Spectrophotometric Determination of Promethazine Hydrochloride by In (III)

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طريقة طيفية لتقدير البروميثازين بواسطة (In III)

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الخلاصة :

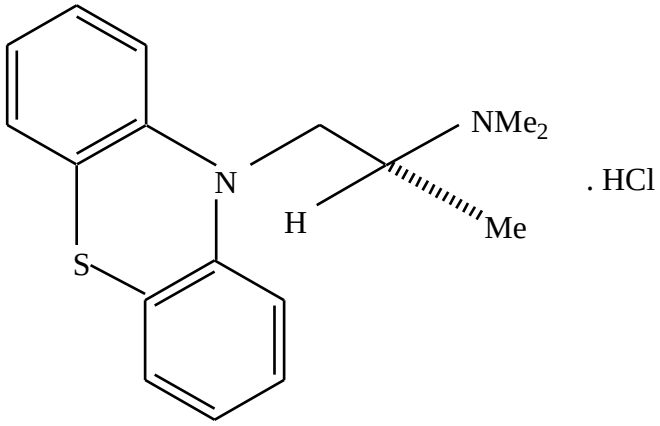
تم وصف طريقة طيفية سهلة وسريعة وحساسة لتقدير كميات ضئيلة من عقار البروميثازين هيدروكلورايد في المحلول المائي . تعتمد الطريقة على تكوين معقد البروميثازين هيدروكلوريد مع In (III) بوجود هيدروكسيد الصوديوم لتكوين ناتج ذائب في الماء ويمتلك اقصى امتصاص عند ٣٠٤ نانوميتر . وجد ان قانون بير ينطبق ضمن مدى التراكيز (٢-٢٠) مايكروغرام / مللتر وبلغت قيمة الامتصاصية المولارية (1.92 × ١٠ ^{٣} لتر / مول . سم) .تم دراسة الظروف المثلى لتكوين المعقد وطبقت الطريقة بنجاح في تقدير البروميثازين هيدروكلورايد في حالته النقية .

Abstract

A simple, rapid and sensitive spectrophotometirc method for the determination of trace amounts of promethazine hydrochloride in the aqueous solution is described. The method is based on the complexation of promethazine hydrochloride with In (III) in the presence of sodium hydroxide to form an soluble product with maximum absorption at 304nm. Beer's law is obeyed over the concentration range of (2-20μg/ml) with molar absorptivity of (1.92×10^3 $L.mol^{-1}.cm^{-1}$). The optimum conditions for all development are described and the proposed method has been successfully applied for the determination of promethazine hydrochloride in bulk drug.

Introduction

Promethazine hydrochloride [(2RS) - N , N – dimethyl -1- (10 h-phenothiazine – 10 – yl) propan-2-amine hydrochloride] (IIIustration 1) is the one of phenothiazine devivatives which is widely used as antihistamine and antiemitic drug.[1]



IIIustration 1. composition of promethazine hydrochloride.

Several methods have been applied to detect promethazine, such as chemiluminescence[2], voltammetry[3,4], chromatography[5], capillary zone electrophoreses[6,7], fluorimetry[8], turbidimetry[9], titrimetric and potentiometric titration methods[10,11]. Besides, the spectrophotometric methods which included charge- transfer complex formation reactions by using chloranil[12] and chloranilic acid[13] as t-acceptors reagents in organic medium, or by extractive spectrophotometric determination using dipicrylamine and picric acid reagents for the determination of promethazine hydrochloride[14], in addition of its spectrophotometric determination by flow injection analysis depending on the oxidation of promethazine by Ce IV[15,16], or electroxidation at gold in sulfuric acid medium[17]. Spectrophotometric method for the determination of promethazine hydrochlorite is proposed and is based on its oxidation by sodium hypochloride and then coupling with sulfanilic acid[18], electrochemical determination of trace promethazine hydrochloride by a pretreated glassy carbon electrode is modified with DNA[19]. In this work, a spectrophotometric method for the determination of promethazine hydrochloride by In (III) in sodium hydroxide medium is presented.

Experimental

Apparatus

- Shimadzu UV- VIS Spectrophotometer.
  UV-160 A Recorder Double beam.
- Phillips Pw,526 conductmeter.

Reagents

Promethazine hydrochlorid standard Samara- Iraq (SDI).
Indium oxide Fluka AG Buchs SG.
Sodium hydroxide Fluka AG Buchs SG.
Hydrochloric acid RIEDEL-DEHAEN AG.

Promrthazine Hydrochloride (1000µg/ml)

A stock solution of (1000µg/ml) of promethazine hydrochloride was prepared by dissolving (0.1 gm) in distilled water and then made up to (100ml) in a volumetric flask with the same solvent working solution of (100µg/ml) was prepared by simple dilution for primary stock solution and was kept ambient bottle away from sun light.

Indium III (1000µg/ml)

A stock solution of (1000µg/ml)of In (III))was prepared by dissolving (0.1209 gm) of Indium oxide in concentrated hydrochloric acide and diluted to (100ml) in a volumetric flask by distilled water. Working solution of (100µg/ml) was prepared by simple dilution of stock solution with distilled water.

Sodium Hydroxide (0.1M)

This solution was prepared by dissolving (0.4 gm) of sodium hydroxide in distilled water and diluted to (100 ml) in a volumetric flask with the same solvent.

Hydrochloric Acide (0.1M)

This solution was prepared by diluting of (1.54 ml) of concentrated hydrochloric acid (%37) and diluted to (250 ml) in a volumetric flask by distilled water.

Recommended procedure

Was taken (0.1, 0.2, 0.3 …. 1.0)ml of standard solution of promethazine hydrochloride (100 µg/ml) and it contained (2-20 µg/ml), they transferred to (5 ml) volumetric flask added (0.25 ml) of (8.7×10^{-4} M) of In (III) and (0.1 ml) of (0.1 M) of sodium hydroxide and complete the solution to the morl with distilled water.

Later, determine the absorbance of solution at λ_{max} = 304 nm by using reagent solution as blank.

Results and Discussions

- Absorption Spectra

The complex is produced from the reaction between promethazine hydrochoride with In (III) in basic medium of sodium hydroxide givining maximum absorbance at λ_{max} = 304 nm as in (Figure 1).

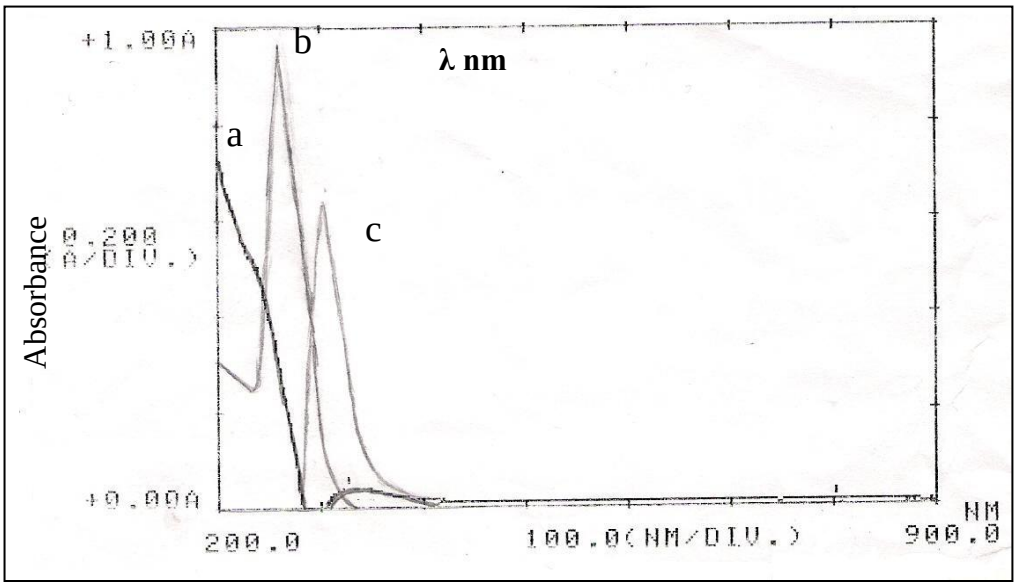


Figure 1: Absorption spectra of (a)50 µg/ml of In(III) (b)200 µg/ml of promethazine. HCl (c) 200 µg/ml of promethazine HCl with 50 µg/ml of In (III) against reagent blank.

Optimum conditions for regulation reaction.

There are many parameters effecting on the complexation reaction and absorbance of complex which is produced.

Effect of In (III) concentration

When various concentrations of In(III) solution (10, 20, ……,80)µg/ml were added to fixed amount of the drug, solution was found (50 µg/ml) of In (III) enough to give a maximum absorption and was considered to be optimum for concentration range of (2-20) µg/ml of promethazine hydrochloride.The results shown in table 1.

Table 1: effect of In(III) concentration of absorbance value of complex .

Con. Of In(III) µg/ml	Absorbance
10	0.033
20	0.061
30	0.102
40	0.126
50	0.160
60	0.162
70	0.161
80	0.162

Effect of In (III) volume

When various volumes of In III solution (0.1, 0.15, ……,0.4)ml of (1000 µg/ml) were added to fixed amount of the drug, solution was found (0.25 ml) of In(III) enough to give a maximum absorption and was considered to be optimum for concentration range of (2-20 µg/ml) of promrthazine hydrochloride.The results shown table 2.

Table 2: effect of In(III) volume solution on absorbance value of complex.

Vol. of In(III) (ml)	Absorbance
0.10	0.080
0.15	0.093
0.20	0.110
0.25	0.118
0.30	0.109
0.35	0.104
0.40	0.102

Effect of sodium hydroxide volume

It was found that the presence of base in reaction solution effect on increasing the intensity of absorbance for the produced complex, NaOH was selected and (0.1 ml) of (0.1M) was found.This base gives high sensitivity which was selected in subsequent experiments.The results shown table 3.

Table 3: effect of sodium hydroxide volume on absorbance value of complex.

Vol. of sodium hydroxide (ml)	Absorbance
0.1	0.166
0.2	0.160
0.3	0.155
0.4	0.150
0.5	0.148
0.6	0.140
0.7	0.136
0.8	0.109
0.9	0.108
1.0	0.103

Effect of hydrochloric acid volume

Existence of hydrochloric acid (0.1-1.0)ml of (0.1M) in reaction solution effect on decreasing the intensity of absorbance for produced complex.The results shown in table 4.

Table4: effect of hydrochloric acid volume on absorbance value of complex

Vol. of hydrochloric acid (ml)	Absorbance
0.1	0.154
0.2	0.150
0.3	0.142
0.4	0.140
0.5	0.135
0.6	0.117
0.7	0.110
0.8	0.109
0.9	0.107
1.0	0.100

Effect of complex time

The results show that the complex produced was not more than stable about 45 minutes but after 60 minutes the absorbance value decreased, that means the complex beginning to dissociated.The results shown in table 5.

Table 5: effect of complex time on absorbance value.

Time (min.)	Absorbance
5	0.160
10	0.160
15	0.161
30	0.162
45	0.162
60	0.130

Effect of temperature

The resulting product of the proposed method was studied at room temperatures (25°C), the absorbance values remain constant.The results shown in table 6.

Table 6: effect of temperature on absorbance value of complex.

Temp.(°C)	Absorbance
20	0.160
25	0.165
30	0.150
40	0.130
50	0.113

- Effect of order of addition

To obtain optimum results, the order of addition of drugs should be followed addition base and In (III).The results shown in table 7.

Table 7: effect of order of addition on absorbance value of complex.

Order of addition	Absorbance
In(III) + promethazine + NaOH	0.075
In(III) + NaOH + promethazine	0.089
promethazine + NaOH + In(III)	0.095
promethazine + In(III) + NaOH	0.090
NaOH + promethazine + In(III)	0.101
NaOH + In(III) + promethazine	0.113

Calibration Graph

Employing the conditions described in the procedure, a linear calibration graph for promethazine HCl is obtained (Figure 2), which shows that Beer's law is obeyed over the concentration range of (2-20 µg/ml) with correlation coefficient of (0.997) and molar absorptivity (ε) (1.92×10^3 $L.mol^{-1}.cm^{-1}$).

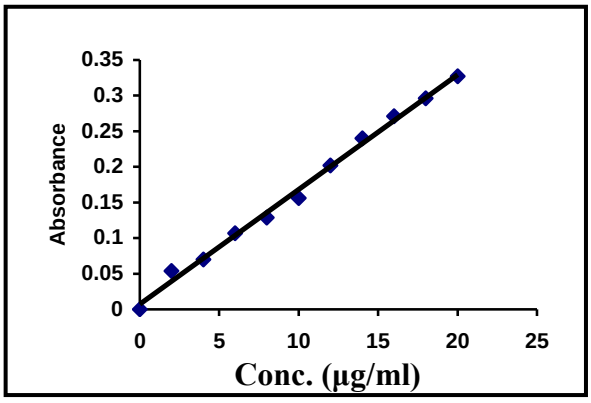


Figure 2: Calibration graph of promethazine hydrochloride.

Precision

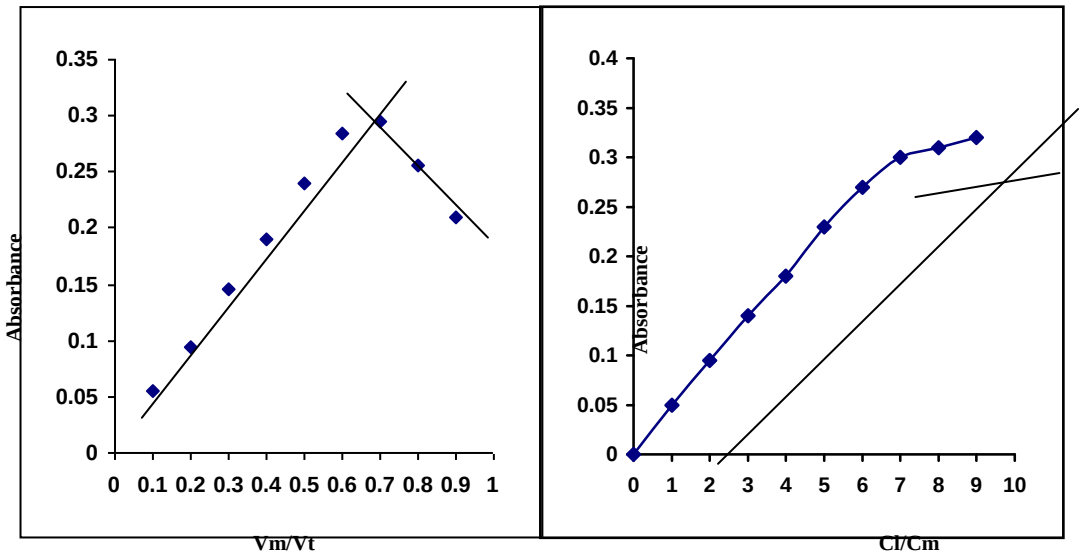
Promethazine HCl was determined at three different concentrations. The results shown in Table 8.

Table 8: Precision of the method

Con. Of promethazine HCl µg/ml	Relative standard deviation % n=5
5	1.0
10	0.8
20	1.0

Structure of the Dye:

The stoichciometry of the complex between promethazine HCl and In (III) was investigated using Job's method and mole ratio method; the results obtained (Figure 3) show that 1:2 In (III) to drug complex was formed at 304 n



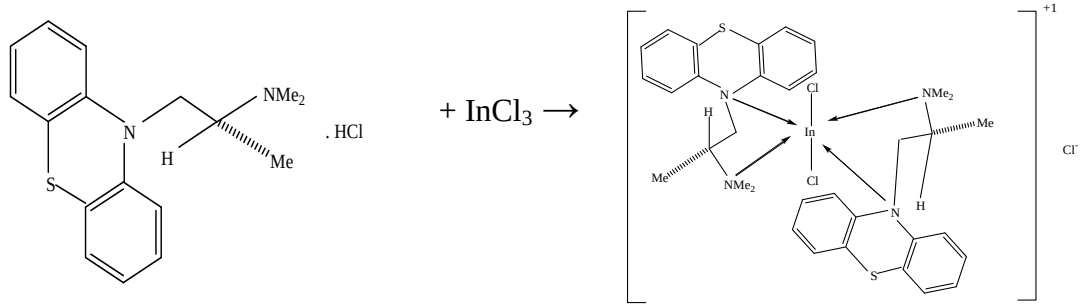
(a) Job's [promethazine.HCl(3.116×10^{-4} M) / promethazine.HCl+In (III) (3.116×10^{-4} M)]

(b) Mole ratio [promethazine. HCl(3.116×10^{-4} M) /In (III) (3.116×10^{-4} M)]

Figure 3: Job's plot method (a) and molar ration method (b) of promethazine. HCl –In (III) in sodium hydroxide medium.

The conductivity of the suggested product was electrolyte type behave(1:1)[20] .Therefore, the formation of the complex produced suggest occuring as follows(IIIustration 2).

$In_2O_3 + 6HCl \rightarrow 2InCl_3 + 3H_2O$



IIIustration 2. suggest product formation pathway.

The promethazine HCl complex was water soluble.

Conclusion

A simple, rapid, precise and sensitive spectrophotometric method has been developed for the determination of trace amounts of promethazine HCl in aqueous solution based on its reaction with In (III) in the presence of sodium hydroxide.

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