International Journal of Pharmacy and Biological Sciences
ISSN: 2321-3272 (Print), ISSN: 2230-7605 (Online)
IJPBS | Volume 8 | Issue 2 | APR-JUN | 2018 | 338-344
Research Article | Pharmaceutical Sciences | Open Access | MCI Approved| ज्ञान-विज्ञान विमुक्तये
|UGC Approved Journal |

DEVELOPMENT AND VALIDATION OF UV SPECTROSCOPIC METHOD FOR THE DETERMINATION OF BISOPROLOL FUMARATE TABLETS

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ABSTRACT

In this study a simple, greenar, cost effective, accurate and precise UV- spectrophotometric method was developed for the estimation of bisoprolol fumarate (BF) in bulk and tablet dosage form. The method was based on measurement of absorbance of BF aqueous solution at 223nm. Validation was conducted in accordance to ICH guidelines. Method development was carried out in solvent water as green solvent at 233 nm. The beer's law was obeyed in the concentration range of 2.0 –12.0 µg/ml (r^2 = 0.9962). The method was tested and validated for various parameters according to ICH guidelines. The detection and quantitation limits were found to be 0.04753 and 0.1584 µg /ml respectively. The proposed methods were successfully applied for the determination of bisoprolol fumarate in pharmaceutical preparations. The results demonstrated that the procedure is accurate, precise and reproducible (R.S.D. < 2%). The recovery percentage was 100.1 ± 2%,

KEY WORDS

Bisoprolol fumarate; UV spectrophotometric method, Eco-friendly.

1. INTRODUCTION

Spectroscopy Methods

Ultraviolet-visible Spectrophotometry

UV-Visible spectrophotometry is one of the most frequently employed technique in pharmaceutical analysis.The fundamental law that governs the quantitative spectrophotometric analysis is the Beer - Lambert law . There are few spectrophotometric methods for the assay of beta blockers and fewer for bisoprolol. It should be noted that the actual spectrophotometric methods used for bisoprolol determination are UV-based. [1,2],

The aim of this method is being to develop and validate a simple, precise and accurate spectrophotometric method for the estimation and quantification of bisoprolol fumarate in bulk material and in tablets. Further, this study is designed to validate the developed methods as per ICH guidelines. This method is based on first-order derivative spectroscopy. Derivative spectrophotometry is a useful technique for qualitative and quantitative analysis and helps in reducing the effects of spectra. Derivative spectroscopy very useful in qualitative analysis, either for characterizing Materials or for identification Derivative spectra can be obtained by optical, electronic, or mathematical methods. The advantages of the mathematical techniques are that derivative spectra may be easily calculated. derivative spectrophotometry was used. [3,4, 5, 6]

Bisoprolol fumarate It is an official in BP, USP pharmacopeia. Bisoprolol fumarate alone (or) in combined formulation with other drugs is reported to be estimated by HPLC and UV/VIS Spectrophotometric methods. A literature review revealed that no HPLC method has been reported for the estimation of Bisoprolol fumarate in Pharmaceutical formulations individually. [3, 4]

Bisoprolol is a cardio selective beta-blocker. It is given as the fumarate in the management of hypertensive, chemically is 1-(propan-2-ylamino)3-[4-(2-propan-2-yloxyethoxymethyl) phenoxy] propan-2-ol. Bisoprolol fumarate is official in USP (USP, 2015), very few analytical methods such as de Several analytical methods have been studied for the determination of BIS in plasma and urine samples. Hypertension is a major public health problem of worldwide distribution and is a major risk factor for cardiovascular disease morbidity and mortality. It is responsible for one half of coronary heart disease (CHD) and about two thirds of cerebrovascular accidents. The relationship between blood pressure and risk of cardiovascular disease events is continuous, consistent and independent of other risk factors. The higher the blood pressure, the greater the chance of myocardial infarction, heart failure, stroke and kidney disease. [3, 4]

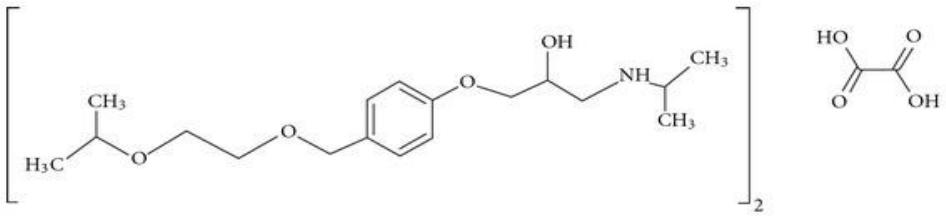

Fig. 1. Chemical structure of Bisoprolol Fumarate

Molecular formula - $C_{40}H_{66}N_2O_{12}$

Molecular Weight: 766.97 g/mol

IUPAC Name- 2E)-but-2-enedioic acid; bis(1-[(propan-2-yl) amino]-3-(4-{[2-(propan-2 yloxy)ethoxy]methyl}phenoxy)propan-2-ol)

This paper presents a new UV spectrophotometric method for the assay of bisoprolol using first order derivative of bisoprolol spectrum at wavelength 223 nm. The developed method was validated using pure substance and pharmaceutical tablets. measured at the selected wavelength and plotted against concentration to obtain the calibration graph. The statistical parameters of the calibration curve, such as the correlation coefficient, regression equation, limit of detection, and limit of quantitation, for bisoprolol fumarate were calculated. [4,5,6]

MATERIALS AND METHODS

Bisoprolol fumarate was a gift sample from Unichem Lab Pvt Ltd. Goa India Ltd. All chemicals and reagents used were of analytical grade and purchased from rajesh chemical Mumbai,India. [5]

Instruments

A double beam UV-VIS spectrophotometer (UV1800 series, Shimadzu, Japan) connected to computer loaded with spectra manager software UV Probe with 10 mm quartz cells was used. The spectra were obtained with the instrumental parameters as follows: [6]

Wavelength range: 200– 400 nm

Scan speed: Medium

Sampling interval: 0.2 and slit width 1.0 mm.

All weights were taken on an electronic balance (Shimadzu Corporation Japan).

Preparation of Stock Standard Solution and Selection of Wavelengths

A stock standard solution was prepared by dissolving 0.010 mg of bisoprolol fumarate in a 10 ml of distilled water to obtain a concentration of 1000 µg/ml. appropriate concentration of 10 µ g/ml was prepared and scanned in the UV-visible over the range 400– 200 nm; the first derivative was recorded. [6]

2.VALIDATION OF THE METHOD

Method validation was performed in terms of sensitivity, specificity, linearity, LOQ, LOD, precision, accuracy and robustness. [5,7,15]

2.1 Study of Linearity Curves

For bisoprolol fumarate, linearity was observed by diluting appropriate aliquots of the working standard stock solution 0.2, 0.40, 0.60, 0.80, and 1.0,1.2 ml into a series of 10-ml volumetric flasks with distiiled water to get a final concentration range of 2–12 µ g /ml. The samples were scanned in the wavelength range 200 to400 nm, and the first-order derivative of the spectrum was taken. The dA/dλ of each of these solutions was measured at the selected wavelength and plotted against concentration to obtain the calibration graph. The statistical parameters of the calibration curve, such as the correlation coefficient, regression equation, limit of detection, and limit of quantitation, for bisoprolol fumarate were calculated. [7,8]

2.2 Precision

The precision of the method was studied as intraday and inter-day variations. Precision was determined by analyzing the 10 µg/ml of bisoprolol fumarate solutions as intra-day and inter-day variations, analyst to analyst variation. [7,8]

2.3 Recovery Studies

To the pre-analyzed sample solutions, a known amount of the stock standard solution was added at different levels, i.e. 80%, 100%, and 120%. The solutions were re-analyzed by the proposed method. [7,8]

2.4 Sensitivity

The sensitivity of measurements of bisoprolol fumarate by the use of the proposed method was estimated in terms of the limit of quantification (LOQ) and limit of detection (LOD). The LOQ and LOD were calculated using equation LOD = 3.3 × N/B and LOQ = 10 × N/B, where 'N' is standard deviation of the absorbance of the drugs (n = 3), taken as a measure of noise, and 'B' is the slope of the corresponding calibration curve. [7,8]

2.5 Specificity

For determining specificity of the method, a tablet dosage form was analyzed. These results demonstrate that there was no interference from other materials in the tablet formulation therefore, conforms the specificity of the method. see figure No. 4 [7,8]

2.6 Limit of detection and limit of quantitation:

The Limit of Detection (LOD) is the smallest concentration of the analyte that gives the measurable response. LOD was calculated using the following formula and the result shown in Table No. 5. [9]

LOD = 3.3 (σ / S)

Where, S = slope of calibration curve, σ = standard deviation of the response.

The Limit of Quantification (LOQ) is the smallest concentration of the analyte, which gives a response that can be accurately quantified. LOQ was calculated using the following formula and the result shown in Table No. 5. [9]

LOQ = 10 (σ / S) Where, S = slope of calibration curve, σ = standard deviation of the response. See Table No.6

2.7 Robustness and stability

Robustness of the proposed method was determined by the analysis of samples and standard solutions (10 µg mL-1) at different wavelength these (± 2 nm), at different solution temperatures (4 and 25 ºC), and at different solution compositions distilled water to assess the stability of bisoprolol fumarate, see Table No.7[10]

The stability study was performed maintaining the Bisoprolol Fumarate, working solution in water for 48 h at 2-8 °C, protected from light, looking for the decrease of absorbance compared with those of freshly prepared solutions. [10,11,12]

2.8 Assay Procedure -

Take weight of 10 tablets of any brand of bisoprolol Fumarate tablet. Crush the tablet in the motor pestle. Accurately weigh the quantity of powder equivalent to 10mg of drug in 100ml volumetric flask and add bisoprolol fumarate to adjust the volume up to 100ml. Pipette out the 1ml into 10 ml volumetric flask make the volume with water to get conc 10µg/ml and analyze the reading on UV visible spectroscopy. Calculate the percentage purity of tablet.

2.9 Standard Solution

From the stock solution, 1 ml was pipped out in 100 ml volumetric flask to have a concentration of 10 µg /ml.

4. RESULTS AND DISCUSSION

This method was validated according to ICH Q2B R1 guidelines for validation of analytical procedures in order to determine the linearity, sensitivity, precision, robustness and accuracy for the analyte. Accuracy and specificity of analysis were determined by performing recovery standard analyte the different concentration of pure drug in the analyzed tablet sample. [12,13]

The method was validated according to ICH Q2B R1 guidelines for the validation of analytical procedure in order to determine the linearity, sensitivity, precision, accuracy and robustness. [13, 14]

Linearity

The linearity of the calibration curve in the pure solution of bisoprolol was checked over the concentration range of 2-12 µg/ml. The regression line relating standard concentrations of Bisoprolol fumarate using regression line, the calibration curve was linear in the study range and equation of the regression analysis was obtained=0.1128x+0.0045; Rs^2 =0.9962 at 223 nm. Fig No.1 and 2. The results obtained were found to be within the specified limits. Regression analysis of Beer's plot showed good correlation in concentration range. See Table No.1.

Accuracy

The accuracy of the method was evaluated by determination of recovery of bisoprolol fumarate at three levels concentration, the results showed good recoveries. The accuracy of the method was expressed

as the amount/weight of the compound of interest analyzed as a percentage of the theoretical amount present in the medium. The accuracy of the proposed method ranging from 98-102%,see table no.5 which improve good recovery for this method.

Precision

The precision of the assay of bisoprolol fumarate was performed by repeatability (intra-day) and intermediate precision the concentration used 10 µg/ml and reported as RSD = 0.872%.

The precision (intra-day, inter -day and analyst to analyst) of the method were found to be within the limit (% RSD < 2). see Table No.3, 4.

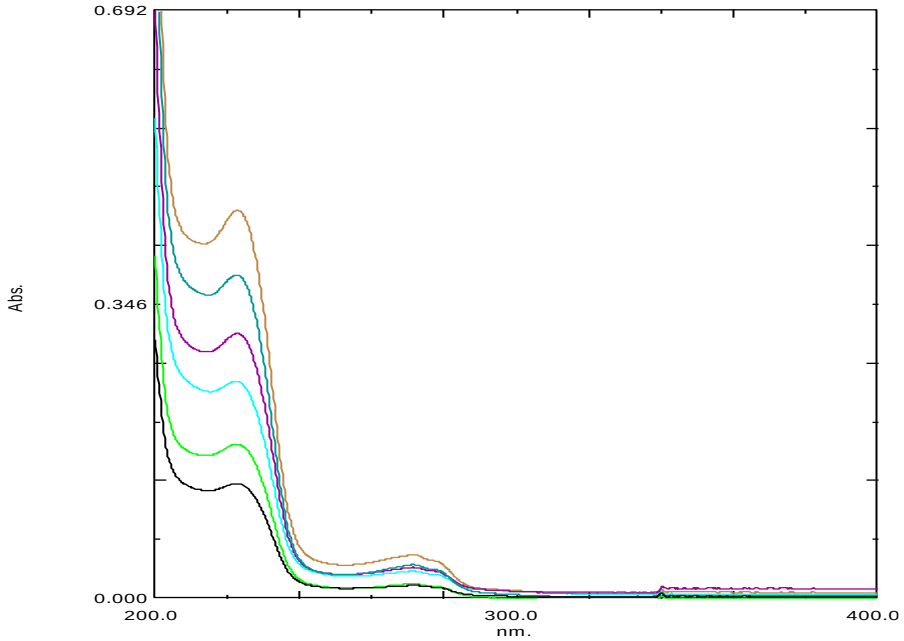

Fig No.2 Overlay of Bisoprolol Fumarate

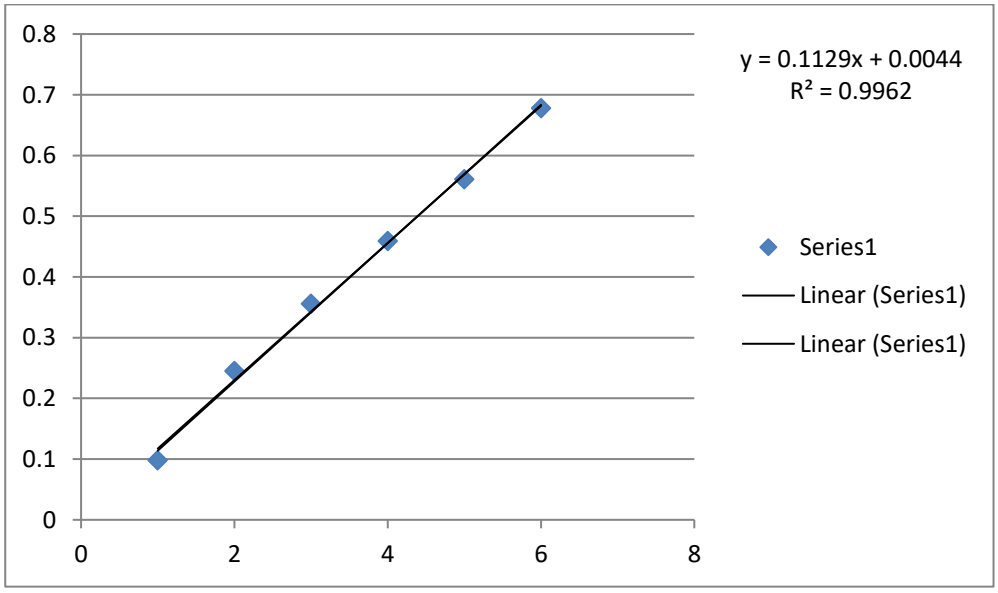

Fig No.3 Calibration curve of Bisoprolol Fumarate

Table No.1 Linearity of Bisoprolol fumarate

Concentration (µg/ml)	Absorbance
2	0.098
4	0.245
6	0.356
8	0.459
1	0.561
1.2	0.678

Table No.2 Linearity data of the developed method

Parameter	Developed method
Conc. range	2 - 12µg/ml
Slope ± ts	0.112
*Intercept ± ts	0.004
Correlation coefficient	0.9962
LOD	0.04753
LOQ	0.1584

Precision

Table No 3-Intraday precision Data

Sr. No Concentration	Absorbance		
	4µg/ml	8 µg/ml	12 µg/ml
1	0.149	0.323	0.472
2	0.151	0.324	0.470
3	0.151	0.324	0.470
4	0.152	0.324	0.471
5	0.152	0.329	0.469
6	0.152	0.328	0.468
Average	0.151	0.3233	0.468
SD	0.001095	0.006055	0.005563
%RSD	0.72546	1.872	0.1886

Table No 4-Interday precision Data

Sr. no Concentration	Absorbance		
	4 µg/ml	8 µg/ml	12 µg/ml
1	0.131	0.283	0.438
2	0.130	0.288	0.438
3	0.132	0.286	0.439
4	0.131	0.284	0.439
5	0.131	0.284	0.439
6	0.129	0.290	0.439
Average	0.1306	0.285	0.438
SD	0.001033	0.00271	0.00056
%RSD	0.790405	0.9495	0.11772

Table No .5 Accuracy

Accuracy level	% Recovery	Average	Statistical Analysis		
			mean	SD	%RSD
80%1	98.40%	99.49%	1.187	0.012	1.0118
80%2	99.49%				
80%3	100.40%				
100%1	100.06%	100.43%	1.464	0.00248	1.0674
100%2	100.01%				
100%3	100.01%				
100%4	100.02%				
100%5	100.48%				
100%6	102.48%	101.50%	1.7183	0.00702	0.408
120%1	101.18%				
120%2	101.47%				
120%3	101.77%				

Table No .6

LOD	0.04753
LOQ	0.1584

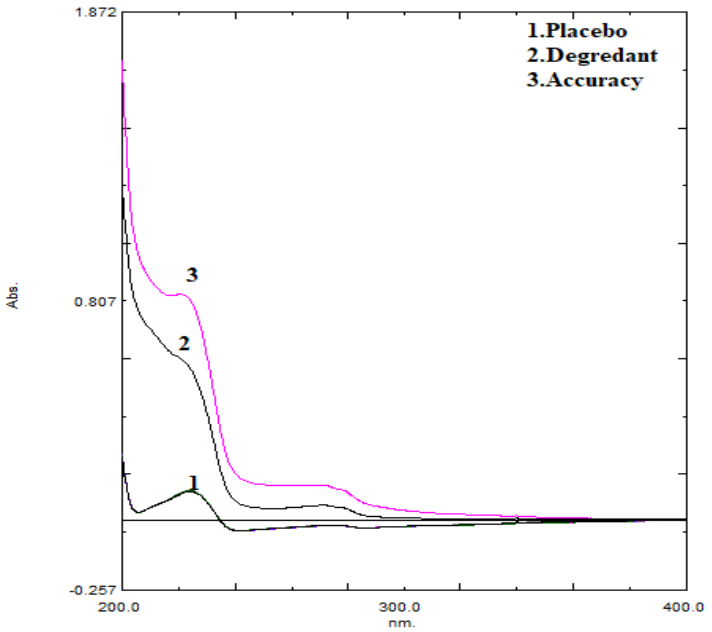

Fig No.4 Specifcity of Bisoprolol Fumarate

Force Degradation

Table No.7: Short term forced degradation data

Sr. No	Stress condition	% Degradation Observed	Remarks
1	0.1N NaOH	99.99%	Stable
2	0.1N HCl	99.99%	Stable
3	Oven	99.99%	Stable
4	Water	99.24%	Stable
5	Photolytic	99.19%	Stable
6	Oxidation	99.05%	Stable

CONCLUSION

An accurate and greener, robust, presice UV spectrophotometric method has been developed and validated for the analysis of bisoprolol fumarate in bulk and tablet dosage form. The percentage recovery and found concentration of active ingredient in pharmaceutical formulation showed that the amount of drug present is consistent with the label claim. Hence this method is very useful simple and accurate, greener, precise for determination of bisoprolol fumarate in bulk and pharmaceutical dosage form .it can be used for the routine analysis of bisoprolol fumarate.

DISCUSSION

This study represents the development and validation of simple U.V method for the determination of Bisoprolol Fumarate in pharmaceutical formulations. The cost of the method is reduced. The method is less time consuming and the sensitivity of the method is comparatively higher. The U.V method developed and validated for the determination of Bisoprolol Fumarate in pharmaceutical formulations, assured the satisfactory precision and accuracy. The method was found to be simple, accurate and precise as per ICH guidelines. The method was successfully used for determination of drugs in their pharmaceutical formulation.

ACKNOWEDGMENTS

The authors are thankful to the management, staff of Channabasweshwar Pharmacy College, Latur (MS) for their kind help and support.

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