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ACCURATE AND SIMPLE UV- SPECTROSCOPIC METHOD FOR THE ESTIMATION OF MONTELUKAST SODIUM IN PURE AND MARKETED FORMULATIONS

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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].This paper describes a simple, accurate, specific and validated method for the estimation of Montelukast sodium in pure and in tablet dosage form. A study was carried out of all the parameters established as per ICH guidelines to validate an analytical method for estimation. The method showed high sensitivity with reproducibility in results. The wavelength maxima (λ_{max}) was found to be 283 nm. The linearity for this method was found to be in the range of 2 – 12 µg/ml. The calibration curve (Fig -2) was drawn by plotting graph between absorbance and concentration. This method showed a correlation coefficient of 0.99967. The regression equation of the curve was Y= 0.04619x+0.005637. Method was successfully validated. In addition, this proposed method was simple, sensitive, easy to apply and requires relatively inexpensive instruments. The proposed method can be used for routine analysis of Montelukast sodium in bulk as well as in the commercial formulations.

INTRODUCTION:

Montelukast sodium is chemically known as 2-[-[[1-[3-[2-[(7-chloro-2-quinolyl]phenyl]-3-[2-(1-hydroxy-1-methyl ethyl) phenyl] propyl] sulfanyl methyl] cyclopropyl] acetic acid sodium salt and shown in fig.1 Montelukast sodium is a leukotriene receptor antagonist (LTRA) used for the maintenance treatment of asthma and to relieve symptoms of seasonal allergies [1-2].

MATERIALS AND METHODS

Pharmaceutical grade of Montelukast sodium was kindly gifted from Hetero Pharmaceuticals, Hyderabad. The brand of Montelukast sodium tablets used was Montene and procured from a local Pharmacy. All the solvents and chemicals used were of analytical reagent grade and procured from Qualigens fine Chemicals (Mumbai).

Instruments:

Shimadzu AX - 220 digital balance, T60 UV-Visible spectrophotometer with 1 cm matched quartz cells, Sonicator Sonica Ultrasonic cleaner model 2200 mH.

METHOD – SIMPLE UV-SPECTROSCOPY

The solubility of Montelukast sodium was determined in a variety of solvent ranging from non polar to polar using essentially a method of Schefter and Higuchi [8].

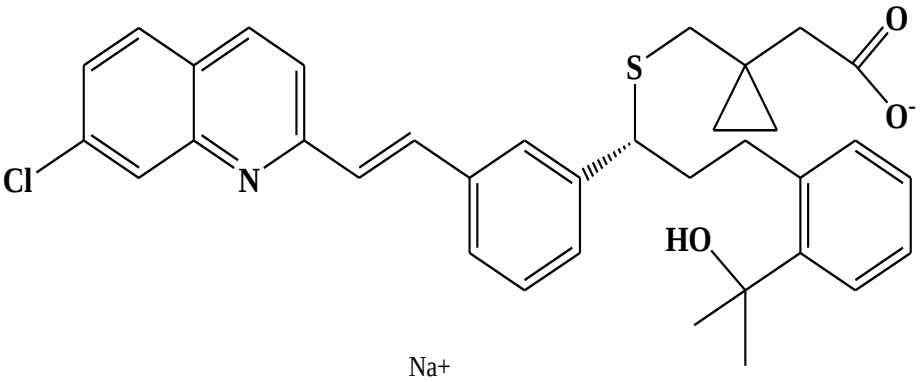

Fig. 1: Structure of Montelukast sodium

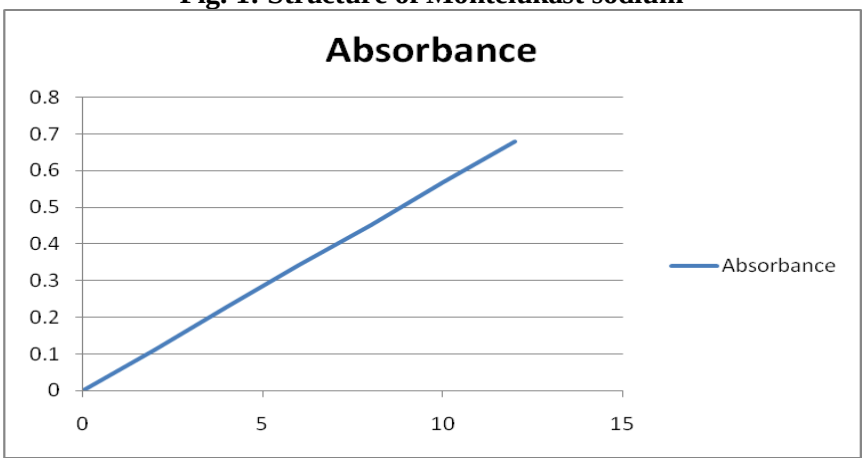

Figure II: Linearity graph

Parameters	Result
λ_{max} (nm)	283
Beers law limit (µg/ml)	2-12
Sandell's sensitivity (µg/cm^2/0.001A.U.)	0.021855
Correlation coefficient (r)	0.99967
Regression equation (y = mx + c)	Y=0.04619x+0.005637
Slope (m)	0.04619
Intercept (c)	0.005637
LOD (µg/ml)	0.33930
LOQ (µg/ml)	1.02820
Standard error of mean	0.001484

Table 1: Optical Characteristics of Montelukast Sodium

S.no	Labelled Amount (mg/Tab)	Amount found (mg/tab)	% obtained	Average %	S.D	%RSD	S.E
1	10	10.06	100.60	99.01	1.830	1.848	0.754
2	10	9.71	97.16				
3	10	9.63	96.33				
4	10	9.93	99.33				
5	10	10.01	100.16				
6	10	10.05	100.50				

SD is standard deviation, % RSD percentage relative standard deviation
*Average of six determinations

Table 2: Results of Analysis of Commercial Formulations

S.no	Amount present (µg/ml)	Amount added (µg/ml)	Amount estimated (µg/ml)	Amount recovered (µg/ml)	% Recovery	Mean of ± S.D	%RSD	S.E
1	6.04	2	7.97	1.97	96.76	99.27 ± 1.9216	1.9351	0.7903
	5.83	2	7.83	2.00	100.00			
	5.78	2	7.76	1.98	99.40			
	5.96	2	8.01	2.05	102.50			
	6.01	2	7.92	1.97	98.50			
	6.03	2	8.00	1.97	98.50			
2	6.04	4	9.91	3.87	97.26	98.51 ± 1.8960	1.9255	0.7861
	5.83	4	9.68	3.85	96.48			
	5.78	4	9.77	3.99	99.87			
	5.96	4	9.99	4.03	100.75			
	6.01	4	10.01	4.0	100.00			
	6.03	4	9.89	3.86	96.71			
3	6.04	6	12.27	6.23	103.87	104.65 ± 1.0190	0.97374	0.397
	5.83	6	12.10	6.27	104.50			
	5.78	6	12.12	6.34	105.66			
	5.96	6	12.15	6.19	103.16			
	6.01	6	12.31	6.30	105.00			
	6.03	6	12.37	6.34	105.76			

*Average of six determinations

Table 3: Results of Recovery Studies

The drug was found to be freely soluble in distilled water, methanol, 0.1 M Hcl, Ethyl acetate and Benzene Sparingly soluble in ethanol, Chloroform and 0.1 M NaoH. Considering the economic factor and the drug were stable in Distilled Water for 3 h. Distilled Water was selected as the solvent for method.

Preparation of standard stock solution:

Required quantity of Montelukast sodium was accurately weighed and transferred into a 100 ml standard flask and dissolved with minimum quantity of Distilled Water and made up to 100 ml with more Distilled Water to get 100 µg /ml.

Selection of λ_{max} and stability studies:

The standard stock solution was further diluted with Distilled Water to get 10 µg/ml concentrations. The solution was scanned between 200 and 400 nm using Distilled Water as blank. From the spectrum obtained, 283 nm was selected as λ_{max} for the analysis of Montelukast sodium. Stability studies were performed and Montelukast sodium was found to be stable for 3 h.

Calibration graph and linearity:

In this method, the aliquots of standard stock solution of Montelukast sodium were transferred into 50 ml standard flasks and made up to the mark with Distilled Water. The absorbance was measured at 283 nm against Distilled Water as blank. The sample solutions were found to be linear from 2-12 µg/ml. The calibration curve was plotted between concentration and absorbance.

Quantification of formulations:

Thirty tablets of formulation (Montene) containing 10 mg of Montelukast sodium were accurately weighed to find out the average weight and powdered. Transferred the powdered tablets equivalent to 25 mg of Montelukast sodium into a 50 ml conical flask, extracted with Distilled Water for three times (3 x 10 ml), sonicated for 15 min and produced to 50 ml with Distilled Water using a standard flask. Half of the solution was filtered using Whatmann filter paper No. 41. From this clear solution, 5 ml was transferred to a 25 ml standard flask and produced to obtain 100 µg/ml

solutions with Distilled Water. The absorbance was measured at 283 nm using Distilled Water as blank. The amount of Montelukast sodium present in each formulation was calculated from the slope and intercept of respective calibration curve [9].

Recovery studies:

From each of the preanalyzed formulation, known quantities were taken and the raw material solution was added in ascending amounts (1, 2, 3, 4, 5 and 6 ml) to 25 ml standard flasks. The contents were mixed well, finally made up to the mark and filtered. The absorbance was measured at 283 nm using Distilled Water as blank and the amount of drug recovered from the each formulation was calculated by the mathematical relation followed by Sane *et al* [10].

Statistical Validation [11]:

The obtained results were treated for statistical validation parameters like Standard Deviation (SD) and Percentage Relative Standard Deviation (% RSD).

Results and Discussion

The solubility profile of Montelukast sodium was determined as per procedure followed by Schefter and Higuchi [8]. Using various polar to non polar solvents and from the solubility studies , the drug was found to be freely soluble in distilled water, methanol, 0.1 M Hcl, Ethyl acetate and Benzene Sparingly soluble in ethanol, Chloroform and 0.1 M NaoH. The optical parameters like Beer's law limits (2-12 µg/ml), Sandell's sensitivity (0.021855), correlation coefficient (0.99967), slope (0.04619), intercept (0.005637), limit of detection (0.33930), and limit of quantification (1.02820) were calculated for Montelukast sodium in Distilled water and produced in Table 1. Quantification of Montelukast sodium from tablets dosage form was performed and the amount present was determined by average of six replicate analyses and the amount in percentage purity is found to be 96.33 – 100.60 % and shown in table 2. To evaluate the accuracy of the method and for knowing the interference from excipients recovery study was performed. The Recovery of Montelukast sodium by UV- Spectroscopic method was found to be 96.48%-105.76% and the results are shown in Table 3. The values of co-efficient of variance were satisfactorily low and recovery was close to 100 % indicating reproducibility of the methods. The excipients in the formulation did not interfere in the accurate estimation of Montelukast sodium in tablet dosage form.

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