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DEVELOPMENT AND STANDARDIZATION OF STABILITY INDICATING UV-SPECTROPHOTOMETRIC METHOD FOR ASSESSMENT OF BILASTINE IN BULK AND PHARMACEUTICAL DOSAGE FORMULATION

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Keywords:

Bilastine, Degradation Studies, standardization, λmax, UV Spectrophotometer.

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ABSTRACT: The objective of the present work is to develop and standardize the UV-Spectrophotometric method for the assessment of Bilastine in bulk and pharmaceutical dosage forms. On account of not much work being reported on the drug Bilastine and also it is a new second-generation anti-histamine molecule. Hence it is necessary in this context to relook into the older methods and further research for new methods to decide on the efficacy, cost, and selectivity of the method. The λ_{max} of bilastine was found at 282.5 nm. Beer's law was obeyed in the concentration range of 10-50 µg/ml. The limit of detection and limit of quantification were found to2.94 µg/ml and 8.92 µg/ml respectively. Recovery of Bilastine in tablet formulation was observed in the range of 96-105%. All the precision, repeatability, and reproducibility studies were performed, and the % RSD was found to be less than 2%. The % degradation of Bilastine by acidic, basic, oxidation, thermal and photolytic degradation was found to be 6.04, 6.97, 10.68, 9.05, 6.5%, respectively. The method for the drug Bilastine was found to be precise, specific, reproducible & economical, and can be used for routine analysis of Bilastine in bulk and marketed dosage form.

INTRODUCTION: Bilastine chemically is {2-[4-[2- [4-[1- (2-ethoxyethyl) benzimidazol-2-yl] piperidin-1-yl] ethyl] phenyl] -2-methylpropanoic acid} [3]. It has less chance to undergo drug-drug interaction [3]. It belongs to class I of Biopharmaceutical classification system [1]. It is a second generation antihistamine medication that is used in the treatment of allergic rhinoconjunctivitis and urticaria [5, 9].

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The dose of bilastine is 20 mg per day [6]. It is also used in the treatment of itchy skin rashes and allergic rhinitis [2]. The chemical structure is given in **Fig. 1**.

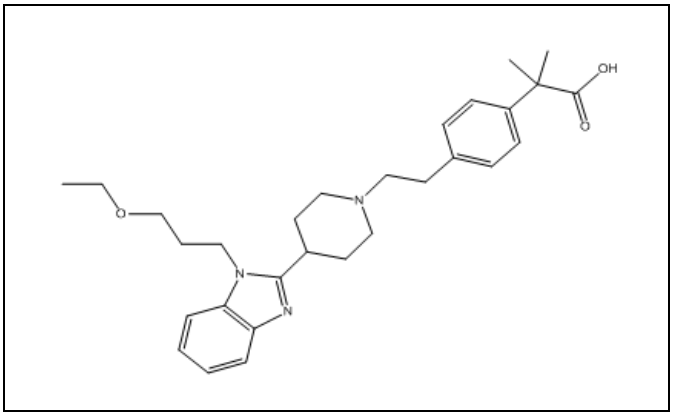

FIG. 1: STRUCTURE OF BILASTINE

MATERIAL AND METHOD: Bilastine standard was obtained as a gift sample from Symed Labs limited Hyderabad, India. Millipore water was collected from the Direct-Q UV water purification system from KLE College of Pharmacy, Belagavi, and Methanol LR grade was collected storehouse KLE College of Pharmacy, Belagavi. Shimadzu UV-1800 with UV Probe software and UV-Spectrophotometer of Shimadzu UV-1900 with Lab Solutions software were used for the determination of Bilastine. Calibrated weighing balance was used for weighing the API standard.

Method Development:

Solvent and Wavelength Detection: Bilastine is soluble in various organic solvents but, to develop a safe and cost-effective method, the ratio of Millipore water and methanol was taken in 80:20v/v was selected throughout the study. Bilastine 10μg/ml of standard solution was scanned in between 400 nm to 200 nm.

Preparation of Stock Solution: An accurately weighed quantity of 10 mg of Bilastine was transfer red into 10 ml clean and dried volumetric flask. The volume was made up to mark with Millipore water and methanol ratio. This was considered as a standard stock solution, having a concentration of 1000 μg/ml. This stock solution was used for making further dilutions.

Standardization of Method:

Specificity and Selectivity: Bilastine showed selectively maximum absorbance at 282.5 nm. The solvent didn't show any absorbance at the λ_{max} of Bilastine. Thus the method was found to be specific.

Method Validation[2]:

Linearity: From the standard stock solution, serial dilutions containing concentrations of 10-50 μg/ml were prepared. The solutions were analyzed and the absorbance was measured at 282.5 nm. Linearity curve was plotted against Concentration on X-axis and Absorbance on Y-axis, and linear regression equation was calculated and found 0.9996.

Precision:

A. System Precision: The system precision was performed in the replicate of six, and the results were found in the accepted range as per the ICH guidelines.

B. Intraday: The intraday precision was performed as in three replicates of three different concentrations 10, 30 & 50 μg/ml. The % RSD was calculated it was performed by a different interval of time in a day. The results were found in the accepted range.

C. Interday: The interday precision was performed by preparing three replicates of three different concentrations of 10, 30 & 50 g/ml of Bilastine. The analysis was performed on three consecutive days. The % RSD was calculated for absorbance.

Ruggedness: The ruggedness parameter was performed by changing the instrument and also by changing the analyst. This parameter was performed in the three replicates at three different concentrations and measuring the absorbance at 282.5 nm.

Robustness: The robustness parameter was performed by minor changes in the wavelength of detection as per method analysis was performed at 282.5nm for the robustness study analysis was performed at 281.5 & 283.5 nm respectively.

Accuracy: Accuracy was performed by the standard addition method. The study was carried out in the three different levels of 50%, 100% & 150%, respectively. Each solution was studied, and the percentage recovery was calculated.

Assay: The developed method was applied for the marketed formulation. Tablets were weighed accurately, and they were triturated, and the equivalent weight was calculated to the standard amount of drug used for the analysis. 56.8 mg of powder was weighed and dissolved in 100 ml of solvent. Further, the dilutions were prepared in terms of 10-50 μg/ml, and the absorbance was measured.

Forced Degradation Studies [8, 9]: Forced degradation studies were performed as per the ICH guidelines for determining the ability of the drug whether it stands its property.

When it undergoes the stress condition. Bilastine was treated with various stress conditions such as acid degradation, alkaline degradation, oxidative degradation, thermal degradation & photolytic degradation.

Acid Degradation: It was carried out using a drug solution with 0.5 ml of 0.1N HCl, and the sample was heated at 60 °C for about 30 min on a water bath. The steered sample was cooled and neutralized with 0.5ml of 0.1N NaOH; the solution was made up to final volume with the solvent in the three replicate, and the absorbance was measured.

Alkaline Degradation: It was carried by treating the drug solution with 0.5 ml of 0.1N NaOH, and then the sample was heated at 60 °C for 30 min on a water bath. The steered sample was cooled and neutralized with 0.5ml of 0.1N HCl and diluted with solvent, and in a replicate of three, the absorbance was measured.

Oxidative Degradation: The oxidative degradation was performed by taking a drug solution with 0.5 ml of hydrogen peroxide, and it was heated for 30 min at 60 °C on a water bath. Then the solution was cooled and diluted with the solvent system. Then the further dilutions were prepared in the replicate of three, and the absorbance was measured.

Thermal Degradation: The thermal degradation was carried out by heating a drug solution for 30 min at 60 °C on a water bath. The solution was kept aside to cool after the solution was cooled, it was diluted with the solvent.

The further dilutions were prepared in the replicate of three, and the absorbance was noted and taking the mean the percentage degradation was measured.

Photolytic Degradation: The photolytic degradation was carried out by keeping the drug sample in direct contact with UV light for 2 h, and then the drug samples dilutions were prepared with the solvent system. Then the further dilutions were made in the replicate of three and the absorbance was measured.

Results: The spectroscopic method was developed using Millipore water and methanol and the UV 1800 instrument, and the results are mentioned in **Table 1.**

TABLE 1: DEVELOPED METHOD PARAMETERS

S. no	Parameters	Specifications
1	Analyte	Bilastine
2	Solvent	Type-III Millipore water : Methanol (80:20)
3	λmax	282.5nm
4	Instrument	Shimadzu 1800 & shimadzu 1900

Specificity and Selectivity: Bilastine showed selectively maximum absorbance at 282.5 nm. The solvent didn't show any absorbance at the λ_{max} of Bilastine. The spectrum is mentioned in **Fig. 2**.

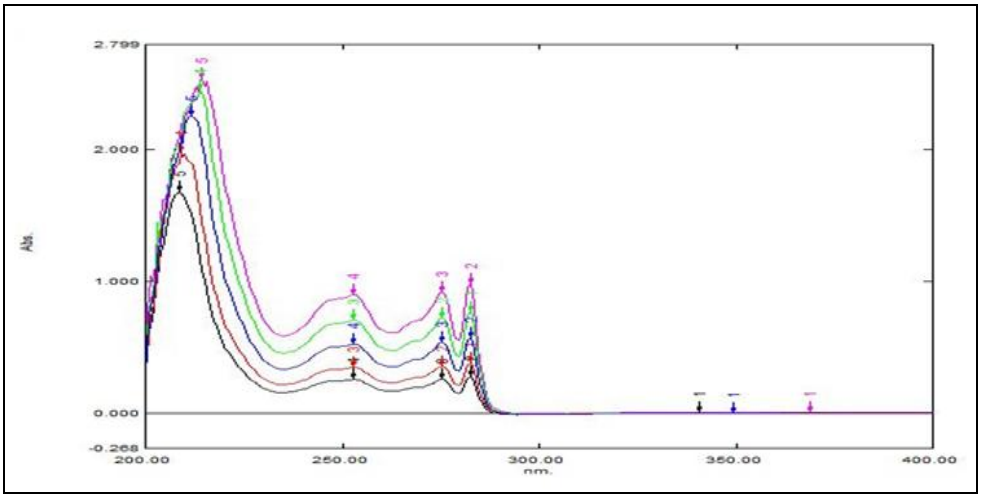

FIG. 2: UV SPECTRUM FOR BILASTINE

Linearity: The dilutions in the concentration range of 10-50 µg/ml were prepared. The solutions were analyzed and the absorbance was measured at 282.5 nm. The results are mentioned in **Table 2,** and the calibration graph is mentioned in **Fig. 3**.

TABLE 2: CONCENTRATION RANGE AND DATA OF BILASTINE

S. no.	Concentration	Absorbance(282.5nm)
1	10µg/mL	0.172
2	20µg/mL	0.311
3	30µg/mL	0.441
4	40µg/mL	0.560
5	50µg/mL	0.694
R^2		0.9996
slope		0.0129
LOD		2.94µg/mL
LOQ		8.92µg/mL

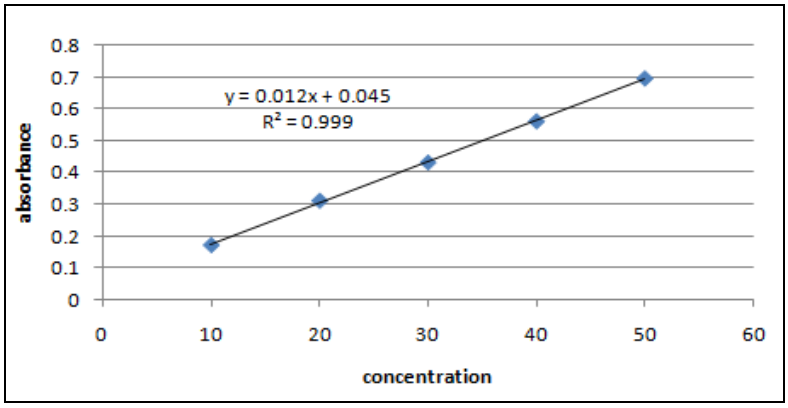

FIG. 3: CALIBRATION GRAPH OF BILASTINE

TABLE 3: SYSTEM PRECISION DATA OF BILASTINE

Concentration (µg/ml)	Absorbance*	Standard Deviation (SD)	% Relative Standard Deviation (%RSD)
10	0.185	0.001612	0.871%
30	0.453	0.002	0.441%
50	0.753	0.0036	0.478%

*= average absorbance of six replicates.

TABLE 4: INTRADAY PRECISION OF BILASTINE

Concentration (µg/ml)	Absorbance*		Standard deviation	% Relative standard deviation
10	Abs 1Hr	0.183	0.0015	0.83%
	Abs 8Hr	0.187	0.0017	0.93%
30	Abs 1Hr	0.441	0.0015	0.35%
	Abs 8Hr	0.464	0.0032	0.69%
50	Abs 1Hr	0.733	0.0006	0.08%
	Abs 8Hr	0.783	0.0026	0.34%

*= average absorbance of three replicates

TABLE 5: INTERDAY PRECISION OF BILASTINE

Concentration(µg/ml)	Absorbance*		Standard Deviation	% Relative Standard Deviation
10	Day 1	0.165	0.002	1.26%
	Day 2	0.174	0.001	0.574%
	Day3	0.165	0.002	1.26%
30	Day 1	0.421	0.0005	0.137%
	Day 2	0.465	0.002	0.430%
	Day 3	0.469	0.0005	0.123%
50	Day 1	0.724	0.002	0.287%
	Day 2	0.792	0.001	0.126%
	Day 3	0.761	0.003	0.401%

*=average absorbance of three replicates.

Precision: The system precision was performed in the replicate of six, and the results were found in the accepted range as per the ICH guidelines. They are mentioned in **Table 3**. The intraday precision was performed as in three replicates of three different concentrations 10, 30 & 50 µg/ml. The %

RSD was calculated. The results are mentioned in **Table 4**. The interday precision was performed in three replicates of three different concentrations of 10, 30 & 50 µg/ml. The % RSD was calculated. The results are mentioned in **Table 5**.

Ruggedness: The ruggedness parameter was performed by changing the instrument and also by changing the analyst. This parameter was performed in three replicates at 282.5 nm. The results are mentioned in **Table 6**.

TABLE 6: RUGGEDNESS DATA OF BILASTINE

Concentration (µg/ml)	Absorbance*		Standard Deviation	% Relative Standard Deviation
10	Analyst 1 UV-1800	0.167	0.0015	0.91%
	Analyst 2 UV-1900	0.169	0.0012	0.68%
30	Analyst 1 UV-1800	0.482	0.0035	0.72%
	Analyst 2 UV-1900	0.484	0.0035	0.72%
50	Analyst 1 UV-1800	0.814	0.0006	0.07%
	Analyst 2 UV-1900	0.842	0.0015	0.18%

*=average absorbance of three replicates.

Robustness: The robustness parameter was performed by minor changes in the wavelength and the solvent system. This parameter was studied at 281.5 nm and 283.5 nm, respectively. The results are mentioned in **Tables 7** & **8,** respectively.

TABLE 7: ROBUSTNESS DATA OF BILASTINE

Concentration (µg/ml)	Change in wavelength	Absorbance*	Standard Deviation	% Relative Standard Deviation
10	281.5	0.168	0.0012	0.69%
	282.5	0.158	0.0021	1.31%
	283.5	0.113	0.0017	1.53%
30	281.5	0.473	0.001	0.21%
	282.5	0.448	0.001	0.22%
	283.5	0.328	0.001	0.30%
50	281.5	0.791	0.0017	0.22%
	282.5	0.747	0.0017	0.23%
	283.5	0.547	0.0021	0.38%

*=average absorbance of three replicates.

TABLE 8: ROBUSTNESS DATA OF BILASTINE

Concentration (µg/ml)	change in solvent ratio	Absorbance*	Standard Deviation	% Relative Standard Deviation
10	Type-III Millipore water : Methanol (79:21)	0.182	0.0012	0.84%
	Type-III Millipore water : Methanol (81:19)	0.163	0.0032	1.97%
30	Type-III Millipore water : Methanol (79:21)	0.454	0.0017	0.38%
	Type-III Millipore water : Methanol (81:19)	0.437	0.001	0.23%
50	Type-III Millipore water : Methanol (79:21)	0.771	0.0026	0.34%
	Type-III Millipore water : Methanol (81:19)	0.791	0.0006	0.07%

*=average absorbance of three replicates.

Accuracy: Accuracy was performed by the standard addition method. The study was carriedout in the three different levels of 50%, 100% & 150%, respectively. The results are mentioned in **Table 9**.

TABLE 9: ACCURACY DATA OF BILASTINE

Level	Standard Conc.	Sample Conc.	Total Conc.	% Recovery
	5	5	10	100%
50%	5	5	10	103.40%

	5	5	10	105.80%
	5	15	20	97.40%
100%	5	15	20	96.14%
	5	15	20	98.60%
	5	25	30	100%
150%	5	25	30	105.50%
	5	25	30	102.70%

Forced Degradation Studies: Forced degradation studies were performed as per the ICH guidelines for determining the ability of the drug whether it withstands its property when it undergoes the stress condition. Bilastine was treated with various stress conditions such as acid degradation, alkaline degradation, oxidative degradation, thermal degradation & photolytic degradation, and the results are mentioned in **Table 10**.

TABLE 10: FORCED DEGRADATION STUDY DATA OF BILASTINE

Stress condition	Absorbance	% Recovery	% Degradation
Acid Degradation	0.403		
(0.1N HCl)	0.408	93.96%	6.04%
	0.406		
Mean	0.405		
Alkaline Degradation (0.1N NaOH)	0.405		
	0.405	93.03%	6.97%
	0.395		
Mean	0.401		
Thermal Degradation	0.39		
	0.394	90.95%	9.05%
	0.392		
Mean	0.392		
Oxidative Degradation	0.382		
	0.384	89.32%	10.68%
	0.391		
Mean	0.385		
Photolytic Degradation	0.402		
	0.404	93.50%	6.50%
	0.403		
Mean	0.403		

DISCUSSION: A stability-indicating UV method was developed using a mobile phase of Millipore water and Methanol for the quantitative analysis of Bilastine and marketed formulation. The above discussion proves that the proposed method is simple, rapid and precise.

Hence, Developed method was standardized in validation parameters such as specificity, selectivity, linear range, precision, robustness, ruggedness, and reproducibility as per ICH guidelines Q2 (R1) 2, 3. The literature revealed that the methods which were developed were reported by using only methanol as a solvent with the precision value % RSD 0.65-1.07. Hence the method was developed by using 80% Millipore water and 20% methanol. Hence we conclude that the developed method is cheap for routine analysis of Bilastine.

CONCLUSION: The developed method for the estimation of Bilastine in bulk and pharmaceutical formulation was precise, accurate, simple, economical and sensitive. This method can also be employed for the routine analysis of the API and the marketed formulation.

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CONFLICTS OF INTEREST: The authors declare that there is no conflict of interest.

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