Original Research Article

Spectrophotometric first order derivative method for simultaneous determination of etoricoxib and paracetamol in tablet dosage form


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Paracetamol
UV spectrophotometry
First order derivative method
ICH guideline

ABSTRACT

This work was aimed to develop a new, sensitive, accurate, precise, and simple UV spectrophotometric method for estimating the Etoricoxib and Paracetamol in tablet dosage form. First order derivative simultaneous estimation was carried out by using the UV-visible double beam spectrophotometer. Etoricoxib and Paracetamol exhibited absorbance at working wavelength 248 nm (Zero crossing point of Paracetamol) and 258.4 nm (Zero crossing point of Etoricoxib), respectively, using methanol as a solvent. Linearity was found 1-8 μg/mL for Etoricoxib and 5.42-43.3 μg/mL for Paracetamol. Accuracy was obtained between 98.96 to 101.38% for Etoricoxib and 98.38 to 101.64% for Paracetamol. LOD an LOQ was found to be 0.122 μg/mL and 0.248 μg/mL for Etoricoxib and 0.075 μg/mL and 0.152 μg/mL for Paracetamol. The developed method was validated as per ICH Guideline. The results confirmed that the proposed method is suitable for the routine analysis for the estimation of Etoricoxib and Paracetamol in tablet dosage form.

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Etoricoxib (ETC) is 5-chloro-3-(4-methanesulfonylphenyl)-2-(6-methylpyridin-3-yl)pyridine [1]. It is a COX-2 selective inhibitor. Etoricoxib selectively inhibits isoform 2 of cyclo-oxygenase enzyme (COX-2), preventing production of prostaglandins (PGs) from arachidonic acid. Paracetamol (PCM) is N-(4-hydroxyphenyl)acetamide[2]. It increases the pain threshold by inhibiting two isoforms of cyclooxygenase, COX-1 and COX-2, which are involved in prostaglandin (PG) synthesis. Prostaglandins are responsible for eliciting pain sensations. Acetaminophen does not inhibit cyclooxygenase in peripheral tissues and, therefore, has no peripheral anti-inflammatory effects. Structures of the Etoricoxib and Paracetamol are presented in Figure 1 [3-4].
Etoricoxib in combination with Paracetamol is widely used in arthritis associated with fever condition in aged patients because Etoricoxib has anti-inflammatory, analgesic action while Paracetamol has antipyretic-analgesic action [5]. Etoricoxib and Paracetanol is available in tablet dosage form of 60 mg and 325 mg, respectively. It was found that, various analytical methods are available such as Simultaneous equation method [5,6], Q absorbance method [5,6], RP-HPLC [7] and stability indicating hplc study [8] were reported for simultaneous estimation of Etoricoxib and Paracetamol. Also alone and in combination with others drugs several techniques are available like simultaneous equation [9], HPLC Assay for Etoricoxib alone[10] and UV method for paracetamol [11], Dual wavelength method for Paracetamol and Nabumetole[12], Vierodt's Method (Simultaneous equation) for Lornoxicam and Paracetamol[13], Vierodt's Method (Simultaneous equation) Nabumetone and Paracetamol[14], Q Analysis for Nabumetone and Paracetamol[15], RP-HPLC method for Paracetamol, Ambroxol hydrochloride, Levocetirizine hydrochloride Phenylephrine hydrochloride[16], RP-HPLC for Zaltoprofen and Paracetamol[17] Stability indicating method for Thiocholchicoside and Etoricoxib[18] is available. However, no first order derivative method was reported using actual marketed dose ratio(30 mg, 325 mg) of 1:5.41 so far. Thus, in present study it was decided to perform the first order derivative method in actual ratio of marketed dosage form and method was validated in compliance with ICH guideline (Q2 R1) [19]. First order derivative spectroscopy was more selective, accurate, precise and simple method for the estimation.

**Material and Method**

**Chemicals and reagents**

Etoricoxib and Paractamol API was provided by B K Mody Govt. Pharmacy College. Methanol (HPLC grade) was used as a solvent of Rankem Pvt. Ltd. UV Visible spectrophotometer (UV-1800 Shimadzu) used, data were processed using UV probe(2.60) software.

**Preparation of standard stock solution**

Standard stock solution of Etoricoxib and Paracetamol 65 μg/mL and 100 μg/mL, respectively, were prepared in methanol used as diluents.

**Selection of wavelength**

By appropriate dilutions of the standard stock solution 6 μg/mL of Etoricoxib and 32.5 μg/mL of Paracetamol were separately prepared and scanned in the UV range 200–400 nm. The overlain zero-order absorption spectra of both drugs were obtained. These absorbance spectra were converted to first order derivative spectra by using UV probe software. After observing overlay firstorder derivative spectra with scaling factor 1 and Δλ 8 for Etoricoxib and Paracetamol, zero crossing points of drugs were selected. The first wavelength selected was 258.4 nm (zero crossing of Etoricoxib), where Paracetamol showed considerable absorbance. The second wavelength selected was 248 nm (zero crossing of Paracetamol), where Etoricoxib showed considerable absorbance.
Method validation

**Linearity** The standard solution was dilute up to obtain concentration of 1, 2, 3, 4, 5, 6, 7, 8 µg/mL for Etoricoxib and 5.42, 10.83, 16.25, 21.7, 27.1, 32.5, 37.9 and 43.3 µg/mL, respectively, from the above stock solution.

**Specificity**

Specificity was performed under 6 replicates at concentration 2 µg/mL of Etoricoxib and 10.83 µg/mL with and without addition of excipients to check the interference of excipient.

**LOD/LOQ**

The limit of detection (LOD) and limit of quantification (LOQ) were calculated by using formula. Calibration curve was repeated for five times and standard deviation (SD) of the intercepts was calculated.

**Accuracy**

The accuracy of the method was carried out by spiking triplicate at three different concentration levels 50, 100 and 150% (3, 4 and 5 µg/mL for Etoricoxib and 16.25, 21.7 and 27.1 µg/mL for Paracetamol) to placebo. The accuracy of method was evaluated by calculating the percentage recovery.

**Precision**

Repeatability was performed under 6 replicates at concentration of 2 µg/mL of Etoricoxib and 10.83 µg/mL. Intra-day and inter-day variations of Etoricoxib and Paracetamol were performed in triplicate at three different concentration levels 50, 100, 150% (1, 2, and 3 µg/mL) for Etoricoxib and (5.41, 10.83 and 16.25 µg/mL) for Paracetamol. The results were presented in the form of RSD.

**Robustness**

The robustness of method was established by introducing small change in experimental condition like wavelength. The changes made in wavelength ± 0.5 nm (248, 246, and 251 nm for Etoricoxib and 258.4, 256.04, 261.04 nm for Paracetamol), respectively. The robustness of the method was evaluated by calculating RSD.

**Assay of tablet dosage form**

Accurately weighed twenty tablets containing Etoricoxib 60 mg and Paracetamol 325 mg with excipients. Than crushed them into a fine powder. From the powder of twenty tablets accurately weighed powder equivalent to 2 mg and 10.83 mg of Etoricoxib and Paracetamol respectively. Then, it was transferred to a 100 mL volumetric flask and
add 60 mL diluents to dissolve it properly and make up volume up to 100 mL, then passed it through watman filter paper. From this solution made 2 µg/mL and 10.83 µg/mL solution of Etoricoxib and Paracetamol, respectively.

**Results and Discussion**

**Linearity**

The calibration curve obtained for Etoricoxib and Paracetamol in the range of 1-8 µg/mL and 5.42-43.3 µg/mL. The correlation coefficient of Etoricoxib and Paracetamol was found to be 0.9985 and 0.9986, respectively. This method was found to be linear. The spectra and graph for linearity are demonstrated in Figure 4 and 5.

![Figure 4. Linearity spectra of (A) ETC (B) PCM](image)
**Specificity:** Excipient interference is not observed at the working wavelength of 248 nm Etoricoxib and 258.04 nm for Paracetamol, the method presented in this study is specific for drugs. % interference was found less than 0.5%. The result are presented in Table 1.

**Table 1.** Specificity study of Etoricoxib and Paracetamol.

<table>
<thead>
<tr>
<th>Conc (μg/mL) (n=6)</th>
<th>Absorbance</th>
<th>Concentration (μg/mL)</th>
<th>Difference</th>
<th>% Interference</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>With excipient</td>
<td>Without excipient</td>
<td>With excipient</td>
<td>Without excipient</td>
</tr>
<tr>
<td>ETC 2</td>
<td>0.0050 ± 0.0015</td>
<td>2.00 ± 0.050</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>PCM 10.83</td>
<td>0.0410 ± 0.0020</td>
<td>10.97 ± 0.030</td>
<td>0.020 ± 0.015</td>
<td>0.277 ± 0.15</td>
</tr>
</tbody>
</table>

**LOD and LOQ:** LOD and LOQ of Etoricoxib and Paracetamol were determined using average of slope and standard deviation of intercepts. LOD and LOQ were found to be 0.122 μg/mL and 0.248 μg/mL for Etoricoxib and 0.075 μg/mL and 0.152 μg/mL for the Paracetamol, respectively.

**Accuracy:** % recovery for Etoricoxib and Paracetamol was found in range of 98.38 to 101.64 % and this method is accurate. Thus data of accuracy is tabulated in Table 2.
Spectrophotometric first order derivative method for...

**Precision:** Repeatability and intermediate precision express in term of RSD. Absorbance were determined and results found satisfactory for RSD < 2% for both intra-day and inter-day precision and including repeatability study. Thus precision is acceptable as shown in Table 3 and 4.

**Table 3.** Repeatability study of ETC and PCM.

<table>
<thead>
<tr>
<th>Drug</th>
<th>Concentration (μg/mL) (n=6)</th>
<th>Conc. found (μg/mL) Mean ± SD</th>
<th>RSD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Etoricoxib</td>
<td>2</td>
<td>2.04 ± 0.016</td>
<td>0.79</td>
</tr>
<tr>
<td>Paracetamol</td>
<td>10.83</td>
<td>11.07 ± 0.07</td>
<td>0.67</td>
</tr>
</tbody>
</table>

**Table 4.** Intermediate study of ETC and PCM.

<table>
<thead>
<tr>
<th>Drug</th>
<th>Level (%)</th>
<th>Absorbance (Mean ± SD)</th>
<th>RSD</th>
<th>Absorbance (Mean ± SD)</th>
<th>RSD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Etoricoxib</td>
<td>50</td>
<td>0.0024 ± 0</td>
<td>1.96</td>
<td>0.0025 ± 0</td>
<td>1.31</td>
</tr>
<tr>
<td></td>
<td>100</td>
<td>0.0044 ± 0</td>
<td>1.73</td>
<td>0.0043 ± 0</td>
<td>1.94</td>
</tr>
<tr>
<td></td>
<td>150</td>
<td>0.0066 ± 0</td>
<td>0.01</td>
<td>0.0065 ± 0</td>
<td>0.01</td>
</tr>
<tr>
<td>Paracetamol</td>
<td>50</td>
<td>0.0225 ± 0</td>
<td>0.37</td>
<td>0.0224 ± 0</td>
<td>0.53</td>
</tr>
<tr>
<td></td>
<td>100</td>
<td>0.0413 ± 0</td>
<td>1.68</td>
<td>0.0414 ± 0</td>
<td>0.36</td>
</tr>
<tr>
<td></td>
<td>150</td>
<td>0.0622 ± 0</td>
<td>0.00</td>
<td>0.0617 ± 0</td>
<td>0.00</td>
</tr>
</tbody>
</table>

**Robustness:** By making a deliberate change in wavelength, RSD of absorbance was found to be less than 2%, specifying that the method was robust. The result was represented in Table 5.

**Table 5.** Robustness study for Etoricoxib and Paracetamol.

<table>
<thead>
<tr>
<th>Conc. (μg/mL)</th>
<th>Absorbance at different (For Etoricoxib)</th>
<th>Conc. (μg/mL)</th>
<th>Absorbance at different (For Paracetamol)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>248 nm</td>
<td>247.5 nm</td>
<td>248.5 nm</td>
</tr>
<tr>
<td></td>
<td>0.0048</td>
<td>0.0050</td>
<td>0.0048</td>
</tr>
<tr>
<td></td>
<td>0.0049</td>
<td>0.0050</td>
<td>0.0049</td>
</tr>
</tbody>
</table>
| Mean ± 0      | 0.0048 | 0.0049 | 0.0047 | 0.0410 ± 0.0412 ± 0.0411 ± 0.
| RSD 1.1945    | 1.1624 | 1.2197 | RSD 0.3722 | 0.7409 | 0.5060 |

**Assay of tablet dosage form:** % drug content of tablet dosage form was found between 98.60-101.23%. The data is given in Table 6.
Table 6. Assay study of synthetic mixture.

<table>
<thead>
<tr>
<th>Conc. µg/mL (Mean ± SD)</th>
<th>Absorbance (n=5) (Mean ± SD)</th>
<th>Conc. Found (µg/mL) (Mean ± SD)</th>
<th>% Drug Content</th>
</tr>
</thead>
<tbody>
<tr>
<td>ETC</td>
<td>PCM</td>
<td>ETC</td>
<td>PCM</td>
</tr>
<tr>
<td>(2:10.83)</td>
<td>0.0048 ± 0.0001</td>
<td>0.0410 ± 0.0001</td>
<td>1.96 ± 0.066</td>
</tr>
<tr>
<td></td>
<td></td>
<td>10.95 ± 0.045</td>
<td>98.60</td>
</tr>
<tr>
<td></td>
<td></td>
<td>101.23</td>
<td></td>
</tr>
</tbody>
</table>

Conclusion

The proposed method for the spectrophotometric determination of the Etoricoxib and Paracetamol is simple, rapid, sensitive, reproducible, robust and specific with good accuracy and precision. As there is no interference of excipient at the working wavelength, it is very fast, with good reproducibility and good response. It also allows reliably the analysis of the Etoricoxib and Paracetamol in tablet dosage form.

Conflict of interest

We have no conflicts of interest to disclose.

References
