SIMULTANEOUS ESTIMATION OF CEFIXIME AND OFLOXACIN IN TABLET DOSAGE FORM

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INTRODUCTION

Cefixime (CFX) is an oral third generation cephalosporin antibiotic. Chemically, it is (6R,7R)-7-{[2-{[2-amino-1,3-thiazol-4-yl]-2(carboxymethoxyimino) acetyl]amino}-3-ethenyl 8-oxo-5-thia-1-azabicyclo-[4.2.0]oct-2-ene-2-carboxylic acid, clinically used in the treatment of susceptible infections including gonorrhea, otitis media, pharyngitis, lower respiratory tract infections such as bronchitis, and urinary tract infections. Ofloxacin (OFL) is a fluoroquinolone derivative. Chemically, it is (+)-9-fluoro-3, 3-dihydro-3-methyl-10-(4-methyl-1-piperazinyl)-7-oxo-7H-pyrido-[1,2,3-de]-1,4-benzoxazin-6-carboxylic acid. Literature review reveals that Cefixime can be estimated spectrophotometrically and Ofloxacin can be estimated spectrophotometrically in combination with other drugs. One method is reported for estimation of Cefixime and Ofloxacin in combination by UV – Visible spectroscopy using methanol as solvent. One method is also reported for estimation of Cefixime and Ofloxacin in combination by using RP-HPLC. So here an attempt has been made to develop simple, accurate, rapid and economic method for simultaneous estimation of Cefixime and Ofloxacin from tablet dosage forms using UV – Visible spectroscopy along with its degradation studies.

EXPERIMENTAL

Instrumentation

The instrument used in the present study was SYSTRONICS double beam UV/Visible spectrophotometer (Model 2201) with slit width fixed at 2 nm. All weighing was done on electronic balance (Model Shimadzu AY-120).

REAGENTS AND CHEMICALS

Analytically pure sample of CFX and OFL was kindly supplied by Torrent Pharmaceuticals Limited and used as such without further purification. The pharmaceutical dosage form used in this study was a Nicholas Piramal India Limited labeled to contain 200 mg of CFX and 200 mg of OFL.

Solvent

Methanol (AR Grade) was used as solvent, procured from Universal Laboratories Private limited, Mumbai.
Stock Solution
100 mg of Cefixime (CFX) and 100 mg of Ofloxacin (OFL) were weighed separately and transferred to two separate 100 ml volumetric flasks. Each drug was dissolved in 20 ml of methanol and shaken gently for 10 min. The volume was made up to the mark with 0.2 M sodium hydroxide and the final strength obtained was 100 μg/ml.

Procedure

Spectral characteristics of CFX and OFL
Solutions of CFX and OFL (100 μg/ml, each), were prepared separately by appropriate dilution of standard stock solution. Both the solutions were scanned in the spectrum mode from 400 nm to 200 nm. Overlay absorption spectra were recorded (Fig. 1).

Preparation of calibration curves
Appropriate dilutions of the standard stock solution were done separately to get 10, 20, 30, 40, 50, 60, 70, 80, 90 and 100μg/ml of CFX and OFL, respectively. The absorption spectra of all solutions were recorded between 400 nm to 200 nm. Overlay spectra were recorded (Fig. 1).

Determination of Absorptive Value of CFX and OFL
Appropriate dilutions of the standard stock solution were done to get 10 μg/ml of each CFX and OFL, respectively. The absorbances were measured for CFX and OFL at 224.0 nm (λmax of CFX), 384.0 nm (λmax of OFL) and 261.6 nm (iso-absorptive point). Beer’s lamberts range for CFX and OFL were selected and working calibration curves of both the drugs were plotted separately.

Application of the proposed method for the determination of CFX and OFL in tablets
Twenty tablets were weighed and average weight was calculated. The tablets were crushed to obtain fine powder. Tablet powder equivalent to 40 mg of CFX was transferred to 100.0 ml volumetric flask, methanol added, ultrasonicated for 10 minutes and volume was made-up to the mark with 0.2 M sodium hydroxide solution and. The solution was then filtered through a Whatmann filter paper (No. 41). The filtrate was further diluted with distilled water to obtain 40μg/ml of CFX and 40μg/ml of OFL. The concentration of both CFX and OFL were determined by measuring the absorbance of the sample at 224.0 nm, 284.0 nm (method A, simultaneous equation method) and at 284.0 nm and 261.6 nm (method B, absorbance ratio method). Concentration of sample solution was determined by using following equations:

Method A- Vierodt’s Method of simultaneous equation
A set of two simultaneous equations obtained by using mean absorptivity values are given below

\[ A1 = 27250 \text{CCEF } + 32825 \text{COFL} \]
\[ A2 = 20850 \text{CCEF } + 46650 \text{COFL} \]

Where A1 and A2 are absorbance of the sample at 224.0 nm and 284.0 nm respectively, 27250 and 20850 are the absorptivity values of CFX at 224.0 nm and 284.0 nm respectively. Similarly 32825 and 46650 are the absorptivity value of OFL at 224.0 and 284.0 nm respectively. CCEF is the concentration of CFX and COFL is the concentration of the OFL.

Method B- The Graphical Absorption Ratio Method (Q-Analysis)
From the following set of equations the concentration of each component in sample can be calculated.

For Cefixime:

\[ C_x = \frac{Q_m - Q_y}{Q_x - Q_y} \cdot A_1 \]

For Ofloxacin:

\[ C_y = \frac{Q_m - Q_x}{Q_y - Q_x} \cdot A_1 \]

Where,

\[ C_x = \text{Concentration of CFX}, \]

\[ C_y = \text{Concentration of OFL}, \]

\[ A_1 = \text{Absorbance of sample at iso-absorptive wavelength 261.6 nm}, \]
a = Mean absorptivity of CFX and OFL at iso-absorptive wavelength 261.6 nm,

\[
Q_m = \frac{\text{Absorbance of sample solution at 284.0 nm}}{	ext{Absorbance of sample solution at 261.6 nm}}
\]

\[
Q_x = \frac{\text{Absorptivity of CFX at 284.0 nm}}{\text{Absorptivity of CFX at 261.6 nm}}
\]

\[
Q_y = \frac{\text{Absorptivity of OFL at 284.0 nm}}{\text{Absorptivity of OFL at 261.6 nm}}
\]

Linearity Studies
Linearity studies were carried out at different level of concentrations. Both the drugs obey Beer's law in the concentration range 10-80 μg mL\(^{-1}\). Results are reported in table 1.

Recovery studies
The accuracy of the proposed method was checked by recovery studies, by addition of standard drug solution to pre analyzed sample solution at three different concentration levels (80%, 100%, and 120%) within range of linearity for both the drugs. Results are reported in table 2.

Degradation studies
Degradation studies were carried out on CFX and OFL. Results are reported in table 3.

RESULT AND DISCUSSION
Method I: Simultaneous Equation Method
UV-spectrophotometric method using simultaneous equation was developed. CFX showed absorbance maxima at 234 nm and OFL at 296.0 nm. Linearity was observed in the concentration rage of 10 - 80 μg/ml for CFX and OFL correlation coefficient was found to be 0.993 and 0.98 at 284 nm and 224 nm respectively. The proposed method was applied for pharmaceutical formulation and % label claim for CFX and OFL was found to be 99.9 and 99.96, respectively. The method is accurate and precise and can be used for routine pharmaceutical analysis.

Method II: Absorbance Ratio Method
UV-spectrophotometric method by using absorbance ratio method was developed. Absorbances selected were 261.6 nm (isoabsorptive point) and 284 nm (λ max of Ofloxacin) Linearity was observed in the concentration range of 10 - 80 μg/ml and correlation coefficient was found to be 0.992 and 0.990 respectively. The proposed method was applied for pharmaceutical formulation; % label claim for CFX and OFL was found to be 99.63 and 100.24, respectively. The low % RSD indicates method is accurate and precise.

CONCLUSION
The methods discussed in the present work provide a convenient and accurate way for simultaneous analysis of Cefixime and Ofloxacin in tablet dosage form. This method is fast, accurate, precise and sensitive hence it can be employed for routine quality control of Cefixime and Ofloxacin tablets in QC laboratories and industries.
Fig. 2: Linearity curve of CFX and OFL

**Table 1: Linearity Studies of CFX and OFL**

<table>
<thead>
<tr>
<th>Method</th>
<th>Range(μg mL⁻¹)</th>
<th>Equation of line</th>
<th>r²</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>CFX</td>
<td>OFL</td>
<td>CFX</td>
</tr>
<tr>
<td>A</td>
<td>10-80</td>
<td>10-80</td>
<td>y = 34.66x</td>
</tr>
<tr>
<td>B</td>
<td>10-80</td>
<td>10-80</td>
<td>y = 47.54x</td>
</tr>
</tbody>
</table>

**Table 2: Tablet Analysis and Recovery Studies of CFX and OFL**

<table>
<thead>
<tr>
<th>Method</th>
<th>Label Claim(mg/tab)</th>
<th>Amount Found* (%)</th>
<th>Standard Deviation</th>
<th>(%) Recovery *</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>CFX</td>
<td>OFL</td>
<td>CFX</td>
<td>OFL</td>
</tr>
<tr>
<td>A</td>
<td>200</td>
<td>200</td>
<td>99.9</td>
<td>99.96</td>
</tr>
<tr>
<td>B</td>
<td>200</td>
<td>200</td>
<td>99.63</td>
<td>100.24</td>
</tr>
</tbody>
</table>

*denotes n=6, average of six estimations
Table 3: Degradation Studies of CFX and OFL

<table>
<thead>
<tr>
<th>S. No.</th>
<th>Method</th>
<th>CFX Degraded (%)</th>
<th>OFL Degraded (%)</th>
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<tbody>
<tr>
<td>1</td>
<td>0.01 M NaOH at 85°C for 1 hr</td>
<td>25.00</td>
<td>1.00</td>
</tr>
<tr>
<td>2</td>
<td>0.01 M NaOH at 85°C for 1 hr</td>
<td>100.0</td>
<td>6.00</td>
</tr>
<tr>
<td>3</td>
<td>0.01 M HCl at 85°C for 2.5 hr</td>
<td>30.00</td>
<td>3.00</td>
</tr>
<tr>
<td>4</td>
<td>0.1 M HCl at 85°C for 7 hr</td>
<td>100.0</td>
<td>10.00</td>
</tr>
<tr>
<td>5</td>
<td>1% H₂O₂ 25°C for 3.5 hr</td>
<td>24.00</td>
<td>100.0</td>
</tr>
<tr>
<td>6</td>
<td>1% H₂O₂ 30°C for 10 min</td>
<td>100.0</td>
<td>100.0</td>
</tr>
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</table>

REFERENCES


