SPECTROPHOTOMETRIC METHOD FOR THE ESTIMATION OF RANOLAZINE IN BULK AND PHARMACEUTICAL FORMULATIONS

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ABSTRACT

The present study describes a simple, accurate, precise and cost effective colorimetric method has been developed for the quantitative estimation of ranolazine in bulk and pharmaceutical dosage forms. This method is based on the reaction of ranolazine with resorcinol to form orange yellow colored chromogen. The \( \lambda_{\text{max}} \) or the absorption maxima of the drug was found to be 447nm. A linear response was observed in the range of 5-25µg/ml with a correlation coefficient of 0.9997. The molar absorptivity, Sandell’s sensitivity, quantitation limit and detection limit of the method was found to be precise and accurate. This method can be used for the determination of ranolazine in quality control of formulation without interference of the excipients.

Keywords: Ranolazine, resorcinol, spectroscopy, \( \lambda_{\text{max}} \) and colorimetry.

INTRODUCTION

Ranolazine is a antianginal drug and chemically it is a piperazine derivative. Structurally it is N-(2,6-dimethylphenyl)-2-[4-[2-hydroxy-3-(2-methoxyphenoxy) propyl] piperazin-1-yl]acetamide. Ranolazine is believed to have its effects via altering the trans-cellular late sodium current. It is by altering the intracellular sodium level that ranolazine affects the sodium-dependent calcium channels during myocardial ischemia. Thus, ranolazine indirectly prevents the calcium overload that causes cardiac ischemia. Ranolazine is indicated for the treatment of chronic angina. Ranolazine may be used with betablockers, nitrates, calcium channel blockers, antiplatelet therapy, lipid-lowering therapy, ACE inhibitors, and angiotensin receptor blockers\(^1\). There are various methods for determination of ranolazine such as UV- Spectrophotometry\(^3\,5\), Liquid chromatography/mass spectrometry (LC/MS)\(^6\,12\) and RP-HPLC\(^13\). Although these techniques are sufficiently sensitive, but they use expensive instrument and time consuming. A simple, sensitive and reproducible Spectrophotometric method has been developed here for the estimation of ranolazine in pure and its pharmaceutical formulations.

MATERIALS AND METHODS

Instrumentation:
A Shimadzu UV/visible double beam spectrophotometer (Model 2450) with 1cm matched quartz cells were used for all the spectral measurements.

Preparation of Standard and Sample Solutions:
About 100 mg of ranolazine was accurately weighed and dissolved in water and volume made up to 100 ml with distilled water (1 mg/ml). The final concentration of ranolazine was made to 100µg/ml with distilled water by dilution. For formulation analysis, twenty tablets of ranolazine each containing 500mg were accurately weighed and finely powdered. An amount equivalent to 100mg of ranolazine was weighed and dilutions were made suitably. Solvents like Hydrochloric acid (0.5% w/v), Sodium nitrite (0.1%w/v), Sodium hydroxide (2% w/v) and Resorcinol (0.5% w/v) were prepared by using distilled water as solvent\(^14\).
ASSAY METHOD:
Aliquots of ranolazine ranging from 0.5 – 2.5 ml (1 ml = 100 µg) were transferred into a series of 10 ml volumetric flasks. To each flask 0.5 ml of Hydrochloric acid (0.5% w/v), 1ml of Sodium nitrite (0.1%w/v), Sodium hydroxide (2% w/v) and 0.5ml of Resorcinol (0.5% w/v) was added. The volumes were made up to the mark with distilled water. The absorbance of the orange yellow colored chromogen was measured at 447 nm against reagent blank. The amount of ranolazine present in the sample was computed from calibration curve.

RESULTS AND DISCUSSION
The optical characteristics such as absorption maxima, Beer’s law limits, molar absorptivity and Sandell’s sensitivity are presented in Table 1. The regression analysis using method of least squares was made for the slope (b), intercept (a) and correlation (r) obtained from different concentrations and the results are summarized in Table 1. The percent relative standard deviation and percent range of error (0.05 and 0.01 level of confidence limits) calculated from the eight measurements at ¾ of the upper Beer’s law limits of ranolazine are shown in Table 1. The results of analysis of tablet formulations are done at three levels recorded in Table 2. To evaluate the validity and reproducibility of the methods, known amounts of the pure drug were added to the previously analyzed pharmaceutical preparations and the mixtures were analyzed by the proposed method. The result of recovery studies are summarized in Table 2. Interference studies revealed that the common excipients and other additives are usually present in the tablet dosage forms did not interfere at their regularly added levels. The result showed that this method has reasonable precision. The proposed method was found to be simple, sensitive, selective, accurate, precise and economical and can be used for determination of ranolazine.

Table 1: Optical characteristics and precision.

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Method</th>
</tr>
</thead>
<tbody>
<tr>
<td>$\lambda_{\text{max}}$ (nm)</td>
<td>447</td>
</tr>
<tr>
<td>Beer’s law limits (µg/ml)</td>
<td>5-25</td>
</tr>
<tr>
<td>Molar absorptivity (L/ mol$^{-1}$, cm$^{-1}$)</td>
<td>$4.15 \times 10^3$</td>
</tr>
<tr>
<td>Sandell’s sensitivity (µg/ml/cm$^2$/0.001 absorbance unit)</td>
<td>0.0102</td>
</tr>
<tr>
<td>Regression equation (Y*)</td>
<td></td>
</tr>
<tr>
<td>Slope (b)</td>
<td>0.0482</td>
</tr>
<tr>
<td>Intercept (a)</td>
<td>0.0171</td>
</tr>
<tr>
<td>Correlation coefficient (r)</td>
<td>0.9997</td>
</tr>
<tr>
<td>% RSD**</td>
<td>1.140</td>
</tr>
<tr>
<td>Range of errors**</td>
<td></td>
</tr>
<tr>
<td>Confidence limits with 0.05 level</td>
<td>0.00542</td>
</tr>
<tr>
<td>Confidence limits with 0.01 level</td>
<td>0.00725</td>
</tr>
</tbody>
</table>

* $Y = bC + a$ where $C$ is the concentration of ranolazine in µg/ml and $Y$ is the absorbance at the respective $\lambda_{\text{max}}$.

** For eight measurements.

Table 2: Evaluation of Ranolazine in pharmaceutical dosage forms

<table>
<thead>
<tr>
<th>Samples (Tablet)</th>
<th>Manufacturer</th>
<th>Labelled amount (mg/Tab)</th>
<th>Amount obtained by(mg) Proposed Method</th>
</tr>
</thead>
<tbody>
<tr>
<td>RANCAD</td>
<td>LUPIN</td>
<td>500</td>
<td>498.89</td>
</tr>
<tr>
<td>RANOZEX</td>
<td>SUN PHARMA</td>
<td>500</td>
<td>499.95</td>
</tr>
<tr>
<td>RANOLAZ</td>
<td>TORRENT</td>
<td>500</td>
<td>499.48</td>
</tr>
</tbody>
</table>

Average ± S.D of eight determinations

CONCLUSION
The proposed method for the spectrophotometric determination of ranolazine samples is simple, rapid and sensitive. The method does not require any heating for the development of colour. The statistical analysis of the results indicates that the methods have good precision and accuracy.

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REFERENCES


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