



Spectrophotometric Determination of Chlorpromazine – HCl Using Potassium Permanganate

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Abstract

Two simple, sensitive, accurate, and precise spectrophotometric methods have been developed for the determination of chlorpromazine – HCl in pure form and pharmaceutical formulation. The first method involved treatment of cited drug with a measured excess of permanganate in acid medium and the unreacted oxidant was measured at 525 nm. The second method involves the reaction of the drug with potassium permanganate in the presence of sodium hydroxide to produce a bluish – green colored manganite which is measurable at 610nm.

All the experimental variables affecting the development of the manganite ions were investigated and conditions were optimized. Working linearity ranges were 5-45 $\mu\text{g}\cdot\text{mL}^{-1}$ and 1-20 $\mu\text{g}\cdot\text{mL}^{-1}$ by two methods respectively. The apparent molar absorptivities are 4.015×10^3 and $18.717 \times 10^3 \text{L}\cdot\text{mol}^{-1}\cdot\text{cm}^{-1}$ respectively, with corresponding Sandell's sensitivity values of 0.0885 and $0.01798 \mu\text{g}\cdot\text{cm}^{-2}$ respectively.

The methods have successfully been applied to the determination of drug in dosage forms.

Key Words: Chlorpromazine – HCl , Potassium Permanganate, Spectrophotometry.

Introduction

Chlorpromazine is chemically (10-[3-dimethylaminopropyl] phenothiazine), is a phenothiazine neuroleptic used for the control of psychoses including schizophrenia and mania and it also used in treatment of vomiting and vertigo because of its sedative and extrapyramidal effect.^[1,2]

Several methods have been reported for the determination of chlorpromazine in both pharmaceutical dosage forms and biological fluids includes HPLC [3,4], GC^[5,6], voltammetry^[7], potentiometry^[8] and spectrophotometry^[9-12]. The aim of the present work is to develop two simple sensitive and cost-effective spectrophotometric methods for the determination of chlorpromazine in pure and pharmaceutical formulations. The methods involve using permanganate as oxidimetric reagent for the determination of chlorpromazine in either acid or alkaline medium. In acidic medium the unreacted permanganate ion is determined at 525 nm, while in alkaline medium the bluish-green color of manganate is measured at 610 nm. The validated methods when applied to the determination of chlorpromazine in dosage form yielded results, which were in agreement with the label claim.

Experimental

Instruments

A centra 5 GBC-Scientific-Equipment UV-Visible double beam spectrophotometer with 10 mm matched quartz cells was used for all absorbance measurements.

Reagents and Materials

All chemicals used were of analytical grade and distilled water was used to prepare all solutions.

For Method A

Potassium permanganate solution (0.0038M) is prepared by dissolving 0.058 gm of KMnO_4 in 50 ml of distilled water and treated as mentioned above, then diluted to the 100 mL by using a volumetric flask.

Sulfuric acid solution (2 M) is prepared by mixing 5.50 mL of concentrated sulfuric (sp.gr 1.84) with 50 mL of distilled water and diluted to the mark in a 100 mL volumetric flask using distilled water.

Standard drug (100 ppm) solution is prepared by dissolving 10 mg of the drug in 10 mL of 0.1 M H_2SO_4 and diluting to the mark in a 100 mL volumetric flask with the same acid.

For Method B

Potassium permanganate solution (0.0126 M) is prepared by dissolving approximately 0.2 gm of KMnO_4 (Riedel-de Haen-Germany) with 50 mL of water, the solution was boiled for 10 minutes to remove any residual manganate (IV) ions, cooled filtered and diluted to 100 mL and standardized.

Sodium hydroxide solution (2 M) is prepared by dissolving 8 gm of NaOH in 100 mL of water.

Acetic acid solution (0.5 M) is prepared by mixing 2.85 mL of concentrated acetic acid (sp.gr. 1.052) with distilled water and making the final volume to 100 mL in a volumetric flask.

Standard drug (100 ppm) solution is prepared by dissolving 10 mg of the drug in 10 mL of 0.5 M acetic acid and diluted to 100 mL in a volumetric flask with distilled water.

General Assay Procedures and Calibration Curves

Method A

Aliquots of the working standard solution of containing chlorpromazine (50-450 μg) were transferred into a series of 10 mL volumetric flasks and the volume was adjusted to 4 mL with distilled water. To each flask, 2 mL of 2 M H_2SO_4 was added followed by 1 mL of 0.0038 M KMnO_4 . The flasks were kept aside for 20 min with occasional shaking before diluting to the mark with distilled water. The absorbance of each solution was measured at 525 nm against a reagent blank.

Method B

Aliquots of the working standard solution of chlorpromazine containing (10-200 μg) were transferred into a series of 10 mL volumetric flask and the volume in each flask was adjusted to 7 mL with distilled water. To each flask, 2 mL of 2 M NaOH were added followed by 1 mL of 0.0126 M KMnO_4 . The flasks were kept aside for 20 min with intermittent shaking before diluting to the mark with water. The absorbance was measured after complete color formation at 610 nm against a reagent blank.

Procedure for the Assay of the Drug in Pharmaceutical Formulation Tablets

An accurately weighed quantity of the mixed content of 10 tablets equivalent to 10 mg of drug was transferred into 100 mL volumetric flask and dissolved with 0.1 M H_2SO_4 , mixed and filtered using a Whatman no 42 filter paper to avoid any suspended or undissolved material before use. The first 10 mL of the filtrate was discarded and the filtered solution was diluted quantitatively with distilled water to obtain suitable concentration for the analysis.

Ampoules

An accurately measured volume of the mixed contents of 5 ampoules equivalent to 25 mg of chlorpromazine were transferred into 50 mL volumetric flask, and diluted to 50 mL with distilled water. The working solutions were freshly prepared by subsequent dilutions and analyzed by the above procedure.

Results and Discussion

Optimization of Experimental Variables

The spectrophotometric properties of the colored product as well as the different experimental parameters affecting the color development were carefully studied. The optimization of experimental conditions is accomplished by sequentially optimizing one variable at a time while keeping all other variables constant, these factors include time required for maximum and stable color development, concentration of potassium permanganate.

Method Development

Potassium permanganate is a strong oxidizing agent that can react with several organic substances. Recently, permanganate was studied to determine pharmaceutical active compounds^[13] in formulation of both in alkaline medium^[14] as well as in acidic medium^[15].

Method A

In order to determine the permanganate concentration which would give a reasonable maximum absorbance, preliminary experiments were performed in sulfuric acid medium at 525 nm (Figure 1).

Hence different concentrations of chlorpromazine ($5.0-45\mu\text{g.mL}^{-1}$) were reacted with 1 mL of 0.0038 M KMnO_4 in acidic medium, and after elapsed the contact time the absorbance of the residual permanganate was measured and related to chlorpromazine concentration.

When different concentrations of chlorpromazine react with a fixed amount of KMnO_4 (60 μg) in H_2SO_4 acid medium the KMnO_4 was consumed in proportion to chlorpromazine concentration and a concomitant fall in the concentration of KMnO_4 will take place as shown by the decreasing absorbance values at 525 nm with the increase of chlorpromazine concentration. The results are represented in Figure 2.

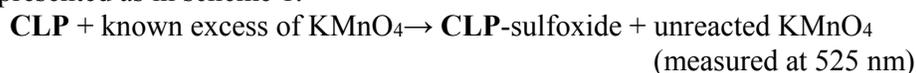
Effect of Reaction Time

To study the effect of reaction time for maximum color development, the method was fixed by carrying out the experiment using 10 $\mu\text{g.mL}^{-1}$ of chlorpromazine. The maximum intensity of color was obtained after 20 minutes and remained constant up to 45 min at room temperature (Figure 3).

Effect of Volume of Sulfuric Acid

Different volumes (0.5 – 3.0) mL of 2 M H_2SO_4 were mixed with 1 mL of chlorpromazine (10 μg), and 1 mL of 0.0038 M KMnO_4 . It was found that the highest color intensity was attained at (2.0-2.5) mL of 2M H_2SO_4 (Figure 4). Excess volume of H_2SO_4 had little effect on the absorbance of chlorpromazine; therefore, 2 mL was selected for recommended procedure.

The possible reaction between the permanganate and the drug in acidic medium could be represented as in scheme 1.



Scheme 1: Proposed reaction in acidic medium.

Method B

In this method a green colored manganate ion MnO_4^{2-} was obtained as a result of reduction of KMnO_4 by chlorpromazine in the presence of NaOH which showed maximum absorption peak at 610 nm against the reagent blank (Figure 5).

Effect of Reaction Time

The optimum reaction time for the development of color intensity at ambient temperature ($25 \pm 2^\circ\text{C}$) was studied and it was found that complete and maximum intensity was obtained at 20 min and remained constant up to 2 hrs. (Figure 6), therefore, 20 min of reaction time was used throughout the determination process.

Effect of Volume of NaOH

The influence of volume of 2M NaOH for green colored manganate ion MnO_4^{2-} was examined in the range of (1 – 3.5 mL). It is apparent from Figure 7, that increasing the volume of NaOH would increase the absorbance of the reaction product upto 2.5 mL; after which further increase in the volume resulted in no change in the absorbance. Thus, 2.5 mL of 2M NaOH was chosen as an optimum value for maximum absorbance.

Effect of Volume of Potassium Permanganate

The effect of the volume of 0.0126 M of KMnO_4 on the intensity of the green colored developed was studied in the range of (0.5-2.5 mL). It is evident from Figure 8 that the maximum absorbance was attained with 1.5 mL KMnO_4 was selected for all the experimental process.

The possible reaction between the permanganate and the drug in alkaline medium could be represented as in scheme 2.



Scheme 2: Proposed reaction in alkaline medium.

Validation of the Proposed Methods

Concentration Range and Calibration Graphs

Under the optimized experimental conditions, the response measured for each methods at the specified working wavelengths was found to be proportional to the analyte concentration Figure 9 and Figure 10.

The linear regression equations were derived by least-squares treatment of the calibration data. (Table 1), summarized the performance data and statistical parameters for the proposed methods.

Sensitivity

Sensitivity of the proposed method was evaluated by calculating limit of detection (LOD) and limit of quantification (LOQ). LOD is the lowest detectable concentration of the analyte by the method while LOQ is the minimum quantifiable concentration. LOD and LOQ were calculated by equations: $\text{LOD} = \frac{(3 \times s)}{\text{slope}}$ and $\text{LOQ} = \frac{(10 \times s)}{\text{slope}}$ respectively, where s is the standard deviation of a blank and m is the slope of the calibration curve. The results Table (2) indicating proposed methods are highly sensitive.

Precision and Accuracy

The competence of the method was statistically evaluated by measuring accuracy and precision of the proposed methods. The accuracy was determined by measuring the relative error percentage (E%), and the results are shown in Table (2). The obtained results were satisfactory and indicate that the proposed methods have a good accuracy and precision.

Application of the Proposed Methods to Pharmaceutical Dosage Forms

It is evident from the aforementioned results that the proposed method gave satisfactory results with the investigated drugs. The results of the application of the recommended procedure are summarized in Table (3).

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Table No(1): Analytical parameters for the proposed methods

Parameter	Method A	Method B
λ_{\max} (nm)	525	610
Concentration range ($\mu\text{g.mL}^{-1}$)	5 – 45	1 – 20
Regression equation	$Y=0.0113x+0.5328$	$Y=0.0587x+0.0333$
Intercept	0.5328	0.0333
Slope	0.0113	0.0587
Correlation coefficient (r)	0.9992	0.9994
Molar absorptivity ($\text{L.mol}^{-1}.\text{cm}^{-1}$)	4.015×10^3	18.717×10^3
Sandell's sensitivity ($\mu\text{g. cm}^{-2}$)	0.0885	0.0180
Limit of detection (LOD) ($\mu\text{g.mL}^{-1}$)	--	0.545
Limit of quantification (LOQ) ($\mu\text{g.mL}^{-1}$)	--	1.652

Tablet No.(2): Evaluation of accuracy and precision for the determination of chlorpromazine-HCl

	Conc. ($\mu\text{g.mL}^{-1}$)		Relative Error %	R .S .D %
	Taken	Found *		
Method A	10	9.920	-0.80	2.016
	20	19.69	-1.515	2.792
	30	39.436	-1.410	1.805
Method B	5	5.121	+ 2.42	0.937
	10	10.038	+1.730	0.508
	20	19.69	-1.515	2.792

*Average of three determinations.

Tablet No.(3): Assay results of different brands of chlorpromazine using the proposed methods.

Method A						
Sample	Labeled Amount (mg)	Found* Amount (mg)	Conc.taken ($\mu\text{g.mL}^{-1}$)	Conc.found ($\mu\text{g.mL}^{-1}$)	R.E %	R.S.D %
Largactil OUBARI Syria	100	102.01	10	10.173	1.730	2.860
Largactil S D I/Iraq	100	101.9	20	20.225	1.125	1.510
Ampoule 25mg/5mL OUBARI Syria	25	23.19	10	9.942	-0.58	1.579
Method B						
Largactil OUBARI Syria	100	101.92	5	5.101	2.02	1.810
Largactil S D I/Iraq	100	100.09	10	10.021	0.21	0.690
Ampoule 25mg/5mL OUBARI Syria	25	24.69	10	9.962	-0.38	0.965

*Average of three determinations.

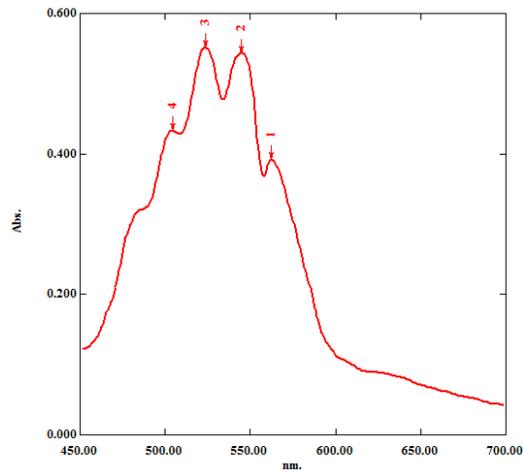


Figure No (1): Visible spectrum of ($60 \mu\text{g.mL}^{-1}$) potassium permanganate in the presence of

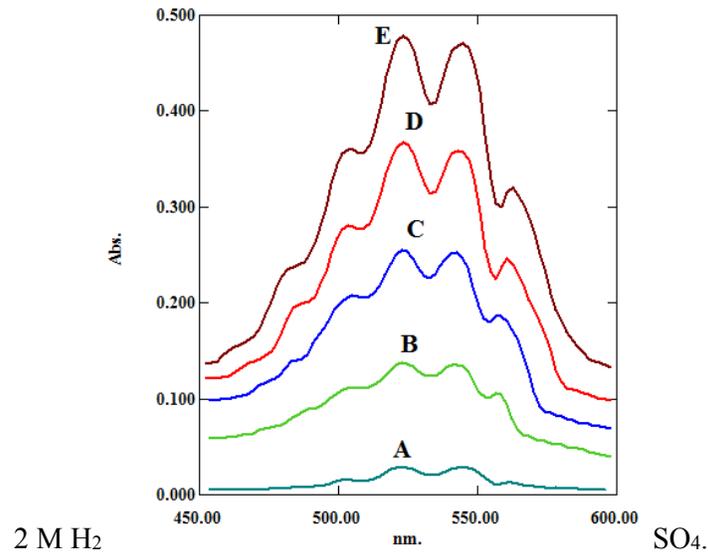


Figure No (2): Effect of chlorpromazine concentration on the absorption spectrum of $60 \mu\text{g.mL}^{-1}$ of KMnO_4 (A for $5 \mu\text{g.mL}^{-1}$, B for $15 \mu\text{g.mL}^{-1}$, C for $25 \mu\text{g.mL}^{-1}$, D for $35 \mu\text{g.mL}^{-1}$, and E for $45 \mu\text{g.mL}^{-1}$).

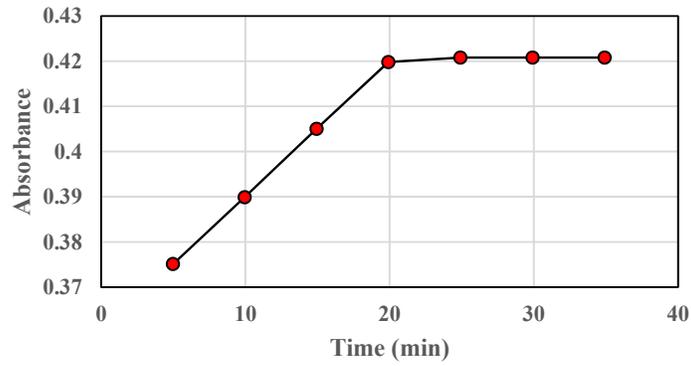


Figure No.(3): Effect of reaction time

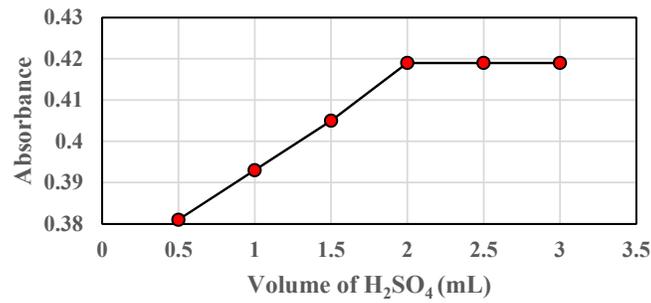


Figure No.(4): Effect of H₂SO₄ volume

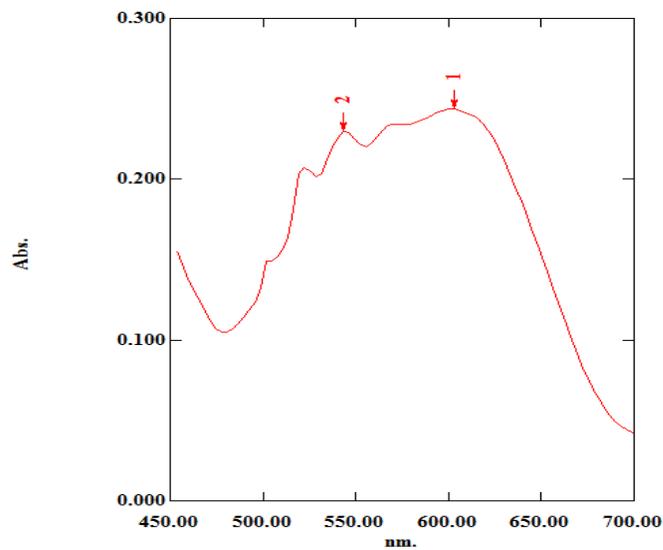


Figure No.(5): Visible spectrum of manganite (MnO₄⁻) in the presence of 2M NaOH.

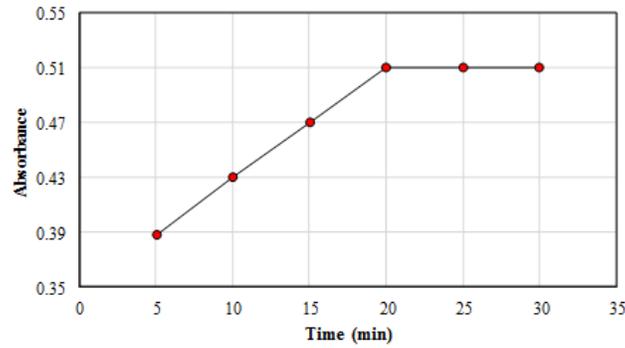


Figure No.(6): Effect of reaction time and stability species.

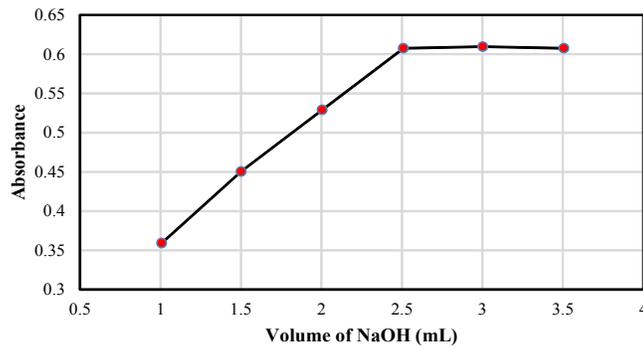


Figure No. (7): Effect of NaOH volume

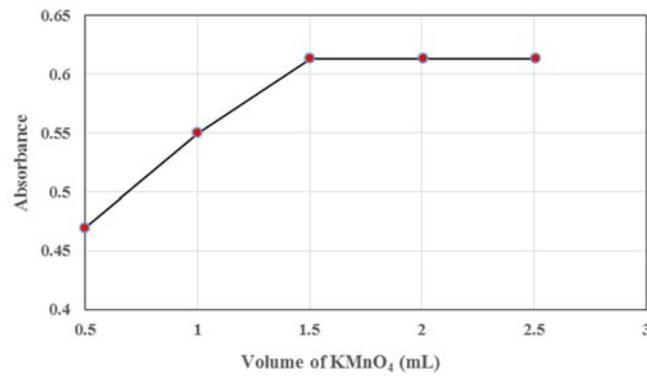


Figure No.(8): Effect of KMnO₄ volume.

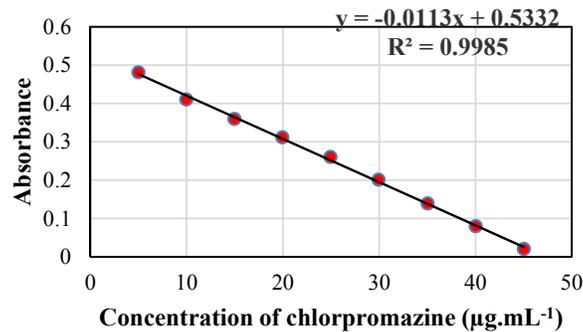


Figure No. (9):Calibration graph of chlorpromazine – HCl under optimum experimental conditions for method A.

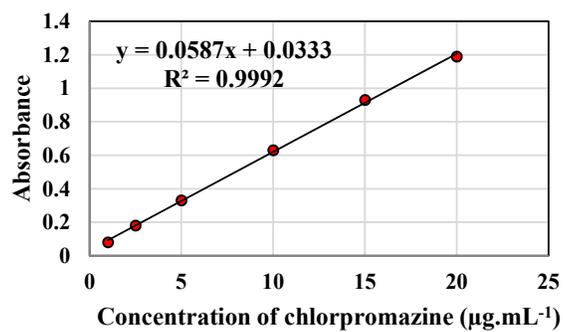


Figure No.(10):Calibration graph of chlorpromazine – HCl under optimum experimental conditions for method B.

التقدير الطيفي لعقار كلوروبرومازين-هيدروكلوريد باستعمال برمنكنات البوتاسيوم

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استلم البحث في: 26 اذار 2014، قبل البحث في: 2 كانون الاول 2014

الخلاصة

اقترحت طريقتان طيفيتان سهلتان وحساستان ودقيقتان لتقدير الكلوروبرومازين-هيدروكلوريد بصورته النقية وفي بعض المستحضرات الصيدلانية. تضمنت الطريقة الأولى معاملة العقار مع محلول برمنكنات البوتاسيوم في وسط حامضي وقياس الامتصاص عند الطول الموجي 525 نانوميتر. أما الطريقة الثانية فتضمنت مفاعلة العقار مع محلول برمنكنات البوتاسيوم في وسط قاعدي وقياس امتصاص لون أيون MnO_4^- الأخضر المزرق عند طول موجي قدره 610 نانوميتر. درست المتغيرات للوصول إلى الظروف الفضلى للتفاعلين، وأظهرت النتائج التي تم الحصول عليها مطاوعة قانون بيير في مدىات تراكيز تراوحت بين 5-45 و 1.0 - 20 مايكروغرام/مل لكلا الطريقتين على التوالي وكانت قيم معاملات الامتصاص المولية 4.015×10^3 و 18.717×10^3 لتر/مول.سم وقيم حساسية ساندل هي 0.0885 و 0.01798 مايكروغرام/سم² على التوالي. طبقت الطريقتان بنجاح لتقدير الكلوروبرومازين في اقراص دوائية وامبولات من مناشئ مختلفة.

الكلمات المفتاحية: المطيافية، برمنكنات البوتاسيوم، كلوروبرومازين -هيدروكلوريد