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Method Development and Validation of Montelukast Sodium by UV-Visible Spectroscopy

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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. Montelukast is usually taken once a day with or without food. The present study describes a simple, accurate reproducible and precise UV-Visible 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, detection limit, quantification limit etc, (as per ICH guidelines). The relative standard deviation (RSD) in case of, accuracy precision, 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.

Keywords : Montelukast Sodium, Validation, Leulotriene receptor, Ruggedness

I. INTRODUCTION

Montelukast sodium is chemically known as **[**R-(E)-**]**-1-**[[[**1-**[**3-**[**2-(7- chloro-2 quinolyl-2-yl**]** Phenyl**]**-3-**[**2-**(**1-hydroxy 1- methylethyl**)**phenyl Propyl **]**thio**]**methyl**]** cyclopropaneacetic acid,Monosodium salt, having a molecular formula $C_{35}H_{36}CINO_3S$, with a Molecular weight-586.2g/mol, comes under Anti-Asthmatic category which is soluble in ethanol, methanol, water and practically insoluble in acetonitrile. The structural is given below **[1].**

In the present situation every year a new product is introduced into the market. These drugs may be either new entities or partial structural modifications of the existing one. Very often there is a time from the date of introduction of a drug into the market to the date of its inclusion in pharmacopoeias. This happens because of the possible uncertainties in the continuous and wider usage of these drugs, reports of new toxicities (resulting in their withdrawal from the market), development of patient resistance and introduction of better drugs by competitors. Under these conditions, standards and analytical procedures for these drugs may not be available in the pharmacopoeias. It becomes necessary, therefore to develop newer analytical methods for such drugs.

MATERIALS

Sodium hydroxide (HPLC grade), Methanol (HPLC grade), Montelukast API, was purchased from Sri Sai Scientific Traders, Distilled water was purchased from local market, Montelukast sodium of Cipla manufactures. is Purchased form th local pharmacy

INSTRUMENTS

UV-Visible spectroscopy Lab India, Analytical Balance conetch, Hot air Oven , Ultra sonicate clearance.

METHOD DEVELOPMENT

In the start of the method development for this drug, different solvents were tested such as water, methanol, and 0.1 N NaOH (sodium hydroxide), In order to select suitable solvent for determination of Montelukast sodium, various solvents were selected for the solubility studies and it was found that Montelukast sodium was freely soluble in methanol was used for all the dilutions since it is economical. Due to greater solubility and reproducible readings of maximum absorbance, 0.1 N NaOH

(Sodium Hydroxide) was taken under consideration for further work.

SELECTION OF WAVELENGTH

The absorbance of the solutions containing Montelukast sodium was determined **[2].**

METHOD VALIDATION

Preparation of stock solution 1: 10 mg of Montelukast Sodium API was accurately weighed and transferred to flask. It was then dissolved by adding sufficient quantity of 0.1 N (NaOH)Sodium Hydroxide and volume was made up to 10 ml using 0.1N (NaOH)Sodium Hydroxide. The concentration of the standard drug stock solution was 1000 µg/ml (1mg/ml).

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Preparation of stock solution 2: 1ml of stock solution was pipette out into a 10 ml standard flask and the volume was made up to mark with 0.1 N (NaOH)Sodium Hydroxide. The concentration of the resulting solution was 100µg/ml.

Preparation of stock solution 3: 1 ml of stock solution was pipette out into a 10 ml standard flask and the volume was made up to mark with 0.1 N (NaOH)Sodium Hydroxide. The concentration of the resulting solution was 10µg/ml

Preparation of standard solution: 10 mg of Montelukast API was accurately weighed and transferred to 10 ml volumetric flask, shaken with 0.1 (NaOH)Sodium Hydroxide and diluted up to mark with a 0.1 N (NaOH)Sodium Hydroxide to get stock solution of 1000µg/ml. Aliquot portions were furteherd diluted with 0.1N (NaOH)Sodium Hydroxide to get concentrations of 10µg/ml of Montelukast. The absorbance of the final solution was read at selected wavelength.

Preparation of Test solution: An accurately weighed quantity of tablet powder equivalent to about 10 mg of Montelukast sodium was transferred to 10 ml volumetric flask, shaken with 0.1 N (NaOH)Sodium Hydroxide and diluted up to the mark with 0.1 N (NaOH)Sodium Hydroxide to get stock solution of 1000µg/ml. Aliquot portion were furthered diluted to get concentrations of 10µg/ml of Montelukast sodium. The absorbance of the final solution was read at selected wavelength.

UV Spectroscopy method

From the stock solution 1 (1000µg/ml), 1ml was pipette out into 10 ml standard flask and the volume was made up to the mark with 0.1 N (NaOH)Sodium Hydroxide (100µg/ml) and 1 ml was pipette out into standard flask from the above solution and volume was made up to the mark with 0.1 N (NaOH)Sodium Hydroxide (10µg/ml) for this stock solution 3 make 2ml,4ml, 6ml, 8ml, and 10 ml solutions were pipette out and made up to the mark using 0.1 N NaOH(Sodium Hydroxide) subsequently the concentrations were obtained. The absorbance of each solution measured at 243 against 0.1 N (NaOH)Sodium Hydroxide as blank. From these stock solutions we can find the Linearity, Range, Standard Regression Equation, slope, Intercept, Correlation Coefficient, Method precision, Accuracy, LOD, LOQ and Assay of Montelukast in API and Formulated form.

II. RESULTS:

Because of the greater solubility and reproducible readings of maximum absorbance with 0.1N Sodium Hydroxide (NaOH). It was taken under consideration for further work. The UV spectrum of Montelukast was obtained by using 0.1N Sodium Hydroxide (NaOH) as a solvent and then validated. The λmax of drug in 0.1N Sodium Hydroxide (NaOH) was determined using UV Spectrophotometer. The λmax was determined by scanning 10µg/mL solution of drug in the 0.1N Sodium Hydroxide (NaOH) in the range of 200-400 nm. The wavelength 243 nm was selected because it showed maximum absorbance by the drug.

Linearity of an analytical method was found to obey Beer's law in the concentration range of 2-10 µg/mL with correlation coefficient (r) values 0.999054.

Method precision of the proposed method was determined by analysis of aliquots from homogeneous slots by different analysts and analyzed under similar operational and environmental conditions. The % RSD reported was found to be 0.3 and 0.3.

The accuracy of the method was determined by recovery studies by adding known amount of the pure drug to the formulation. Thus, for accuracy, recovery studies were carried out and it was found to be within the range of 99.6% - 102%, which was within the recommended limits, indicating that the method has required accuracy.

The percentage of assay for the drug was to be 99.30801%w/v. The individual % Assay of Montelukast should not be less than 98.0% and not more than 102.0%.

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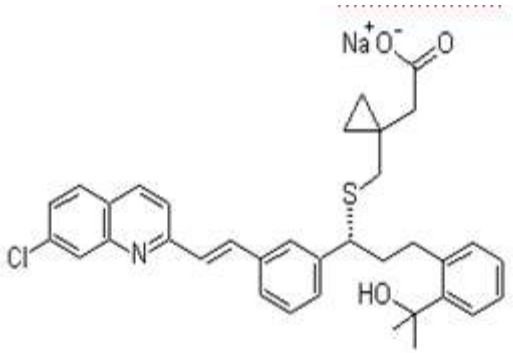
1. Structure of Montelukast



2. **OPTICAL CHARACTERISTICS**

Table no:. I optical characteristics results of Montelukast sodium by UV-Visible spectroscopic method:

S.NO	Parameter	Result
1	Absorption Maximum (nm)	243 nm
2	Linearity Range (µg/ml)	0.4- 0.16 µg/ml
3	Standard regression equation	y = 0.014x + 0.022
4	Slope	0.014
5	Intercept	0.022
6	Correlation Coefficient (r)	0.999157
7	Accuracy (% Recovery)	98-102%
8	Precision (Intra day)% RSD (Inter day) % RSD	0.3 0.3
9	LOD(µg/ml)	1.16
10	LOQ(µg/ml)	3.53

3.Maximum absorbance and 4.Linearity & Range of Montelukast

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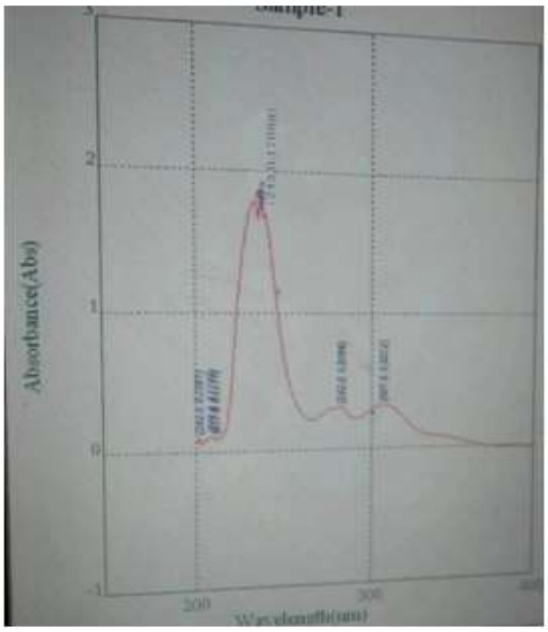

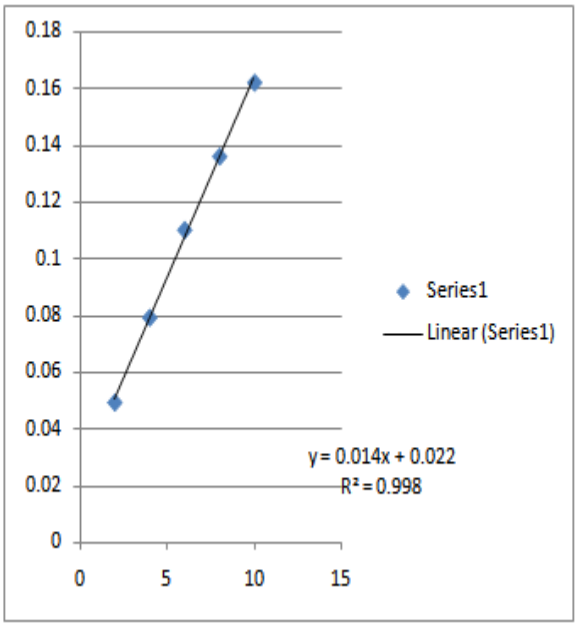

5. LINEARITY AND RANGE

Table No: 5.I Absorbance of various concentrations of drug solutions

S.NO	Concentration µg/Ml	Absorbance
1	2	0.049
2	4	0.079
3	6	0.110
4	8	0.136
5	10	0.162

6. PRECISION:

Table no. 6.I Intra-day precision and Inter-day precision

Concentration Taken	Precision		SD		%RSD	
	Intra-day	Inter-day	Intra-day	Inter-day	Intra-day	Inter-day
Sample-1	98.7	98.6	0.3	0.3	0.3	0.3
Sample-2	99.5	99.2				
Sample-3	98.7	99.6				
Sample-4	99.0	99.2				
Sample-5	99.3	99.5				

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Sample-6	99	99.1
Avg	**99**	**99.2**

%RSD for Sample absorbance, Concentration found ,%Assay for 6 Samples was found to be not more than 2%

7. ACCURACY

Accuracy Level	Concentration (µg/ml)		Absorbance	% Recovery	Statistical Analysis
	Amount added	Amount found			
80%	18	18.02	0.2770	100.1	Mean=1.1913 SD=0.005033 %RSD=0.4224
80%	18	18.09	0.2779	100.5	
80%	18	18.13	0.2785	100.7	
100%	20	20.01	0.3050	100.05	Mean =1.31 SD=0.005568 %RSD=0.4250
100%	20	20.07	0.3059	100.35	
100%	20	20.19	0.3075	100.95	
120%	22	22.31	0.3375	101.4	Mean=1.4283 SD=0.003512 %RSD=0.2458
120%	22	22.42	0.3390	101.9	
120%	22	22.46	0.3395	102.0	

Table.No: 7.I- Net Accuracy Table

8. ASSAY

Table no: 8.I

S.NO	SAMPLE	ABSORBANCE
1	Standard	0.160
2	Test-1	0.157
3	Test-2	0.159

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TEST – 1 :

$$= \frac{0.157}{0.160} x \frac{10}{10} x \frac{5}{100} x \frac{10}{9.9} x \frac{100}{5} x \frac{99.9}{100} x100$$

=0.981 x1 x 0.05 x 1.01 x 20 x 0.999 x 100

=98.02%w/v

TEST – 2 :

$$= \frac{0.159}{0.160} x \frac{10}{10} x \frac{5}{100} x \frac{10}{9.9} x \frac{100}{5} x \frac{99.9}{100} x100$$

= 0.99 x 1 x 0.05 x 1.01 x 20 x 0.999 x 100

=100.2%w/v

AVERAGE $= \frac{98.2+100.2}{2}$

$= \frac{198.22}{2}$

=99.11

Acceptance criteria:

The individual % Assay of Montelukast should not be less than 98.0% and not more than 102.0%

III. SUMMARY AND CONCLUSION

An efficient UV Spectrophotometric method was developed and validated for estimation of Montelukast in bulk and tablet dosage forms.

The method was developed using 0.1N Sodium Hydroxide (NaOH) as solvent and the λmax was found to be 243 nm. The method was validated with respect to system suitability, linearity, precision, and accuracy. The method was established according to ICH guidelines and definition. Accuracy was investigated by analyzing marketed formulation and percentage recovery was found to be within the limits. Therefore it can be said that the method was highly accurate. The relative standard deviation (RSD) values were obtained in low percentage. This indicated that the precision of the method was found to be good. The proposed method based on UV spectrophotometer is precise, accurate, simple to perform and economy in practice. It do not require expensive or sophisticated equipments and chemicals.

Hence the method can easily and conveniently adopt for the estimation of Montelukast bulk and pharmaceutical dosage form

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REFERENCES

[1]. Peters-Golden M, Gleason MM, Togias A: Cysteinyl leukotrienes: multi-functional mediators in allergic rhinitis. Clin Exp Allergy 2006;36:689-703.

[2]. Fal AM, Kopec A: Status of leukotrienes in the pathophysiology of asthma. Necessity for antileukotrienes treatment (in Polish). Pneumonol Alergol Pol 2010;78:68-73.

[3]. Shirasaki H, Kanaizumi E, Seki N, Fujita M, Kikuchi M, Himi T: Localization and up-regulation of cysteinyl leukotriene-2 receptor in human allergic nasal mucosa. Allergol Int 2013;62:223-228.

[4]. Kanda T, Tanio H, Wu C, Nishihara H, Nogaki F, Ono T: Churg-Strauss syndrome with severe granulomatous angiitis and crescentic glomerulonephritis, which developed during therapy with a leukotriene receptor antagonist. Clin Exp Nephrol 2010;14:602-607.

[5]. Sircar G, Saha B, Bhattacharya SG, Saha S: Allergic asthma biomarkers using systems approaches. Front Genet 2014;4:308.

[6]. Masoli M, Fabian D, Holt S, Beasley R: The global burden of asthma: executive summary of the GINA Dissemination Committee report. Allergy 2004;59:469-478.