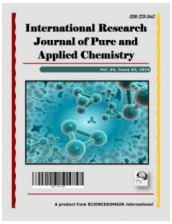

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UV Derivative Spectrophotometric Method for Determination of Bisoprolol Fumarate in Bulk and Tablet Formulation

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Authors' contributions

This work was carried out in collaboration between all authors. All authors read and approved the final manuscript.

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ABSTRACT

Simple, cost effective, accurate and reproducible UV derivative-spectrophotometric method were developed and validated for the estimation of bisoprolol fumarate in pharmaceutical preparations. Bisoprolol fumarate was estimated at 233 nm in 50% methanol. The beer's law was obeyed in the concentration range of 2.0 –10.0 µg/ml (r^2 = 0.9995). The apparent molar absorptivity and Sandall's sensitivity coefficient were found to be 391 L· mol^{-1}·cm^{-1} and 2.51-g·cm–^{2} /0.001 respectively, indicating the high sensitivity of the proposed method. The method was tested and validated for various parameters according to ICH guidelines. The detection and quantitation limits were found to be 0.0267 and 0.0808 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%).

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Keywords: Bisoprolol fumarate; UV-spectrophotometric method; first order derivative spectroscopy; assay.

1. INTRODUCTION

1.1 Spectroscopy Methods

It is the branch of science dealing with the study of interaction between Electromagnetic radiation and matter. It is a most powerful tool available for the study of atomic and molecular structure/s and is used in the analyses of wide range of samples. Optical spectroscopy includes the region on electromagnetic spectrum. The regions of electromagnetic spectrum are: Visible 400-750 nm, UV 200-400 nm.

1.2 Ultraviolet-visible Spectrophotometry

UV-Visible spectrophotometry is one of the most frequently employed technique in pharmaceutical analysis. It involves measuring the amount of ultraviolet or visible radiation absorbed by a substance in solution. Instrument which measure the ratio, or function of ratio, of the intensity of two beams of light in the Invisible region are called Ultraviolet-Visible Spectrophotometers.

In qualitative analysis, organic compounds can be identified by use of spectrophotometer, if any recorded data is available, and quantitative spectrophotometric analysis is used to ascertain the quantity of molecular species absorbing the radiation. Spectrophotometric technique is simple, rapid, moderately specific and applicable to small quantities of compounds. The fundamental law that governs the quantitative spectrophotometric analysis is the Beer -Lambert law [1].

There are few spectrophotometric methods for the assay of beta blockers and fewer for bisoprolol [2]. It should be noted that the actual spectrophotometric methods used for bisoprolol determination are UV-based.

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. [3].

Bisoprolol fumarate is official in USP (USP, 2015), very few analytical methods such as derivative spectrophotometry was used [4].

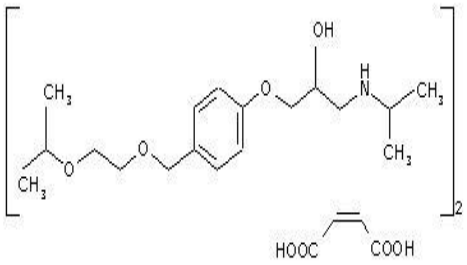

Fig. 1. Chemical structure of bisoprolol fumarate

Several analytical methods have been studied for the determination of BIS in plasma and urine samples. Among these methods, high-performance liquid chromatography (HPLC, liquid chromatography–tandem mass spectrometry (LC–MS-MS), liquid chromatography–electrospray ionization mass spectrometry (LC–ESI-MS) and electrophoresis have been utilized for the determination of BIS [5].

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 [6].

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 [7-9].

This paper presents a new UV-spectrophotometric method for the assay of bisoprolol using first order derivative of bisoprolol spectrum at wavelength 233 nm. The developed method was validated using pure substance and pharmaceutical tablets.

2. MATERIALS

Bisoprolol fumarate was a gift sample from Aurobindo Pharma India Ltd. All chemicals and reagents used were of analytical grade and purchased from SDFCL SD fine Chem limited India.

2.1 Instruments

A double beam UV-VIS spectrophotometer (UV-1800 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: 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 (Sartorius CAP 224S. Germany).

2.2 Preparation of Stock Standard Solution and Selection of Wavelengths

A stock standard solution was prepared by dissolving 100 mg of bisoprolol fumarate in a 100 ml of 50% v/ v methanol 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.

3. VALIDATION OF THE METHOD

Method validation [10,11] was performed in terms of sensitivity, specificity, linearity, LOQ, LOD, precision, accuracy and robustness.

3.1 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 ml into a series of 50-ml volumetric flasks with 50% methanol to get a final concentration range of 2–10 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 d*A*/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.

3.2 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.

3.3 Precision

The precision of the method was studied as intra-day 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.

3.4 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.

3.5 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.

3.6 Analysis of Marketing, Formulation

Twenty tablets of each different brands were accurately weighed, average weight determined and ground into fine powdered. A quantity of powder equivalent to 2.5 and 5mg of tablets was transferred into a 100-ml volumetric flask containing 30 ml of 50% *v/v* methanol, sonicated for 15 min, the volume was adjusted to the mark using the same solvent and filtered through Sartorius filter paper grade 292. An appropriate volume 10 ml was transferred into a 25-ml volumetric flask and the volume was adjusted to the mark to obtain the desired concentration of

10 µg /ml for 2.5 mg of tablet, and 5 ml was transferred into 25 volumetric flasks to obtain 10 µg for 5 mg of tablet.

3.7 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 studies by spiking different concentration of pure drug in the analyzed tablet sample.

A first-order derivative is the rate of change of absorbance with respect to wavelength, a first order derivative starts and finishes at zero. It also passes through zero at the same wavelength as the ƛ max of the absorbance band.

Figs. 2, 3 and 4 showed the zero order and first order spectra of bisoprolol fumarate, the first order derivative yield an absorption band at 233 nm in bisoprolol working standard and tablet of bisoprolol.

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.

4.1 Linearity

The linearity of the calibration curve in the pure solution of bisoprolol was checked over the concentration range of 2-10 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=0.0391x+0.0023; R2 =0.9995 at 233 nm. The results obtained were found to be within the specified limits. Regression analysis of Beer's plot showed good correlation in concentration range.

4.2 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 99.5-100.2%, which improve good recovery for this method, Table 1.

4.3 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 = 0.098%.

The precision (intra-day, inter -day and analyst to analyst) of the method were found to be within the limit (% RSD < 2).

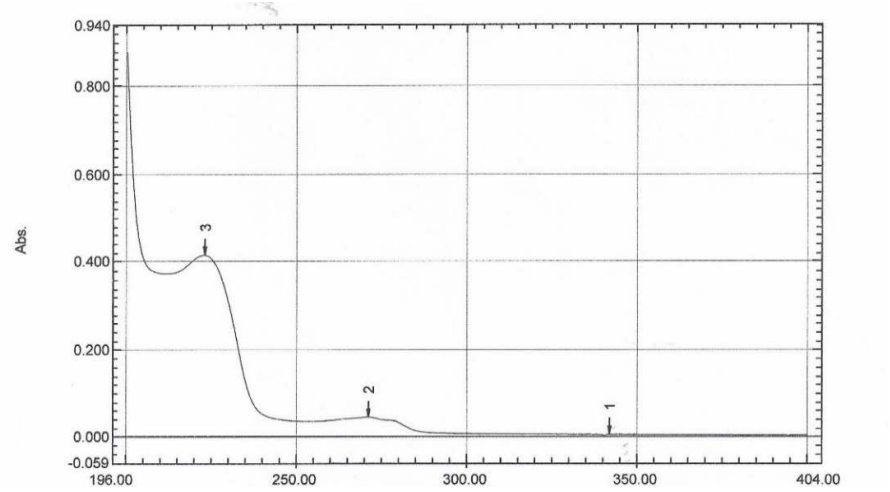

Fig. 2. Zero order absorption spectrum of bisoprolol fumarate

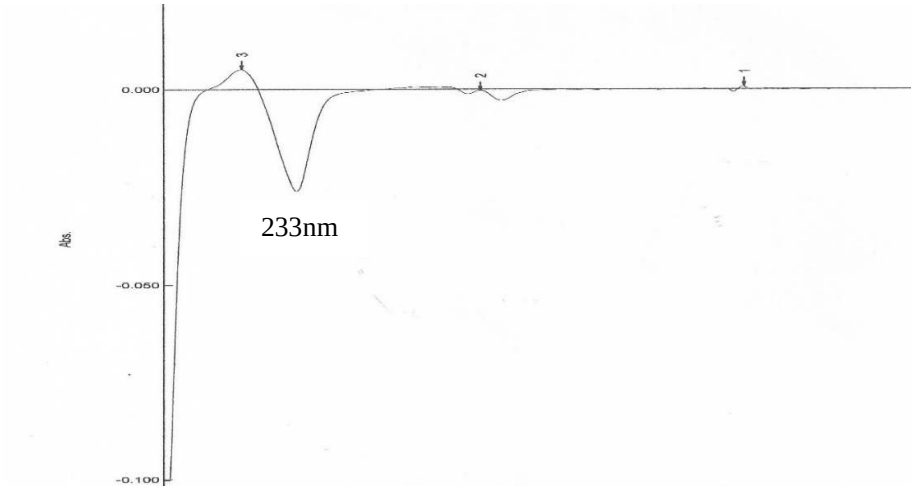

Fig. 3. First derivative absorption spectrum of bisoprolol fumarate working standard.

Fig. 4. First order absorption spectrum derivative of bisoprolol fumarate tablet

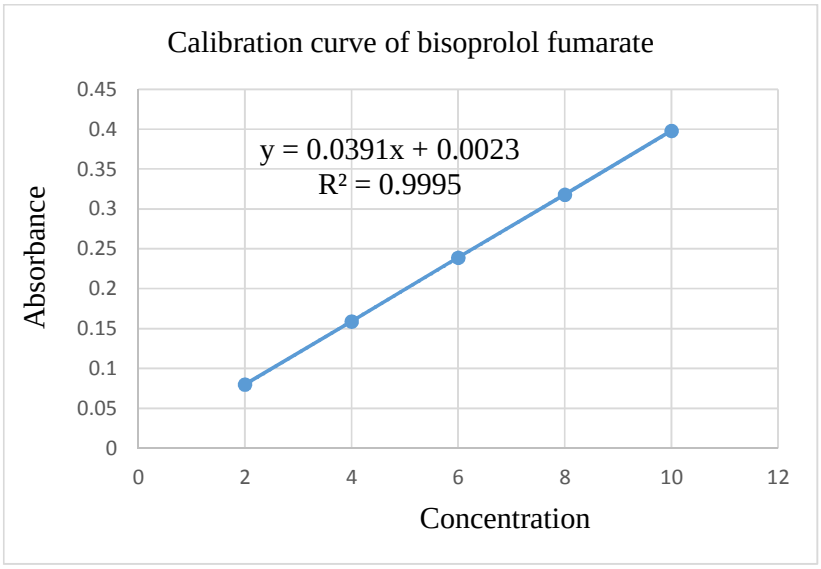

Fig. 5. Calibration curve of bisoprolol fumarate

4.4 Assay of Market Tablets

The results of analysis the bisoprolol fumarate in dosage form tablet different strength by the proposed UV derivate method was highly reliable and are in good agreement with the labeled claim of the drug Table 4.

Table 1. Results of recovery study test for bisoprolol fumarate

Level of addition %	Drug	Tablet strength (n=3) µg/ml	The amount added (n=3) µg/ml	Average amount recovery	Recovery
80	Bisoprolol	5.0	4.0	3.98	99.50
100	Bisoprolol	5.0	5.0	5.01	100.2
120	Bisoprolol	5.0	6.0	5.98	99.67
				Average	99.61
				RSD %	0.0985

Table 2. Results of Intra-day precision of bisoprolol fumarate

Repeatability precision		Run	Absorbance at 233 nm	Assay	% RSD N =6
Sample	Concentration				
Bisoprolol fumarate	10 µg/ml	1	0.387	99.74	0.473
		2	0.386	99.50	
		3	0.388	100.00	
		4	0.385	99.22	
		5	0.389	100.25	
		6	0.384	99.00	

Table 3. Results of inter-day precision

Repeatability precision		Run	Absorbance at 233 nm	Assay	% RSD N =6
Sample	Concentration				
Bisoprolol fumarate	10 µg/ml	1	0.388	100.21	0.68
		2	0.385	99.44	
		3	0.384	100.47	
		4	0.389	100.99	
		5	0.391	99.18	
		6	0.386	99.7	

Table 4. Assay of bisoprolol fumarate in tablet formulation

Drug	Label claim mg/tablet	Amount found*	% RSD
Amicor	2.5	2.506	1.00
Bisocard	5.0	4.95	1.30
Emocor	5.0	4.97	0.81

** Average of three estimations*

Table 5. Results of precision analyst to analyst

Concentration	Analyst 1	Analyst 2
10 µg/ml	0.385	0.379
	0.387	0.384
	0.388	0.385
	0.384	0.382
	0.383	0.380
	0.386	0.381
Average	0.386	0.382
SD	0.0017	0.0021
RSD	0.48	0.61

Table 6. Method validation parameters

Parameters	Results
Linear range	2 -10 µg/ml
Molar absorptivity	391.0
Regression equation	Y = 0.0391x+0.0023
Correlation coefficient (r^2)	0.9995
Sandall's sensitivity	2.51
Slope	0.0391
Intercept	0.0023
LOD µg/ml	0.0266
LOQ µg/ml	0.0808

5. CONCLUSION

The proposed method is found to be accurate, sensitive, selective, and precise for derivative spectroscopic estimation of bisoprolol fumarate. Moreover, the method is economical, simple and rapid, it can be used for routine analysis of bisoprolol fumarate dosage form.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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