Chlorpromazine Hydrochloride Determinations by Spectrophotometric Method via Oxidation with Sodium Periodate

Ali Mohammed Abbed

Iraq, Mustansiriyah University, College of Science, Department of Chemistry

Abstract

Phenothiazine rings are regarded a nucleus or basic compounds for its derivatives, such as chlorpromazine that are used as best drugs in antiemetic and antipsychotic. Chlorpromazine hydrochloride could be determined by many analytical techniques published. But in the present study it can be determined in raw material powder, depending on oxidation via NaIO$_4$ by a simple, sensitive and rapid spectrophotometric method, for determination small amount of chlorpromazine hydrochloride in acidic aqueous solution. The results of this work demonstrated a formation new peak at scanning (1100-200) nm that appears in visible region (526) nm, with intensive rose color through oxidation of chlorpromazine with oxidative agent (NaIO$_4$), and is stable for 2hours. And calibration curve for this reaction which was found obeyed Lamberts Beer law in concentration range (5-60) µg/ml of drug at optimum pH (1.5) and preferable concentration (10 µg/ml) of NaIO$_4$; to give desirable analytical statistical value that equal to (DL=7 µg/ml, sensitivity=0.3 µg/ml).

Key words:- Chlorpromazine, Sodium periodate (NaIO$_4$), oxidation.
تقدير الكلوربرومازين-هيدروكلوريد بطريقة طيفية بواسطة الأكسدة مع بيروидات الصوديوم
علي محمد عبد
العراق ، الجامعة المستنصرية
كلية العلوم ، قسم الكيمياء

الخلاصة
تعتبر حميات الفينوثيازين النواة أو المركب الأساسي لمشتقاتها، كمثال على ذلك، الكلوربرومازين-هيدروكلوريد من الممكن تقديره بعدة تقنيات تحميمية منشورة، ولكن في الدراسة الحالية نستطيع تقديره وهو على شكل باودر كمادة دوائية خام بالاعتماد على اکسدةه بواسطة بيرويدات الصوديوم بطريقة طيفية بسيطة وحساسة وسريعة لتقدير كميات قليلة في محلال مائية حامضية. أوضحت النتائج في هذا العمل تكوين قمة جديدة عند إجراء مسح طيفي يتراوح ما بين (0.011 - 0.11) نانومتر، حيث ظهرت تلك القمة في المنطقة المرئية عند طول موجي (526) نانومتر مع لون وردي غامق وذلك من خلال اکسدة الكلوربرومازين-هيدروكلوريد مع عامل مؤكسد (NaIO₄) ومثمر لمدة ساعتين. حيث وجد منحنى المعايرة لهذا التفاعل أنه يطيع قانون لامبرت بير ضمن مدى من التركيز (0.5 - 10) مايكروغرام/مللتر من الدواء في ظروف الدالة الحامضية المثلث التي تعادل (1.5) والتركيز الأمثل لمادة NaIO₄ ما يعادل (10) مايكروغرام/مللتر ليعطي قيم احصائية تحايلية مرغوبة والتي تساوي (حد الكشف = 7 مايكروغرام/مللتر، وحساسية = 0.3 مايكروغرام/مللتر).
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Introduction

Chlorpromazine was the breakthrough in psychiatric practice. Pharmacotherapy with chlorpromazine started in polish hospital in autumn and winter 1954, and the first paper covering clinical experiences regarded and started to be published in 1955, which was discovered in 1950 (1). One of the phenothiazine derivatives is chlorpromazine as shown in [fig.1] (2), and phenothiazine was regarded as a nucleus molecule of chlorpromazine which could characterized via a tricyclic rings that contain sulfur atom and nitrogen atom located in 5 and 10 position. They exhibit oxidation by many oxidizing agents to produce colored products (1, 3). The chemical name of Chlorpromazine is 2-chloro-10-[(N,N,N-dimethyl amine) broby]phenothiazin Hydrochloride (4). The physical and chemical properties it is white powder color and dark color when exposure to light; melting point equal to 60 C°, dissolved in alchohol, alkaline solution, chloroform and ether (5). It is widely used in human medicine in the treatment of epilepsy, therapy of migraine headaches, anti dopamine receptor, ill dwelling and the organic psychoses. In veterinary medicine it is used as tranquilizer and anti emetics agent (6, 7).

Figure (1):- Chemical structure of Chlorpromazine.

Sodium periodate classified inorganic salt, composed of periodate anion and sodium cation (8). Periodic acid exists in
solution as tetrahedral ion IO$_4^-$, as well as in several hydrated forms. The main equilibria in acid solution are:

\[
\begin{align*}
H_5IO_6^- &= H^+ + H_4IO_6^- & K &= 1 \times 10^{-3} \\
H_4IO_6^- &= IO_4^- + 2H_2O & K &= 29 \\
H_4IO_6^- &= H^+ + H_3IO_6^{2-} & K &= 2 \times 10^{-7}
\end{align*}
\]

In aqueous solution at 25°C the periodate anion IO$_4^-$ predominates. The free acid H$_5$IO$_6$ can be dehydrated to H$_4$I$_2$O$_9$ at 82°C and to HIO$_4$ at 100°C (9). But in alkaline solution periodate became dimerizes:

\[
2IO_4^- + 2OH^- \rightarrow H_2I_2O_{10}^{4-}
\]

**Experimental Materials**

Chlorpromazine – Hydrochloride powder as standard or raw material was provided from the state company for industries of drugs and medical appliances in Samara city – Iraq (SDI).

Carried out scanning (1100-200) nm for Chlorpromazine hydrochloride with NaIO$_4$ to determination of a new peak.

Chlorpromazine-HCl raw material powdered was weighted 0.005 and dissolved in 50 ml distilled water to be 100 ppm, taking different volume to prepare (10, 20, 30, 40, 50, 60, 70) µg/ml in 10 ml volumetric flask, before adding drug to all those volumetric flasks must be containing on constant concentration of sodium periodate that equal to (20 µg/ml) by preparation stock solution from NaIO$_4$, results are shown in figure (3).

Carrying out scanning (1100-200)nm to determine the peaks of the reactions constituents in different conditions.
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Prepare aqueous stock solution of chlorpromazine hydrochloride and sodium periodate in middle range that equal to (30) and (10) µg/ml. Scanning was made to the following solutions [1. Chlorpromazine in acidic media and distilled water as shown in figure (2)]. [2. Sodium periodate by dissolving in water and acidic media to make scanning for drug with sodium periodate when the drug as blank and another time the sodium periodate as blank and make scanning for the drug with acidic sodium periodate as shown in figures (7, 8)]. [3. Acidic sodium periodate alone, drug with and without sodium periodate in different conditions].

**Determination of pH Optimum.**

Preparing the stock solution of Chlorpromazine hydrochloride in distilled water: prepare six volumetric flask containing equal concentration of chlorpromazine (30 µg/ml) and NaIO₄ (10 µg/ml) and add drops HCl 1 N until the reading of PH meter reach to (0.5, 1.0, 1.25, 1.5, 2.0, 2.5) and reading the absorbance at (526 nm).

**Studying the effect of (NaIO₄) Concentration as Oxidizing Agent.**

Preparation the stock solution from the drug by weight 0.002gm and dissolved in 10ml distilled water in volumetric flask to be 200 µg/ml. And preparing the stock solution from NaIO₄ by weight 0.0025gm and dissolved in distilled water at 25ml volumetric flask to be 100 µg/ml and pulling from stock solution of drug equal to volume 1.25ml volumetric flask 5ml to be 50 µg/ml in all volumetric flask and to nine volumetric flask pull (0.25, 0.5, 0.75, 1, 1.25, 1.5, 1.75, 2, 2.5) ml from stock solution of sodium periodate in to the same volumetric flask to be (5, 10, 15, 20, 25, 30, 35, 40, 50) µg/ml and add drops HCl (1N) and measured pH by pH meter until reach (1.5) as pH optimum and complete the volume with distilled water to 5ml and read the absorbance at (526nm).
Calibration Curve in Optimum Conditions.

Weight 0.005gm from the drug and dissolve in 50ml distilled water at volumetric flask, prepare stock solution from NaIO₄ by dissolving 0.001gm in 10ml distilled water to 10ml volumetric flask. Take seven volumetric flask (5ml) and put constant volume from NaIO₄ that equal to (0.5ml) to all volumetric flask to be 10 µg/ml as a perfect concentration. And add different volume from stock solution of the chlorpromazine as (0.25, 0.5, 1, 1.5, 2, 2.5, 3) ml to be (5, 10, 20, 30, 40, 50, 60) µg/ml, and after measuring pH by adding drop by drop from HCl (1N) until the PH reach to 1.5 by PH meter after completing those are treatments, the volume in distilled water read absorbance at the wave length (526nm).

Results

The results that obtained from the proposed chemical oxidation reaction in the present study demonstrated appearing of a new peak in visible region at wave length (526nm) as shown in figure (3) and disappear in all chart in figure (4-8) that is not containing drug and NaIO₄ together, which indicates to oxidation of Chlorpromazine via NaIO₄ and formation a new functional group to give a new wave length with intensive rose color in visible region stable for 2hour; when compared with that of Chlorpromazine hydrochloride alone (λ_max=256 nm) as shown in figure (2), through carrying out scanning in two state at (1100-200)nm.

We could distinguish the linearity through the calibration curve at figure (13) ranking in range (5-60) µg/ml from the drug, with constant concentration of NaIO₄ (10) µg/ml that represents optimum concentration is proved in figure (12) at optimum pH = (1.5) is proved in figure (11) that gives highest absorbance in this conditions; and does not deviate from Lambert Beer law but obeys, and these series of test tube read
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at 526nm. Therefore it can calculate some of analytical statistical values from standard curve and other diagram as shown in the table (1).

Table (1):- Statistical value that obtained from calibration curve of reaction between drug and NaIO₄ in optimum conditions.

<table>
<thead>
<tr>
<th>Statistical terms</th>
<th>S D</th>
<th>RS D</th>
<th>Detection limit (DL)</th>
<th>Sensitivity</th>
<th>Correlation coefficient (R)</th>
<th>Molecular absorption coefficient (a)</th>
<th>pH optimum</th>
</tr>
</thead>
<tbody>
<tr>
<td>Values</td>
<td>0.1</td>
<td>13%</td>
<td>7 µg/ml</td>
<td>0.3 µg/ml</td>
<td>0.993</td>
<td>15 L/gm* Cm⁻¹</td>
<td>1.5</td>
</tr>
</tbody>
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Figure (2):- Chlorpromazine hydrochloride dissolved in (0.1N)HCl, Blank=HCl.
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Figure (3):- Drug with NaIO₄ in acidic media, Blank=HCl. To found (λₘₐₓ=526).

Figure (4):- NaIO₄ dissolve in distilled water, Blank=distilled water.

Figure (5):- Drug dissolve in distilled Water, Blank=distilled water.
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Figure (6):- NaIO₄ in acidic media, Blank=HCl.

Figure (7):- Drug with NaIO₄, Blank=drug.

Figure (8):- Drug with NaIO₄, Blank=NaIO₄.

Figure (9):- Drug with acidic NaIO₄, Blank=acidic NaIO₄.
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Figure (10):- Acidic drug with NaIO₄, Blank=NaIO₄.

Figure (11):- Determination the pH optimum.

Figure (12):- Determination the perfect of NaIO₄ concentration at constant the

Figure (13):- Calibration curve for reaction constituents of drug with NaIO₄ in optimum conditions.

Y=0.015x
R²=0.993
Discussion

The nucleus or basic structure of Chlorpromazine is Phenothiazine that can be oxidized to sulfoxide and sulfones via many oxidative agents such as KMnO₄; Phenothiazine nitrate at positions Para to the nitrogen atom, but sulfoxide formation take place simultaneously (10). Thereby likelihood oxidation sulfur atom of hetero cyclic phenothiazine ring.

The sodium periodate been a mild oxidation which is recorded in previous studies such as Ouabain, also causes a cleavage in rhamnose ring bond between C₂ and C₃ (11). Sodium periodate could be oxidized aliphatic alcohol and alkene alcohol by converts the glycerol to formic acid, formaldehyde, ethylene glycol is oxidized to formaldehyde, and the propylene glycol to formaldehyde and acetaldehyde (12). Therefore we can believe or credit the sodium periodate to be as cleaver of aliphatic amine series of chlorpromazine and produced oxidized phenothiazine. Appearing of this new peak due to possibility of this drug oxidized to radical and cations (13), also undergoing charge-transfer complex formation; and ion-association complex formation (14-19).

Conclusion

We could conclude that chlorpromazine determination by this method it possible to apply on pharmaceutical dosage form of chlorpromazine; by using optimum conditions (10 µg/ml oxidative agent, pH equal to 1.5 and molecular absorption coefficient 15L/gm.Cm or 0.015L/mg.Cm). And read at 526nm to find the concentration of drug in dosage form by Lambert Beer equation(A= a.b.c).
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