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"UV SPECTROPHOTOMETRIC METHOD DEVELOPMENT AND VALIDATION FOR THE ESTIMATION OF BILASTINE IN PHARMACEUTICAL DOSAGE FORM"

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ABSTRACT

Bilastine is approved in the European Union for the symptomatic treatment of allergic Rhino conjunctivitis and urticarial. Bilastine is anti-histaminic drug class H1 anti-histamine second generation. Bilastine has been effective in treatment of disease of allergies including Rhino conjunctivitis, Sneezing, Runny nose, Dry cough, skin allergies. The work was to develop a simple suitable Spectrophotometric method for estimation of Bilastine in Pharmaceutical dosage forms UV Spectrophotometric method showed good linearity from 5-25 µg/ml. The method has been validated as per ICH guidelines. Accuracy (% recovery) for zero order (99.6 – 101.46%) and for first order (98 – 100.5 %) The limit of detection (LOD) for zero order was found to be 0.088µg/ml. and for first order was found to be 0.098 µg/ml while the limit of Quantitation (LOQ) for zero order was found to be 0.253µg/ml and for first order was found to be 0.296µg/ml. The developed Spectrophotometric methods were validated as per ICH guideline and can be used for routine analysis of Bilastine in Pharmaceutical dosage form.

Key Words : Bilastine, UV Visible Spectrophotometric method, Derivative Spectroscopy, Method Validation, ICH Guidelines

Introduction

Bilastine is a selective, second- generation H1- Antihistamine. It was first approved in European Union in 2010. It was developed in spain by FAES farma. Bilastine is now available in approximately 100 countries worldwide. Bilastine is use for the symptomatic treatment of allergic rhinitis and rhino-conjunctivitis and urticaria in adults. **Bilastine** (Trade name-**Bilson** Marketed by –**Unison**) Bilastine has been effective in treatment of disease of allergies including Rhino conjunctivitis, Sneezing, Runny nose, Dry cough, skin allergies.

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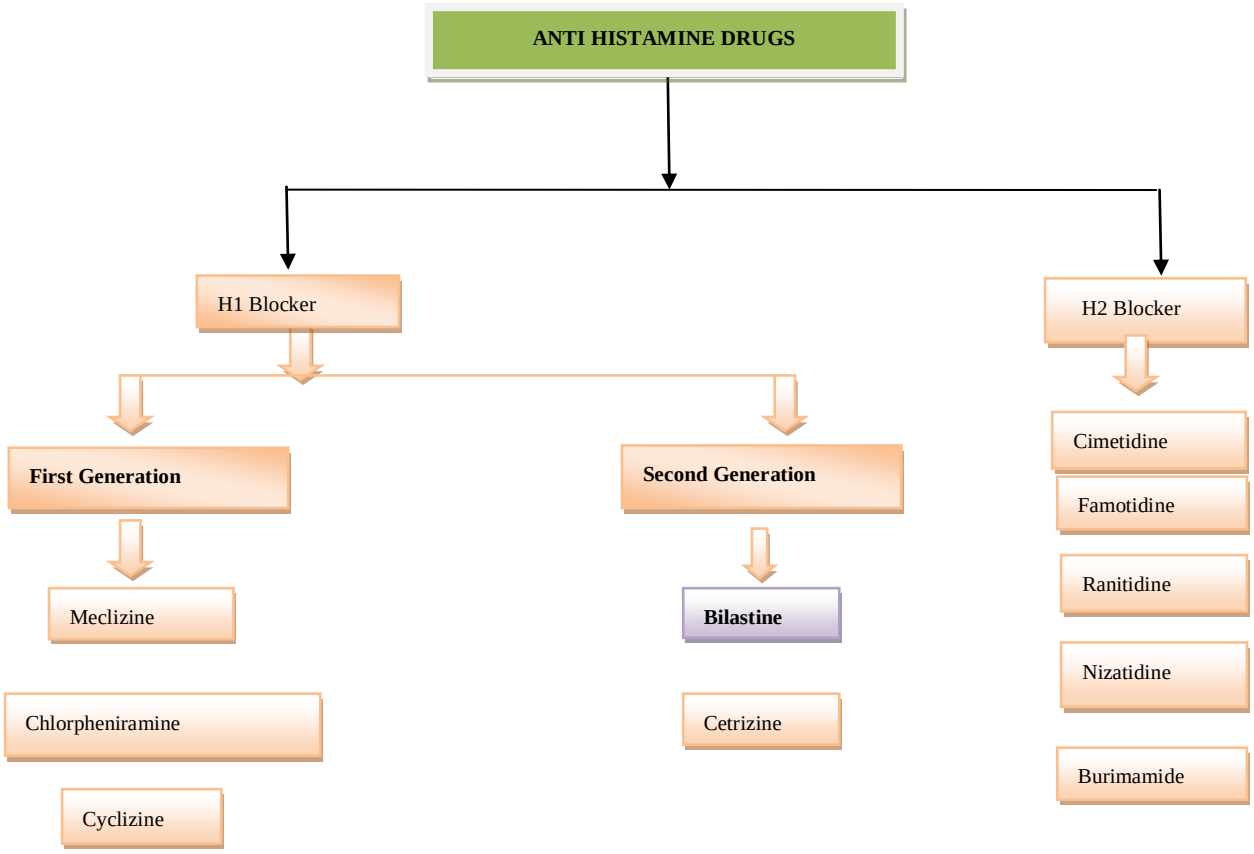


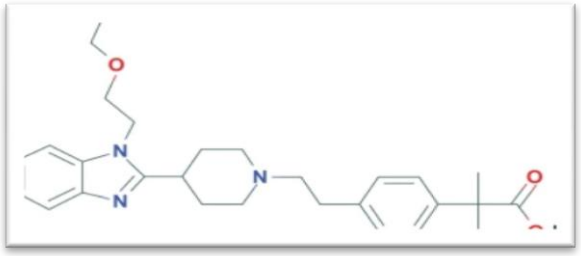


Figure: 1 Structure of Bilastine

Chemistry of Bilastine is IUPAC name is -[4-[2-[4-[1-(2-ethoxyethyl)benzimidazol-2-yl]piperidin-1-yl]ethyl]phenyl]-2-methylpropanoic acid its Chemical formula : $C_{28}H_{37}N_3O_3$. Bilastine is in white solid crystalline powderand the Molecular weight is 463.622 gm./mole.

Mechanism of Action:

Bilastine is a new oral highly selective H1-receptor antagonist developed for the symptomatic treatment of allergic rhino-conjunctivitis and urticaria. It is an antiallergic agent whose main mechanism of action is the **inhibition of immune system reactions mediated by the interaction of histamine on its H1- receptor**.

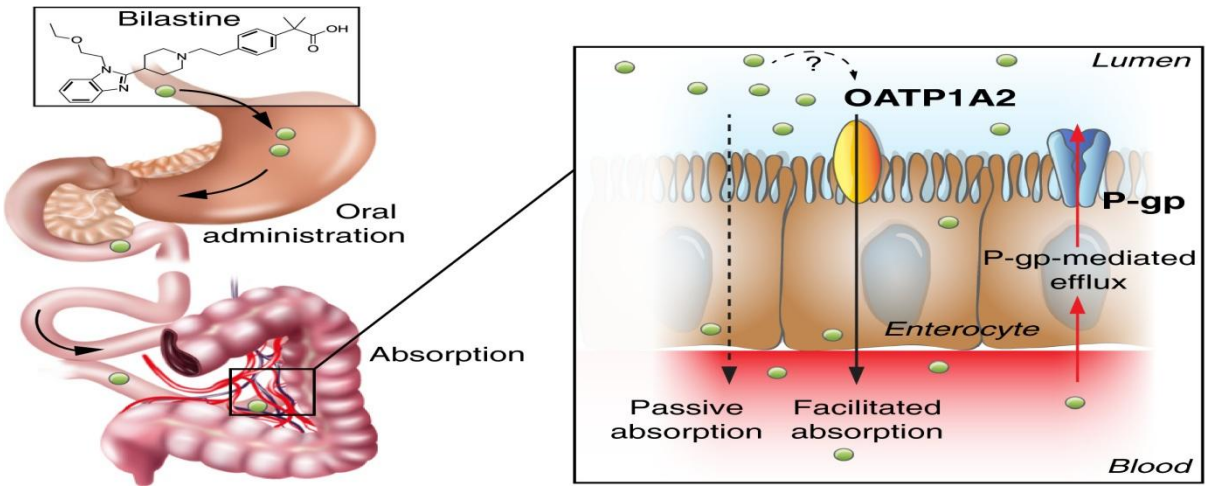


Figure- 2 Mechanism of Action

Literature survey has revealed that various methods like HPLC, HPTLC and LC-MS were reported for estimation of bilastine. No one can report derivative spectrophotometric methods for the estimation of bilastine. It is proposed to improve the existing spectrophotometric methods with derivatization of spectra and to develop new methods for the Estimation of Bilastine in pharmaceutical dosage forms. Hence, on the basis of literature survey it was thought to develop a precise, accurate, simple and reliable, less time-consuming derivative spectrophotometric method for estimation of bilastine in pharmaceutical dosage form and validated method with according to ICH guidelines.

MATERIALS AND METHODS:

Instrumentation

UV Visible spectrophotometer (Shimadzu model 2600 with UV-probe version 2.35 software).

Materials

Bilastine tablets API, ARgrade Methanol (India), ARgrade Water (India)

Preparation of standard stock solution of Bilastine:

Accurately weighted quantity of Bilastine 10mg was transferred into 10ml volumetric flask, dissolved & diluted up to the mark with Methanol this was given a stock solution having strength of 1000µg/ml.

Preparation of working standard Solution of Bilastine:

100 µg/ml of Bilastine working standard solution was prepared by diluting 1ml of std. stock solution with Methanol in 10ml volumetric flask up to the mark.

Selection of wavelength for measurement:

1 ml of working standard solution (100 µg/ml) of Bilastine was diluted with 10 ml Methanol to get 10µg/ml solution. This solution was scanned between 200 - 400 nm against Methanol. It is evident that Bilastine show an absorbance at 280nm respectively.

Preparation of Sample Solution:

Twenty tablets were weighed and average weigh was calculated. The tablet were powdered, a quantity of powder equivalent to 10 mg Bilastine was weighed and transferred to a 10mL of volumetric flask containing 5 ml Methanol and solicited for 20 minutes. The flask was allowed to stand at room temperature for 5min and the volume was made-up to the mark with Methanol to obtained the sample stock solution (1000µg/ml) the solution was filtered through Whatman filter paper. From this solution pipette Solution pipette out 0.5 ml and volume adjusted to mark with 10 ml volumetric flask. This was working sample solution having solution strength 5 µg/ml of Bilastine.

METHOD VALIDATION:

Linearity and Range:

Linearity is expressed in terms of correlation co-efficient of linear regression analysis.

Calibration curve for Bilastine:

Aliquots of working solution (100 µg/ml) of Bilastine (0.5, 1.0, 1.5, 2.0 and 2.5ml) were transferred into 10ml volumetric flask. The volume was adjusted to the mark with the Methanol to get concentrations (5, 10, 15, 20 and 25µg/ml). The absorbance of each solution was measured at wavelength 211.80nm using Bilastine as blank. The graph of absorbance versus concentration was plotted for zero order and first order respectively.

Precision:

Intra-day Precision:

Intra-day precision was determined by analyzing solution (10,15 and 20µg/ml) for three times on the same day. The results were reported in terms of %RSD.

Inter-day precision:

Inter-day Precision was determined by analysing the solution (10, 15 and 20 µg/ml) for three times on the different day. The results were reported in terms of %RSD.

Accuracy:

Accuracy was determined by calculating recovery of Bilastine the standard addition

method. Knows amounts of standard solutions Bilastine (1.5, 2, and 2.5) µg/ml were added to quantified test solution of Bilastine (2µg/ml).Each solution was measured in triplicate, and there covery was calculating by measuring absorbance.

Limit of Detection and Limit of Quantitation:

They were measured using standard deviation of Y-intercept and slop of calibration curve as per ICH guideline. The LOD and LOQ were calculated using following formula

LOD =3.3×σ/s **LOQ**=10×σ/s

Where, σ = the standard deviation of response

S = the slope of the calibration curve

Analysis of tablet dosage form:

Analysis of Working Sample solution (10µg/ml) of Bilastine & the absorbance of solution were measured at wavelength 211.80nm and % assay was calculated from regression equation. Response was an average of three determinations.

RESULT AND DISCUSSION:

Selection of wavelength for measurement:-

To determine wavelength for measurement, standard spectra of Bilastine was scanned between **200 – 400 nm** against water. It is evident that zero order absorption spectra of Bilastine was shown at **211.80 nm**. All zero order spectra was converted into first order derivative spectrum using delta lambda **2nm** and scaling factor 1.0 the first order derivative wave length was measured at **284.40nm.** The spectra of Bilastine show in figure 3 a) & b)

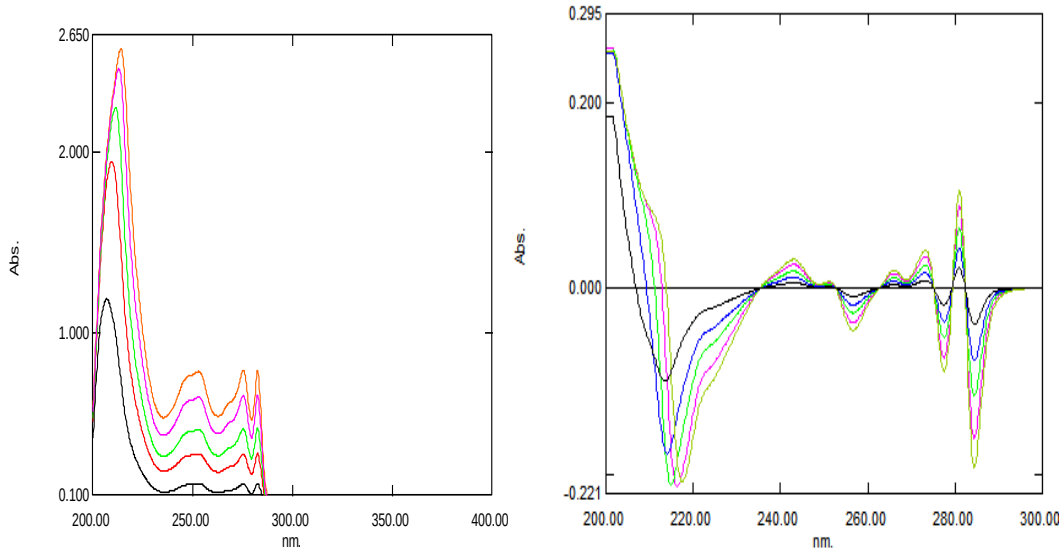
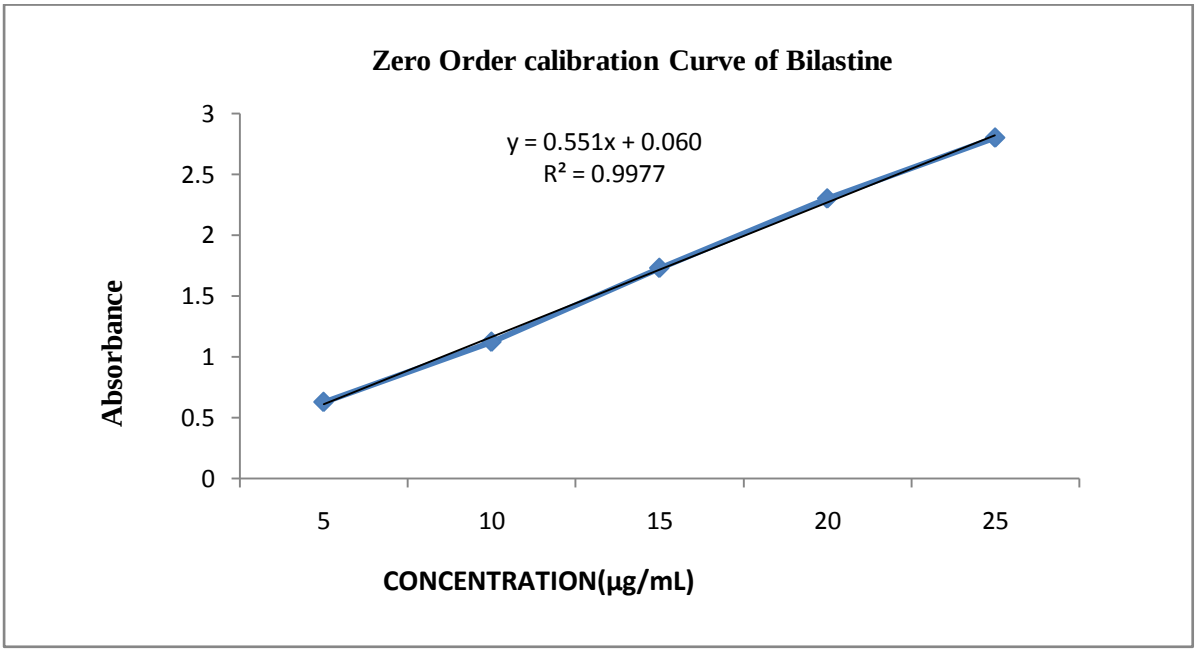


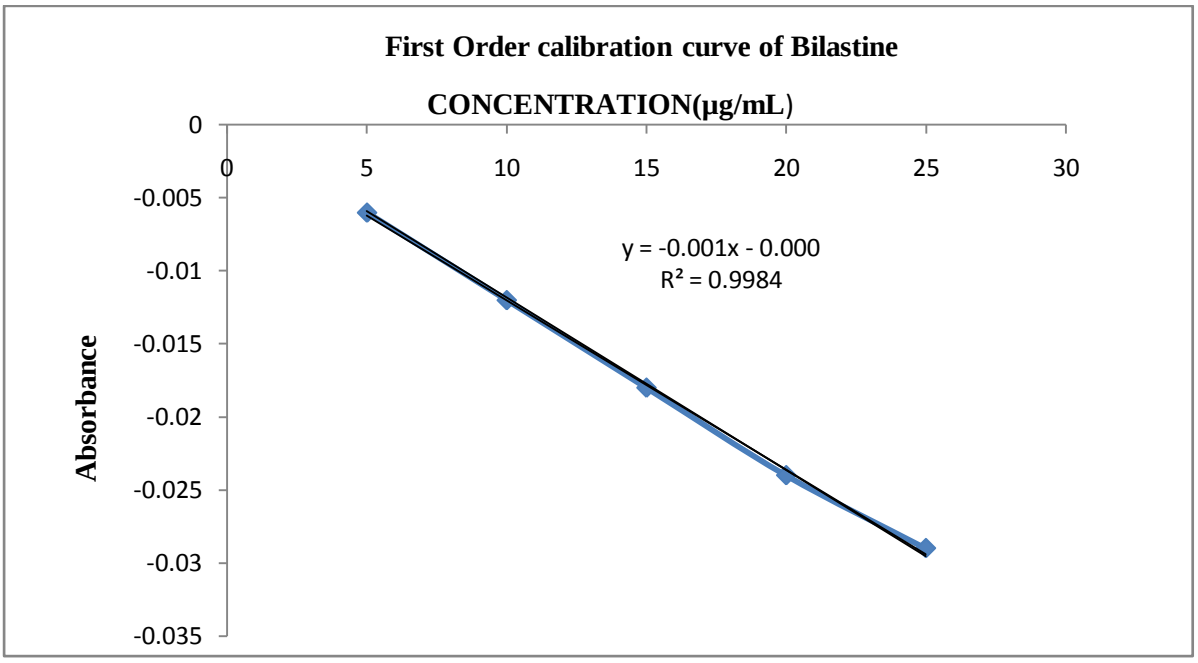
Figure 3 - Standard UV spectra of Bilastine a) Zero order and b) first Order

LINEARITY

The linearity range for bilastine was found to be in the range of 5-25 µg/ml Calibration plot was shown in figure 3a & 3b and the correlation coefficient of Bilastine was found to be 0.9977 and 0.9984 for zero and first order respectively.



(a)



(b)

Precision:

Intra-day precision:

The data for Intra-day precision is shown in Table 1 The % RSD for zero order intra-day was found to be (0.13-0.21%) and for first order intra-day was found to be (0.007-0.033%).

Table: 1 Intra-day precision data of Bilastine for zero and first order

Sr.No	ZERO ORDER			FIRST ORDER		
	Conc.(µg/ml)	Abs.*± SD	%RSD	Conc. (µg /ml)	Abs.*± %SD	%RSD
1	10	1.234±0.004	0.13	10	-0.012±0.002	0.006
2	15	1605±0.006	0.21	15	-0.018±0.001	0.033
3	20	1.869±0.005	0.16	20	-0.024±0.001	0.033

*Average of three determination

Inter-day precision:

The data for Inter-day precision is shown in Table 2 The % RSD for zero order inter-day was found to be (0.07–0.17%) and for first order inter-day was found to be (0.07-0.13%).

Table: 2 Inter-day precision Zero order and First order

Sr. No	Zero order			1st order		
	Concentration (µg/ml)	Absorbance* ± SD	% RSD	Concentration (µg/ml)	Absorbance* ± SD	% RSD
1	10	1.234 ±0.002	0.07	10	-0.013 ±0.002	0.07
2	15	1.606 ±0.004	0.13	15	-0.018 ±0.003	0.11
3	20	1.868 ±0.005	0.17	20	-0.022 ±0.004	0.13

*Average of three determination

Accuracy:

Accuracy of the method was confirmed by recovery study from marketed formulation at three level of standard addition. Percentage recovery for bilastine the drug is in range for zero order (99.61% - 101.46 %) and for first orders (98% - 100.5%) that shown in the Table 3 Accuracy data of bilastine for zero order and first order

Table: 3 Accuracy data of bilastine for zero order and first order

Zero order					
Drug	**% Level**	**Conc. of sample taken (go/ml)**	**Conc. of Std. added (go/ml)**	**Amount Recovered (go/ml) Mean ± SD**	**% Recovery**
Bilastine	80	2	1.5	1.51 ±0.04	101.46
	100	2	2	2.01 ±0.03	100.05
	120	2	2.5	2.49 ±0.02	99.61
First order					
Drug	**% Level**	**Conc. of sample taken (go/ml)**	**Conc. of Std. added (go/ml)**	**Amount Recovered (go/ml) Mean ± SD**	**% Recovery**
Bilastine	80	2	1.5	1.47 ±0.04	98
	100	2	2	2.01 ±0.07	100.5
	120	2	2.5	2.51 ±0.03	100.4

Limit of Detection and Limit of Quantitation:

The limit of detection (LOD) for zero order was found to be 0.088µg/ml and for first order was found to be 0.098 µg/ml while the limit of Quantitation (LOQ) for zero order was found to be 0.253 µg/ml and for first order was found to be 0.296µg/ml the results are shown in table 4

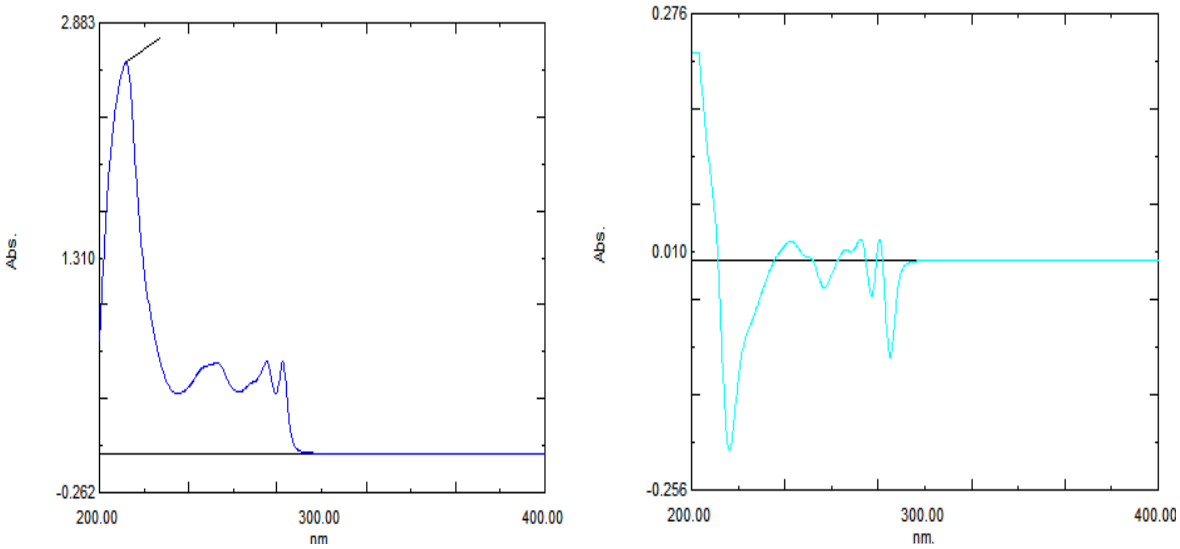
Table: 4 LOD and LOQ data of bilastine

Zero order		**First order**	
LOD (µg/ml)	**LOQ (µg/ml)**	**LOD (µg/ml)**	**LOQ (µg/ml)**
0.088	**0.253**	**0.098**	**0.296**

Estimation of Bilastine in Marketed Tablet

The developed method was used to estimate Bilastine in the tablet form. Tablet of Bilastine from **UNISON PHARMACUTICAL PVT. LTD.** was analysed by proposed method. The percentage of assay of Bilastine was found from the regression line equation of Bilastine (table 5). The test spectra

of Bilastine was shown in figure 4 a) & b)



(a) **(b)**

Figure: 4 Test UV spectra of Bilastine a) Zero order and b) First Order

Table: 5 Estimation of bilastine in tablet by simple UV spectroscopy

Formulation	**Order**	**Labeled Claim (mg/tablet)**	**Amount found* ± S.D (mg/tablet)**	**%Recovery* ± S.D**
BLSON – 20	Zero	20	19.86 ± 0.14	99.03 ± 0.7
	First	20	20.18 ± 0.18	100.9 ± 0.9

*Average of three determinations

Conclusion

UV Visible Spectrophotometric methods such as zero order and first order derivative Spectrophotometric method were developed for estimation of bilastine. The methods were validated according to ICH guidelines. Results of assay and validation study were found to be satisfactory.

The proposed procedures can be applied for the determination of bilastine in pharmaceutical formulations. Moreover, the method sarerapid, sensitive, precise, and selective and can be used in routine and quality control analysis.

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