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ANALYTICAL METHOD DEVELOPMENT AND VALIDATION FOR DETERMINATION OF MONTELUKAST BY UV-SPECTROSCOPY IN API& IN PHARMACEUTICAL DOSAGE FORMS

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ABSTRACT

An accurate, precise, and specific method developed for estimation of Montelukast in bulk. The API is used for the method development by UV spectroscopy with alcohol. The calibration curve method showed wavelength maxima for Montelukast at 345 nm with alcohol. This method obeys Beer's law in the concentration range of 5-30µg/ml with correlation coefficient 0.999 for Montelukast. The precision results are not more than 2%. The percentage assay of Montelukast in API and in pharmaceutical dosage form was 100.50% and 99.08% respectively. The results of analysis have been validated in order to verify linearity, precision, and accuracy for the goal intended and further implementation for the quantification analysis in the pharmaceutical dosage form. The newly developed spectroscopic method is used for the routine analysis for Montelukast in pharmaceutical dosage forms.

KEY WORDS

Method development, Montelukast, Validation, UV spectroscopy

INTRODUCTION

Montelukast sodium (MTKT), 1-[({(R)-m-[(E)-2-(7-chloro-2-quinolyl) vinyl]-α-[o-(1-hydroxyl-1-methylethyl) phenethyl] benzyl} thio) methyl] cyclopropaneacetate sodium. [1, 2] It has a molecular formula of $C_{35}H_{36}ClNO_3S$. The molecular weight of Montelukast Sodium is 586.18 g/mol (Fig. 1). It is white colored powder. It is freely soluble in ethanol, methanol, and water and practically insoluble in acetonitrile. [2, 3]

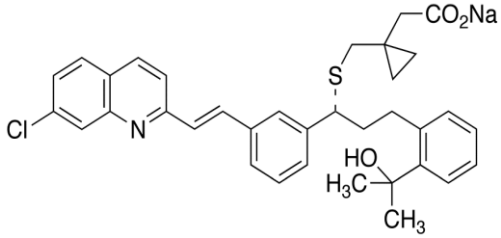

Figure 1: Chemical structure of montelukast

Montelukast sodium is potent, selective Cysteinyl leukotriene receptor antagonist; it blocks the action of leukotriene D4 on the cysteinyl leukotriene receptor in lungs and bronchial tubes. This reduces the bronchoconstriction caused by the leukotriene and results in less inflammation. This inhibits bronchospasm, allergic rhinitis. It inhibits exercise induced asthma and decrease both early and late responses to inhaled allergen. It relaxes the airways in mild asthma. [2, 4, 5]

Montelukast used for the treatment of asthma in children and adult and individuals with aspirin-sensitive asthma. It is indicated for prophylaxis and also used to relieve symptoms of seasonal allergies. [1, 4, 5, 6]

Literature survey reveals that methods which have been reported for estimation of Montelukast Sodium single dosage as well as in combined forms by spectrophotometry [1, 7, 8], RP-HPLC [2-6]. The present study illustrates development and validation of simple, accurate and precise procedure for "Development and validation of analytical method for determination of Montelukast by UV-spectroscopy in API & in pharmaceutical dosage forms".

EXPERIMENTAL

Chemicals and Reagents- Montelukast sodium was available in-house. The alcohol of AR grade was selected as solvent for developing spectral characteristics of drug. The all other chemical reagents and apparatus are of analytical grade.

Instrument- Single beam Agilent Carry 60 UV spectroscopy, 1 cm quartz cells with a fixed slit width, the wavelength range (200-400) nm.

Procedure-

Preparation of Standard Drug Solution- Standard stock solution was prepared by dissolving 50mg of Montelukast in 50 ml of volumetric flask with sufficient amount of alcohol. It was then sonicate for 10 minutes and the final volume of the solution was made up to 50 ml with alcohol to get stock solutions containing 1000µg/ml.

Determination of Absorption Maxima- Dilute 1 ml of standard drug solution with alcohol in 10 ml volumetric flask up to the mark. The solution containing 10 µg/ml of MONT was scanned at the range of 200- 400 nm to determine the wavelength of maximum absorption for MONT at 345 nm. (Fig.2).

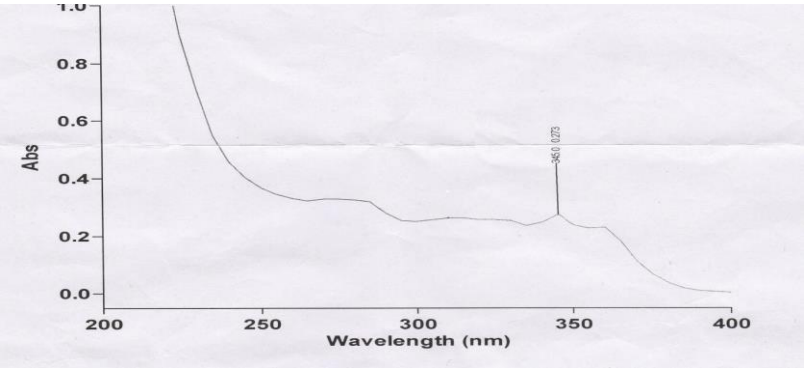

Figure 2: UV spectrum of Montelukast in Alcohol

Preparation of calibration curve- A series of solutions were prepared by diluting 1, 2, 3, 4, 5 and 6 ml of (100µgm/ml) standard solution of Montelukast sodium and transfer into separate 10 ml volumetric flasks. Alcohol was added and then the volumes were made up to the mark to obtain the solutions in the concentration range of 5, 10, 15, 20, 25 and 30 µg/ml of drug.

Absorbance of the resultant solution was measured at 345 nm using Alcohol as blank. A graph was plotted between the concentrations and their respective absorbance (Fig. 3).

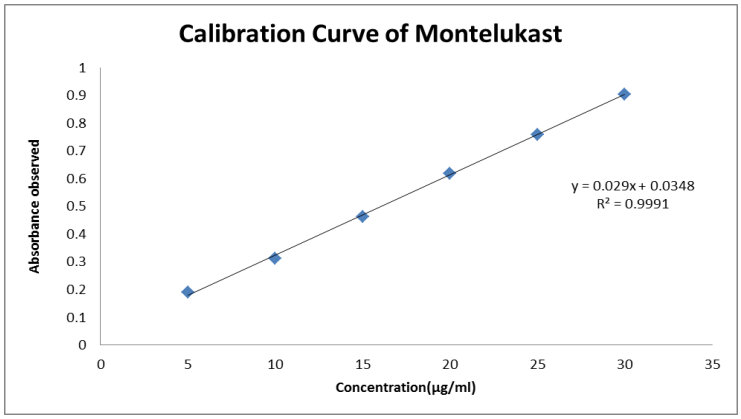

Figure 3: Calibration curve of Montelukast

METHOD VALIDATION PARAMEERS

Validation of the developed method performed according to ICH guidelines [9]

1.Linearity and Range- The linearity of the analytical procedure was obtaining at five concentrations corresponding to 5-30 µg/ml of Montelukast using alcohol. A calibration curve was plotted over a concentration range (5-30 µg/ml) of Montelukast at 345 nm. The regression analysis was performed for the line equation was found to be y = 0.029x + 0.0348 and correlation coefficient was found to be 0.999.

Table No. 1: Data of the standard solutions of Montelukast (Concentration and Absorbance)

S.No.	Concentration(µg/ml)	Absorbance(nm)
1.	5	0.1908
2.	10	0.312
3.	15	0.4639
4.	20	0.6199
5.	25	0.7601
6.	30	0.905

2. Precision:

Repeatability: Pipette out 0.9 ml working solution and transfer into 10 ml volumetric flasks. Dilute it to 10 ml with Alcohol to get 10 µg/ml solution. Six replicates of 10 µg/ml solutions of the drug were prepared. Absorbance of the resultant solutions was measured at 345 nm using, alcohol as blank. The result obtained is in the table 2.

Table No.2: Results of repeatability

Nominal Conc.(µg/ml)	Absorbance	Observed Conc.(µg/ml)	Mean Conc.(µg/ml)	SD	%RSD
10	0.1220	9.60	9.671	0.07	0.58
	0.1128	9.98			
	0.1226	9.44			
	0.1129	10.01			
	0.1231	9.44			
	0.1127	9.56			

Table No. 3: Results of Intra-day Precision

Nominal Conc. (µ g/ml)	Absorbance			Observed Conc.(µg/ml)			Mean Conc. (µg/ml)	SD	%RSD
	0 hrs	3 hrs	6 hrs	0 hrs	3 hrs	6 hrs			
3	0.1582	0.1576	0.1542	3.37	3.31	3.27	3.31	0.056	1.691
8	0.4221	0.4232	0.4345	8.23	8.19	8.17	8.19	0.030	0.366
16	0.8307	0.8312	0.8469	16.76	16.82	16.74	16.77	0.040	0.238
Mean									0.765

Intra-day precision:

Pipette out 0.3, 0.8- and 1.6-ml working solution and transfer into separate 10 ml volumetric flasks. Dilute the solution with alcohol to get solution of concentrations 3, 8 and 16µg/ml, respectively. Absorbance of the resultant solutions was measured at 345 nm using Alcohol as blank. It is determined by analyzing the corresponding responses three times within a day at 0, 3 and 6 hrs. interval. The result obtained is in the table 3.

Inter-day precision:

Pipette out 0.3, 0.8- and 1.6-ml working solution from standard stock solutiuon and transfer into separate 10 ml volumetric flasks. Dilute the solutions to 10 ml with alcohol to get solution of concentrations 3, 8 and 16µg/ml, respectively. Absorbance of the resultant

solutions was measured at 345 nm using acohol as blank. It is determined by analyzing the solutions once on three consecutive days 0, 24 and 48hrs interval. The result obtained is in the table 4.

Table No. 4: Results of Inter-day Precision

Nominal Conc. (µ g/ml)	Absorbance			Observed Conc.(µg/ml)			Mean Conc. (µg/ml)	SD	%RSD
	0 hrs	3 hrs	6 hrs	0 hrs	3 hrs	6 hrs			
3	0.1523	0.1545	0.1512	3.30	3.23	3.27	3.26	0.0351	1.07
8	0.4234	0.4562	0.4234	8.12	8.14	8.17	8.14	0.0251	0.30
16	0.8236	0.8235	0.8345	16.61	16.53	16.70	16.61	0.0850	0.51
Mean									1.88%

3. Accuracy-

Pipette out 0.5 ml working solution and transfer into 10 ml volumetric flasks. Nine such transfers are made. Pipette out three of the solutions with 0.4 ml of working solution and dilute each to 10 ml with alcohol to get 10 µg/ml solutions. Pipette out another three of the solutions with 0.5 ml of working solution and dilute each to 10 ml with alcohol to get 20 µg/ml solutions. Pipette out last three of the solutions with 0.6 ml of working solution and dilute each to 10 ml with alcohol to get 30 µg/ml solutions. Absorbance of the resultant solutions was measured at 345 nm using Alcohol as blank. The result obtained is in the table 5.

Table No. 5: Results of accuracy

Level %	Conc. µg/ml	Amt. Rec µg/ml	Recovery %	%RSD
10	10	38.96	99.56	0.28
	10	39.01	100.11	
	10	38.99	99.89	
20	20	49.80	98.00	0.80
	20	49.89	98.90	
	20	50.73	97.30	
30	30	60.93	100.18	0.69
	30	60.98	100.73	
	30	60.84	99.36	
Mean			99.34	0.59

4. Specificity:

Specificity study was carried out by observing any interference in absorbance of drug in the presence of common excipients like starch, talc, lactose, magnesium stearate etc. Absorbance of 10 µg/ml drug solution with and without excipients was measured at 345 nm using Alcohol as blank. The result obtained is summarized in the table 6.

Table No. 6: Results of specificity

S. No.	Conc. (µg/ml)	Before addition of excipients		After addition of excipients		% interference
		Abs.	Conc.	Abs.	Conc.	
1	10	0.217	19.87	0.218	20.01	-0.14
2	10	0.218	19.11	0.216	19.87	-0.76
3	10	0.217	19.83	0.220	19.99	-0.16
4	10	0.215	19.86	0.213	20.05	-0.19
5	10	0.221	18.54	0.222	19.21	-0.67
6	10	0.218	19.21	0.215	20.05	-0.84
Mean						0.46

The absorbance, E1% 1cm, Absorptivity and molar absorptivity values of Montelukast in different concentration at λ_{max}= 345nm: Table 7.

Table No. 7: Data of absorptivity

S.No.	Conc. (µg/ml)	Absorbance	Absorbance/ Conc.(A/C)	E1% 1cm (A/C*10000	Absorptivity (E1%/10)	Molar absorptivity
1.	5	0.1908	0.03816	381.6	38.16	23207.729
2.	10	0.312	0.0312	312	31.2	18974.872
3.	15	0.4639	0.03092	309.2	30.92	18804.585
4.	20	0.6199	0.03099	309.9	30.99	18847.157
5.	25	0.7601	0.03040	304	30.4	18488.337
6.	30	0.905	0.03016	301.6	30.16	18342.377
			Mean =	319.7166	31.97	19444.176

Estimation of Montelukast in pure form: Weigh accurately 50 mg of the drug and dissolve it in. Alcohol make up the volume to 50 ml with alcohol in volumetric flask. Pipette out 5 ml of the solution and transfer into a 50 ml volumetric flask. Dilute it to 50 ml with alcohol. Pipette out 1 ml of the resultant solution and transfer into 10 ml volumetric flasks. Dilute it to 10 ml with alcohol. Absorbance of the final solution was measured at 345 nm using Alcohol. The above procedure was repeated for three times. The result obtained is in the table 8.

Table No. 8: Results of Assay (API)

S. No.	Absorbance	Conc.(µg/ml)	Dil. Factor	Content (mg)	Weight Taken (mg)	% Assay
1	0.3250	10.16	5000	50.82	50	101.65
2	0.3190	9.97	5000	49.89	50	99.78
3	0.3200	10.00	5000	50.04	50	100.09
						100.50

Estimation of Montelukast in pharmaceutical dosage form (Montecip, 10mg)- Weigh 10 tablets and calculate the average weight. Powder those tablets. Weigh accurately a quantity of powdered tablets containing about 50 mg of Montelukast and transfer it into 50 ml volumetric flask. Add 35 ml Alcohol and sonication for 15 minutes. Make up the volume to 50 ml, mix and filter. Dilute 5 ml of the filtrate to 50 ml with Alcohol. Further dilute 1 ml of the resulting solution to 10 ml with Alcohol. Measure the absorbance of the resulting solution at 345 nm.

The above procedure was repeated for three times. The result obtained is in the table 9**.**

Table No. 9: Results of assay (Montecip)

S No.	Absorbance	Conc.(µg/ml)	Dil. Factor	Content (mg)	Label Claim (mg)	% Assay
1.	0.3146	9.84	5000	49.20	10	98.40
2.	0.3200	10.0	5000	50.04	10	100.0
3.	0.3160	9.88	5000	49.42	10	98.84
Mean						99.08%

RESULTS and DISCUSSION

The solubility of Montelukast studied and alcohol is selected as a solvent. For calibration curve method Montelukast showed wavelength maxima at 345 nm. The drug follows Beer-Lambert's law over the concentration range of 5-30 µg/ml with a correlation coefficient of 0.999. The present study of proposed method showed precision in terms of the repeatability and, reproducibility is found to be not more than 2%. The recovery results are in the range of 98 to 102%. Hence, the results of the analysis are validated as per ICH guidelines. Quantitative determination of Montelukast in API and tablet dosage form by employed the method, the assay values found 100.50% and 99.08%, respectively.

CONCLUSION

The newly developed method of Montelukast is simple, precise, and validate in terms of linearity, precision, accuracy, reproducibility. Therefore, the developed spectroscopic method used for routine estimation of Montelukast in tablet dosage form.

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