

Chlorpromazine Hydrochloride Determinations by Spectrophotometric Method via Oxidation with Sodium Periodate

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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 Lambert's Beer law in concentration range (5-60) $\mu\text{g/ml}$ of drug at optimum pH (1.5) and preferable concentration (10 $\mu\text{g/ml}$) of NaIO_4 ; to give desirable analytical statistical value that equal to (DL=7 $\mu\text{g/ml}$, sensitivity=0.3 $\mu\text{g/ml}$).

Key words:- Chlorpromazine, Sodium periodate (NaIO_4), oxidation.

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تقدير الكلوربرومازين-هيدروكلوريد بطريقة طيفية بواسطة الأكسدة مع بيرايودات الصوديوم

علي محمد عبد

العراق ، الجامعة المستنصرية

كلية العلوم ، قسم الكيمياء

الخلاصة

تعتبر حلقات الفينوثيازين النواة او المركب الأساسي لمشتقاته، كمثال لهذه المشتقات الكلوربرومازين والذي يستخدم ضد التقيؤ والاضطرابات النفسية. الكلوربرومازين-هيدروكلوريد من الممكن تقديره بعدة تقنيات تحليلية منشورة، ولكن في الدراسة الحالية نستطيع تقديره وهو على شكل باودر كمادة دوائية خام بالأعتماد على اكسدته بواسطة بيرايودات الصوديوم بطريقة طيفية بسيطة وحساسة وسريعة لتقدير كميات قليلة في محاليل مائية حامضية. اوضحت النتائج في هذا العمل تكوين قمة جديدة عند اجراء مسح طيفي يتراوح ما بين (1100-200) نانومتر، حيث ظهرت تلك القمة في المنطقة المرئية عند طول موجي (526) نانومتر مع لون وردي غامق وذلك من خلال اكسدة الكلوربرومازين- هيدروكلوريد مع عامل مؤكسد (NaIO_4) ومستقر لمدة ساعتان. حيث وجد منحنى المعايرة لهذا التفاعل انه يطيع قانون لامبرت بير ضمن مدى من التركيز (5-60) مايكروغرام/ملتر من الدواء في ظروف الدالة الحامضية المثلى والتي تعادل (1.5) والتركيز الأمثل لمادة NaIO_4 ما يعادل (10) مايكروغرام/ملتر ليعطي قيم احصائية تحليلية مرغوبة والتي تساوي (حد الكشف = 7 مايكروغرام/مل، وحساسية = 0.3 مايكروغرام/ملتر).

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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-dimethyl amin). brobryl]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).

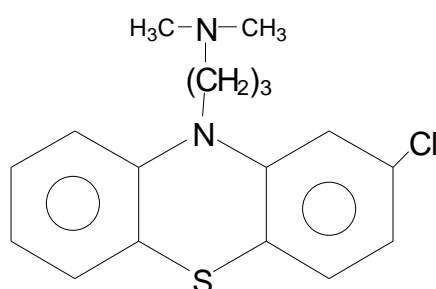


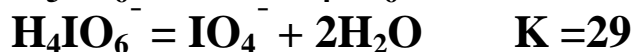
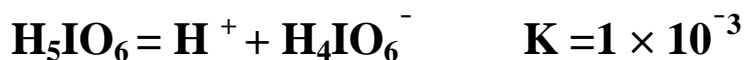
Figure (1):- Chemical structure of Chlorpromazine.

Sodium periodate classified inorganic salt, composed of periodate anion and sodium cation (8). Periodic acid exists in

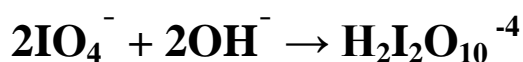
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solution as tetrahedral ion IO_4^- , as well as in several hydrated forms. The main equilibria in acid solution are:-



In aqueous solution at 25°C the periodate anion IO_4^- predominates. The free acid H_5IO_6 can be dehydrated to $\text{H}_4\text{I}_2\text{O}_9$ at 82°C and to HIO_4 at 100°C (9). But in alkaline solution periodate became dimerizes:-



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) $\mu\text{g}/\text{ml}$ 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 $\mu\text{g}/\text{ml}$) by preparation stock solution from NaIO_4 , results are shown in figure (3).

Carrying out scanning (1100-200)nm to determinate 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) $\mu\text{g/ml}$. 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 Chlorpromazin hydrochloride in distilled water : prepare six volumetric flask containing equal concentration of chlorpromazine (30 $\mu\text{g/ml}$) and NaIO_4 (10 $\mu\text{g/ml}$) 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 (NaIO_4) 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 $\mu\text{g/ml}$. And preparing the stock solution from NaIO_4 by weight 0.0025gm and dissolved in distilled water at 25ml volumetric flask to be 100 $\mu\text{g/ml}$ and pulling from stock solution of drug equal to volume 1.25ml volumetric flask 5ml to be 50 $\mu\text{g/ml}$ 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) $\mu\text{g/ml}$ 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).

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Calibration Curve in Optimum Conditions.

Weight 0.005gm from the drug and dissolve in 50ml distilled water at volumetric flask, prepare stock solution from NaIO_4 by dissolving 0.001gm in 10ml distilled water to 10ml volumetric flask. Take seven volumetric flask (5ml) and put constant volume from NaIO_4 that equal to (0.5ml) to all volumetric flask to be 10 $\mu\text{g}/\text{ml}$ 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) $\mu\text{g}/\text{ml}$, 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 NaIO_4 together, which indicates to oxidation of Chlorpromazine via NaIO_4 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 ($\lambda_{\text{max}}=256 \text{ nm}$) 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) $\mu\text{g}/\text{ml}$ from the drug, with constant concentration of NaIO_4 (10) $\mu\text{g}/\text{ml}$ 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.

Statistic al terms	S D	RS D	Detection limit (DL)	Sensitivi ty	Correlati on coefficient (R)	Molecul ar absorpti on coefficient (a)	pH optimu m
Values	0.1	13 %	7 µg/ml	0.3 µg/ml	0.993	15 L/gm* Cm ⁻¹	1.5

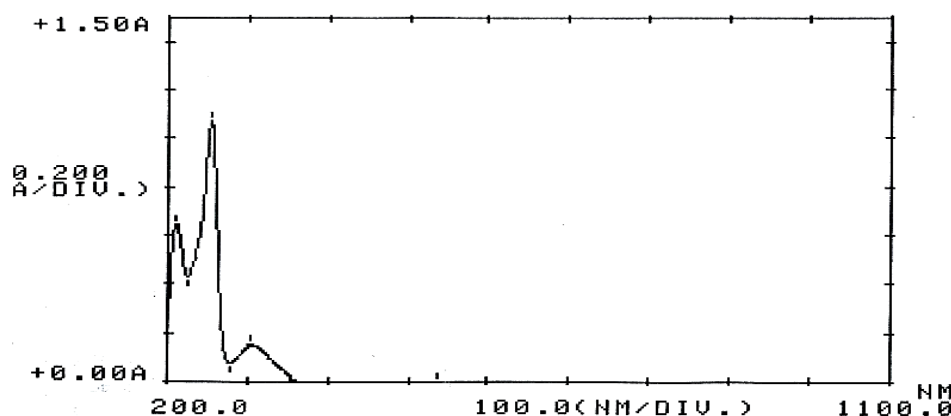


Figure (2):- Chlorpromazine hydrochloride dissolved in (0.1N)HCl, Blank=HCl.

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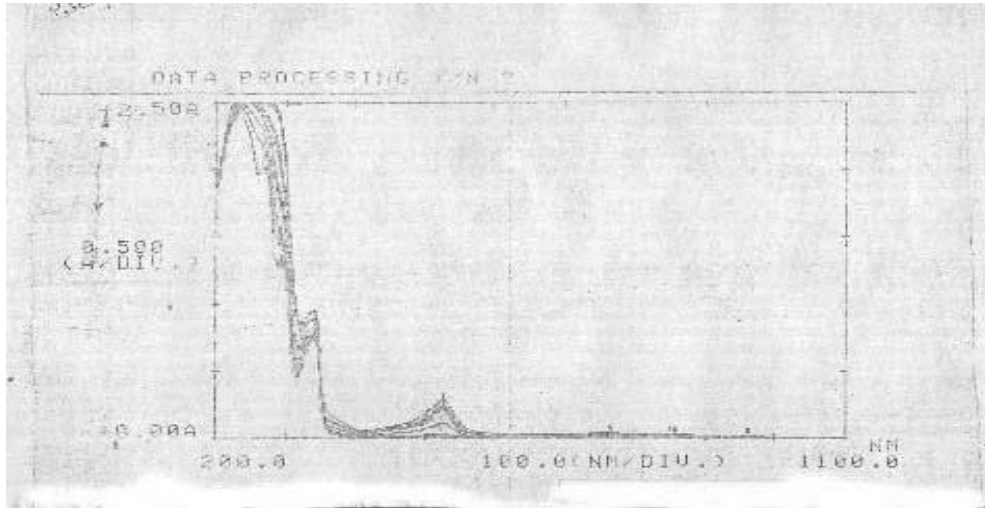


Figure (3):- Drug with NaIO_4 in acidic media, Blank= HCl . To found ($\lambda_{\text{max}}=526$).

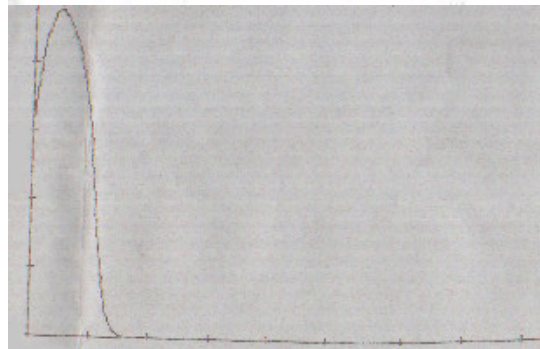
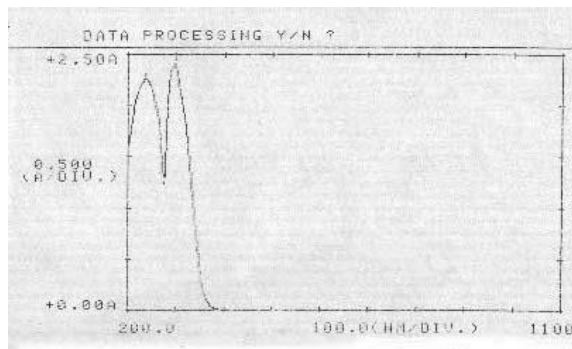


Figure (4):- NaIO_4 dissolve in distilled water, Blank=distilled water.

Figure (5):- Drug dissolve in distilled Water, Blank=distilled water.

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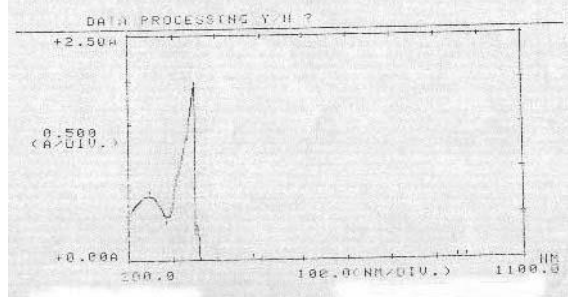


Figure (6):- NaIO_4 in acidic media, Blank=HCl.

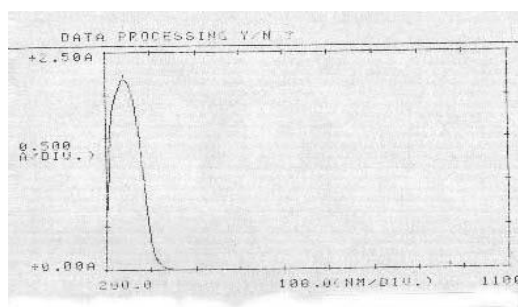


Figure (7):- Drug with NaIO_4 , Blank=drug.

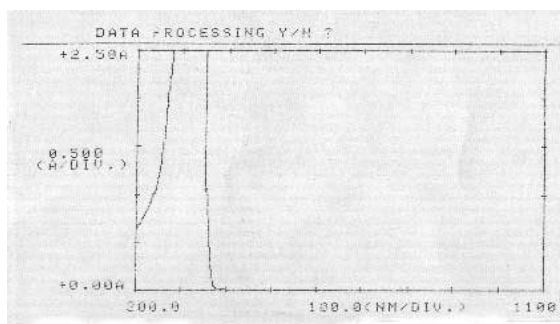


Figure (8):- Drug with NaIO_4 , Blank= NaIO_4 .

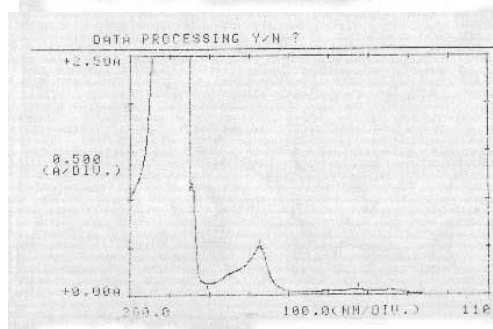


Figure (9):- Drug with acidic NaIO_4 , Blank=acidic NaIO_4 .

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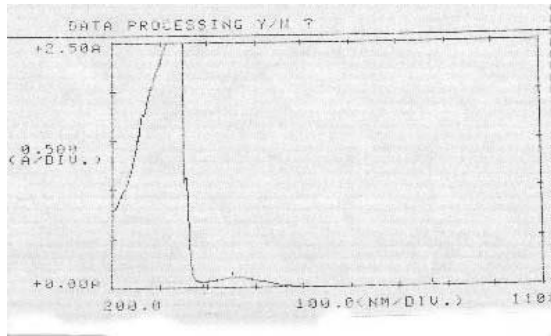


Figure (10):- Acidic drug with NaIO_4 , Blank= NaIO_4 .

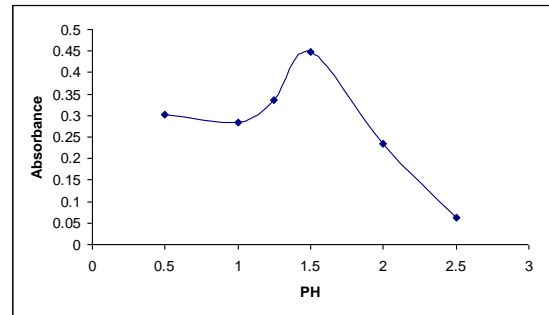


Figure (11):- Determination the pH optimum.

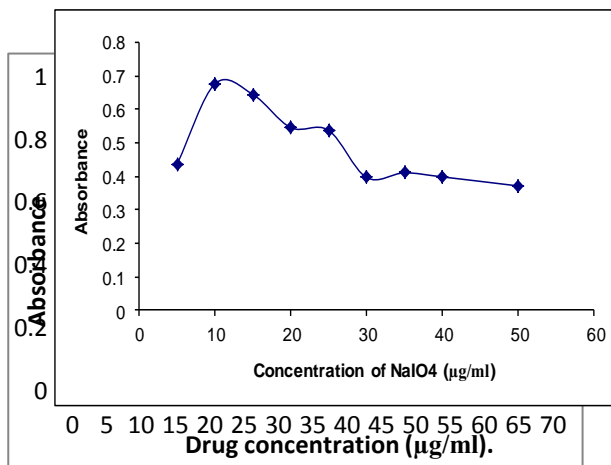


Figure (12):- Determination the perfect of NaIO_4 concentration at constant the

$$Y=0.015x$$

$$R^2=0.993$$

Figure (13):- Calibration curve for reaction constituents of drug with NaIO_4 in optimum conditions.

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Discussion

The nucleus or basic structure of Chlorpromazine is Phenothiazine that can be oxidized to sulfoxide and sulfones via many oxidative agents such as KMnO_4 ; 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 C_2 and C_3 (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 ($10 \mu\text{g/ml}$ 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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