ULTRA VIOLET AND DERIVATIVE SPECTROPHOTOMETRIC METHODS
FOR ESTIMATION OF METOLAZONE IN PHARMACEUTICALS

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ABSTRACT
Four new simple, precise, accurate spectrophotometric methods have been developed and validated for the routine estimation of Metolazone in bulk drug and pharmaceutical formulations. Metolazone exhibits absorption maxima at 237nm in water (Method A), 270nm in alcohol (Method B) and in first order derivative spectra a sharp peak is shown in water at 229.6nm (Method C). The system obeyed Beers law in the concentration range of 10-50µg/ml (Method A, and C) and 1-5µg/ml (Method B). Repeatability, intraday and interday precision of metolazone for all the four methods were found to be precise. The accuracy of the developed methods was 98.0-99.04%. The methods developed were fast and economical and also selective and sensitive for the desired range. The results of analysis were validated as per ICH guidelines and by recovery studies. No interference was observed from common tablet adjuvants. These methods have been successfully applied to the pharmaceutical preparations containing Metolazone.

Key words: Metolazone, UV spectroscopy, First order derivative.

INTRODUCTION
Metolazone\(^{[1-4]}\) is chemically 7-chloro-1,2,3,4-tetrahydro-2-methyl-3-(2-methyl phenyl)-4-oxo-6-quinazoline Sulfonamide. Metolazone is an oral diuretic drug. It is primarily used to treat congestive heart failure and high blood pressure. Metolazone indirectly decreases the amount of water reabsorbed into the blood stream by the kidney, so that blood volume decreases and urine volume increases. This lowers blood pressure and prevents excess fluid accumulation in heart failure.

Objective
Survey of literature showed RP-HPLC\(^{[5,7]}\) method and UV Spectrophotometric method in methanol\(^{[6]}\) for the estimation of Metolazone in pharmaceutical preparations. To the best of our knowledge there is no report of UV Spectrophotometric method in
water and alcohol, first order derivative Water being economical and easily available an attempt was made to develop simple UV and derivative Spectrophotometric method for the estimation of Metolazone in bulk drug and formulations.

**EXPERIMENTAL**

All spectral measurements were done on double beam shimadzu 1700 UV-Visible Spectrophotometer.

**Reagents**

Double distilled water and distilled Alcohol was used. Pure Metolazone was obtained from Centaur Pharmaceuticals Pvt.Ltd. Mapusa Goa.

**Standard and Sample Solutions**

About 100mg of Metolazone (pure or equivalent formulation) was accurately weighed and dissolved in 20ml of distilled water in 100ml volumetric flask and diluted up to the mark with distilled water (1µg/ml). The final concentration was brought to 100µg/ml with distilled water (Method A and C). For method B the standard solution was prepared in alcohol.

**Method-A UV in water**

Aliquots of Metolazone ranging from 1-5ml (1ml=100µg) were transferred into a series of 10ml volumetric flask and diluted to the mark with distilled water. The absorbance of the solution was measured at 237nm against solvent blank. The amount of drug was completed from calibration curve.

**Method-B UV in Alcohol**

Aliquots of Metolazone ranging from 0.1-0.5ml (1ml=100µg) were transferred into a series 10ml volumetric flasks and diluted to the mark with alcohol. The absorbance of the solutions was measured at 270nm against solvent blank. The amount of drug was completed from calibration curve.

**Method-C First Order Derivative Spectroscopy**

In this method 30µg/ml solution of Metolazone was prepared by appropriate dilution of standard solution and scanned in the spectrum mode from 400nm to 200nm. First order derivate Spectra was selected for analysis of drug. First Order Derivative spectra of the drug showed a sharp peak at 229.6nm and was selected for its quantitation. The calibration
The curve was plotted in the concentration range of 10-50µg/ml at wavelength 229.6nm. The amount of drug was computed from calibration curve.

RESULTS AND DISCUSSION

The Optical characteristics such as absorption maxima, Beer’s law limits, molar absorptivity are presented in Table 1.

**TABLE – 1 OPTICAL CHARACTERISTICS OF METOLAZONE**

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Method A</th>
<th>Method B</th>
<th>Method C</th>
</tr>
</thead>
<tbody>
<tr>
<td>$\lambda_{\text{max}}$ (nm)</td>
<td>237</td>
<td>270</td>
<td>229.6</td>
</tr>
<tr>
<td>Beer’s Law Limit (µg/ml) (C)</td>
<td>10-50</td>
<td>1-5</td>
<td>10-50</td>
</tr>
<tr>
<td>Molar absorptivity (L mole$^{-1}$ cm$^{-1}$)</td>
<td>$6.925 \times 10^3$</td>
<td>$5.121 \times 10^4$</td>
<td>$5.499 \times 10^3$</td>
</tr>
<tr>
<td>Regression Equation ($Y^*$)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Slope (b)</td>
<td>0.0190</td>
<td>0.0134</td>
<td>0.0149</td>
</tr>
<tr>
<td>Intercept (a)</td>
<td>0.0095</td>
<td>0.0165</td>
<td>0.0064</td>
</tr>
<tr>
<td>Correlation Coefficient (r)</td>
<td>0.9999</td>
<td>0.7425</td>
<td>1.000</td>
</tr>
<tr>
<td>$%$RSD</td>
<td>0.0567</td>
<td>0.761</td>
<td>0.2785</td>
</tr>
<tr>
<td>Range of errors**</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Confidence limits with 0.05 level</td>
<td>± 0.0010</td>
<td>± 0.0011</td>
<td>± 0.0013</td>
</tr>
<tr>
<td>Confidence limits with 0.01 level</td>
<td>± 0.0015</td>
<td>± 0.0017</td>
<td>± 0.0019</td>
</tr>
<tr>
<td>Limit of Detection (LOD)</td>
<td>0.1734</td>
<td>0.0278</td>
<td>0.2765</td>
</tr>
<tr>
<td>Limit of Quantification (LOQ)</td>
<td>0.5254</td>
<td>0.0843</td>
<td>0.8379</td>
</tr>
</tbody>
</table>

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

** For Eight measurements.

The regression analysis using the method of least squares was made for the slope (b), intercept (a) and correlation coefficient (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, ¾ of the upper Beer’s law limits of Metolazone are given in Table -1.
TABLE – 2 EVALUATION OF METOLAZONE IN PHARMACEUTICAL PREPARATIONS

<table>
<thead>
<tr>
<th>S. No</th>
<th>Brand</th>
<th>Labeled amount (mg)</th>
<th>Amount obtained (mg)*</th>
<th>%Recovery</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>Metoz</td>
<td>5</td>
<td>4.82</td>
<td>98.3%</td>
</tr>
<tr>
<td>II</td>
<td>Metoral</td>
<td>5</td>
<td>4.91</td>
<td>99.1%</td>
</tr>
</tbody>
</table>

*Average of Six determinations

To evaluate the validity and reproducibility of the method, known amount of pure drug was added to the analyzed sample of tablet powder and the mixture analyzed for the drug content using the proposed method. The percentage recovery was found to be within range as shown in Table-2. The results obtained by proposed method are in good agreement with the label claims (Table - 2). The additives and excipients usually present in tablets did not interfere. The results indicate that the proposed methods are simple, precise, accurate and economical and can be used for the routine determination of Metolazone in bulk drug and Pharmaceutical preparations.

**Figure a**
UV Spectrum of Metolazone using Water

**Figure b**
Calibration curve of Metolazone
REFERENCES


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