Spectrophotometric Determination of Chlorpromazine -HCl by Ion - Pair Complex Formation with Acid Dyes

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Abstract

A simple, rapid, accurate and sensitive spectrophotometric method is proposed for the determination of chlorpromazine -HCl in pure form and in pharmaceutical formulation. This method is based on the formation of ion association complexes of drug with either thymol blue or bromophenol blue in an acidic buffer at pH values 4.17 and 3.68, respectively.

The ion-pair complexes formed exhibit absorption maxima at 410nm for both thymol blue and bromophenol blue. These complexes are quantitatively extracted with chloroform. The calibration graphs are linear and obeyed Beer's law in a concentration range of 50-250µg/ml and 10-120µg/ml with molar absorpitivites of $1.0374x10^3$ and $1.7613x10^3$ $l.mol^{-1}cm^{-1}$ for thymol blue and bromophenol blue, respectively.

Statistical treatment of the experimental results indicated that the method is precise, accurate and the procedure was successfully applied to the determination of the bulk drug and its pharmaceutical formulations.

Introduction

Chlorpromazine -HCl is chemically [3-(2- chlorophenothiazin-10-yl) propyl] dimethylamine hydrochloride (1), is an antipsychotic drug, a group of drugs includes phenothiazines, butyrophenones and thioxanthenes. Chlorpromazine -HCl is one of the phenothiazines, useful in violent patients and also used in severe anxiety (short-term), terminal illness, intractable hiccup and as antiemetic. (2)

Several procedures have been reported in the literature for the analysis of chlorpromazine -HCl. These methods are spectrophotometry (3-7), high-performance liquid chromatography (8-10), gas chromatography (11-12) and flow –injection with different types of detection system (13-14).

Ion –pair extraction spectrophotometry has been received considerable attention for quantitative estimation of pharmaceutical compounds. Bromophenol blue (BPB), bromothymol blue (BTP), bromocresol green (BCG), methylene blue (MB), thymol blue (TB) and light Green FCF has been reported to form an ion-pair complexes, thus offering simple and rapid spectrophotometric determination of a number of organic pharmaceutical compounds [15-20].

This paper described a newly developed procedure for the determination of chlorpromazine –HCl, based on the complexation of the drug with TB and BPB at pH 4.17 and 3.68 respectively, to form ion-pair complexes. The method is simple, sensitive and applied successfully in different tabulated dosage with good accuracy and precision.

Experimental

Apparatus

Absorbance measurements were carried out using a Beckman DU-65 single beam spectrophotometer with 10mm glass cells. The pH measurements were made with a Philips model a PW-9421 pH- meter.

Materials and Reagents

All chemicals used were of analytical reagent grade:

- Chlorpromazine –HCl standard powder material (purity 99.0%) was provided from the state company for drug industries and medical appliances Samara-Iraq (SDI).

Largactil tablets (labeled to contain 25mg Chlorpromazine -HCl) were provided from (Ciba) Switzerland.

Largapromactil tablets (labeled to contain 25mg Chlorpromazine -HCl) were provided from (SDI).

MIPROM- 25 tablets (labeled to contain 25mg Chlorpromazine –HCl) were provided from (Mission Pharmaceuticals Limited-INDIA).

Chlorpromazine tablets (labeled to contain 25mg Chlorpromazine -HCl) were provided from (Pharmadex S.A.L. Syria).

- Thymol blue, $1x10^{-3}$ M solution prepared by dissolving 46.7mg thymol blue in 100ml 0.1NaOH solution.
- Bromophenol blue, $1x10^{-3}$ M solution (prepared by dissolving 67.0 mg bromophenol blue in 5 ml methanol and completed to 100ml by distilled water).

Phthalate buffer (pH =3.60). To 250ml of 0.2M potassium hydrogen phthalate, 11.90ml of 0.2 M HCl was added, and then the solution was diluted to a final volume 1000ml with water (21).

Standard stock solutions

Solutions for Ion-Pair formation procedure

Half mg/ml standard solution of Chlorpromazine was prepared by dissolving 25mg of Chlorpromazine -HCl in 50ml of methanol by using volumetric flask.

General analytical procedures and calibration graphs

Ion-pair formation Procedure

-Method using thymol blue

One ml from each solution-containing (0.05-0.40mg) drug was transferred into 25-ml separating funnel. The solution was then treated with 1-ml of thymol blue solution. Five ml phthalate buffer (pH=3.60) was added and the complex was extracted for 1min with two portion of 5-ml chloroform. The organic layer was passed through anhydrous sodium sulphate into a 10-ml volumetric flask, then the volume was completed with chloroform and the absorbance was measured at the wavelength of maximum absorption (410nm) against reagent blank treated similarly Table (1).

-Method using bromophenol blue

One ml from each solution-containing (0.02-0.14mg) drug was transferred into 25-ml separating funnel .The solution was then treated with 1-ml of bromophenol blue solution. Five ml phthalate buffer (pH=3.60) was added and the complex was extracted for 1min with two portion of 5-ml of chloroform. The organic layer was passed through anhydrous sodium sulphate into a 10-ml volumetric flask, then the volume was completed with chloroform and the absorbance was measured at the wavelength of maximum absorption (410nm) against reagent blank treated similarly Table (1).

Procedure for pharmaceutical formulations
Applying Ion-pair formation Procedure

Twenty tablets were washed from the color coat using distilled water, dried, weighed and finely powdered. A quantity of powdered tablets equivalent to 25 mg chlorpromazine -HCl was dissolved by shaking with 5-ml methanol and the volume was made to 50-ml with either 0.1M HCl for the procedure using thymol blue or distilled water for procedure using bromophenol blue. The solution was filtered and the procedure was continued as described under procedure for calibration curves.

Results and discussion

Ion-pair formation

Absorption spectra

Fig (1): shows the absorption spectra of the chlorpromazine -thymol blue ion-pair complex and of the reagent blank in chloroform. An intense yellow color was formed immediately, which become stable for at least two hour. The absorption maximum of the ion-pair in chloroform is at 410nm; in contrast to the reagent blank, which show negligible absorption over the range (380-540nm). Therefore, a wavelength of 410nm was used for the examination of the conditions for the determination of chlorpromazine -HCl. On the other hand, a solution of chlorpromazine and bromophenol blue exhibits a pale-yellow color with maximum absorption band at 410nm in contrast to the reagent blank Fig.(2). Therefore, all absorbance measurements were made at 410nm.

Optimization of variables

pH dependence

One- milliliter from thymol blue and bromophenol blue solutions was mixed with specified volume of chlorpromazine -HCl solution, and then the pH was adjusted to a pH between 3.0-4.6 with hydrochloric acid –phthalate buffer solution. Maximum and constant absorbances were obtained in the pH range 3.90-4.18 and 3.30-3.68 for thymol blue and bromophenol blue respectively Fig. (3). The absorbance decreased at pH values above the optimum range, Hence, a pH of 4.18 and 3.68 were used in all the subsequent experimental work.

Effect of reaction time

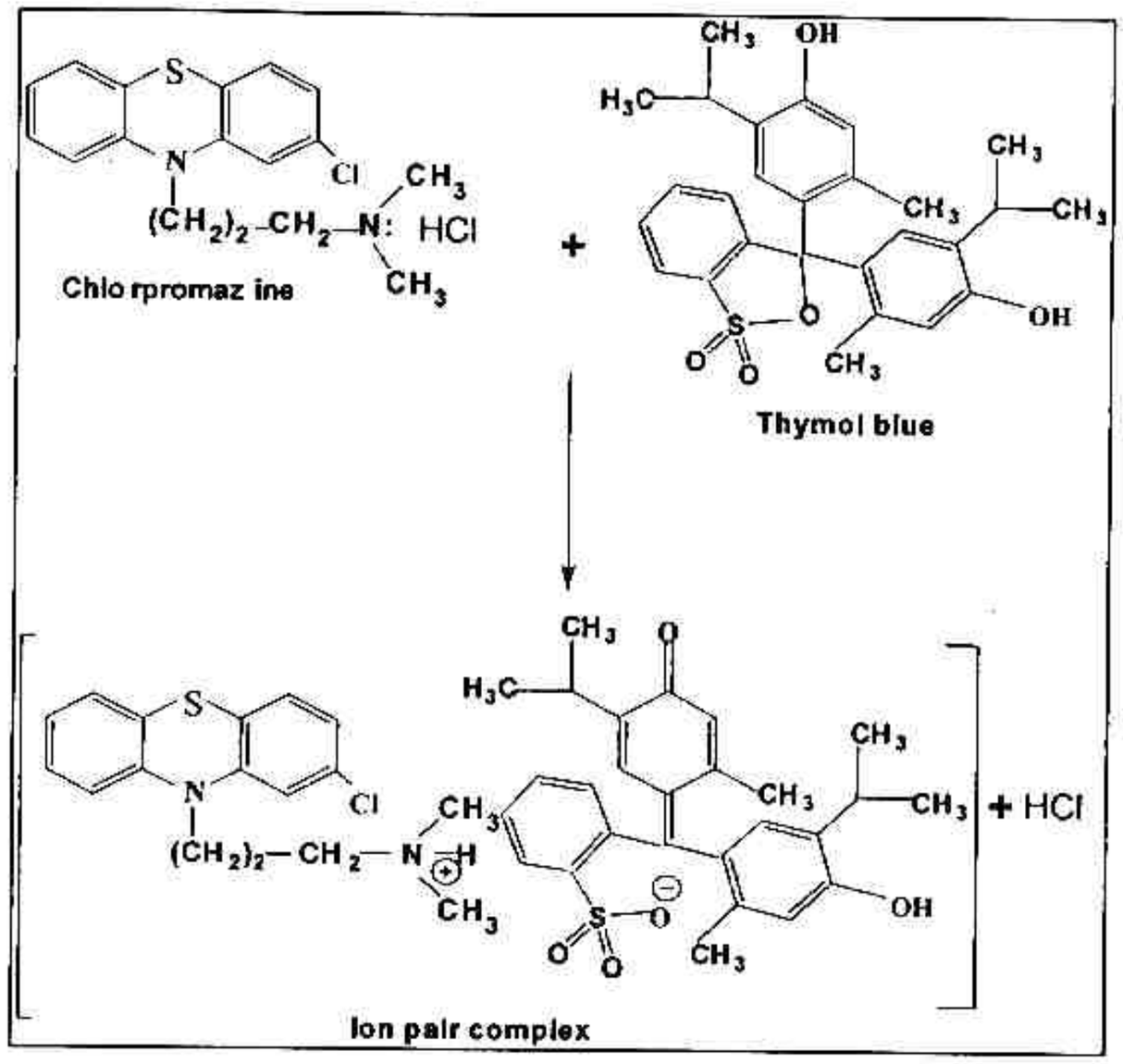
The optimum reaction time was determined by following the color development at ambient temperature ($25C^0 \pm 2$). It was found that the reaction is instantaneous. Hence the product attained maximum and constant absorbance immediately after the chlorpromazine -HCl has been reacted with thymol blue or bromophenol blue and the color obtained remained strictly unaltered for 24 hr.

Calibration graphs (Beer s law and sensitivity)

Employing the conditions described under procedure, a linear calibration graph for chlorpromazine with thymol blue and bromophenol blue was obtained. The correlation coefficient, intercept and slope for all calibration data are calculated by using least square methods Table (2).

Stoichiometric relationship

Applying Job's method of continuous variation, the reaction stiochiometry of the ion-pair complexation of chlorpromazine -HCl with thymol blue and bromophenol blue was found to be 1:1 Fig. (4)
The formation of the complex is shown in the reaction scheme given below, taking thymol blue as an example (Scheme 1):



(Scheme 1)

Accuracy and precision

The reproducibility and precision of the proposed method was tested by estimating three different concentrations of the cited drug within the Beers law limits. The analytical results are summarized in Table (3).

Analytical applications

The applicability of the proposed method to the assay of simple dosage form was examined by analyzing four types of pharmaceutical marked tablets containing chlorpromazine -HCl; the results are summarized in Table (4).

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Table (1) Optimum conditions for the color development of chlorpromazine -HCl using ion- pair formation.

Item	Chlorpromazine -HCl	
	Thymol blue	Bromophenol blue
Conc. range of the drug (mg/ml)	0.005-0.40	0.020-0.180
Conc. of acceptor (% w/v) or molar	1ml ($1x10^{-3}$M)	1ml ($1x10^{-3}$M)
Reaction time (min)	At once	At once
λ_{max} (nm)	410	410
Stability of complex	More than 2hr	More than 2hr
Drug dissolving solvent	Methanol	Methanol
Diluting solvent	0.1M HCl	Water

Table (2) Optical characteristics and statistical data of the regression equations for determination of Chlorpromazine -HCl using ion–pair formation

Parameters	Chlorpromazine -HCl	
	Thymol blue	Bromophenol blue
Linearity range of the drug (µg/ml)	50-250	10-120
Molar absorpitivites ($l.mol^{-1}.cm^{-1}$)	$1.037x10^3$	$1.761x10^3$
Regression equation		
Intercept (a)	0.0300	0.0354
Slope (b)	0.00292	0.00495
Correlation coefficient (r)	0.9997	0.9993
Relative standard deviation (%)	0.49	0.59
Detection limit (D.L)	0.0541	0.0418

A=a + bc, A=Absorbance, c=Concentration

Table (3) Test of precision and accuracy of the method for samples of pure chlorpromazine -HCl.

Method	Amount of chlorpromazine (µg/ml)		Recovery % n=3	R.S.D % n=3
	Taken	Found		
Thymol blue	70	69.6346	99.4781	2.4743
	90	89.0410	98.9345	-
	120	119.8630	99.8858	-
Bromophenol Blue	30	29.8433	99.4777	3.1492
	50	50.0168	100.0336	2.0377
	70	70.1902	100.2717	2.0377

Table (4) Spectrophotometric determination of chlorpromazine -HCl in pharmaceutical formation using ion-pair method.

Sample	Wt.of tablet mg	Labeled amount mg	Method	Amount taken µg/ml	Amount found µg/ml	Recovery n=5 (%)	R.S.D n=5 (%)
Largactil Switzerland	99.0	25	Thymol-blue	65	64.7260	99.5785	1.0210
				80	79.7940	99.7431	1.0412
			Bromophenol-blue	50	49.9495	99.8991	0.9677
				90	89.8930	99.8812	0.4648
Largaprom actil (SDI)	181.9	25	Thymol-blue	65	64.3835	99.0516	1.2562
				80	79.4520	99.3150	1.0452
			Bromophenol-blue	50	49.7478	99.4956	0.9711
				90	89.4567	99.3963	-
Miprom-25 India	242.5	25	Thymol-blue	65	64.0410	98.5247	1.2620
				80	79.1095	98.8869	0.8567
			Bromophenol-blue	50	49.5460	99.0920	0.7957
				90	90.0948	100.1053	0.5681
Chlorproma zine Syria	210.8	50	Thymol-blue	65	63.6986	97.9978	1.0352
				80	78.7671	98.4589	-
			Bromophenol-blue	50	49.3443	98.6887	-
				90	89.4896	99.4329	0.9336

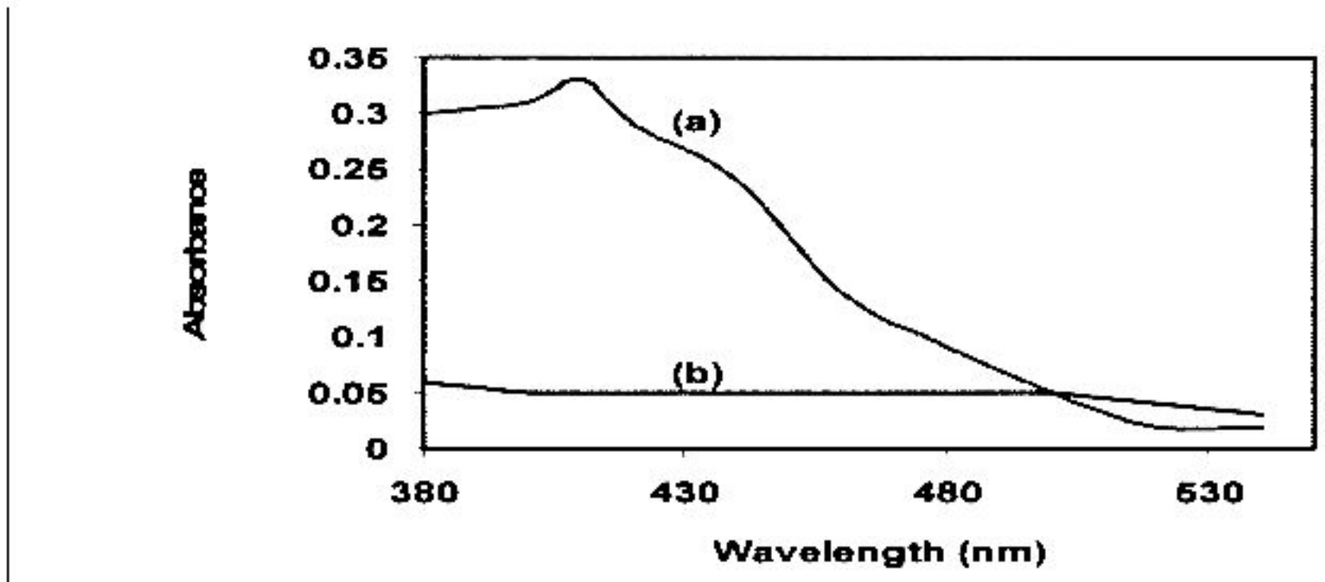

Fig (1) Absorption spectra of :
(a) : 1 x 10^{-4} M Thymol blue , 0.1 mg/ml chlorpromazin at pH =4.18
(b) : blank , solvant of extract (chloroform).

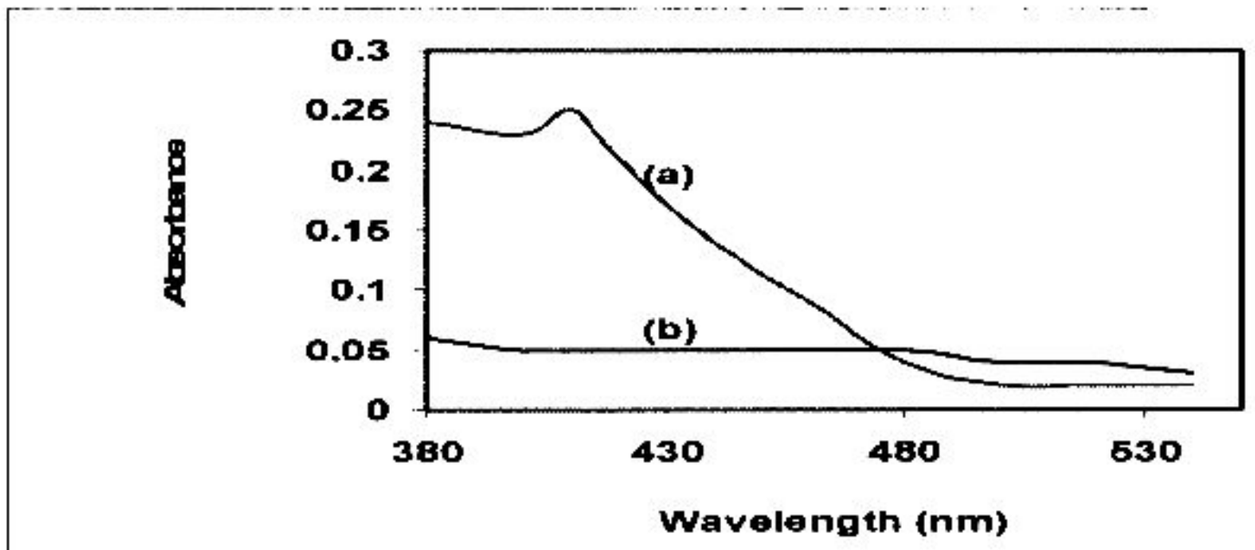

Fig (2) Absorption spectra of :
(a): 1 x 10^{-4} M Bromophenol blue , 0.04 mg/ml chlorpromazine at pH = 3.68
(b): blank , solvent of extract (chloroform).

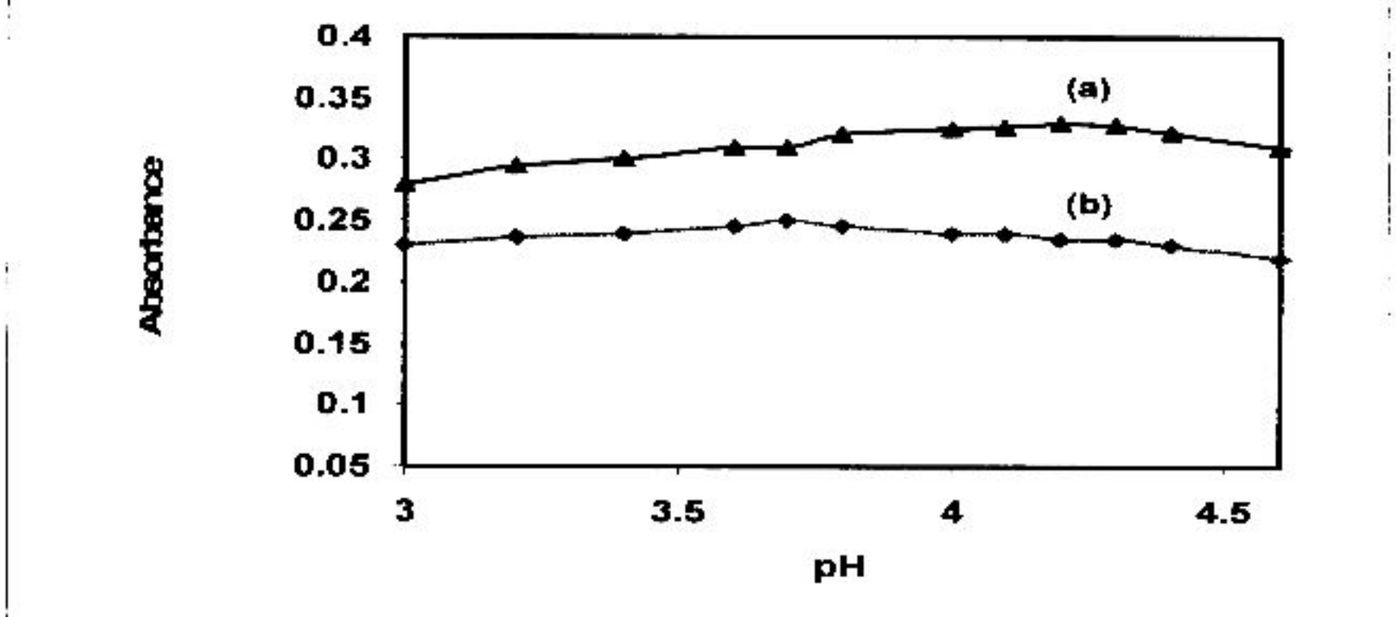

Fig (3) Effect of pH on the absorbance of :
(a): 1×10^{-3} M thymol blue ; 3.15×10^{-4} M chlorpromazine.
(b): 1×10^{-3} M bromophenol blue ; 1.26×10^{-4} M chlorpromazine .

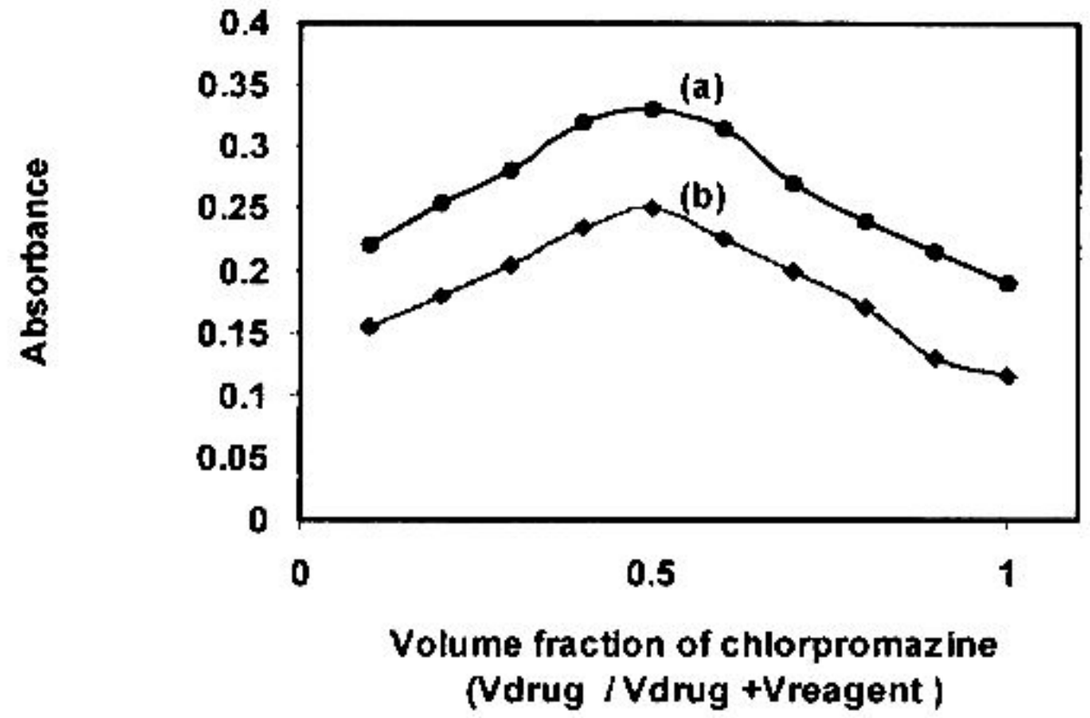

Fig (4) Continuous variation plot of :
(a) : [Thymol blue] = [chlorpromazine] = 3.15×10^{-4} M .
(b) : [Bromophenol blue] = [chlorpromazine] = $1,36 \times 10^{-4}$ M .

التقدير الطيفى للكلوربرومازين – هيدروكلورايد بتكوين معقدات الأزواج الأيونية مع الصبغات الحامضية

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الخلاصة

عرضت طريقة طيفية بسيطة وسريعة و ذو دقة وحساسية عالية لتقدير الكلوربرومازين–هيدروكلورايد في الصورة النقية وفي المستحضرات الدوائية. تستند هذه الطريقة الى تكوين معقدات الأرتباط الأيوني للدواء مع صبغة الثايمول الازرق او البروموفينول الازرق في بفر حامضي عند دالة حامضية مقدارها 4,17 و 68، 3 للصبغتين على التوالي.

ان معقدات الزوج الأيوني المتكونة أظهرت إمتصاصا أعظم عند طول موجي 410 نانوميتر لمعقدي الثايمول الازرق و البرومو فينول الازرق' وأن دوال المعايرة أظهرت أستقامة ومطاوعة لقانون بير ضمن مدى التراكيز (50–250) ،(10–120)مايكروغرام/مل مع امتصاصية مولارية مقدارها 1,0374 × 10 ^{3} و 7613 ،1 × 10 ^{3} لتر.مول $^{-1}$.سم $^{-1}$ لمعقدى الثايمول الازرق و البروموفينول الازرق على التوالي.

إن المعالجة الإحصائية لنتائج التجارب تشير الى ان هذه الطريقة تمتاز بالدقة و الحساسية، وان هذه الطريقة تم تطبيقها بنجاح لتقدير الدواء في الصورة النقية و في المستحضرات الدوائية.