ANALYTICAL DETERMINATION FOR CHLORPROTHIXENE.HCL DRUG IN PURE FORM AND MEDICINAL TABLETS BY SPECTROPHOTOMETRIC DERIVATIVES

Aayad Ammar Sayhood1*, Bayan Jabr Hussein2, Mohanad Hazim Halboos3

1Department of Basic Sciences, Faculty of Dentistry, University of Kufa, Najaf, Iraq
2Department of Oral Histology, Faculty of Dentistry, University of Kufa, Najaf, Iraq
3Department of Ecology, Faculty of Science, University of Kufa, Najaf, Iraq

Abstract
Quantitative measurement, easy, accurate, and reproducible analysis of chlorprothixene.HCl medications (COT) using one of chemometrics method, the spectrophotometric derivatives method of zero (D0), first (D1) and second (D2) order. These suggested methods had been used to determine the (COT) between the range (0.4-3) μg.mL⁻¹, 196.6 and 258.4 nm for 0th order; in (D1) range at 215.8, 247.2 and 268.4 nm; and in (D2) range derivative spectrophotometry at 223.2 and 257.4 nm, respectively. The precise and accurate results of the methods employed have been calculated and are very satisfactory. The limit of detection was estimated in this study, and it ranged between (0.0531-0.0611) μg.mL⁻¹; As for the limit of quantification, it ranged between (0.1776-0.2044) μg.mL⁻¹. This method has been applied to some medicinal doses consisting of this drug (COT), and the results have been impressive.

1. INTRODUCTION
chlorprothixene.HCl (C₁₈H₁₈N₂Cl.HCl), Figure (1), N,N-dimethyl-3-(9H-thioxanthen-9-ylidene)prop-1-amine hydrochloride, (COT), where used in anti-psychotic field [1]. This is a class of drugs used for trying to treat hallucinations [2]. For this drug, there are several analytical techniques that are certified, such as; Liquid chromatography [3, 4]; HPLC [5–7]; GC [8]; RP-TLC [9]; Potentiometric [10–12]; Voltammetry [13–15]; Spectrophotofluorometric [16]; Spectrophotometric [17–19].

Because of the previous studies in the literature, 0th, 1st and second derivatives were not combined to estimate the medicinal product of (COT). We have proposed a quick, easy, new and inexpensive method in this scientific research, where do not need additional material such like reagent to estimate drug (COT) as it is and in pharmaceutical dosage forms, means of a method of spectral analysis resulting from the drug concentration and the measurement of λmax at (D0), (D1) and (D2).

![Figure 1. Structure of chlorprothixene.HCl](image)

2. EXPERIMENTAL PART
Double beam Shimadzu UV visible spectrophotometer; model UV1800 PC has the software UV-Probe 2.34 used for spectral measurement, ultrasonic from Homogenizer, and balance sensitive ± 0.0001g from Mettler-Toledo. The pure (COT) drug form has been obtained from (SDI) company in Iraq.

It is dissolving 0.0100 g pure chlorprothixene.HCl in distilled water was done, and transferring to a 1L volumetric flask, diluted with water in a mark; stowed at < 10 °C to prepare ten μg.mL⁻¹ (COT). Every day freshly prepares in range (0.4-3) μg.mL⁻¹ solutions.

The following research has been done to apply this approach to drug substances; the weights and crushed to powder were calculated for fifty tablets, each containing 0.5 mg COT. Powder of 10 mg (COT) equivalent has been transferred to a 1L volumetric flask. Added and sonicated with ultrasonic a limited quantity of sterile water for 10 minutes, then the solution was purified and mixed with fresh water.

3. RESULTS AND DISCUSSION
For measure the linearity by the (D0), (D1) and (D2) order spectrum methods, the system showed the linear correlation under the experimental conditions qualified [20–24]. A regression study was performed for R², intercept, and slope, as seen in figure (2-4). Figure (2) displays concentration spectrum to (COT) drug (0.4-3) μg.mL⁻¹ calibration curve for (D0), the regression equation was:
y=0.1189x + 0.5643 (R²=0.9994) at 196.6 nm; and
Analytical Determination For Chlorprothixene.Hcl Drug In Pure Form And Medicinal Tablets By Spectrophotometric Derivatives

$y=0.0762x + 0.3093$ (R$^2=0.9995$) at 258.4 nm

Figure 2. (1); (D$_0$) spectrum of (COT). (2); calibration curve for (COT) at 196.6 nm; (3) calibration curve for (COT) at 258.4 nm

Figure (3) displays concentration spectrum of (COT) drug (0.4-3) $\mu$g.mL$^{-1}$ calibration curve for (D$_1$), the regression equation was
$y=-0.0066x - 0.0323$ (R$^2=0.9992$) at 215.8 nm; and
$y=0.003x + 0.0134$ (R$^2=0.9993$) at 247.2 nm; and
$y=-0.0026x - 0.0111$ (R$^2=0.9991$) at 268.4 nm

Figure (4) displays concentration spectrum of (COT) drug (0.4-3) $\mu$g.mL$^{-1}$ calibration curve for (D$_2$), the regression equation was
$y=0.001x + 0.0041$ (R$^2=0.9996$) at 223.2 nm; and
$y=-0.0006x - 0.0026$ (R$^2=0.9992$) at 257.4 nm.

The standard additions method [25] can be used to ensure the accuracy of the results in this study. 60%, 100% and 140% of 1 mg.mL$^{-1}$ (COT), standard solutions were used to evaluate in terms of the accuracy of the suggested method by (D$_0$), (D$_1$) and (D$_2$). Five determinations were made at each level, the percentage of error, the percentage of recovery, and the percentage of RSD (table 1).

Figure 3. (1); (D$_0$) spectrum of (COT). (2); calibration curve for (COT) at 215.8 nm; (3) calibration curve for (COT) at 247.2 nm; (4) calibration curve for (COT) at 268.4 nm
Analytical Determination For Chlorprothixene.HCl Drug In Pure Form And Medicinal Tablets By Spectrophotometric Derivatives

Table 1. Accuracy of spectrophotometric 0th, 1st, and 2nd derivatives determination of COT

<table>
<thead>
<tr>
<th>Method</th>
<th>COT* µg.mL⁻¹</th>
<th>Standard Added* µg.mL⁻¹</th>
<th>Found* µg.mL⁻¹</th>
<th>E%</th>
<th>R%</th>
<th>RSD%</th>
</tr>
</thead>
<tbody>
<tr>
<td>(D₀)</td>
<td>1</td>
<td>0.6</td>
<td>1.6049</td>
<td>0.3116</td>
<td>100.3116</td>
<td>0.1537</td>
</tr>
<tr>
<td></td>
<td></td>
<td>1</td>
<td>1.9986</td>
<td>-0.0656</td>
<td>99.9343</td>
<td>0.2701</td>
</tr>
<tr>
<td></td>
<td></td>
<td>1.4</td>
<td>2.4055</td>
<td>0.2296</td>
<td>100.2296</td>
<td>0.1483</td>
</tr>
<tr>
<td>(D₁)</td>
<td>1</td>
<td>0.6</td>
<td>1.6023</td>
<td>0.1476</td>
<td>100.1476</td>
<td>0.1364</td>
</tr>
<tr>
<td></td>
<td></td>
<td>1</td>
<td>2.0039</td>
<td>0.1968</td>
<td>100.1968</td>
<td>0.2006</td>
</tr>
<tr>
<td></td>
<td></td>
<td>1.4</td>
<td>2.4028</td>
<td>0.1202</td>
<td>100.1202</td>
<td>0.1305</td>
</tr>
<tr>
<td>(D₂)</td>
<td>1</td>
<td>0.6</td>
<td>1.5971</td>
<td>-0.1804</td>
<td>99.8195</td>
<td>0.1076</td>
</tr>
<tr>
<td></td>
<td></td>
<td>1</td>
<td>2.0013</td>
<td>0.0656</td>
<td>100.0656</td>
<td>0.0962</td>
</tr>
<tr>
<td></td>
<td></td>
<td>1.4</td>
<td>2.4002</td>
<td>0.0109</td>
<td>100.0109</td>
<td>0.0764</td>
</tr>
</tbody>
</table>

*Average of 5 measurements

Table 2. The precision of spectrophotometric 0th, 1st, and 2nd derivatives determination of COT

<table>
<thead>
<tr>
<th>Method</th>
<th>COT µg.mL⁻¹</th>
<th>RSD% interday precision</th>
<th>RSD% intraday precision</th>
</tr>
</thead>
<tbody>
<tr>
<td>(D₀)</td>
<td>1</td>
<td>0.2351</td>
<td>0.1975</td>
</tr>
<tr>
<td>(D₁)</td>
<td>1</td>
<td>0.2671</td>
<td>0.2167</td>
</tr>
<tr>
<td>(D₂)</td>
<td>1</td>
<td>0.2167</td>
<td>0.1784</td>
</tr>
</tbody>
</table>

*Average of 5 measurements

Table 3. LOD and LOQ of spectrophotometric 0th, 1st and 2nd derivatives determination of COT

<table>
<thead>
<tr>
<th>Methods</th>
<th>LOD; µg.mL⁻¹</th>
<th>LOQ; µg.mL⁻¹</th>
</tr>
</thead>
<tbody>
<tr>
<td>(D₀)</td>
<td>0.0531</td>
<td>0.1776</td>
</tr>
<tr>
<td>(D₁)</td>
<td>0.0595</td>
<td>0.1990</td>
</tr>
<tr>
<td>(D₂)</td>
<td>0.0611</td>
<td>0.2044</td>
</tr>
</tbody>
</table>

To study the accuracy of this method to determine (COT) in medicinal tablets, 3 assessed tablet solution concentration of 0.8, 1.5, and 2.6 µg.mL⁻¹ to determine by derivative methods of (D₀), (D₁) and (D₂) order. Five determinations were made at each level, the percentage of error, the percentage of recovery, and the percentage of RSD (table 4).

Table 4. Medicinal tablets analysis

<table>
<thead>
<tr>
<th>Method</th>
<th>Taken * µg.mL⁻¹</th>
<th>Found * µg.mL⁻¹</th>
<th>E%</th>
<th>R%</th>
<th>RSD%</th>
</tr>
</thead>
<tbody>
<tr>
<td>(D₀)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(D₁)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(D₂)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

(LOQ) quantification limit, and (LOD) detection limit are calculated for this suggested method to depend on standard deviation, and the result is displayed in table 3.
### 4. CONCLUSIONS

The zero-, first- and second-order derivative spectrometry procedure makes quantitative analyzes of (COT) drugs easy to specify, accurate, and replicable. The techniques were validated as specified, linearity, accuracy, precision, detection limit (LOD), quantification limit (LOQ), and reproducibility by ICH Guidelines. To the quality control and the routine test for drugs in bulk or/and medicinal tablets analysis, the proposed design can be used.

### REFERENCES


Analytical Determination For Chlorprothixene.Hcl Drug In Pure Form And Medicinal Tablets By Spectrophotometric Derivatives