take by mouth[3]. Montelukast is usually taken once a day with or without food[3]. The present study describes a simple, accurate reproducible and precise uv spectrophotometric method for the estimation of Montelukast Sodium in bulk and in tablet dosage form. The absorbance maxima (λmax) for Montelukast Sodium were found to be 286.5nm. The method was validated for different parameters such as molar absorptivity, accuracy precision, ruggedness, robustness, detection limit, quantification limit etc, (as per ICH guidelines). The relative standard deviation (RSD) in case of, accuracy precision, ruggedness, robustness was less than 2.0% proving that method was highly accurate, precise and robust. This method can be used for determination of Montelukast Sodium in pharmaceutical formulations without interference of the excipients.

INTRODUCTION: Montelukast sodium (MNLT), (S, E) – 2 - (1-((1-(3-(2- (7-chloroquinolin-2-yl) vinyl) phenyl) – 3 - (2-(2- hydroxypropan-2-yl) phenyl) propylthio)methyl)cyclopropyl)acetic acid. It is a leukotriene receptor antagonist (LTRA) used for the maintenance treatment of asthma and to relieve symptoms of seasonal allergies. It is usually administered orally. Montelukast is a CysLT1 antagonist; it blocks the action of leukotriene D4 (and secondary ligands LTC4 and LTE4) on the cysteinyl leukotriene receptor CysLT1 in the lungs and bronchial tubes by binding to it.

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This reduces the bronchoconstriction otherwise caused by the leukotriene and results in less inflammation. The chemical structure of MNLT is shown in **Fig.1**.

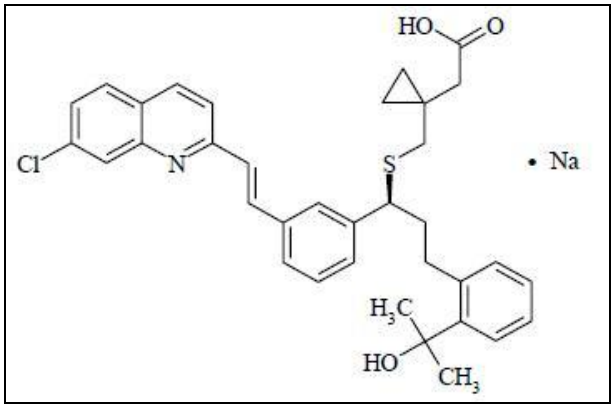

FIG. 1

The drug is commercially available in various forms of once daily oral dosage formulations

including oral granules. In oral dosage form, each packet contains Montelukast Sodium equivalent to 10 mg of Montelukast. Several analytical methods have been reported for determination of Montelukast including derivative spectroscopic [4], by colorimetry [5], by flouorimetry [6], by TLC [7], by HPTLC [8], by simultaneous UV determination in combination drug formulation [9], by voltametry [10], by high performance liquid chromatography (HPLC) [11] and by LCMS [12]. To our knowledge, there is no simple and accurate UV spectrophotometric method for quantitative determination of Montelukast Sodium in its bulk and in its tablet dosage forms.

The objective of study to develop and validate a simple, eco-friendly UV spectrophotometric method for the determination of Montelukast in Montelukast Sodium oral dosage forms (strength is 10 mg as Montelukast). Also method should be capable to apply in routine Quality control analysis. Analytical parameters for the method have also been established and compared with those established and existing HPLC method.

MATERIALS AND METHODS:

A shimadzu - 1700 double beam uv/vis. spectrophotometer with 1cm matched quartz cells was used for absorbance measurements. Montelukast sodium was a gifted sample obtained from Sanofi India Ltd., Ankleshwar, India.

Double distilled water was used for analysis. Montelast (Cadila pharma) and Montair (Cipla pharma) were marketed formulation of Montelukast sodium procured from local pharmacy. Water, methanol and sodium hydroxide (loba chemical ltd.,) were of analytical grade was used. Drug was dissolved in methanol and further dilutions made with 0.1N NaOH. All the reagents used were of analytical reagent grade.

Preparation of stock and standard solution:

Stock solution of Montelukast sodium was prepared by dissolving 10 mg in methanol and final dilution was made by 0.1 N NaOH. Suitable aliquots of the stock solution of Montelukast sodium were pipette and transferred separately into 10ml volumetric flasks. The volume was made up with the same solvent.

Determination of Absorption maxima:

Working standard solutions were scanned in UV range of (200-400nm) using a Shimadzu 1700 UV-Visible spectrophotometer with cells of 10mm length against the same solvent used as blank. It was scanned in the range of 200-400 nm and it shows absorbance maxima at 286.5 nm.

Procedure for Analysis of Tablet Formulation:

Twenty tablets were weighed and powdered. An accurately weighed tablet powder equivalent to10 mg of Montelukast sodium transferred in to 25 ml volumetric flask, small amount of methanol was added and sonicated for 15 min. Volume was made up to the mark with 0.1 N NaOH then solution was filtered through whatman filter paper no.41. From this stock solution, necessary dilutions were made with 0.1 N NaOH to get final concentration of 10 µg/ml. The above solution was then analyzed for the content of Montelukast sodium.The amount of Montelukast sodium present in each formulation was calculated from the respective calibration curve.

TABLE 1: OPTICAL CHARACTERISTICS AND PRECISION OF THE PROPOSED METHOD

Parameters	Results
Wavelength	286.5 nm
Beer's law limit (µg/mL)	5-25
Regression equation (Y= mx+C)	Y = 0.034x + 0.035
Slope (m)	0.034
Intercept (C)	0.035
Correlation Coefficient (r)	0.999

TABLE 2: MEAN ABSORBANCE VALUE AND STATISTICAL DATA OF THE CALIBRATION CURVE

Conc.	Abs 1	Abs 2	Abs 3	Mean	Std Dev.	%RSD
5	0.1369	0.1399	0.1379	0.138233	0.001528	1.105034
10	0.2994	0.3036	0.3091	0.304033	0.004864	1.599988
15	0.4858	0.4994	0.491	0.492067	0.006862	1.39462
20	0.6675	0.6618	0.6699	0.6664	0.004161	0.624329
25	0.8241	0.8221	0.8243	0.8235	0.001217	0.14773

Analytical method validation: The method was validated for different parameters like linearity, specificity, selectivity, accuracy, precision, robustness, and ruggedness, limit of quantification (LOQ) and limit of detection (LOD)[13-14]

Linearity and Range:
Solutions containing 5, 10, 15, 20, and 25µg / ml of Montelukast sodium were prepared from standard solution to determine the linearity range. The detection was carried out at 286.5 nm. Spectrums were recorded and absorbance was recorded for all the concentrations. A calibration plot of concentration over the absorbance was constructed against the corresponding concentrations to obtain the calibration graphs and was shown in **Fig.2** The optical characteristics such as Beer's law limits, regression equation and correlation coefficient, mean absorbance value, and statistical data of the calibration curve were calculated and results are presented in **Table 1 Linearity** was checked by calculating regression coefficient[14].

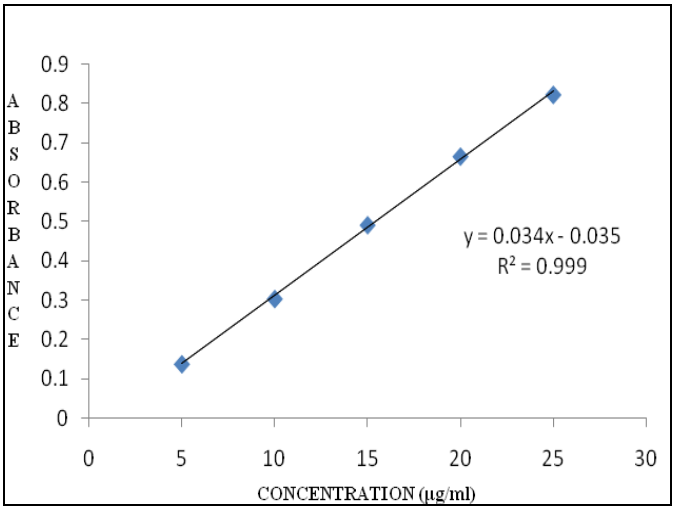

FIG.2: STANDARD CALIBRATION CURVE OF MONTELUKAST SODIUM SOLUTION IN 0.1 N NAOH

Specificity and selectivity:
Specificity and selectivity of the selected method was determined by preparing 10µg/ml of Montelukast sodium solution in 0.1 N NaOH along with and without common excipients (Lactose, Hydroxypropyl methylcellulose and starch) separately. All the solutions were scanned from 200-400 nm at fast speed and analyzed for any change in absorbance and percentage drug recovery at respective wavelengths.

Accuracy:
The accuracy of the method was determined by calculating percentage drug recovery of Montelukast at a concentration of 10 µg/ml (n=6)[14].

Precision:
The precision of proposed method was determined by varying the practical conditions. Inter-day, intra-day and inter-analyst variations were studied to determine the intermediate precision of proposed analytical method. Drug concentrations of Montelukast, mixture was prepared at three different times in a day and studied for intra-day variation. The same procedure was followed for six days in order to study inter-day variations. Developed method was performed by three different analysts for inter analyst studies and by same analyst at six different times for intra analyst studies. The percent relative standard deviation (% RSD) of prepared concentrations was analyzed for precision studies[14].

Limit of detection and Limit of quantification:
Limit of detection (LOD) and Limit of quantification (LOQ) of Montelukast, mixture by proposed method were determined using calibration standards. LOD and LOQ were calculated as 3.3σ/S and 10σ/S respectively. Where, σ is standard deviation of y-intercept of regression equation and S is the slope of the calibration curve[14].

Ruggedness and Robustness:
Ruggedness and robustness was evaluated by analyzing Montelukast, mixture under variable experimental conditions (a) Sample solution containing 10µg/ml was assayed for six times prepared from different stock solution and the percentage recovery was checked in each case. (b) Sample solution containing 10µg/ml was analyzed by changing the UV apparatus (Apparatus 1: Shimadzu-1800; Apparatus 2: Cintra) to check the inter-instrument variation in the absorbance. (c) Robustness in the form of stability of Montelukast, in prepared solution was also checked at room temperature. The concentration of drug in solvent was checked at time of preparation and at the interval of twenty-four hours[14]

Stability:
Stability of the solutions of Montelukast, used for preparing the calibration curves in the method, was ascertained by observing for changes in the absorbance at their analytical wavelengths over a period of 24 h.

RESULTS AND DISCUSSION:

Standard calibration curve The UV scan of standard solution of Montelukast between 200-400 nm gives the absorption maxima at 286.5nm. The regression coefficient for calibration curve of Montelukast in 0.1 N NaOH was found to be 0.999 with regression equation of $Y_{286.5nm} = 0.034x$. The optical and regression characteristics are given in **Table 1.**

Analytical method validation:
Linearity The linearity was found in the range of 5-25µg/ml for Montelukast in 0.1N NaOH supported by high regression coefficient.

Specificity:
The UV-Spectrum of Montelukast showed no change in the presence of common excipients used for the formulation. Absorption spectrum of pure drug sample was matching with the sample mixed with excipients. **Table 2** shows the values for specificity studies of Montelukast in 0.1 N NaOH. The excellent percentage recovery of shows that there is no effect of excipients on the absorbance.

TABLE 2: RESULTS OF SPECIFICITY AND SELECTIVITY STUDIES OF APPLIED METHOD OF UV ESTIMATION OF MONTELUKAST

	Excipient	Amount taken: Excipient added	% Drug recovery ± RSD
Conc. of drug taken = 10µg/ml (N=6)	--	1:0	100.89±1.325
	Lactose	1:1	101.90±1.53
	HPMC	1:1	99.89 ±1.45
	Starch	1:1	99.65±1.87

Accuracy:
The accuracy of the method was checked by determining the percentage recovery values. Percentage drug recovery (± RSD) of above concentrations of Montelukast in 0.1 N NaOH is shown in **Table 3**. In all the cases RSD was not more than 2% depicting the accuracy of the developed method.

TABLE 3: RESULTS OF ACCURACY STUDIES OF APPLIED METHOD OF UV ESTIMATION OF MONTELUKAST

Accuracy of recovery studies (N=6)	Conc. of drug taken (µg/ml)	% Drug recovery ± RSD
	10	100±0.65

Precision:
The precision of the developed method was determined by studying the repeatability of the developed method. In this, the percentage recovery of Montelukast in 0.1 N NaOH was calculated by inter-day, intra-day, inter-analyst and intra analyst conditions over a short interval of time. Results of percentage drug recovery obtained from intra-day studies, inter-day studies and inter-analyst studies are shown in **Table 4**. From obtained data, it was found that in all the precision studies, RSD was not more than 2 indicating that developed method has excellent repeatability.

TABLE 4: RESULTS OF PRECISION STUDIES OF APPLIED METHOD OF UV ESTIMATION OF MONTELUKAST (CONC. OF DRUG TAKEN 10µg/ml)

Studies done for precision	Observed Conc. ± RSD
A. Intra-day studies (N=3)	99.940±1.34
B. Inter-day studies (N=3)	100.56±0.89
C.Inter-analyst studies (N=3)	101.40±1.05

Limit of Detection and Limit of Quantification:
LOD and LOQ were calculated to be 0.471µg/ml and 1.42 µg/ml respectively.

Robustness:
Robustness of the selected method was checked by inter-stock solution, inter-instrument, and by calculating percentage drug recovery after twenty-four hours of preparation of stock solution (**Table 5**). Overlaid spectra of stock solution at zero and twenty-four hours (**Fig. 7**) showed no change in absorbance and λ_{max} of the solution. Further, data

showed that in all the above cases, RSD was found to be less than 2 confirming the robustness of the developed method.

TABLE 5: RESULTS OF ROBUSTNESS STUDIES OF APPLIED METHOD OF UV ESTIMATION OF MONTELUKAST (CONC. OF DRUG TAKEN 10µg/ml)

Studies done for robustness	Observed Conc. ± RSD
A. Inter-stock solution (N=6)	101.45±1.09
B. Inter Instrument (N=2)	100.98±1.56
C. Robustness of stability of solution (N=6)	98.476±1.58

CONCLUSION: The most striking feature of this method is its simplicity and rapidity, non-requiring- consuming sample preparations such as extraction of solvents, heating, degassing which are needed for HPLC procedure. These are new and novel methods and can be employed for routine analysis in quality control analysis. The described methods give accurate and precise results for determination of Montelukast, sodium in marketed formulation.

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