Simultaneous Spectrophotometric Determination of Valdecoxib and Tizanidine in Tablets

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Two simple, precise and accurate methods for simultaneous estimation of valdecoxib and tizanidine in combined dosage form, have been described. Method 1 involves formation of Q-absorbance equation at 239.6 (isosbestic point) and at 241 nm, while method 2 involves formation of simultaneous equation at 241 and 229 nm, using methanol as solvent. Both the methods were validated, and the results were compared statistically. They were found to be precise, accurate, and specific. The proposed methods were successfully applied to estimation of valdecoxib and tizanidine in combined tablet formulation.

Valdecoxib (VAL) is chemically a diaryl substituted isoxazole. The chemical formula is 4-(5-methyl-3-phenyl-4-isoxazolyl) benzene sulfonamide. It is a non-steroidal antiinflammatory agent, a selective inhibitor of cyclooxygenase–2 (COX–2) indicated for oral administration, for the treatment of Osteoarthritis and Rheumatoid arthritis. Valdecoxib is official only in the Martindale Extra Pharmacopoeia. A survey of literature reveals that valdecoxib is estimated by Solid phase LC in urine samples. Tizanidine hydrochloride (TZN), 5-Chloro-N-(4,5-dihydro-1H-imidazol-2-yl)-2,1,3-benzothiadiazol-4-amine is an α adrenergic receptor agonist, which is a centrally active skeletal muscle relaxant, and is chemically different from other muscle relaxants. In addition to its muscle relaxant properties and central analgesic effect, TZN also has gastroprotective effect. TZN is an imidazoline derivative, and not official in any of the Pharmacopoeia. Several analytical methods for the estimation of tizanidine using HPLC, isocratic SFC, colorimetry, and UV spectrophotometry, have been reported. Reddy et al. reported simultaneous spectrophotometric estimation of tizanidine and nimesulide from combined dosage forms, using methanol as a solvent. Moreover, the literature survey revealed that so far, no method has been reported for estimation of TZN and VAL in combined dosage forms, hence we attempted to develop a simple, accurate, and economic analytical method. This paper describes two simple UV spectrophotometric methods for simultaneous estimation of TZN and VAL in tablets, using methanol as solvent.

An UV/Vis double beam spectrophotometer, Shimadzu model-1601, with 1 cm matched quartz cells was used. TZN standard stock solution (100 µg/ml) was prepared by weighing a 25 mg portion of TZN (Blue Cross Laboratories Ltd., Mumbai) standard, it was transferred to a 25 ml volumetric flask, and volume made to 25 ml with methanol. From this solution, an aliquot of 2.5 ml was withdrawn, and it was diluted to 25 ml with methanol. VAL standard stock solution (100 µg/ml) was prepared by weighing a 25 mg portion of VAL standard in to a 25 ml volumetric flask, and volume was made up to 25 ml with methanol. From this solution, an aliquot of 2.5 ml was withdrawn, and it was diluted up to 25 ml using methanol.

For selection of analytical wavelength for the Q-absorbance method (Method 1), the stock solutions of VAL and TZN were separately diluted in methanol, to get concentrations of 10 µg/ml each, and scanned in the wavelength range of 200-400 nm. From the overlain spectra of both drugs, (Fig. 1) wavelengths 239.6 nm (isosbestic point) and 241 nm (λmax of VAL) were selected for the formation of Q-absorbance equation. For calibration curves, stock solutions of VAL and TZN were appropriately diluted to obtain concentration range of 5-30 µg/ml for each drug. The absorbance of VAL measured at 241 nm and 239.6 nm, and calibration curves were plotted. Similarly the absorbance of TZN measured at 239.6 nm and 241 nm, and calibration curves were plotted. The absorptivities (A1%, 1 cm) of each drug at both the wavelengths were also determined.

The absorbance and absorptivity values at the particular wavelengths were calculated and substituted in the following equation, to obtain the concentration.
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\[
C_{\text{VAL}} = \frac{C_{\text{VAL}}}{A_{\lambda_1}} - \frac{A_{\lambda_1}}{A_{\lambda_2}} = \frac{C_{\text{TZN}}}{A_{\lambda_1}} - \frac{A_{\lambda_1}}{A_{\lambda_2}}
\]

where, \(C_{\text{VAL}}, C_{\text{TZN}}\) are concentration of VAL and TZN, respectively, \(A_{\lambda_1}\) is the absorbance of sample at 239.6 nm, \(a_{\lambda_1}\) is the absorptivity of VAL at 239.6 nm, \(Q_1\) was obtained by using the equation, (absorptivity of VAL at 241 nm)/(absorptivity of VAL at 239.6 nm), \(Q_2\) was obtained from (absorptivity of TZN at 241 nm)/(absorptivity of TZN at 239.6 nm) and \(Q_m\) from, (absorbance of sample at 241 nm)/(absorbance of sample at 239.6 nm).

For the selection of analytical wavelength in simultaneous equation method (Method 2), the spectra of VAL and TZN of the method 1 were used, and wavelength 229 and 241 nm (lmax of TZN and VAL, respectively) were selected for the formation of the simultaneous equations. For calibration curves, stock solutions of VAL and TZN were appropriately diluted to obtain VAL and TZN in the concentration range of 5-30 \(\mu\)g/ml. The absorbance of VAL and TZN were measured at 241 and 229 nm, and calibration curves were plotted. The absorptivities of both the drugs at both the wavelengths were determined.

The proposed methods were successfully used to estimate the amount of VAL and TZN, present in two of the marketed tablet formulations containing VAL and TZN. The assay values for both the tablets were found to be satisfied for VAL (X) and TZN (Y), respectively. Where \(A_1, A_2\) represents the absorbance of the mixture at \(\lambda_1\) and \(\lambda_2\), \(a_{\lambda_1}\) and \(a_{\lambda_2}\) denote absorptivities of X at \(\lambda_1\) and \(\lambda_2\), and \(a_{\lambda_1}\) and \(a_{\lambda_2}\) denote absorptivities of Y at \(\lambda_1\) and \(\lambda_2\), respectively. In this context, the above criteria was found to be satisfied for VAL (X) and TZN (Y), where \(\lambda_1\) is 239.6 nm and \(\lambda_2\) 241 nm for Q-absorbance method, and \(\lambda_1\) is 241 nm and \(\lambda_2\) 229 nm for simultaneous equation method.

Three wavelengths that could serve as isoabsorptive points were 222 nm, 239.6 nm, and 280.2 nm, as determined by evaluation of overlain spectra. By comparing the absorptivity of both the drugs at these wavelengths, 239.6 nm was found suitable for the analysis, since both the drugs gave same absorptivity at this wavelength. The other wavelength i.e. the \(\lambda_{\text{max}}\) of VAL selected at 241 nm. Hence 239.6 and 241 nm were selected for the formation of Q-absorbance equation.

In simultaneous equation method, two wavelengths i.e. \(\lambda_{\text{max}}\) of both the drugs were required. The spectra of TZN showed two distinct peaks, one at around 229 nm, and other at 371 nm. The former was selected for analysis of TZN. The \(\lambda_{\text{max}}\) of VAL was 241 nm, which was used for its estimation.

The proposed methods were successfully used to estimate the amount of VAL and TZN, present in two of the marketed tablet formulations containing VAL and TZN. The assay values for both the tablets were
The authors thank Blue Cross Laboratories Ltd., Mumbai, for the sample of pure tizanidine hydrochloride and Novartis India Ltd., Mumbai for the pure sample of Valdecoxib.

REFERENCES


TABLE 1: SUMMARY OF VALIDATION PARAMETERS

<table>
<thead>
<tr>
<th>Parameters</th>
<th>VAL (%)</th>
<th>Method 1</th>
<th>TZN (%)</th>
<th>Method 2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Linearity range (µg/ml)</td>
<td>2.5-15</td>
<td>1.3</td>
<td>2.5-15</td>
<td>1.3</td>
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<tr>
<td>Correlation coefficient (r²)</td>
<td>0.999a</td>
<td>0.997a</td>
<td>0.999b</td>
<td>0.997b</td>
</tr>
<tr>
<td>Intercept</td>
<td>0.00195a</td>
<td>0.00867a</td>
<td>0.00195a</td>
<td>0.00867a</td>
</tr>
<tr>
<td>Slope</td>
<td>0.0607a</td>
<td>0.0508a</td>
<td>0.0607a</td>
<td>0.0508a</td>
</tr>
<tr>
<td>Accuracy (%)</td>
<td>98.8-102</td>
<td>98.2-98.8</td>
<td>97.5-99.5</td>
<td>100.2-100.9</td>
</tr>
<tr>
<td>Repeatability (RSD)</td>
<td>0.472</td>
<td>0.0058</td>
<td>0.467</td>
<td>0.0051</td>
</tr>
<tr>
<td>% Recovery</td>
<td>98.5±1.8</td>
<td>102±0.3</td>
<td>99.5±1.8</td>
<td>101±0.2</td>
</tr>
</tbody>
</table>

Method 1 is Q-absorbance method while Method 2 is the Simultaneous equation method, RSD is the relative standard deviation while r² is the correlation coefficient, a; at 241 nm, b; at 239.6 nm, c; at 229 nm.

TABLE 2: ANALYSIS OF COMMERCIAL FORMULATIONS

<table>
<thead>
<tr>
<th>Method</th>
<th>Tablet A</th>
<th>Tablet B</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>% VAL</td>
<td>% TZN</td>
</tr>
<tr>
<td>Method 1</td>
<td>98.5±1.8</td>
<td>100±0.3</td>
</tr>
<tr>
<td>Method 2</td>
<td>98.4±1.8</td>
<td>101±0.2</td>
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</table>

Method 1 is Q-absorbance method while Method 2 is the Simultaneous equation method. Values for recovery are mean±SD for three determinations. Tablet A: Zulu-V (Unichem Ltd) and Tablet B: Valeron (CFL Pharmaceuticals), containing 2 mg tizanidine hydrochloride and 20 mg valdecoxib.

The authors thank Blue Cross Laboratories Ltd., Mumbai, for the sample of pure tizanidine hydrochloride and Novartis India Ltd., Mumbai for the pure sample of Valdecoxib.

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