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Quantitative Determination and Validation of Bilastine in Bulk and Pharmaceutical Dosage Form by Using UV-Spectroscopy

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T. Anju*, Sk. Hakeema, G. Divya Jyothi, Md. Harshad, P. Anusha, L. Sai Kalyan, T. Satyanarayana

Department of Pharmaceutical Analysis, Mother Teresa Pharmacy College, Kothuru, Sathupally, Khammam -507303 (TS) India.

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ABSTRACT

A simple, accurate, and precise UV spectroscopy method has been developed for the estimation of Bilastine. It is a medication used for the treatment of allergic rhinoconjunctivitis and itchy skin rashes. It inhibits the H1 histamine receptors. Here we have developed a UV spectroscopic method for the quantitative determination of Bilastine in the bulk and tablet dosage forms. The parameters linearity, precision, accuracy, the limit of detection, and the limit of quantification were studied according to an international conference on harmonization guidelines (ICH). The determination was carried out at an absorption maximum of 271nm using 10% glacial acetic acid as solvent. In the present method, linearity over the concentration range of Bilastine was found to be 5-30µg/ml, with a correlation coefficient of 0.9998. The results of the analysis have been validated statistically for linearity, accuracy, precision, LOD, and LOQ of the processed method. The developed method was successfully applied for the quantitative analysis of commercially available dosage forms.

INTRODUCTION:

Bilastine is a new second-generation H1-antihistamine and chemically as 2-[4-[2-[4-[1-(2-ethoxyethyl)benzimidazol-2-yl]piperidin-1-yl]ethyl]phenyl]-2-methylpropanoic acid.

Bilastine is a selective histamine H1 receptor antagonist (ki=64Nm) Label. During allergic response mast, cells undergo degranulation which releases histamine and other substances. By binding to and preventing activation of the H1 receptor, Bilastine reduces the development of allergic symptoms due to the release of histamine from mast cells. Bilastine is a medication that is used to relieve the symptoms of allergic rhinoconjunctivitis (sneezing, itchy nose, nasal secretion, nasal congestion, and red streaming eyes) and other forms of allergic rhinitis. It can also be used to treat itchy skin rashes (Wheals or Urticaria).Adverse effects of Bilastineareabdominal pain, dizziness, headache, somnolence, fatigue. Contraindications of Bilastine the risk or severity of QTc prolongation can be increased when Bilastine is combined with Amiodarone. The risk or severity of QTc prolongation can be increased when Bilastine is combined with Amisulpride.

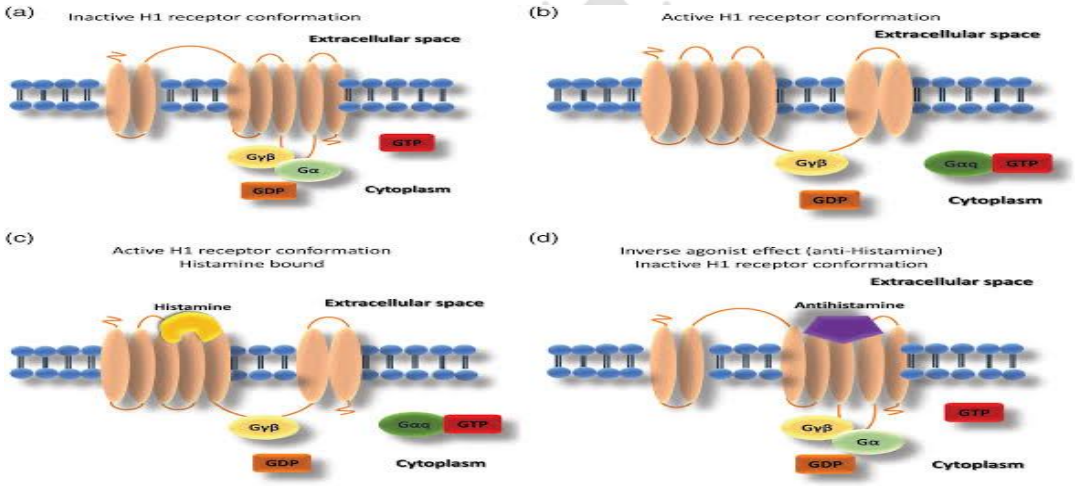

Figure no 1: Mechanism of Bilastine

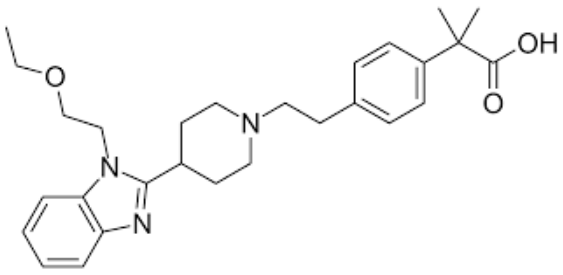

Figure no 2: Structure of Bilastine

MATERIALS AND METHODS:

MATERIALS:

Drug Sample

Bilastine was obtained as a gift sample from OPTRIX Pharmaceuticals Pvt. Ltd., Hyderabad.

Formulation Used

"BILASURE" Tablets containing 20 mg of Bilastine was purchased from local Pharmacy.

Instruments Used:

KERRO P5 Series Precision Electric Balance, Model BL-3003, T-60 UV-Visible Spectrophotometer.

Chemicals and Solvents

All the following chemicals used were of analytical grade.

Distilled water, Chloroform, Methanol, Ethanol, 0.1N Hydrochloric acid, Glacial acetic acid, Ether, Acetone, Benzene, 0.1N Methanolic Hydrochloric acid, NaOH, Chemicals, and solvents are from Qualigens India Pvt. Ltd., and LobaChemie India Ltd.

METHOD: UV SPECTROSCOPIC METHOD

Selection of Solvent

The solubility of Bilastine was determined in a variety of solvents as per Indian Pharmacopoeia standards. Solubility test for Bilastine was carried out in different polar and non-polar solvents. From the solubility studies, 10% glacial acetic acid was selected as a suitable solvent for the proposed method.

Preparation of Standard Stock Solution

100 mg of Bilastine raw material was accurately weighed and transferred into the 100 ml volumetric flask and dissolved in a minimum quantity of 10% glacial acetic acid and made up to 100 ml with 10% glacial acetic acid.

Selection of λ_{max}

The standard stock solution was further diluted with 10% glacial acetic acid to get a 10 µg/ml concentration. The solution was scanned between 200 and 400 nm range using 10% glacial acetic acid as blank. From the UV Spectra 271nm was selected as λ_{max} for analysis of Bilastine. The stability of the Bilastine in 10% glacial acetic acid was studied by measuring the same solution at this λ_{max} at different time intervals. It was observed that Bilastine in 10% Glacial acetic acid was stable for 5 hours.

Calibration Graph

In this aliquots of stock solution of Bilastine (0.5 - 03 ml) were transferred into 100 ml volumetric flask and made up to the mark with 10% glacial acetic acid. The absorbance of different concentration solutions was measured at 271 nm against blank. The samples were found to be linear from 5-30 µg /ml. The calibration curve was plotted using concentration Vs absorbance. The curve obtained was linear in the concentration range of 5-30 µg /ml.

Quantification of formulation

Contents of twenty Tablets of formulation (**BILASURE**) containing 20mg of Bilastine were accurately weighed to find out the average weight. Tablets powder equivalent to 100 mg of Bilastine was transferred into 100 ml volumetric flask added 10% glacial acetic acid and made up to the volume. Then the solution was sonicated for 15 minutes. After sonication, the solution was filtered through Whatman filter paper No.41. From the clear solution, further dilution was made to bring a 10 µg /ml using 10% glacial acetic acid. The prepared solution was measured at 271nm. The amount of Bilastine was determined by using slope and intercept values from the calibration graph.

Recovery Studies

To the pre-analyzed formulation, a known quantity of standard solution (2, 7, 12, 17, 22, and 27µg/ml solution) was added and the contents were mixed well, finally made up to the volume with 10% glacial acetic acid. Absorbance was measured at 271nm. The amount present was calculated from slope and intercept. Then the % recovery was determined by using the following formula.

$$\% \text{ Recovery} = \frac{N \sum xy - \sum x \sum y}{N \sum x^2 - (\sum x)^2} \times 100$$

Where, N = Number of observations

X = Amount Added in microgram/ml

Y = Amount recovered in microgram/ml

Limit of Detection (LOD) and Limit of Quantification (LOQ)

The preparation of the calibration curve from the serial dilutions of the standard was repeated six times. The limit of detection and limit of quantification was calculated by using the average value of slope(s) and standard deviation of intercept.

$$\textbf{Limit of detection:} = \frac{3.3 \times \sigma}{S}$$

Units - (mcg/ml)

Where: σ= The standard deviation of the response.

S = The slope of the calibration curve.

$$\textbf{Limit of quantitation} = \frac{10 \times \sigma}{S}$$

Unit- (mcg/ml)

Where: σ= The standard deviation of the response

S = The slope of the calibration curve

Repeatability

The repeatability of the method was checked by repeating the measurement of formulation six times.

RESULTS AND DISCUSSION

UV-Spectroscopic Method

The solubility of Bilastine was determined in a variety of solvents ranging from nonpolar to polar using essentially a method of Schefter and Higuchi. The drug was found to be freely soluble in ethanol, chloroform, glacial acetic acid (10%, 20%,30% & 50%), 0.1 N HCl, 0.1N NaOH, and Sparingly soluble in Benzene, distilled water, methanol, and insoluble in acetone.

100 mg of Bilastine raw material was accurately weighed and transferred into the 100 ml volumetric flask and dissolved in a minimum quantity of 10% glacial acetic acid and made up to 100 ml with 10% glacial acetic acid, resulting in 100 µg/ml and made further dilution to get 10 µg/ml concentration by using 10% glacial acetic acid. It was scanned in the range of 200-400 nm and it shows constant λ_{max} at 271 nm this is shown in Fig.3. The stability of the absorbance at their λ_{max} was also checked for up to 5 hours. The linearity of the drug Bilastine was found, its calibration curve was constructed and is shown in Fig 4, the optical characteristics such as Beer's law limit (5-30µg/ml), Sandell's sensitivity (0.0054901), correlation coefficient (0.9998), slope(0.02034) and intercept(0.02053), molar absorbtivity ($1.20481x10^2$), were calculated and shown in Table 1.

The limit of detection and the limit of quantification was determined from the linearity studies. The limit of detection was found to be 1.5522µg/ml and the limit of quantification was found to be 1.6250µg/ml. It is shown in Table 1 and Table 2 shows the result of formulation quantification on **BILASURE** tablets repeatability also found to be within the limits 95.32– 101.04 (98.08 ± 0.8325743210) %RSD value 0.8488726763 and SE value 0.3398970432.

To evaluate the accuracy of the method, a known amount of pure drug (2, 7, 12, 17, 22, and 27 µg/ml solution) was added to the previously analyzed solution containing pharmaceutical formulation, and the mixture was analyzed by the proposed method and the recoveries were calculated. The percentage recovery of the Bilastine sample was found within the limit 97.59%-100.35% Mean of SD 0.418066 (%RSD 0.419998, SE 0.1706751). These values were given in Table 3.

The precision of the method was studied by making repeated analyses of the sample and it was carried out three times in a day and repeated for 2 days. The percentage standard deviation for inter-day and intra-day analysis was found for recovery and assay and is mean ±

SD value 0.3441801853 and 0.2891366458, % RSD value 0.3460140598 and 0.2905311955for interday and intraday values.

Further, Intraday and Interday recovery analyses were performed. The recovery analysis of formulation was carried out on the same day and for three consecutive days. The percentage RSD value was found to be 0.8488726763, 0.2789478575 for inter-day and intra-day recovery analysis of Bilastine respectively. The reports of analysis are shown in Tables 4 and 5.

Table no 1: Optical characteristics of Bilastine by UV method

Parameters	**Method Values**
λ_{max}(nm)	271
Beer's law limit(µg/ml)	5-30
Sandell's sensitivity (µg/cm^2/0.001 AU)	0.0054901
Molar absorbtivity(L mol^{-1} cm^{-1})	1.20481x10^2
Correlation Coefficient (r)	0.9998
Regressionequation (Y=mx+c)	Y=0.02034x+0.02053
Slope(m)	0.02034
Intercept(c)	0.02053
LOD(µg/ml)	1.5522
LOQ(µg/ml)	1.6250
Standard error of the mean of the regression line	0.01633

Table no 2: Quantification of formulation- bilasure by UV method

S.No	Labelled Amount (mg/Tab)	Amount found (mg/Tab)	% Obtained	Average %	S. D	%RSD	S. E
1	20	20.26	101.3	99.23	0.956743	0.964167	0.390588
2	20	19.81	99.05				
3	20	19.05	95.25				
4	20	19.90	99.5				
5	20	20.01	100.05				
6	20	20.05	100.25				

SD is standard deviation, % RSD percentage relative standard deviation

Table no 3: Recovery studies for formulation- Bilasureby UV method

S.No.	Amount present (µg)	Amount Added (µg)	Amount found (µg)	Amount Recovered (µg)	% Recovery	Average %	SD	%RSD	SE
1	3	2	4.9518	1.9518	97.59	99.54	0.418066	0.419998	0.170675
2	3	7	10.0246	7.0246	100.35				
3	3	12	14.9219	11.9219	99.34				
4	3	17	20.0082	17.0082	100.04				
5	3	22	24.9385	21.9385	99.72				
6	3	27	30.0605	27.0605	100.22				

*Average of six determinations

Table no 4: Repeatability for quantification of formulation – BILASURE by UV Method

S.NO.	INTERDAY*	INTRADAY*
1	97.78	99.18
2	95.32	100.27
3	98.12	99.78
4	101.04	98.78
5	99.59	98.38
6	96.65	99.25
Mean	98.08	99.27
SD	0.8325743210	0.2769115382
% RSD	0.8488726763	0.2789478575
SE	0.3398970432	0.1130486620

* mean of six observations

Table no 5: Repeatability for Recovery Studies of Formulation of BILASURE by UV Method

S.NO.	INTERDAY*	INTRADAY*
1	99.02	99.02
2	99.05	100.23
3	100.78	99.34
4	100.29	100.54
5	98.70	98.74
6	99.03	99.25
Mean	99.47	99.52
SD	0.3441801853	0.2891366458
% RSD	0.3460140598	0.2905311955
SE	0.1405109722	0.1180395413

* mean of six observations

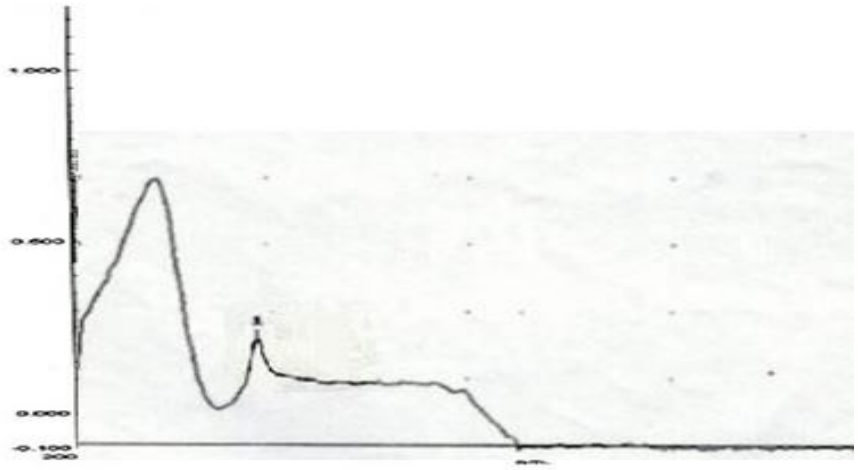

Figure no 3: UV-Spectroscopic spectrum

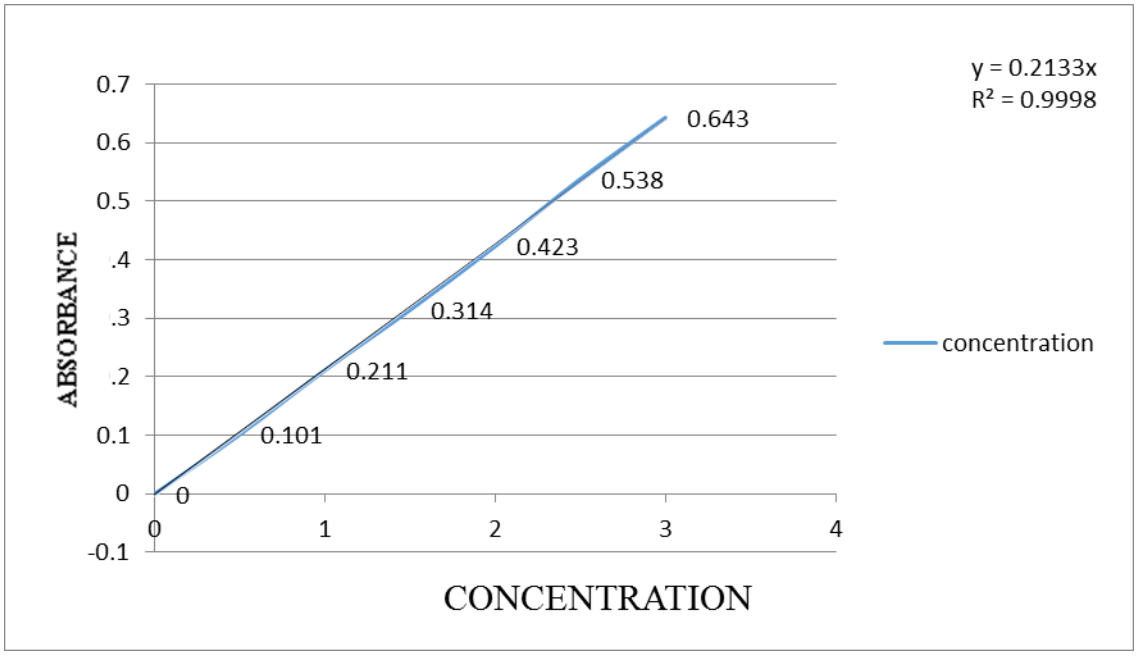

Figure no - 4: Linearity graph

CONCLUSION:

The proposed analytical methods are simple, reliable, rapid, sensitive, reproducible, and accurate for the estimation of Bilastine. The method adopted for our studies is the simple UV-Spectroscopic method. The drug samples were analyzed by UV spectroscopy using 10% glacial acetic acid as solvent and the average content of the drug present in the formulation was found to be 99.23 mg (99.23%). The above method does not suffer from any interference due to common excipients. Therefore, it was shown that the proposed method could be

successfully applied to estimate commercial Pharmaceutical products containing Bilastine. Thus, the above studies and findings will enable the quantification of the drug for future investigation in the field of analytical chemistry.

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