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DEVELOPMENT AND VALIDATION OF UV SPECTROPHOTOMETRIC METHOD FOR BISOPROLOL FUMARATE IN BULK AND TABLET DOSAGE FORM

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ABSTRACT

A simple, precise, accurate and cost effective Area under curve UV Spectrosphotometric method was developed for estimation of Bisoprolol fumarate in pharmaceutical dosage form. The principle for AUC method is "the area under two points on the mixture spectra is directly proportional to the concentration of the component of interest." Drug follows Beers law over the concentration range 5-25µg/ml with Regression of coefficient 0.997. The accuracy of the method was found to be 100%. The developed method was validated with respect to linearity, precision and accuracy. UV Spectrosphotometric method was developed and the results were validated statistically as per ICH Q2 (R1) guidelines and were found to be satisfactory.

KEYWORDS: Bisoprolol fumarate; Area under curve; validation; UV Spectrophotometer.

I INTRODUCTION

Bisoprolol fumarate is chemically 2-propanol,-[4-[[2-(1-methylethoxy) ethoxy] methyl] phenoxy]-3-[(1-methylethyl) amino]-, (±)-, (E)-2-butenedioate (Fig.1).[1-2] Bisoprolol fumarate is a white crystalline powder, which is readily soluble in water, methanol, ethanol, and chloroform.[3] It is a racemic mixture of S (-) and R (+) enantiomers. Bisoprolol fumarate is a synthetic, β_1-selective (cardioselective) adrenoreceptor blocking agent.[4] Bisoprolol fumarate competitively blocks the activation of (Gs protein and cAMP) which ultimately

leads to increased contractility and increased heart pacemaker. So, Decreased adrenergic tone shows less contractility of heart muscle and lower heart rate of pacemaker. It is used as an antihypertensive drug.[5-7]

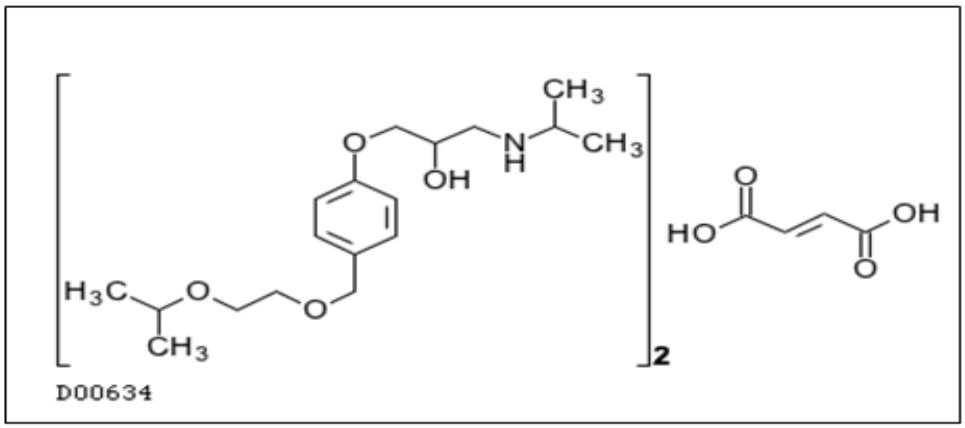

Fig. 1: Structure of Bisoprolol fumarate.

Molecular Formula: $(C_{18}H_{31}NO_4)_2.C_4H_4O_4$

Molecular Weight: 767.0 g/mol

The objective of the present work was to develop new analytical UV spectrophotometric method and its validation parameters for the proposed method according to ICH guidelines for the estimation of Bisoprolol fumarate in bulk and tablet dosage form. The developed method can be applied for routine analysis of Bisoprolol fimarate in bulk and pharmaceutical dosage form.[6]

II. MATERIALS AND METHODS

Chemical and reagents

Bisoprolol fumarate [bulk drug] used were of analytical reagent grade purchased from Unichem laboratories Ltd, Pharmaceutical Company in Goa Industrial Estate, Goa, India. Double distilled water was used throughout the analysis.

Instrumentation

A shimadzu1800UV/VIS double beam spectrophotometer with 1cm matched quartz cells was used for all spectral measurements.

Selection of solvent

Solubility of drug was checked in water, methanol and chloroform. As compare to other solvent water not only shows good result but also cost effectively. So; water is best choice as mobile phase for this method.

Preparation of standard stock solution

Accurately weighed 10mg of Bisoprolol fumarate (bulk drug) was transferred in 10 ml volumetric flasks, dissolved, sonicated and diluted to the mark with water to obtain standard solution (1000µg/ml) of drug.

Area under curve

For the determination of Bisoprolol fumarate using the area under curve(AUC) method, suitable dilutions of the working stock solution(1000µg/ml) of Bisoprolol fumarate were prepared in water and Scanned in the UV-region i.e. 400nm to 200nm. For Area under curve method, the sampling wavelength ranges from 217-229nm (Fig.2) selected for estimation of Bisoprolol fumarate and area were integrated between these selected wavelength range, which showed linear response with increasing concentration hence the same wavelength range were used for estimation of tablet formulations.

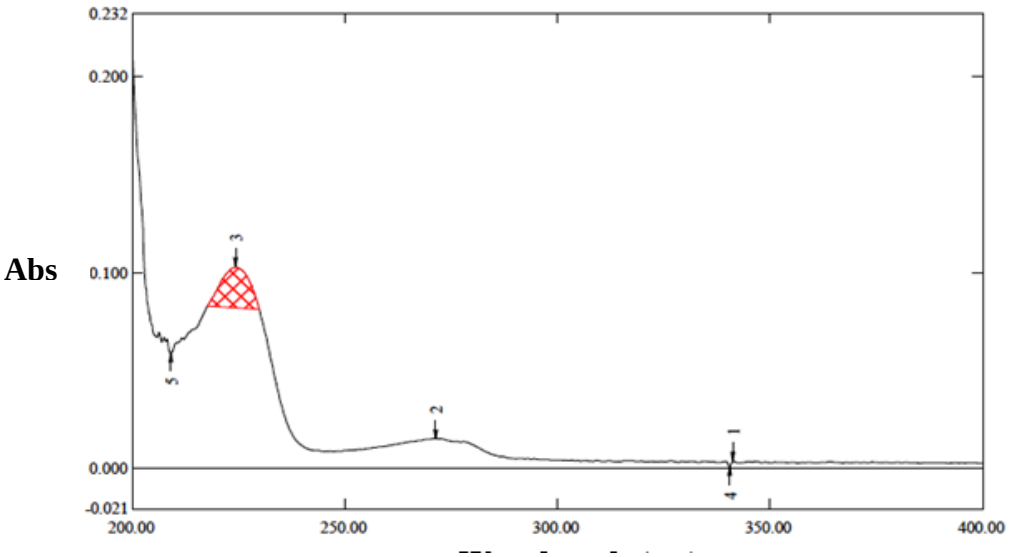

Fig. 2: AUC spectrum of Bisoprolol fumarate.

Analysis of marketed formulation

Ten tablets of Besicor brand was weighed and powdered (Each tablet contains Bisoprolol fumarate 5mg). Powder equivalent to 10mg of Bisoprolol fumarate transferred to 10 ml volumetric flask and was diluted with water and volume made to 10ml (1000µg/ml) with water. Solution was filtered and further dilutions were made with mobile phase to get the final concentration of 5µg/ml of Bisoprolol fumarate. AUC determined in the wavelength range between 219-229nm six times.

Table 1: Analysis of marketed formulation.

Sr. No.	Area	Amount Recovered(µg/ml)	% Recovery
1	0.137	4.91	98.28
2	0.139	4.97	99.42
3	0.142	5.05	101.14
4	0.143	5.08	101.71
5	0.140	5	100
6	0.138	4.94	98.85
Mean	0.139	4.971	99.90
%RSD	1.656	1.325	1.325

Validation of the Method[8 9 10 11]

1. Linearity

The linearity of an analytical procedure is its ability to obtain test results which are directly proportional to the concentration (amount) of analyte in the sample. Calibration graph was found to be linear that is adherence to the system of Beer's law which was found over the concentration range of 5-25µg/ml of Bisoprolol fumarate (Fig.3). The regression data as given in Table 2, showed a good linear relationship.

Table 2: Linearity values of Bisoprolol fumarate.

Parameter	Bisoprolol fumarate
Range	5-25µg/ml
Slop	0.035
Intercept	-0.035
Correlation coefficient	0.997

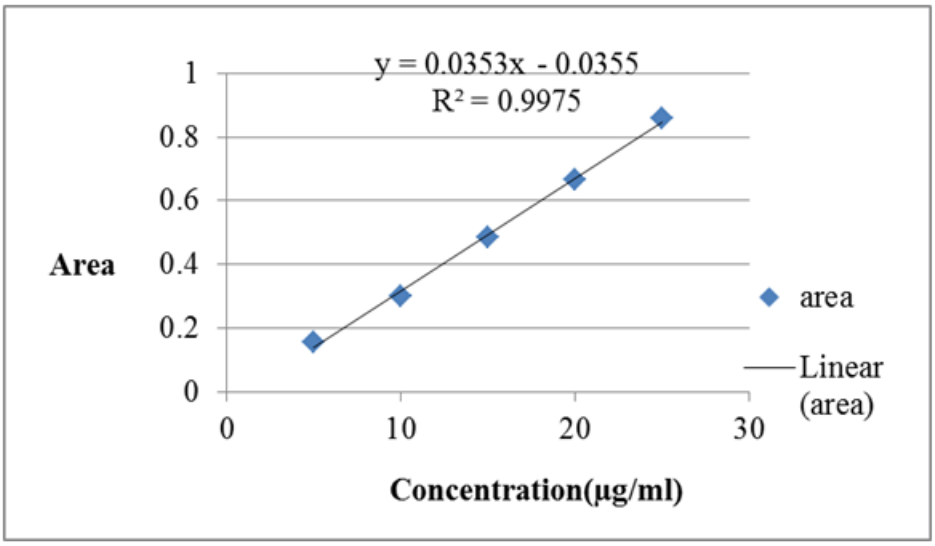

Fig. 3: Linearity graph of Bisoprolol fumarate.

2. Precision

The precision of the method was established by Intra-day and Inter-day variation studies. In the Intraday precision was found by carrying out the analysis of standard drugs at three different concentrations in the linearity range of the drugs for three times on the same day. Each concentration was applied in triplicates and % RSD was calculated. For the Inter day precision was found by carrying out the analysis of the standard drugs at three different concentrations in the linearity range of the drugs for three days and % RSD was calculated. The results obtained for Intraday and Inter day variations studies of above method are shown in Table 3&4.

Table 3: Intraday precision study.

Conc. µg/ml	Area			Mean Area	SD	%RSD
	Trial 1	Trial 2	Trial 3			
5	0.158	0.156	0.157	0.157	0.001	0.6369
10	0.305	0.304	0.302	0.303	0.0015	0.5030
15	0.484	0.485	0.487	0.485	0.0015	0.3147

Table 4: Intraday precision study.

Conc. µg/ml	Area			Mean Area	SD	%RSD
	Trial 1	Trial 2	Trial 3			
5	0.159	0.158	0.157	0.158	0.001	0.632
10	0.306	0.307	0.305	0.306	0.001	0.326
15	0.489	0.487	0.488	0.488	0.001	0.204

3. Accuracy (Recovery studies)

Known amounts of Bisoprolol fumarate were spiked to placebo at 50%, 100% and 150% of specification in triplicate and analyzed as per the proposed method to determine the accuracy of the method. Percentage recovery was calculated from the amount found and amount added. The percentage recovery is within the acceptance criterion, which indicates the accuracy of the method. The results are shown in Table 5.

Table 5: Recovery studies

Level	Conc.(µg/ml)		Area	% Recovery	Mean% Recovery ±%RSD
	Sample	Std.			
50%	10	5	0.501	102.09	101.46±0.573
			0.495	100.95	
			0.497	101.33	
100%	10	10	0.665	100	100.47±0.820
			0.675	101.42	
			0.665	100	
150%	10	15	0.858	102.05	100.68±1.201
			0.838	99.77	
			0.842	100.22	

4. Limit of detection (LOD) and Limit of Quantification (LOQ)

LOD and LOQ were calculated as 3.3 σ/S and 10 σ/S respectively. Where (σ) is the standard deviation of the response (y-intercept) and (S) is the mean of the slop of calibration plot. The LOD and LOQ value of Bisoprolol fumarate was found to be 1.518654µg/ml and 4.601981µg/ml respectively.

III. RESULT AND DISCUSSION

In area under curve method, the area under curve in the range of 217-229 nm was selected for analysis of Bisoprolol fumarate. In above method linearity was observed in the concentration range 5-25µg/ml with Regression of coefficient 0.997.The results of assay are presented in Table1. The accuracy and reproducibility is evident from the data as results are 100%and low % RSD value (<2) coupled with low standard deviation makes the proposed method highly suitable for accurate and precise determination of Bisoprolol fumarate in tablet dosage forms. Results of precision studies are shown in Tables 3&4. Results of recovery studies are shown in Table 5. The proposed method is simple, economic, rapid, precise and accurate. Hence this can be used for routine analysis of Bisoprolol fumarate in tablet dosage form.

IV. CONCLUSION

The developed Area under curve UV spectrophotometric method was found to be simple, accurate, precise, economical and rapid. This developed method provides suitable quantification of Bisoprolol fumarate without any interference from the excipients. Above developed method was validated as per the ICH guidelines. Therefore the developed method can be applied for routine quantitative and qualitative analysis of Bisoprolol fumarate in bulk and pharmaceutical dosage form.

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