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Determination of Etoricoxib in Pharmaceutical Formulations by HPLC Method

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A simple, precise and rapid RP-H PLC method was developed for the estimation of etoricoxib in pharmaceutical dosage forms. The method was carried out on a Kromasil 100, RP-C18 column using a mixture of acetonitrile: methanol: 10mM potassium dihydrogen phosphate (pH 3.0 adjusted with orthophosphoric acid). The detection was carried out at 234 nm using rofecoxib as an internal standard. The linearity was found to be 25 to 400 ng/injection with correlation coefficient of 0.9996. The intra-day and inter-day precision (% RSD) were in the range of 0.28 to1.6 and 0.35 to 1.39, respectively. The percentage recovery was found to be 99.52±1.51 to 100.59±1.16. The result of analysis of marketed formulation was found to be 100.32±0.96 to100.95±0.69. The proposed method was successfully applied for the estimation of etoricoxib in pharmaceutical dosage forms.

Etoricoxib, a newer cyclo-oxygenase-2 inhibitor, is mainly used in the management of osteoarthritis, rheumatoid arthritis and acute gouty arthritis1-4. Chemically, etoricoxib is a 5-chloro-6'-mehtyl-3-[4-(methylsulfonyl)phenyl]-2,3'-bipyridine, and is not yet official in any Pharmacopoeia. Its impurities studies and HPLC/MS-MS methods in matrix have been reported5-8. The availability of an HPLC method with high sensitivity and selectivity will be very useful for the estimation of etoricoxib in pharmaceutical dosage forms.

Etoricoxib working standard was a gift sample from M/S Sun Pharmaceutical Industries Ltd., Vapi, India, whereas rofecoxib was obtained from M/S Torrent Research Centre, Ahmedabad, India. Potassium dihydrogen phosphate (AR grade), methanol and acetonitrile (HPLC grade, E. Merck Limited, Bombay, India), orthophosphoric acid (LR grade, S. D. Fine-Chemicals Ltd., Mumbai, India) and triple distilled water were used in the study. Commercially available etoricoxib tablets claimed to contain 60, 90 and 120 mg of the drug were procured from the local market. Quantitative HPLC was performed on a isocratic high pressure liquid chromatograph (Shimadzu HPLC Class 10A series) with LC-10AS pumps, a multi wavelength UV/VIS detector (SPD-10A) and Kromasil 100 C-18 column (250 mm×4.6 mm i.d., particle size 5 µ). The HPLC system was equipped with the software Class CR-10 series version (Shimadzu).

The mobile phase was prepared by mixing acetonitrile, methanol and 10 mM potassium dihydrogen phosphate (pH 3.0 adjusted with 1% v/v ortho-phosphoric acid) in the ratio of 35:35:30 v/v. The mobile phase was filtered through a 0.45 µm membrane filter, degassed by ultrasonication for 15 min and pumped from the
solvent reservoir to the column at a flow rate of 1 ml/min, which yielded a column back pressure of 120-140 kg/cm². The run time was set at 8 min. The volume of injection loop was 20 µl. Prior to injection of the drug solutions, the column was equilibrated for at least 30 min with the mobile phase flowing through the systems. The eluents were monitored at 234 nm and the data were acquired, stored and analyzed with the software Class CR-10 series version.

Working standard solution of etoricoxib (100 µg/ml) was prepared by suitable dilution of the stock solution (1000 µg/ml in methanol) with the mobile phase. Different volumes (0.125, 0.25, 0.50, 1.00, 1.50, 2.00 ml) of working solution were taken in 10 ml volumetric flasks, rofecoxib solution (150 µl, 1000 µg/ml) was added to it as an internal standard and diluted up to mark with mobile phase to get concentrations of 1.25, 2.50, 5.0, 10.0, 15.0, 20.0 µg/ml. Each of these drug solutions (20 µl) was injected three times into the column and the peak area and retention time was recorded.

Twenty tablets were weighed to obtain the average tablet weight and powdered. A sample of the powdered tablets, equivalent to 25 mg of the etoricoxib was taken in a 25 ml volumetric flask containing 10 ml of methanol, sonicated it for 15 min and diluted to mark with methanol. The solution was filtered through a 0.45 µm membrane filter. An aliquot of solution (1.0 ml) was transferred to a 10 ml volumetric flask, rofecoxib solution (150 µl, 1000 µg/ml) was added as an internal standard and diluted with mobile phase to get a concentration of 100 µg/ml. From this, an aliquot (1.0 ml) was transferred to a 10 ml volumetric flask, and diluted with mobile phase to obtain 10 µg/ml of test concentration. The resulting solution (20 µl) was injected to HPLC system. All determinations were performed in triplicate.

The calibration curve of etoricoxib was constructed by plotting the ratio of the peak area of etoricoxib to the peak area of internal standard (Y) against concentration of etoricoxib (X). It was found to be linear with a correlation coefficient of 0.9996, the representative linear regression equation being $Y = 0.0092 + 0.1483X$. The relative standard deviations, based on the peak area ratios for triplicate injections were found to be 0.34 to 1.38% (Table 1). The developed method was validated for its intra-day and inter-day precision in the range of 25 to 400 ng/injection. The intera-day and inter-day (3 days, n= 3) precision were expressed as relative standard deviation in range of 0.28 to 1.36% and 0.35 to 1.39%, respectively (Table 2).

The HPLC method developed in the present study was used to quantify etoricoxib in tablet dosage forms. Etoricoxib tablets (60 mg, 90 mg and 120 mg) were analyzed. The obtained results are given in Table 3. The average drug content was found to be 100.67% of the labeled amount. No interfering peaks

### TABLE 1: CALIBRATION DATA OF THE PROPOSED HPLC METHOD

<table>
<thead>
<tr>
<th>Concentration of etoricoxib (ng/injection)</th>
<th>Mean peak area ratio (n=3)</th>
<th>% RSD</th>
</tr>
</thead>
<tbody>
<tr>
<td>25</td>
<td>0.1931</td>
<td>0.84</td>
</tr>
<tr>
<td>50</td>
<td>0.3946</td>
<td>0.34</td>
</tr>
<tr>
<td>100</td>
<td>0.7438</td>
<td>1.38</td>
</tr>
<tr>
<td>200</td>
<td>1.4520</td>
<td>0.51</td>
</tr>
<tr>
<td>300</td>
<td>2.2862</td>
<td>0.56</td>
</tr>
<tr>
<td>400</td>
<td>2.9544</td>
<td>0.98</td>
</tr>
</tbody>
</table>

Regression equation: $Y = 0.0092 + 0.1483X$ (r = 0.9996)

### TABLE 2: INTERDAY AND INTRADAY PRECISION OF PROPOSED METHOD

<table>
<thead>
<tr>
<th>Concentration of etoricoxib (ng/injection)</th>
<th>Intraday precision</th>
<th>Interday precision</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean (n=3)</td>
<td>%RSD</td>
</tr>
<tr>
<td>25</td>
<td>24.88</td>
<td>1.26</td>
</tr>
<tr>
<td>50</td>
<td>51.80</td>
<td>0.82</td>
</tr>
<tr>
<td>100</td>
<td>99.25</td>
<td>1.15</td>
</tr>
<tr>
<td>200</td>
<td>194.66</td>
<td>0.28</td>
</tr>
<tr>
<td>300</td>
<td>307.82</td>
<td>0.32</td>
</tr>
<tr>
<td>400</td>
<td>392.93</td>
<td>0.78</td>
</tr>
</tbody>
</table>

### TABLE 3: ANALYSIS OF PHARMACEUTICAL DOSAGE FORMS BY PROPOSED METHOD

<table>
<thead>
<tr>
<th>Dosage forms code</th>
<th>Labeled amount (mg/tab)</th>
<th>Amount found (mg/tab)</th>
<th>% Purity*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tablet-1</td>
<td>60</td>
<td>60.57±0.42</td>
<td>100.95±0.69</td>
</tr>
<tr>
<td>Tablet-2</td>
<td>90</td>
<td>90.29±0.86</td>
<td>100.32±0.96</td>
</tr>
<tr>
<td>Tablet-3</td>
<td>120</td>
<td>120.88±0.41</td>
<td>100.73±0.34</td>
</tr>
</tbody>
</table>

Table-1 stands for tablet of Dr Reddy Lab., Hyderabad (brand name-Retoz, strength-60 mg), tablet-2 stands for tablet of Wockhardt Limited, Mumbai (brand name- Etoxix-90, strength-90 mg) and tablet-3 stands for tablet of Torrent Pharmaceuticals Ltd., Ahmedabad (brand name-Torcoxia-120, strength-120 mg). *Mean±SD of three determinations

### TABLE 4: RECOVERIES OF ETORICOXIB TABLETS BY PROPOSED METHOD

<table>
<thead>
<tr>
<th>Concentration of etoricoxib (ng/injection)</th>
<th>Amount found (ng/injection)</th>
<th>% Recovery*</th>
</tr>
</thead>
<tbody>
<tr>
<td>150</td>
<td>201.18±0.12</td>
<td>100.59±1.16</td>
</tr>
<tr>
<td>150</td>
<td>299.49±0.08</td>
<td>99.83±0.55</td>
</tr>
<tr>
<td>150</td>
<td>398.06±0.30</td>
<td>99.52±1.51</td>
</tr>
</tbody>
</table>

*Mean±SD of three determinations
were found in the chromatogram, indicating that the tablet excipients did not interfere with the estimation of the drug by the proposed HPLC method. Also, when a known amount of the drug solution was added to a powdered sample of the tablet dosage form and subjected to an estimation of the drug by the proposed method, there was a high recovery (Table 4) of etoricoxib (99.98±0.55%), indicating that the proposed procedure for the estimation of etoricoxib in the tablet dosage forms is accurate. The results of the study showed that the proposed RP-HPLC method for analysis of etoricoxib in pharmaceutical dosage forms is simple, rapid, precise and accurate. It will be useful for the determination of etoricoxib in its pharmaceutical dosage forms.

ACKNOWLEDGEMENTS

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