Development and Validation of UV Spectrophotometric Method for Determination of Bisoprolol Fumarate in Bulk and Pharmaceutical Dosage Forms

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Abstract: In this study a simple, 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 271 nm. Validation was conducted in accordance to ICH guidelines. The calibration curve was linear in the concentration range 5–25 µg/mL with correlation coefficient not less than 0.9986. The limit of detection and limit of quantification were 0.22 µg/ml and 0.66 µg/ml, respectively. Intraday and intermediate precision of the developed method were reflected by the low RSD% values (1.19 and 0.854, respectively). The recovery percentage was 105.0 ± 1.3%, n=3. The proposed method was applied for the assay of BF in three different brands.

Keywords: Bisoprolol fumarate; UV spectrophotometric method; Brands.

Introduction

Bisoprolol fumarate (BF; Figure 1) is a selective beta-blocker. It is used for the treatment of hypertension, angina pectoris 1,2. Several methods were reported for the determination of BF in bulk and dosage form as single component, combined with other drugs or in biological fluids. These methods include electrochemical 3, UV spectrophotometric methods 4,7 and HPLC methods 8-12. The official method for its analysis is an HPLC method which considered time consuming and expensive specially in developing countries.

On the other hand, UV spectrophotometry is fast, simple, economic and universally accepted in pharmaceutical analysis. A literature survey revealed that no UV spectrophotometric method has been reported for the estimation of BF in pharmaceutical formulations individually.

Thus, the present study describes a direct, simple and accurate method for the estimation of BF in bulk and in tablet dosage forms.

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Experimental

Materials:
Bisoprolol fumarate reference standard (100.5%) was kindly provided by Azal Pharma, Sudan. Pharmaceutical products of the three commercial brands (Tablets; 5mg) were purchased from the local market.

Instrumentation: UV-Vis spectrophotometer, Jenway 7315 single beam.

Methodology:
Preparation of stock solutions
BF standard solution
Accurately weighed amount (5 mg) of BF standard was dissolved in about 70 ml of distilled water. The solution was then transferred into 100 ml volumetric flask and volume completed to mark with distilled water (solution A; 50 µg/ml).

BF sample solution
Twenty tablets were weighed and powdered. An equivalent weight to 5mg was transferred to 100ml volumetric flask, dissolved in distilled water and shaken for 15 minutes. The volume was then completed to mark with distilled water. The solution was then filtered (solution B; 50 µg/ml).

Estimation of maximum wavelength
Solution A was scanned between 240 to 400 nm to establish the maximum wavelength of absorption (λmax).

Construction of Calibration curve
Aliquot volumes of solution A (1-5 ml) were transferred into a set of volumetric flasks (10ml). The volumes were then completed to mark with distilled water to obtain concentration range of 5-25 µg/ml. The absorbance values of these solutions were measured at 271nm against blank (distilled water). Calibration curve was constructed by plotting absorbance values vs concentration.

Method Validation
The developed method was validated as per the ICH guidelines in terms of linearity, precision, accuracy and specificity.

Linearity
LOD, LOQ, slope error and intercept error were calculated from the concentration range, absorbance data and slope.

Precision
Different concentrations within the linearity range were prepared and analysed three times within the same day and between days to evaluate the precision of the developed method. The mean, standard deviation and relative standard deviation values were calculated.

Accuracy
Two ml each of solution B were transferred into three volumetric flasks. Study was carried out through spiking solutions at 50%, 100% and 150% levels. The absorbance values were measured and the recovery percentage was calculated. The procedure was repeated three times.

Assay of tablets dosage form
The absorbance of sample and standard solutions with the same concentration was measured at 271nm. The procedure was repeated three times and the content percent was calculated as follows.

\[
\% = \frac{\text{Absorption of the sample}}{\text{Absorption of the standard}} \times 100\%.
\]

Results and Discussion
Although UV spectrophotometry lacks selectivity, it is the most widely used method for quantitative analysis of raw materials and pharmaceutical dosage forms. This is due to its simplicity and accuracy.

The developed method describes the analysis of BF using direct UV method. Aqueous solution of BF showed maximum absorption at 271nm (Figure 2).
Method validation

**Linearity**
The linearity of the method was checked in pure solution of BF. Regression analysis of Beer's plots showed good correlation in concentration range of 5-25 µg/ml with good correlation coefficient (Figure 3).

The obtained regression analysis data was summarized in Table 1.

![Figure 3. Calibration curve of BF](image)

**Table 1. Linearity data of the developed method.**

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Developed method</th>
</tr>
</thead>
<tbody>
<tr>
<td>Conc. range</td>
<td>5 - 30µg/ml</td>
</tr>
<tr>
<td>Slope ± ts_b,*</td>
<td>0.035 ± 0.48</td>
</tr>
<tr>
<td>Intercept ± ts_y,**</td>
<td>0.018 ± 0.056</td>
</tr>
<tr>
<td>Correlation coefficient</td>
<td>0.9986</td>
</tr>
<tr>
<td>LOD</td>
<td>0.22µg/ml</td>
</tr>
<tr>
<td>LOQ</td>
<td>0.66µg/ml</td>
</tr>
</tbody>
</table>

*Standard error of slope calculated at 95% confidence limit for n-2 degrees of freedom.

**Precision**
The precision of the developed method was assessed in terms of repeatability and intermediate precision by analyzing replicate for three different concentrations. RSD% values were 1.19 and 0.854 reflecting the precision of the developed method (%RSD < 2).

**Accuracy**
The accuracy of the method was determined by recovery experiments. The recovery studies were carried out at spiking levels of 50%, 100% and 150% of test concentration. Results of assay and recovery were presented in Table 2.

The obtained results reflect the accuracy of the method and its freedom of interferences by excipients.

**Table 2. Accuracy of the developed method**

<table>
<thead>
<tr>
<th>Amount of sample (µg/ml)</th>
<th>study level (%)</th>
<th>Amount of drug added (µg/ml)</th>
<th>Recovery % ± SD; n=3</th>
</tr>
</thead>
<tbody>
<tr>
<td>20</td>
<td>50</td>
<td>10</td>
<td>105.9 ± 1.36</td>
</tr>
<tr>
<td></td>
<td>100</td>
<td>20</td>
<td>107.4± 1.90</td>
</tr>
<tr>
<td></td>
<td>150</td>
<td>30</td>
<td>105.5± 1.30</td>
</tr>
</tbody>
</table>

**Assay of BF tablets dosage forms by developed method**
The developed method was applied for the assay of BF in three commercial brands collected from Sudan market.

The obtained results showed good content percent of BF in the three brands which complies with the stated percent (90-105%), Table 3.
Table 3. Assay of BF tablets dosage form by developed method

<table>
<thead>
<tr>
<th>Brand code</th>
<th>Labeled amount (mg/tablet)</th>
<th>Content % ± SD; n=3</th>
</tr>
</thead>
<tbody>
<tr>
<td>B1</td>
<td>5</td>
<td>105.1± 0.17</td>
</tr>
<tr>
<td>B2</td>
<td>5</td>
<td>100 ± 0.001</td>
</tr>
<tr>
<td>B3</td>
<td>5</td>
<td>90.48± 0.35</td>
</tr>
</tbody>
</table>

Conclusion

An accurate and precise 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 formulations showed that the amount of drug present is consistent with the label claim. Hence, this method is very useful simple and accurate for determination of Bisoprolol fumarate in bulk and pharmaceutical dosage form. It can be used for the routine analysis of BF.

References