ABSTRACT
A novel analytical UV spectrophotometric method has been developed in the present research work for simultaneous estimation of Lornoxicam and Paracetamol in pharmaceutical dosage form. In the proposed Absorption correction method, linearity range was observed in the concentration range of 1-6 µg/ml for Lornoxicam and 12-32 µg/ml for Paracetamol with r² values 0.9990 and 0.9987 respectively. The wavelengths selected were 376 nm and 257 nm, for Lornoxicam and Paracetamol in 0.1 N Sodium Hydroxide respectively. The limit of detection for Lornoxicam and Paracetamol were found to be 0.018 µg/ml and 0.027 µg/ml respectively. Limit of quantification were found to be 0.055 µg/ml and 0.084 µg/ml for Lornoxicam and Paracetamol respectively. Validation of the proposed method was carried out for its accuracy and precision according to ICH guidelines. The accuracy of the method was checked by recovery experiment performed at three different levels of 80%, 100% and 120%. The percentage recoveries of Lornoxicam and Paracetamol were found to be in the range of 100.24-100.95% and 99.25-99.95% respectively. The low values of % relative standard deviation (RSD) are indicative of the accuracy and reproducibility of the method. The precision of the method was studied as an intra-day, inter-day variations and repeatability. The % RSD value less than 2 indicate that the method is precise. The method was found to be rapid, simple, accurate and precise.
KEYWORDS: Lornoxicam, Paracetamol, Absorption correction UV spectrophotometric method, validation.

INTRODUCTION
Lornoxicam belongs to the chemical class oxicams, which includes piroxicam, tenoxicam and meloxicam. It has non steriodial anti-inflammatory activity. It is used to treat inflammatory diseases of the joints, osteoarthritis, pain after surgery, and sciatica. It works by blocking the action of cyclooxygenase, an enzyme involved in the production of chemicals, including some prostaglandins in the body.[1,2] Chemically, Lornoxicam (LOR) is (3E)-6-chloro-3-[hydroxy(pyridine-2-ylamino)methylene]-2-methyl-2,3-dihydro-4H-thieno[2,3-e][1,2]thiazin-4-one-1,1-dioxide.[3] Lornoxicam is not official in any Pharmacopoeia, but listed in the Merck Index.[4] Few analytical methods for determination of lornoxicam using UV method,[5,6] Bio-analytical method,[7] spectro-fluorimetry method,[8] HPLC,[9,10] RP-HPTLC,[11,12] stability indicating HPLC method[13] have been reported.

Paracetamol is chemically 4-hydroxy acetanilide. It is a centrally and peripherally acting non-opioid analgesic and antipyretic.[14,15] Paracetamol is official in I.P,[16] B.P,[17] and USP.[18] Literature survey reveals that there are UV method[19,20] and UV and HPTLC methods of Paracetamol with other drugs[21,22] have been reported for the estimation of Paracetamol in Pharmaceutical formulations.

Extensive Literature survey reveals that there are some UV method, i.e. simultaneous equation method and absorbance Q ratio method,[23,24] RP- HPLC methods[25] have been reported for simultaneous estimation of Lornoxicam and Paracetamol in combined dosage form.

However, Absorption correction method has not been reported yet for simultaneous estimation of both drugs in combination. This paper presents simple, rapid, reproducible and economical method for the simultaneous analysis estimation of both the drugs from
pharmaceutical dosage form. The proposed method was optimized and validated in accordance with International Conference on Harmonization (ICH) guidelines.

MATERIALS AND METHODS

Instrumentation: UV - Visible spectrophotometer Shimadzu-1800

Chemicals and reagents: Lornoxicam and Paracetamol working standards were procured from Stallion Laboratories Pvt. Ltd., Ahmedabad and Dolphin Pharmaceutical Ltd, Surat. The tested pharmaceutical marketed formulation (Lornoxi-P - Lornoxicam 8mg, paracetamol 325mg) were procured from commercial pharmacy. Reagents were of suitable analytical grade.

Marketed tablet preparation used was

<table>
<thead>
<tr>
<th>Trade Name</th>
<th>Company Name</th>
<th>Dose</th>
<th>Batch Number</th>
<th>Manufactured Date</th>
<th>Expiry Date</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lornoxi-P</td>
<td>Hetero Labs Limited</td>
<td>Lornoxicam-8mg,</td>
<td>3114306</td>
<td>May2014</td>
<td>Apr2016</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Paracetamol-325mg.</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Preparation of standard solution

Accurately weighed 100mg quantity of Lornoxicam and Paracetamol were transferred into different 100 ml volumetric flasks, dissolved and diluted up to mark with 0.1N NaOH to get 1000μg/ml. From this solution 100μg/ml of Lornoxicam and Paracetamol solutions were prepared by diluting 10 ml of 1000μg/ml solutions to 100 ml with 0.1N NaOH.

Preparation of working standard solutions

The standard solutions were further diluted to get working standard solutions of analytes in the concentration range of 1-6 μg/ml and 12-32 μg/ml for Lornoxicam and Paracetamol respectively.

Analysis of Tablet Formulation

Twenty tablets were weighed and crushed to fine power. The amount of powder equivalent to 325mg of Paracetamol (8 mg of Lornoxicam) was weighed and transferred to 100ml volumetric flask. The drug content was shaken with 25ml of 0.1N NaOH and was kept in ultra sonicator for 15 min. Finally, the volume was made up to the mark with 0.1N NaOH. The solution was filtered through whatman filter paper No.41. The filtrate was further diluted to obtain 0.8 µg/ml and 32.5 µg/ml concentrations of Lornoxicam and paracetamol respectively. The spectras were scanned in the range of 400-200 nm.
Validation Parameters

1. Linearity & Range
Linearity was found in the range of 1-6µg/ml for Lornoxicam and 12-36µg/ml for Paracetamol. Co-relation Co-efficient was found to be 0.999 and 0.9987 respectively.

2. Precision
The precision expressed as standard deviation or relative standard deviation.

Intraday precision
Lornoxicam and Paracetamol were taken in a ratio was analyzed at three levels of concentration for three times in a day. Absorbances of the solutions were measured. The % RSD for Lornoxicam and Paracetamol were found to be less than 2% for the method.

Interday precision
Lornoxicam and Paracetamol were taken in a ratio was analyzed at three levels of concentration for three consecutive days. Absorbances of the solutions were measured. The % RSD for Lornoxicam and Paracetamol were found to be less than 2% for the method.

3. Accuracy
The accuracy of the method was established using recovery technique i.e. external standard addition method. The known amount of standard was added at three different levels to preanalyzed sample. Each determination was performed in triplicate. The result of recovery study is presented in Table.

4. Sensitivity
The sensitivity of measurements of FH by the use of the proposed method was estimated in terms of the limit of quantification (LOQ) and limit of detection (LOD).

Formula:

$$\text{LOD} = 3.3 \times M/S$$

$$\text{LOQ} = 10 \times M/S$$

Where, M is the standard deviation of y-intercepts of regression lines and S is the slope of the calibration curve.

5. Ruggedness
Ruggedness of the method was determined by analysis of aliquots from homogeneous slot by two analyst using same operational and environmental conditions.
RESULT AND DISCUSSION
In this Absorption correction method overlain spectra showed that Paracetamol has zero absorbances at 376nm whereas Lornoxicam has substantial absorbance. Thus Lornoxicam was estimated directly at 376nm without interference of Paracetamol. Both the drugs Lornoxicam and Paracetamol obeyed linearity range 1-6µg/ml and 12-32µg/ml respectively and correlation coefficient ($r^2$) were found to be 0.9990 and 0.9989 for Lornoxicam at 376nm and 257 nm respectively and 0.9987 for Paracetamol at 257nm. The percentage purity of drugs in combined dosage form was found to be 100.91% for Lornoxicam and 100.12% for Paracetamol. The accuracy of the method was determined by performing recovery study by standard addition method. The % recoveries were found within 100.24-100.95% and 99.25-99.95% for Lornoxicam and Paracetamol respectively. The experiment was repeated three times in a day for intra-day and on three different days for inter-day precision. The method was found to be precise as % RSD for intra-day and inter-day precision were < 2. The limit of detection for Lornoxicam and Paracetamol were found to be 0.0184µg/ml and 0.0278µg/ml respectively. Limit of quantification were found to be 0.055µg/ml and 0.0843µg/ml for Lornoxicam and Paracetamol respectively.

Selection of wavelength for Absorption correction method
In this Absorption correction method overlain spectra showed that Paracetamol has zero absorbances at 376nm whereas Lornoxicam has substantial absorbance. Thus Lornoxicam was estimated directly at 376nm without interference of Paracetamol.

Figure 1: Absorption correction method overlain spectra of Lornoxicam (1-6 µg/ml) and Paracetamol (12-36 µg/ml), at 257nm and 376nm.
Figure 2: calibration curve for Lornoxicam (1-6 µg/ml) at 376nm.

Figure 3: calibration curve for Lornoxicam (1-6 µg/ml) at 257nm.

Figure 4: calibration curve for Paracetamol (12-36 µg/ml) at 257nm.
Table 1: Accuracy studies: % Recovery of Lornoxicam and Paracetamol using Absorption correction method.

<table>
<thead>
<tr>
<th>Assay Level</th>
<th>Tablet content taken eq. to (mg)</th>
<th>Standard added (mg)</th>
<th>Total drugs recovered (mg)</th>
<th>% Recovery of standard added (n=3)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Lor</td>
<td>Pcm</td>
<td>Lor</td>
<td>Pcm</td>
</tr>
<tr>
<td>Blank</td>
<td>8</td>
<td>325</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>80%</td>
<td>8</td>
<td>325</td>
<td>6.4</td>
<td>260</td>
</tr>
<tr>
<td>100%</td>
<td>8</td>
<td>325</td>
<td>8</td>
<td>325</td>
</tr>
<tr>
<td>120%</td>
<td>8</td>
<td>325</td>
<td>9.6</td>
<td>390</td>
</tr>
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</table>

Table 2: Precision study: Intra-Day and Inter-Day Precision

<table>
<thead>
<tr>
<th>Drug</th>
<th>Concentration [µg/ml]</th>
<th>Amount found [µg/ml n=3]</th>
<th>% R.S.D.</th>
<th>Inter-day Amount found [µg/ml n=3]</th>
<th>% R.S.D.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lor</td>
<td>2</td>
<td>99.79±1.10</td>
<td>1.109</td>
<td>99.82±1.08</td>
<td>1.085</td>
</tr>
<tr>
<td></td>
<td>3</td>
<td>99.79±1.09</td>
<td>1.100</td>
<td>100.12±1.21</td>
<td>1.216</td>
</tr>
<tr>
<td></td>
<td>4</td>
<td>99.19±0.71</td>
<td>0.725</td>
<td>99.42±0.94</td>
<td>0.947</td>
</tr>
<tr>
<td>Pcm</td>
<td>16</td>
<td>99.81±0.60</td>
<td>0.606</td>
<td>99.61±0.47</td>
<td>0.475</td>
</tr>
<tr>
<td></td>
<td>20</td>
<td>99.89±0.42</td>
<td>0.422</td>
<td>99.75±0.52</td>
<td>0.523</td>
</tr>
<tr>
<td></td>
<td>24</td>
<td>98.91±0.79</td>
<td>0.796</td>
<td>98.99±0.23</td>
<td>0.235</td>
</tr>
</tbody>
</table>

Table 3: LOD and LOQ

<table>
<thead>
<tr>
<th>Absorption correction method</th>
<th>Lornoxicam</th>
<th>Paracetamol</th>
</tr>
</thead>
<tbody>
<tr>
<td>LOD (µg/ml)</td>
<td>0.01840</td>
<td>0.02783</td>
</tr>
<tr>
<td>LOQ(µg/ml)</td>
<td>0.05576</td>
<td>0.08439</td>
</tr>
</tbody>
</table>

Table 4: Assay: Analysis of pharmaceutical tablet dosage form

<table>
<thead>
<tr>
<th>Tablet content taken eq. to (mg)</th>
<th>Amount found (mg)</th>
<th>Assay (% Estimated) (n=3)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lornoxicam</td>
<td>Paracetamol</td>
<td>Lornoxicam</td>
</tr>
<tr>
<td>8</td>
<td>325</td>
<td>8.06</td>
</tr>
</tbody>
</table>

CONCLUSION

The validated UV method proved to be simple, less expensive, fast, accurate, and precise and thus can be used for routine analysis of Lornoxicam and Paracetamol in tablet dosage forms.

ACKNOWLEDGEMENTS

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