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Research Article

NEW CHROMOGENIC REAGENT FOR THE SPECTROPHOTOMETRIC DETERMINATION OF CHLORPROMAZINE HCL IN AQUEOUS SOLUTIONS AND PHARMACEUTICAL FORMULATIONS

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ABSTRACT

Objective: Simple, rapid and accurate spectrophotometric method has been developed for the determination of Chlorpromazine HCl in pure and pharmaceutical formulations.

Method: The method is based on the formation of violet color product as a result to interaction of mentioned drug with P-amino acetanilide as new chromogenic reagent in the presence of ferric chloride hexahydrate. The experiential conditions have been studied by UV-Vis spectrophotometric analysis.

Results: The calibration curve was linear in the range 4-32ppm with a correlation coefficient of 0.9990 with a maximum absorbance at 590nm, while the limit of detection(L.O.D) was1.7ppm. The results compare favorable with those of official methods.

Conclusion: The proposed method is simple and economical and can be used in the estimation of chlorpromazine HCl in bulk and pharmaceutical formulations.

Keywords: Spectrophotometric**,** p-aminoacetanilid, New chromgenic reagent, Chlorpromazine HCl.

INTRODUCTION

Several N-substituted phenothazines are commonly employed in medicine and therefore their determination in pharmaceutical formulations is of considerable importance[1]. Chlorpromazine was discovered in the early 1950s as important antipsychotic agent and the advent of even more powerful phenothaizinic psychopharmacological agent represent a landmark in the history of the medical and psychiatric science[2,3]. Chlorpromazine HCl(CPH) as shown in figure(1) is [3-(2-chlorophenothazine-10-yl)propyl] dimethylamine hydrochloride, and it is one of family of drugs commonly known as neuroleptic tranquilizers, which used as sedatives, antihistamines, antiemetics and anaesthetics[4].

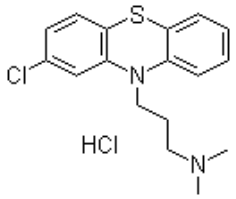


Fig. 1: Chemical Structure of chlorpromazine HCl (CPH).

Several methods for the determination of chlorpromazine using different techniques, including spectrophotometry[5-9], spectrofluorimetry[10], chemiluminescece[11], spectroelectrochemistry[12], polarography[13], voltammetry[14], potentiometry with an ion-selective electrode[15-16], liquid chromatography[17-18], capillary electrophoresis[19] and flow injection analysis[20], have been reported. In the last decade methods based on spectrophotometric determination have been reported for determination of Amiloride [21] and Cilnidipine[22].

We here proposed a simple and accurate spectrophotometric method for the determination of chlorpromazine hydrochloride. It was based on the using new chromogenic reagent of p-Aminoacetanilide(PAA) that reacts with the mentioned drug in the presence of ferric chloride hexahydrate as oxidizing agent leading to formation an intense violet product having a maximum absorption at λ_{max}(590nm). The method was successfully applied to the determination of chlorpromazine hydrochloride in aqueous solutions and pharmaceutical formulations.

MATERIALS AND METHODS

Apparatus

- All spectral and absorbance measurements were carried out on Shimadzu UV-Vis 1800 double beam spectrophotometer using 1cm glass cell.

- Four digital balance type Denever instrument / Germany.

- Labtech digital water bath.

- Charisma ice bath.

Reagents

All chemicals used were of analytical grade reagents unless otherwise stated, CPH pure powder was provided from SDI company-Iraq.

CPH stock solution(500ppm)

0.05gm of pure CPH was dissolved in 100ml of distilled water in a volumetric flask of 100ml.

PAA reagent ($1x10^{-2}$M)

Prepared by dissolving 0.1501gm in 100ml distilled water.

Ferric chloride hexahydrate(30%V/V)

10gm of Ferric chloride hexahydrate was dissolved in 100ml of 0.1M of HCl to prepare 10%W/V. 30ml from this solution was diluted with 0.01M HCl to 100ml volumetric flask.

Standard HCl solution(0.1M)

This solution was prepared from the gradual dilution of stock HCl and was standardized with sodium carbonate solution.

Methodology

Into a series of calibrated flask(25ml), transfer increasing volumes of CPH solutions to cover the range of calibration curve(4-32ppm) in a final volume of 25ml, then added 1ml of $1x10^{-2}$M PAA and shake well. Add 2ml of ferric chloride hexahydrate(30%v/v); dilute the mixture to the mark with distilled water, and allow the reaction to stand for 20min at room temperature. Measure the absorbance at 590nm against reagent blank but containing no CPH. The preferred conditions were optimize using 20ppm of CPH in a final volume of 25ml.

Analysis of pharmaceutical formulations

Largactile tablets(50 and 25mg CPH):

Ten tablets of mentioned drugs were weighted, crushed and grinded. Extracted an accurately weighted portions of the powder equivalent to about 500ppm of CPH; then dissolved in 100ml distilled water using 100ml volumetric flask. The undissolved materials was filtered and use 0.8ml aliquot of 500ppm solution in a final volume 25ml volumetric flask for the formation of violet color product via reaction with PAA and ferric chloride hexahydrate as described under calibration curve.

RESULTS AND DISCUSSION

Determination of Wavelength(λ_{max}) of color product

The combination and order of the addition of the chemicals are involved in the formation of violet colored product, i.e. reaction of CPH(20ppm) with PAA(1x10^{-2}M) in the presence of ferric chloride hexahydrate(30%v/v). This violet colored product that formed was scanned from 400-750nm for the measurement of absorbance versus wavelength. The scanning shows that a maximum absorbance at 590nm(figure(2)) was obtained against reagent blank (i.e. mixture of PAA and ferric chloride hexahydrate). Therefore, the λ_{max} of 590nm was used in all subsequent experiments.

Optimization of experimental conditions

A series of experiments were conducted to establish the conditions for the production of maximum well defined intensity for the violet color product.

Effect of PAA reagent concentration

When variable volumes of PAA(1x10^{-2}M) were added to a fixed amount of CPH(20ppm/25ml); followed by addition of 1.5ml (30%v/v) ferric chloride hexahydrate and dilute the mixture to the mark with distilled water; allow the mixture to stand for 20min at room temperature. 1ml of 1x10^{-2}M of PAA was found enough to develop the violet color product to it's maximum intensity and gave a minimum absorbance blank. Therefore, 1ml was considered to be the preferred volume of PAA (1x10^{-2}M) as shown in figure(3).

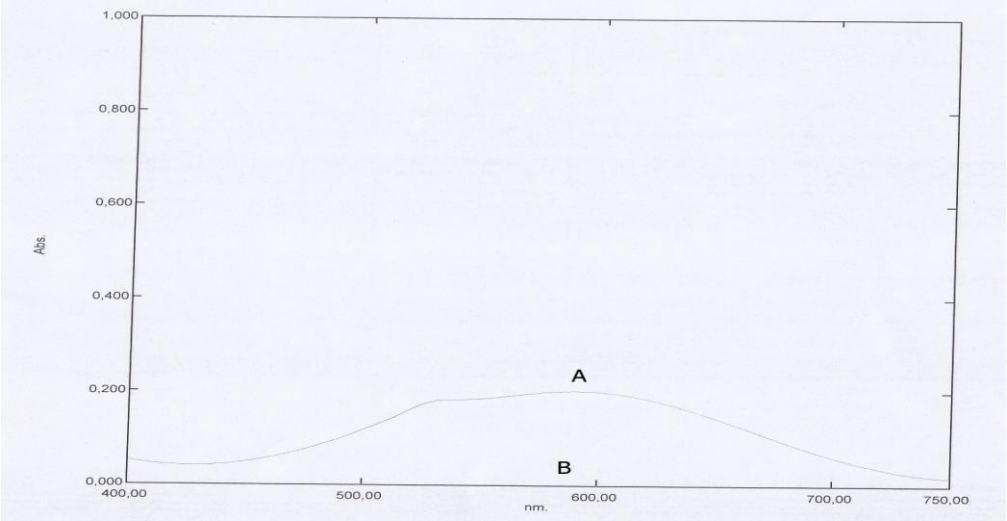


Fig. 2: Absorption spectra of A(20ppm) of CPH treated as described under recommended procedure and measure against B reagent blank.

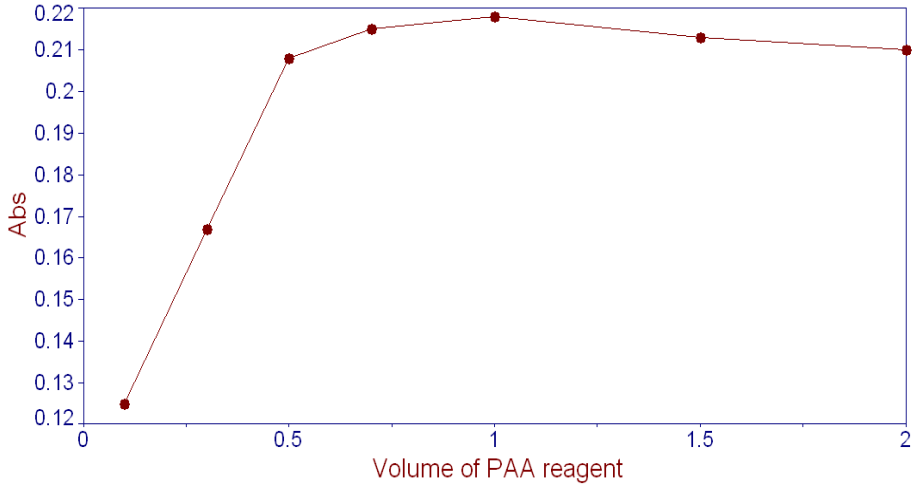


Fig. 3: Effect of variation of reagent volume(ml) on the intensity of the colored product.

Effect of oxidant concentration

Using the optimum variable achieved in previous section. A variable volumes of ferric chloride hexahydrate solution(30%v/v) ranging 0.5-3ml were used to establish the optimum concentration of the oxidant. The maximum product formation was achieved when using 2ml of ferric chloride hexahydrate as shown in figure(4). Therefore, 2ml of the oxidant concentration was used in all subsequent experiments.

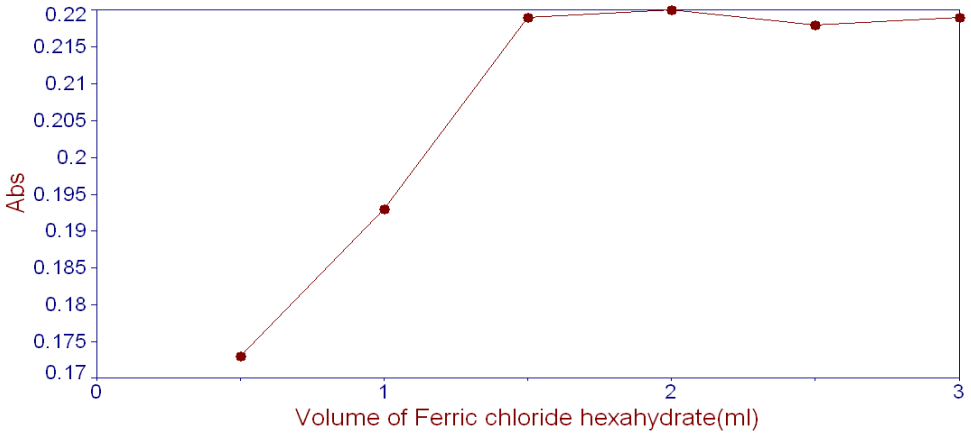


Fig. 4: Effect of variation of the oxidant concentration on the absorbance of violet color product.

Effect of order of addition

The measurements obtained indicated that the order of addition of the chemicals involved in the formation of colored product have no effect on the sensitivity and intensity of the product formed. Thus, the recommended addition shown in calibration curve construction was used through out this work.

Effect of temperature

The effect of temperature on the color intensity of the violet dye was studied. In practice, the absorbance of the sample was low at 10°C whereas at 50°C a high value for the blank was obtained. Therefore, it is recommended that the color reaction be carried out at room temperature(25°C).

Development time and stability period

The color intensity reached a maximum after the aromatic amine solution had been reacted completely with CPH in the presence of the oxidant for 20min. The obtained violet color was stable for an additional 25min, after which a slightly decrease was observed as shown in figure(5). Therefore, 20min was used as preferred reaction time and allow several measurements to be performed sequentially.

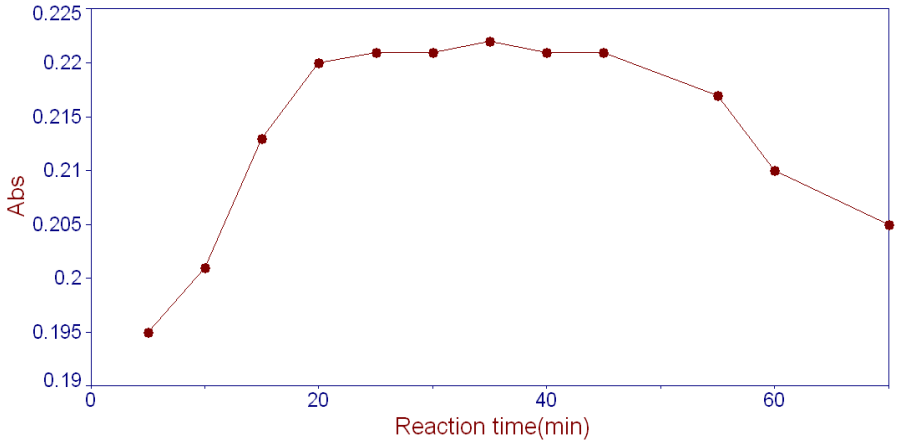


Fig. 5: Effect of reaction time and stability period on the intensity of the violet colored product.

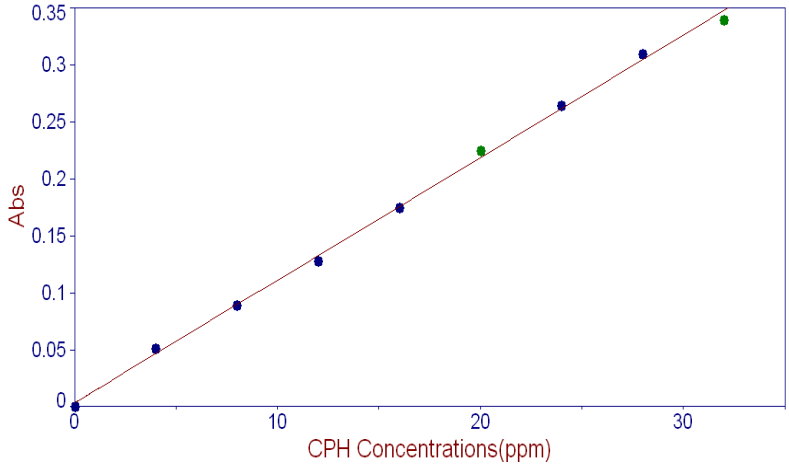


Fig. 6: Linear calibration curve for the variation of absorbance of colored product with CPH concentration.

Construction of calibration curve

Fixing all the achieved parameters in previous sections . A series of CPH standard solutions were prepared, a calibration curve for the variation of intensity of colored product with CPH concentrations is obeyed over the concentration range 4-32ppm as shown in figure(6). The obtained results were tabulated in table(1).

The conditional molar absorptivity(ε) of violet color product was found to be $3.923x10^3 L.mol^{-1}.cm^{-1}$ and the sandell sensitivity(S) was $9.05x10^{-5} \mu g.cm^{-2}$.

Accuracy and precision of proposed method

Chlorpromazine HCl was determined at two different selected concentrations(16, 24ppm). The obtained results were tabulated in table(2), indicated that the proposed method for determination of CPH using PAA as new chromgenic reagent was quite satisfactory in reality on the used of both procedure and parameters.

Limit of detection (L.O.D)

The limit of detection of CPH for the proposed method was measured using the successive gradual dilution of the minimum concentration of CPH drug that was used in the calibration curve which was 4ppm, a limit of detection of 1.7ppm. Table(3) summarizes the limit of detection of CPH conducted through two methods.

Nature of the violet product

The reaction between CPH and PAA was investigated using molar ratio method. The obtained results is shown in figure(7); which shows that a 1:1 product might be formed between CPH drug and PAA reagent at wavelength 590nm. On this base, the formation of product might be probably occurs as follows[23].

Table 1: Summary of linear regression for the variation of absorbance with CPH concentration using first degree equation of known form y=a+bx.

Concentration (ppm)	Linear range (ppm)	Straight Line equation Abs=a+b[X]	Correlation coefficient (r)	Percentage Linearity (r^2%)	Calculated t-value $\frac{/r/\sqrt{n-2}}{\sqrt{1-r^2}}$	Molar absorptivity(ε) $L.mol^{-1}.cm^{-1}$
0-40	4-32	Abs=0.0034+0.010[X]	0.9990	99.82	57.63	$3.92x10^3$

Table 2: Accuracy and precision of the proposed method for the determination of CPH in aqueous solutions

CPH Concentration(ppm)		%Recovery*	%R.S.D*
Taken	Found		
16	15.80	98.75	0.36
24	24.62	102.58	0.38

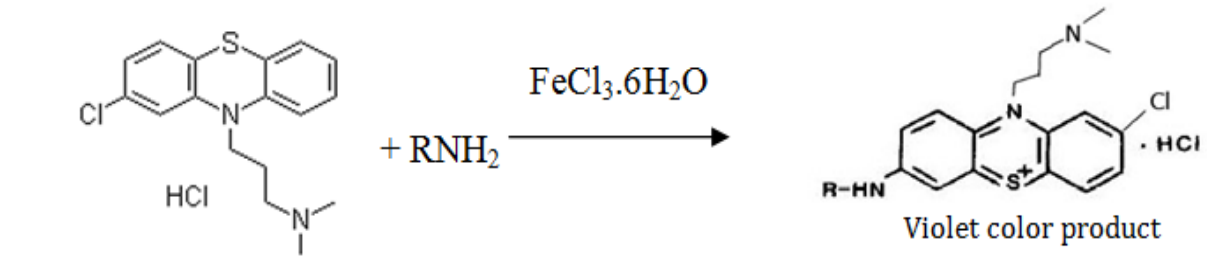
* Average of three determination

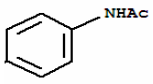
Table 3: Limit of detection of CPH for the proposed method

Practically based on gradual dilution for the minimum concentration	Theoretical based on the value of slope $X=3S_B/slope$
1.7ppm	1.4ppm

X=value of L.O.D based on slope.

S_B=standard deviation of blank solution.



Where R= 

The applications

Two types of pharmaceutical formulations containing CPH have been analyzed as described under recommended procedure; a good accuracy and precision were obtained. The obtained results were summarized in table(4), which confirm the reality and applicability of the proposed method for the determination of CPH in pharmaceutical formulations.

T-test was carried out as shown in table(5), indicated that there was no significant difference between the developed method and the official method at 95% confidence interval as the calculated t-value(0.59) is less than tabulated t-value(2.78).

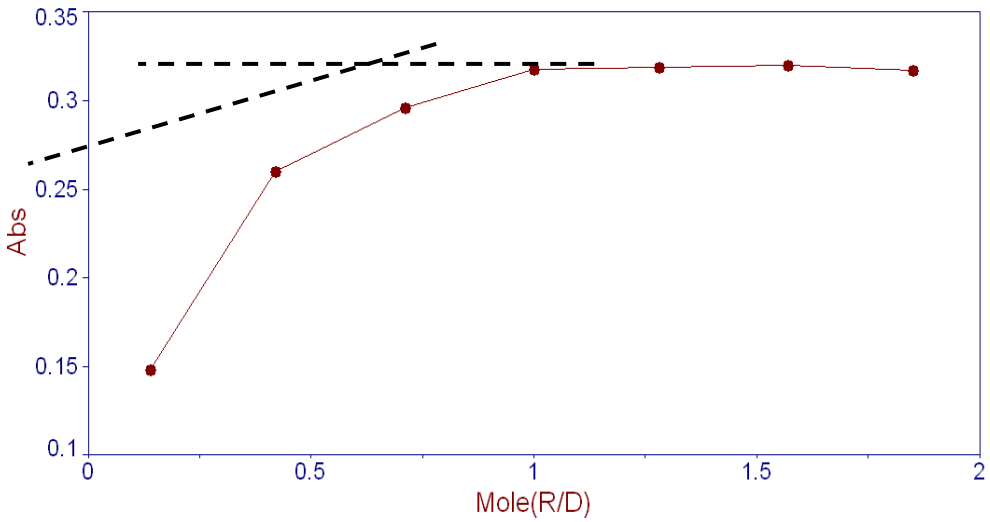


Fig. 7: Molar ratio method for the reaction between CPH(D) and PAA(R) in the presence of ferric chloride hexahydrate.

Table 4: Application of the proposed method for the determination of CPH in pharmaceutical tablets

Tablet sample	Weight of CPH(mg)	Amount of CPH taken(ppm)	Amount of CPH found(ppm)	%R.S.D*	%Recovery*
Largactile SDI /Iraq	50	16	16.17	0.64	101.06
Largactile Oubari / Syria	25	16	15.69	0.91	98.08

* Average of three determinations.

Table 5: Comparison of new method with official method

Sample No	Drug sample	% Recovery	
		New method	Official method*
1	Pure CPH	100.66	100
2	Largactile/SDI	101.06	98.56
3	Largactile/Oubari	98.08	99.03

*U.S.P Standard method

CONCLUSIONS

Although chlorpromazine HCl has been determined by a variety of techniques, the method described here is simple, highly sensitive (spectrophotometry), convenient and don't require special working conditions, unlike many other reagents. Moreover, owing to the advantages of the new reagent(PAA) for the estimation of CPH in aqueous solutions and pharmaceutical formulations, PAA can be used for routine analysis.

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