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Research Article

Simultaneous Estimation Of Bilastine And Montelukast In Bulk And Pharmaceutical Dosage Form By UV Spectroscopy

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ABSTRACT

The ultraviolet (UV) method was developed for the purpose of determining the amount of bilastine and montelukast present in bulk and pharmaceutical dosage form. An ultraviolet-visible spectrophotometer was utilized in order to carry out the identification and quantification processes. The mixture of 0.1% perchloric acid and acetonitrile was employed as a diluent for the preparation of samples and standards, as well as a blank. Researchers discovered that the wavelength of the medicine Montelukast was 254 nm, while the wavelength of the drug Bilastine was 270 nm An effort has been made to construct a UV method for the estimation of Bilastine and Montelukast in bulk and pharmaceutical dosage form, as well as to validate the method that has been developed in accordance with the guidelines established by ICH Q2 (R1).

INTRODUCTION

Montelukast is widely recommended for the primary purpose of preventing and treating the symptoms of mild to moderate asthma, as well as preventing the asthma from becoming more severe. persons who suffer from asthma were also administered it to help them breathe easier, particularly when they exercised (a condition known as exercise-induced asthma), as well as persons who suffer from seasonal allergies, which include symptoms such as sneezing, itching, and runny nose (allergic rhinitis). The treatment of urticaria that lasts for more than six weeks may also involve the administration of Montelukast to patients who do not have asthma sometimes . The new therapeutic molecule known as bilastine is a member of the oral second-generation H1 antihistaminic receptor antagonist class. It possesses a subatomic load of 463.6 Daltons and a basic drug moiety that is piperidinyl-

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benzimidazole. The chemical known as bilastine was initially approved by the European Union (EU) for the treatment of allergic rhinoconjunctivitis and urticarial.

UV Spectrophotometric Method

1. Method Parameters:

a. Diluent: 0.1% Perchloric acid : Acetonitrile (50: 50%, v/v)

Preparation of 0.1% Perchloric acid:

Add 0.1 ml of Perchloric acid in 100 ml of Water, Mix and filtered.

b. Wavelength: λ1 = 270nm; λ2 = 254 nm

2. Standard Preparation:

a. Bilastine Standard Stock Solution-I (BSSS-I):

i. To begin, prepare a Standard Stock Solution (BSSS-I) by adding 10 mg of Bilastine to a volumetric flask containing 10 ml of liquid. Then, add 5 ml of diluent to the flask, stir for two minutes, and proceed to bring the volume up to 10 ml with the diluent. The concentration of Bilastine is 1000 µg/ml.

b. Montelukast Standard Stock Solution-II (MSSS-II):

i. Then prepare a Standard Stock Solution (MSSS-II) of Montelukast by adding 5 mg in 10 ml volumetric flask & add 5 ml diluent, mix for 2 minutes and make the volume to 10 ml with diluent. (Conc. of Montelukast = 500 µg/ml).

c. Then add 0.1 ml of BSSS-I &0.1 ml MSSS-I in 10 ml volumetric flask and add 5 ml diluent and vortex and make up the volume with diluent. (Conc. of Bilastine= 10µg/ml &Montelukast = 5µg/ml).

3. Selection of Wavelength:

10µg/ml of BIS Working Standard and 5µg/ml of MTLWorking Standardwere scanned in the UV range of 190-400 nm. The overlay of both the spectrum was recorded. From the overlain spectra wavelengths 270 nm (λmax of BIS) and 254 nm (λmax of MTL) were selected for analysis of both drugs using simultaneous method. (λ1-270 nm and λ2-254 nm). The absorbance at λ1 and λ2 was measured and the concentration was calculated using following formula;

$$Cx = \frac{A2ay1 - A1ay2}{ax2ay1 - ax1ay2}$$

$$Cy = \frac{A1ax2 - A2ax1}{ax2ay1 - ax1ay2}$$

Where,

In this equation, Cx and Cy represent the concentrations of bilastine and montelukast, two different medications.

A1 and A2 are the absorbances of sample at λ1 and λ2, respectively,

ax1 and ax2 are the absorptivity of Bilastine at λ1 and λ2, respectively,

ay1 and ay2 are the absorptivity of Montelukast at λ1 and λ2, respectively.

Validation of UV method:-

a. Linearity:

i. 5 samples of varying concentrations ranging from 80% to 120% were made.

ii. The concentrations are given below

iii. The sample preparations are given as below;

X ml of BSSS-I and Y ml of MSSS-II was diluted to 10 ml.

X ml of MSSS-I	Y ml of ASSS-II	Diluted to	Conc. of BIS (µg/ml)	Conc. of MTL (µg/ml)
0.08	0.08	10 ml	8	4
0.09	0.09	10 ml	9	4.5
0.10	0.10	10 ml	10	5
0.11	0.11	10 ml	11	5.5
0.12	0.12	10 ml	12	6

LOD/ LOQ:

iv. Can be calculated by using AVONA Technique.

$$LOD = \frac{3.3 \times Std\ Error\ of\ Intercept}{Coefficient\ of\ X\ variable\ 1}$$

$$LOD = \frac{10 \times Std\ Error\ of\ Intercept}{Coefficient\ of\ X\ variable\ 1}$$

c. Repeatability :

A single sample was prepared as described and 6 injections were made from same sample; checked for RSD.

d. Accuracy:

i. Samples were made of 80%, 100% and 120% concentration as per Table 1.

ii. In order to determine the percentage of relative standard deviation, samples were injected three times.

iii. The percentage of recovery was also computed.

% Conc	BIS Conc. (µg/ml)	MTL Conc. (µg/ml)
80	12	36
100	15	45
120	18	54

e. Intra- & Inter-day Precision:

- The working standard and drug product samples were freshly prepared and analysed in morning and evening for Intra-day precision.
- The same working standard and drug product were used for analysis on 2nd day for inter-day precision.
- % RSD for Assay was calculated for the confirmation of precision.

RESULT AND DISCUSSION:

Selection of Wavelength

The Standard and Sample solution was scanned from 190 to 400 nm by using UV-VIS spectrophotometer against Diluent (0.1% Perchloric acid: Acetonitrile (50:50)) as blank and the maximum absorption of standard and sample solution were recorded.

RESULT:

a. The maximum absorption for Bilastine was found to be 270 nm.

b. The maximum absorption for Montelukast was found to be 254 nm.

The UV scans for both the drugs is given below:

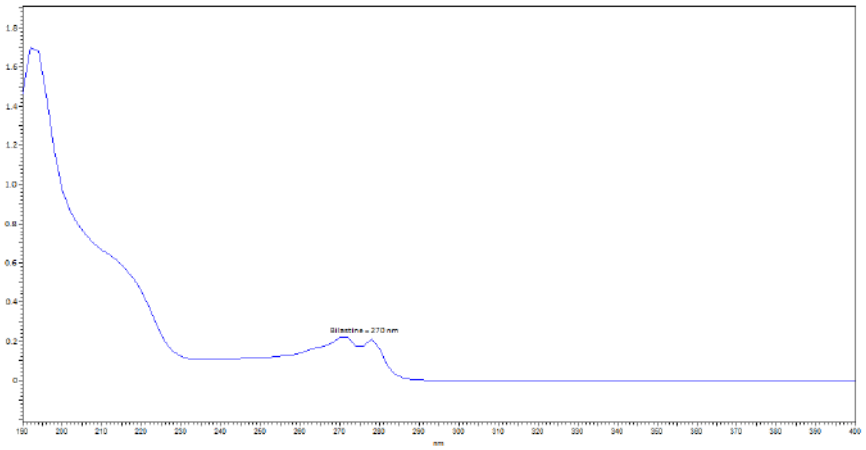

Figure 1: UV scan of Bilastine

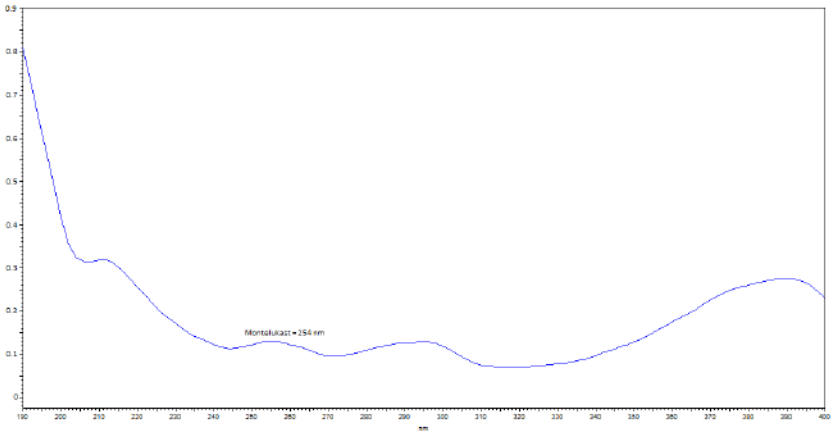

Figure 2: UV scan of Montelukast

Validation of UV Method

a. Specificity

It was confirmed with blank and working standard run that there was zero absorbance of blank at set lambda in UV Spectrophotometer.

b. Linearity

Within the range of 8-12µg/ml, it was discovered that the peak reaction is directly proportional to the concentration of the drug, and it was also found to be linear. The linearity data for Bilastine and Montelukast is give below:

Table 2: Linearity data for Bilastine

Bilastine		
% Level	**Concentration (ug/ml)**	**Absorbance**
80	8	0.189
90	9	0.209
100	10	0.231
110	11	0.254
120	12	0.279

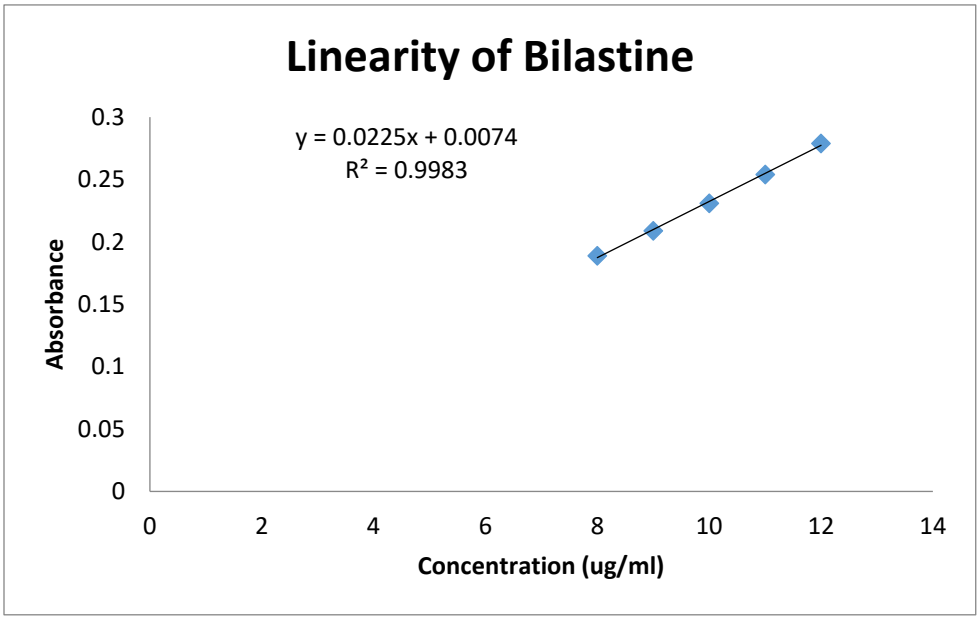

Figure 3: Linearity graph of Bilastine

Table 3: Linearity data for Montelukast

Montelukast		
% Level	**Concentration (ug/ml)**	**Absorbance**
80	4	0.115
90	4.5	0.129
100	5	0.144
110	5.5	0.161
120	6	0.175

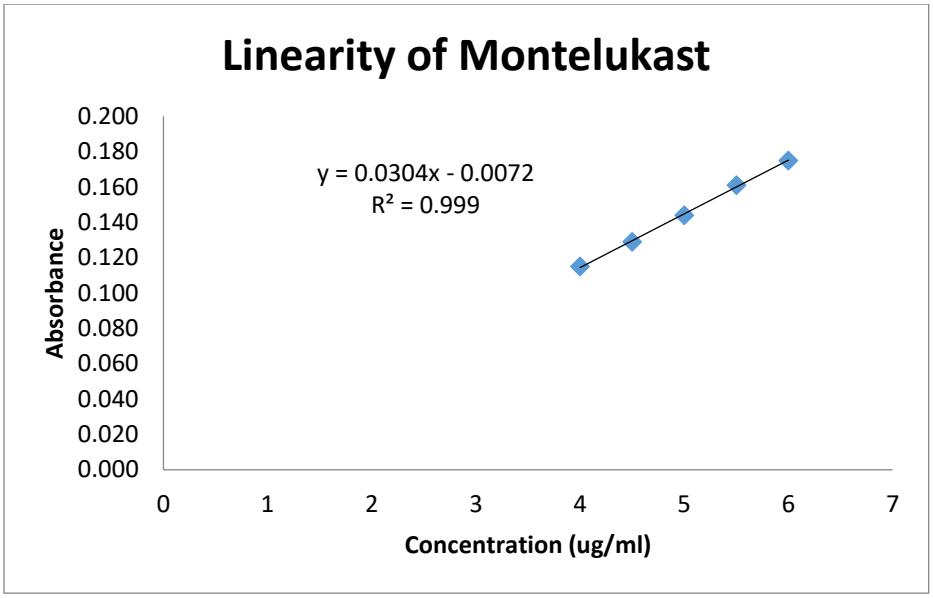

Figure 4: Linearity graph of Montelukast

From the above data it was found that the correlation coefficient of Bilastine and Montelukast were 0.998 and 0.999 respectively, which was found to be within the acceptance criteria of 0.998.

c. LOD and LOQ

Based on the linearity data, LOD and LOQ was calculated and reported as below:

Table 4: LOD & LOQ of Bilastine

Regression Statistic	
Multiple R	0.999141847
R Square	0.99828443
Adjusted R Square	0.997712573
Standard Error	0.001702939
Observations	5

ANOVA

	df	SS	MS	F	Significance F
Regression	1	0.0050625	0.0050625	1745.689655	3.01735E-05
Residual	3	8.7E-06	2.9E-06		
Total	4	0.0050712			

	Coefficients	Standard Error	t Stat	P-value
Intercept	0.0074	0.00543875	1.360606793	0.266839705
X Variable 1	0.0225	0.000538516	41.78145109	3.01735E-05

LOD	0.80	ug/ml
LOQ	2.42	ug/ml

Table 5: LOD & LOQ of Montelukast

Regression Statistic	
Multiple R	0.999481014
R Square	0.998962297
Adjusted R Square	0.998616396
Standard Error	0.000894427
Observations	5

ANOVA

	df	SS	MS	F	Significance F
Regression	1	0.0023104	0.0023104	2888	1.41917E-05
Residual	3	2.4E-06	8E-07		
Total	4	0.0023128			

	Coefficients	Standard Error	t Stat	P-value
Intercept	-0.0072	0.002856571	-2.520504151	0.086138631
X Variable 1	0.0304	0.000565685	53.74011537	1.41917E-05

LOD	0.31	ug/ml
LOQ	0.94	ug/ml

From the above data it was found that:

1. The LOD & LOQ for Bilastine were found to be 0.80 µg/ml and 2.42 µg/ml.
2. The LOD & LOQ for Montelukast were found to be 0.31 µg/ml and 0.94 µg/ml.

d. Repeatability

Repeatability was performed for both the APIs, the recorded absorbance is shown below:

Table 6: Repeatability of Bilastine and Montelukast

Sample ID	BIS ABS	MTL ABS
100% Rep 1	0.231	0.144
100% Rep 2	0.237	0.143
100% Rep 3	0.234	0.145
100% Rep 4	0.233	0.144
100% Rep 5	0.235	0.143
100% Rep 6	0.235	0.145
AVG	0.234	0.144
STDEV	0.002	0.00
%RSD	0.87	0.62

From the above data, it can be seen that the %RSD for 6 replicate injections of Bilastine and Montelukast are 0.87% and 0.62% respectively. The percentage RSD (<2) values obtained showed that the method developed was precise at repeatability precision level.

e. Accuracy

The accuracy was performed at 3 different levels i.e. 80%, 100% and 120%. The accuracy data for Bilastine and Montelukast is given below:

Table 7: Accuracy for Bilastine

Bilastine								
% Level	**Reps**	**Spiked Conc (ug/ml)**	**Abs**	**Amount Recovered (ug/ml)**	**% Recovery**	**AVG**	**STDEV**	**RSD**
80	Rep 1	8.00	0.189	8.08	100.96	100.07	0.82	0.82
	Rep 2	8.00	0.187	7.99	99.89			
	Rep 3	8.00	0.186	7.95	99.36			
100	Rep 1	10.00	0.231	9.87	98.72	100.00	1.28	1.28
	Rep 2	10.00	0.237	10.13	101.28			
	Rep 3	10.00	0.234	10.00	100.00			
120	Rep 1	12.00	0.279	11.92	99.36	99.95	0.54	0.54
	Rep 2	12.00	0.281	12.01	100.07			
	Rep 3	12.00	0.282	12.05	100.43			

- The %RSD of three replicates of Bilastine for accuracy level 80%, 100% and 120% was found to be 0.82%, 1.28% and 0.54% respectively.
- The % recoveries for accuracy level 80%, 100% and 120% was found to be 100.07%, 100.00% and 99.95% respectively.

Table 8: Accuracy for Montelukast

Montelukast								
% Level	**Reps**	**Spiked Conc (ug/ml)**	**Abs**	**Amount Recovered (ug/ml)**	**% Recovery**	**AVG**	**STDEV**	**RSD**
80	Rep 1	4.00	0.115	3.99	99.83	100.69	0.87	0.86
	Rep 2	4.00	0.117	4.06	101.56			
	Rep 3	4.00	0.116	4.03	100.69			
100	Rep 1	5.00	0.144	5.00	100.00	100.00	0.69	0.69
	Rep 2	5.00	0.143	4.97	99.31			
	Rep 3	5.00	0.145	5.03	100.69			
120	Rep 1	6.00	0.175	6.08	101.27	100.31	0.88	0.88
	Rep 2	6.00	0.173	6.01	100.12			
	Rep 3	6.00	0.172	5.97	99.54			

- The %RSD of three replicates of Montelukast for accuracy level 80%, 100% and 120% was found to be 0.86%, 0.69% and 0.88% respectively.
- The % recoveries for accuracy level 80%, 100% and 120% was found to be 100.69%, 100.00% & 100.31% respectively.

f. Intra & Inter day Precision

The Standard solution of Bilastine and Montelukast were examine for Intra and Inter day Precision, the data is shown below:

Table 9: Intra & Inter day Precision of Bilastine and Montelukast

Condition	Sample ID	Interval	Bilastine		Montelukast	
			Conc (ug/ml)	% Assay	Conc (ug/ml)	% Assay
Intraday	WS	Morning	10.00	-	5.00	-
	DP	Morning	9.98	99.80	4.96	99.20
	WS	Evening	10.00	-	5.00	-
Interday	DP	Evening	9.95	99.50	4.95	99.00
	WS	Day 2	10.00	-	5.00	-
	DP	Day 2	9.93	99.30	4.96	99.20
%RSD			0.25		0.12	

- The % Assay for Bilastine for Morning, Evening and Day 2 were found to be 99.80%, 99.50% and 99.30%, respectively.
- The % Assay for Montelukast for Morning, Evening and Day 2 were found to be 99.20%, 99.00% and 99.20%, respectively.
- In terms of intraday and interday precision, the relative standard deviation (%RSD) for bilastine and montelukast was determined to be 0.25% and 0.12%, respectively. Since there was no discernible change in the working standard of bilastine and montelukast over the course of two days, it may be concluded that the standard is stable.

CONCLUSION

The purpose of this study was to develop and validate a UV and RP-HPLC method for the quantification of bilastine and montelukast in tablet formulations and bulk quantities.. The proposed methods were found to be appropriate due to its simplicity, reliability, sensitivity, rapidness and selectivity for detection at very low concentrations. The short chromatographic time makes this method suitable for processing of multiple samples in short time. The method showed no interference of the Excipients present in Bilastine and Montelukast. The statistical parameters and recovery data reveals the good accuracy and precision of the proposed methods. The UV and method developed for the estimation of Bilastine and Montelukast was validated as per the ICH guidelines. Validation data demonstrates that, these methods are accurate, precise, simple and economic and can be used in the routine analysis of Bilastine and Montelukast in various formulations.

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