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Spectrophotometric Determination of Chlorpromazine Hydrochloride Using 4-Nitroanilline by Oxidative Coupling Reaction

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Abstract:

A simple, rapid spectrophotometric method has been established for the determination of chlorpromazine hydrochloride (CPZ) in its pure form and in a tablet formulations. The suggested method is based on the oxidative coupling reaction with4-nitroainlline using KIO_3 in acidic solution to produce a violet colored product with maximum absorption at λ=526 nm.The analytical data obtained throughout this study could be summarid as follows: 1ml of 1M HCl (pH=2.2), 1 ml of 4-nitroanilline ($1x10^{-2}$M), and 1.5ml of ($1x10^{-2}$)KIO_3 per 25 ml reaction medium. The order of additions, coupling reaction time, and temperature in addition to the type of solvent were studied.

The Beer′s law is obeyed over the concentration range of(5–40) µg ml^{-1}, but the detection limit and quantification limit are 0.34 besides 1.03 µg ml^{-1} respectively. The correlation coefficient (r) for the calibration graph was found to be 0.9980, molar absorptivity of 10. 25 × 10^3 L.mol $^{-1}$.cm^{-1}, and Sandell′s sensitivity index of 0.03467 µg.cm^{-2}. The precision and accuracy of the method were tested by calculating the percentage of relative standard deviation (RSD%) (<1.831%) and the average recovery percent (99.22%) average error percent $E_{rel\%}$(0.558).

Direct and standard addition procedures were applied to both standards and specimens of pharmaceutical and the results indicate that the suggested method was successfully applied for the determination of CPZ.

Key words: Chlorpromazine Hydrochloride Determination, KIO_3, 4-nitroanilline, Spectrophotometric.

Introduction:

Chlorpromazine Hydrochloried (CPZ) is the most important compound in the group of phenothiazine derivatives. CPZ is widely used as a healing agent for treating various psychological and personality illnesses (1-3). It is 3-(2-chloro-10H-phenothiazin-10-yl)-N,N-dimethylpropan-1-aminehydrochloride $C_{17}H_{19}ClN_2S.HCl$ (Fig.1). Like other phenothiazine derivatives it contains heterogeneous rings containing sulfur and nitrogen atoms.

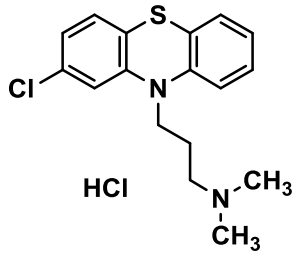

Figure 1. The structure of chlorpromazine hydrochloride.

A number of methods have been applied for the determination of chlorpromazine hydrochloride in pure and dosages. These include HPLC (4-5), liquid-mass spectroscopy (6), potentiometry (7-9), LC-MS/MS (10), GC (11), flow injection analysis (12-13), voltammetry (9), Among the spectrophotometric methods, several methods were proposed depending upon the oxidation of drug using various oxidizing agents (14-17).

In this work, a study of the spectrophotometric determination of CPZ-HCl relying on the oxidative coupling of the drug with 4-nitroaniline using potassium iodate as oxidation reagent in acidic medium.

Materials and Methods:

T90 UV-Visible Spectrophotometer PG Instrumental Ltd, UK with 10 mm quartz cell was used for all spectrophotometric quantities, Jenway 3310 pH meter was used to check the pH of solutions, and Sartorius Balance 210S kern was used to perform all weight measurements.

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Reagents

Fully chemicals used were of analytical grade and chlorpromazine. HCl typical material was provided from State Company for Drug Industries and Medical Appliance (SDI) Samarra-Iraq. Distilled water was used to prepare all solutions.

A 1000 µg/ml (2.814×10^{-3} M))CPZ of solution was prepared by dissolving 0.100gm in100ml distilled water and stored in dark and used, for at least one month, as stock solution. More dilute working solutions of the drug were prepared by serial dilutions with distilled water. 4-nitoanilline solution (1.000×10^{-2} M) was freshly ready daily by dissolving0.0345gm in 5ml ethanol and completed by distilled water to 25ml , while the calculated weight of KIO_3 0.2140gm dissolved in 100ml distilled water was required to prepare (1.000×10^{-2} M) solution. 1.000×10^{-1} M solution of each of sodium hydroxide and hydrochloric acid was prepared and used.

General procedure

In a 25 ml volumetric flask, 1 ml of 1.000×10^{-2} M 4-nitroanilline (R) solution is mixed with 1.500 ml of 1.000×10^{-2} M KIO_3. To this mixture 3 ml aliquot of CPZ solution is added and the mixture is rendered acidic by the addition of 1. 000ml of 1.000 M HCl (11.8N). The mixture is then diluted and the value of absorbance is measured at 526 nm after letting the mixture to stand for 15 minutes in the dark.

Application to various dosage forms

A portion equivalent to 0.1075 gm of a homogenized powder of 10 tablets Largactil (Aubrey Pharmaceutical Industries - Aleppo/Syria with distinction from the company Avnitis – France 25mg/tablet) was weighed and dissolved in 100 ml water. Dissolution of the drug was assisted by means of magnetic stirring and an ultrasonic bath. The resulted solution was cleaned through a Whatman filter paper No.1. and the volume was made up to the dent with distilled water in 100ml calibrated flask. The drug gratified of an aliquot of this solution was found by applying the general procedure as pronounced above.

Results and Discussion:

When CPZ was treated according to the recommended procedure, the recorded absorption spectrum of the formed reaction product for the range of 450 to 600 nm against reagent blank shows an extreme absorption at 526 nm, while, the blank does not have any significant absorbance in this region, as it is shown in (Fig.2).

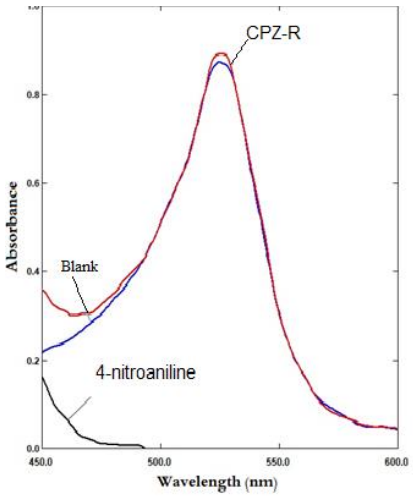


Figure 2. The absorption spectra of 30 µg/ml CPZ- R coupling product against reagent blank solution, 30 µg/ml CPZ -R coupling product against distilled water, and reagent blank solution against distilled water.

Optimization of reaction conditions:

The effect of the amount of HCl, 4-nitroanilline, and potassium periodate was investigated. The results show that use of 1.000 ml of 1.000 M hydrochloric acid (i.e. pH=2.2) with 1.500ml of 1.000×10^{-2} M of KIO_3, and 1ml of 1.000×10^{-2} M of coupling reagent give best results (Fig.3 a, b and c respectively).

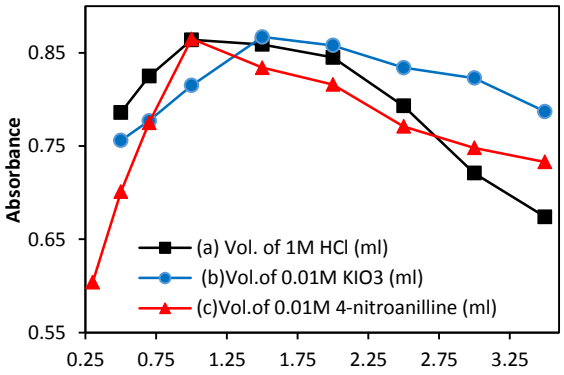


Figure 3. Effect of (a) HCl, (b) KIO_3, and (c) 4-nitroanaline on the on the formation of the colored product.

The order of addition of the reactants should be followed, as cited in the recommended procedure. Moreover, optimum time for full color development was found to be 10minutes, and room temperature15C^{o} was found the most favorable for the color development of the reaction product, Fig.4 (a and b respectively).

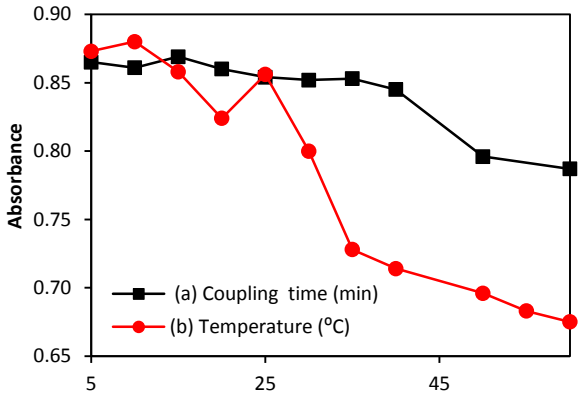


Figure 4. Effect of (a) coupling time, (b) Temperature, on the formation of the colored product.

Furthermore, water was found to be the best solvent among different solvents (viz: water, ethanol, acetone and diethyl ether) tried to solvate the reaction medium and to obtain the perfect absorbance, Fig.5.

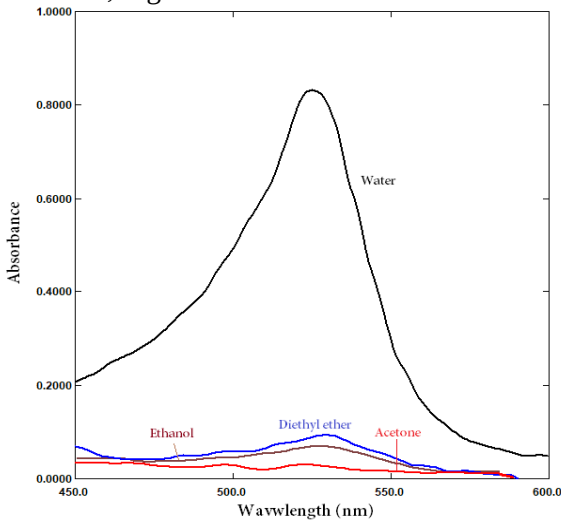


Figure 5. Effect of solvent.

Calibration graph and the statistical data

Using the obtained optimum conditions, a calibration curve was built (Fig.6). The graph shows that the violet colored product obeys Beer's law in the range of concentration of 5 – 40 µg/ml of CPZ. Table 1.depicts the statistical information of the calibration curve of spectrophotometric determination of CPZ.

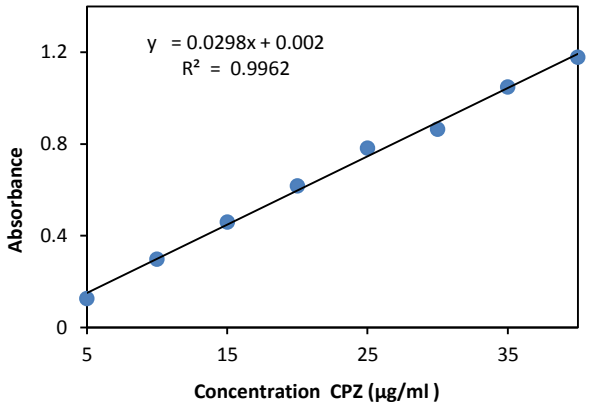


Figure 6. Calibration curve for the determination of chlorpromazine hydrochloride under optimal condition.

Table 1. Statistical data of the calibration curve for the spectrophotometric determination of CPZ.

Parameter	Value
λ_{max} nm	526
Color	Violet
Linear range (µg/mL)	5-40
Regression equation	A = 0.0298 [CPZ] +
Molar absorptivity (L/mol.cm)	1.025×10^4
Correlation coefficient	0.9980
Intercept	0.002
Slope	0.0298
S_b	0.0307
S_a	0.197
LOD (µg/mL)(18)	0.0930
LOQ (µg/mL)(18)	1.03
Sandell's sensitivity (µg/cm^2)	0.03467

precision and Accuracy

The capability of the method was statistically evaluated via measuring accuracy as relative error percentage (E_{rel}%), and precision as relative standard deviation percent of the proposed methods. Table 2 illustrates that the results obtained for seven replicates at three concentration levels of CPZ were satisfactory which indicate that the proposed methods have a good precision and accuracy.

Table2. Evaluation of precision and accuracy for determination of CPZ .

Conc.of CPZ (µg /ml)		$E_{rel\%}$	*RSD %
Taken	Found		
10	10.20	2.00	1.831
30	29.80	-0.600	0.231
40	40.11	0.275	0.255

* n=7

Stoichiometry of reaction

The stoichiometry of the response between CPZ and the mixture was investigated using Job's method and mole- ratio method. The consequences

obtained via the two methods indicate that the stoichiometry of the water-soluble coupling product between drug and the reagent is 1:1 (Fig. 7 and Fig. 8)(15).

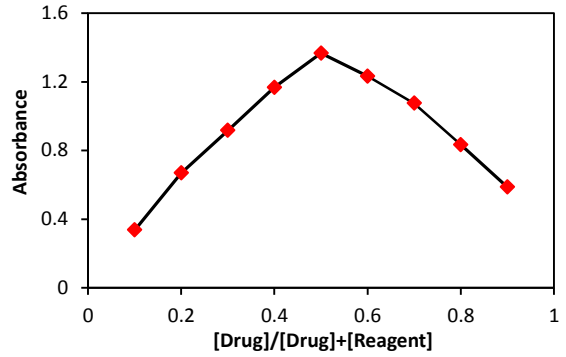


Figure 7. Job's method.

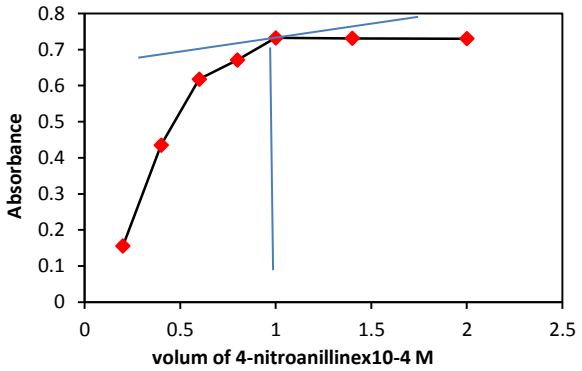
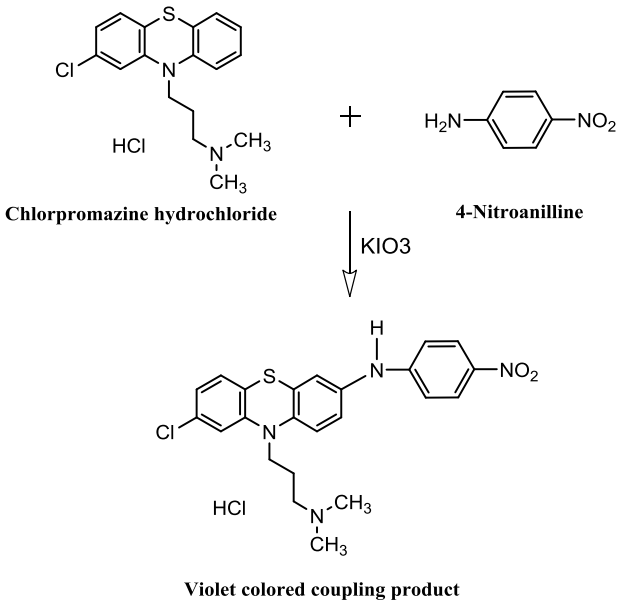


Figure 8. Mole ratio for reaction of (CPZ) with reagent.

Accordingly, a mechanism for formation of the colored product upon the reaction between CPZ and reagent in presence KIO_3 is founded in scheme 1:



Scheme 1. The suggested mechanism for formation of the colored product.

Analysis of CPZ in pharmaceutical preparations

Two procedures (direct calibration and standard additions) were followed using the proposed method to determine CPZ in Largactil tablets. The obtained results are shown in Table 3 and in Fig.9. Good agreement in results was found for both procedures.

Table 3. Determination CPZ in Largactil Tablets (25 mg/tablet), by direct calibration and standard addition method.

Procedure	Conc. of CPZ (µg/ml)		AE	SD	RSD%	E_{rel} %	Recovery %
	Taken	Found					
Direct calibration.	10	10.06	0.06	1.41	0.009	0.68	100.68
	40	40.27	0.27	1.45	0.360	0.675	100.675
Standard additions	25	23.94	-1.06	1.42	0.589	-4.219	95.780

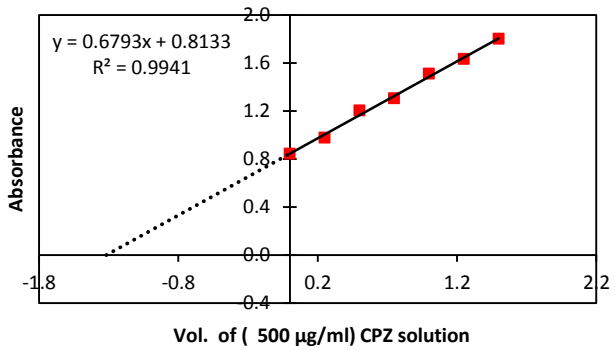


Figure 9. Standard additions plot.

Conclusion:

A rapid, simple and precise spectrophotometric method has been suggested for the determination of chlorpromazine hydrochloride in aqueous solution based on oxidation with 4-nitroanilline and KIO_3 in the acidic solution. The suggested method does not require temperature control or the solvent extraction step, the method was applied, successfully for the determined of amounts commercial CPZ drug.

Conflicts of Interest: None.

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التقدير الطيفي لعقار كلوبرومازين هيدروكلوريد باستخدام 4-نايترو انلين بوساطة تفاعل الاقتران بالاكسدة

أسماء أحمد محمد الراشدي عبد الرحمن خضير عبد الحسين الطائي مهند فيصل شريف

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الخلاصة:

تم تطوير طريقة طيفية بسيطة و سريعة لتقدير عقار كلوبرمازين هيدروكلوريد بشكله الحر وفي بعض مستحضراته الصيدلانية الطريقة تتضمن تفاعل تاكسدي باستخدام الكاشف العضوي 4-نايترو انلين في محلول حامضي مع KIO_3 فاعطى معقد بلون بنفسجي سجل اعلى امتصاص له عند الطول الموجي 526نانومتر . ويمكن ايجاز الظروف التحليلة المدروسة كالاتي: امل من 1مولاري حامض الهيدروكلوريك اي بدالة حامضية (2.2) 1مل من الكاشف 4-نايترو انلين بتركيز $1X10^{-2}$ مولاري ، 1.5مل من العامل المؤكسد KIO_3 تركيزه $1X10^{-2}$ مولاري في حجم نهائي مقداره 25مل وقد تم دراسة تسلسل الاضافة وزمن تفاعل الازدواج واختيار المذيب الانسب عند درجة حرارة المختبر. و كانت قيمة حدي الكشف النوعي والكمي 0.34 و 1.034مكغم/مل على التوالي، معامل الارتباط 0.9980،معامل الامتصاص المولاري 1.025×10^4 لتر.مول$^{-1}$سم$^{-1}$ ،حساسية ساندل0.03467 مكغم/سم^{2}كما ان دقة وتوافقية الطريقة لوحظت من خلال القيم الواطئة للخطأ النسبي والعالية للاستردادية المئوية وقيمة الانحراف القياسي النسبي المئوي (0.558،99.22%،(1.831%>) على التوالي، كما طبقت الطريقتان المباشرة وطريقة اضافة القياس لتطبيق الطريقة على المستحضر الصيدلاني ولاقت نجاحاً.

الكلمات المفتاحية: المطيافية، تقدير،4-نايترو انلين، هيدروكلوريد الكلوبرومازين، KIO_3.