

***Spectrophotometric Determination of  
Promethazine Hydrochloride by In (III) .***

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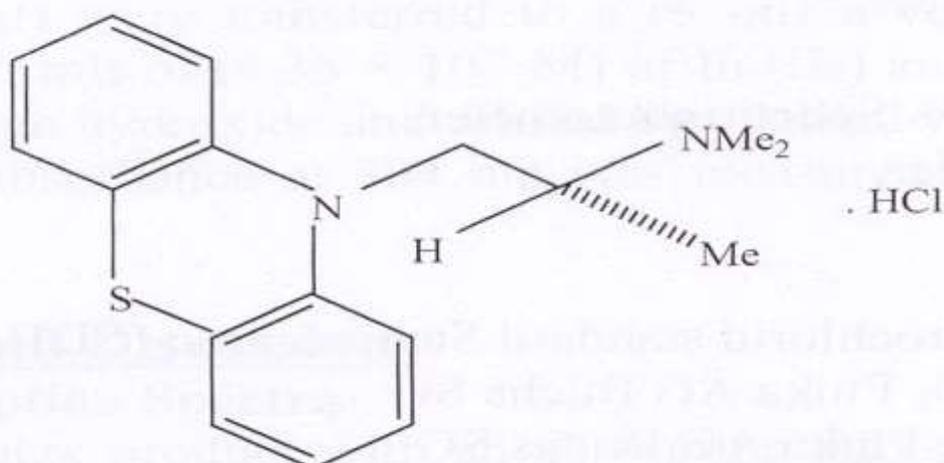
**Abstract :**

A simple, vapid and sensitive spectrophotometric metho) determination of trace amounts of promethazine hydrochloric aqueous solution is described. The method is based on complication of promethazine hydrochloride with In(III) in presence of sodium hydroxide to form an intense product maximum absorption at 304nm. Beer's law is obeyed over concentration range of (2-20ug/m1) with molar adsorptively The optimum conditions for (5.006x 10<sup>3</sup> L.mol<sup>-1</sup> .cm<sup>-1</sup> ).

development are described and the proposed method has successfully applied for the determination of promote hydrochloride in bulk drug.

**Introduction :**

Promethazine hydrochloride ( (2RS) - N , N - dimethyl -1- , 10 h- phenothiazine - 10 - yl ) propan-2-amine hydrochloride ( Illustration 1) is the one of phenothiazine derivatives which is widely used as antihistamine and antiemetic drug.



**Illustration 1. composition of promethazine hydrochloride.**  
Several methods have been applied to detect promethazine, voltammetry(2,3) chromatography(4) such as chemiluminescence, voltammetry(2,3), fluorimetry<sup>7</sup> turbidimetry<sup>8</sup> capillary zone electrophoresis(5,6),

Beside the titrimetric and potentiometric titration methods (9,10). spectrophotometric methods which included charge-transfer (11) and chelation complex formation reactions by using chloranil(11) in organic medium, or by extractive acid as acceptor reagents spectrophotometric acid reagents hydrochloride determination oxidation of promethazine by (16) in sulfuric acid medium. determination using in flow the addition dipicrylamine and picric acid determination of promethazine of its by spectrophotometric depending on the injection analysis reduction at gold Ce IV, Or electrooxidation spectrophotometric method for the determination of promethazine hydrochloride is proposed and is based on its oxidation by sodium hypochlorite and then coupling electrochemical determination of trace with sulfanilic acid, electrochemical determination of trace.

promethazine hydrochloride by a pre-treated glassy carbon electrode modified with DNA.

In this work, a spectrophotometric method for the determination of promethazine hydrochloride by In (III) in sodium hydroxide medium.

### **Experimental**

#### **Apparatus**

**Shimadzu UV- VIS Spectrophotometer.**

**UV-160 A Recorder.**

#### **Reagents**

**Promethazine hydrochloric standard samara- Iraq (SDI).**

**Indium oxide  $IO_2O_3$  Fluka AG Buchs SG.**

**Sodium hydroxide Fluka AG Buchs SG.**

**Hydrochloric acid RIEDEL-DEHAEN AG.**

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

**Indium (111) (1000ug/ml)** A stock solution of (1000ug/ml) of In 111 was prepared by dissolving of (0.1209 gm) of Indium oxide  $In_2O_3$  in hydrochloric acid concentration and diluted to (100ml) in a volumetric flask in distilled water. The working solution of (100ug/ml) was prepared by simple dilution of stock solution and kept protected.

**Sodium Hydroxide (0.1M)**

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

**Hydrochloric Acid (0.1M)**

This solution was prepared by dissolving of (2.07 ml) of hydrochloric acid concentration (%37) and diluted to (250 ml) in a volumetric flask in distilled water.

**Recommended procedure** Aliquots of standard solution of promethazine hydrochloride : 2-20 ug/ml) were transferred to a (5 ml) a volumetric flask to which (0.25ml) of ( $4.35 \times 10^{-4}M$ ) of In (111) and (0.1 ml) of (0.1

M of sodium hydroxide and diluted by distilled water.

The absorbance at 304 nm was measured against a reagent blank.

**Results and Discussions**

- Absorption Spectra

Complex product with an absorption maximum at 304nm is formed when promethazine hydrochloride was allowed to

react with In (111) in basic medium of sodium hydroxide. Figure 1 shows the absorption spectra of product formed and of the reagent blank.

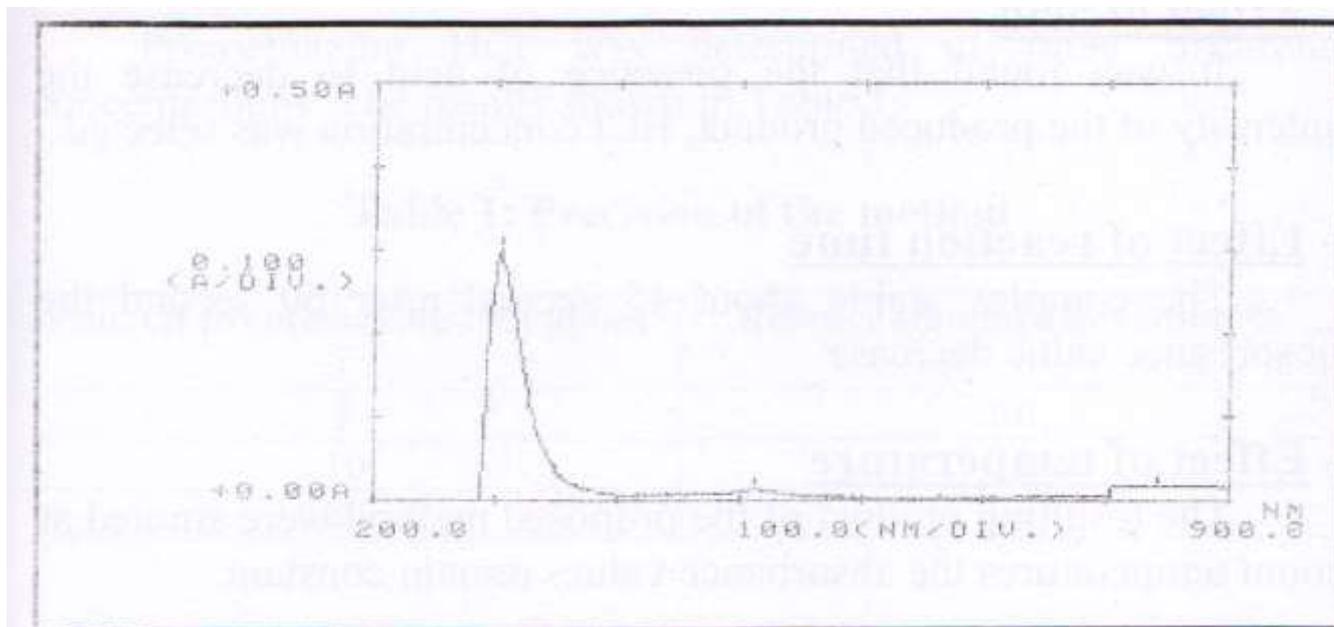


Figure 1: Absorption spectra of 20 µg promethazine. HCl with In (III) against reagent blank.

$\lambda$  nm

**Study of the optimum reaction conditions** The effect of various parameters on the absorption intensity of the dye formed was studied and the reaction conditions are optimized.

#### **- Effect of In 111**

When various concentrations of In (111) solution were added to fixed amount of the drug solution, (0.25 ml) of ( $4.35 \times 10^{-4}$  M) solution was found enough to give a maximum absorption and was considered to be optimum for concentration range of (2-20 µg/ml) of promethazine hydrochloride .

**- Effect of base** It was found that the presence of a base led to increase the intensity of the produced product, NaOH was selected which was found that (0.1 ml) of this base give high sensitivity which selected in subsequent experiments.

**- Effect of acid** It was found that the presence of acid to decrease the intensity of the produced product, HCl concentration was selected.

**- Effect of reaction time** The complex stable about 45 absorbable value decrease.

second after 60 second the **- Effect of temperature** The resulting product of the proposed method were studied at room temperatures the absorbable values remain constant.

**- Effect of order of addition** To obtain optimum results the order should be followed addition base and In (111) .  
of addition of drugs

### **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 ug/ml) with correlation coefficient of (0.997) and molar absorptivity ( $5.006 \times 10^3 \text{ L mol}^{-1} \text{ cm}^{-1}$ )

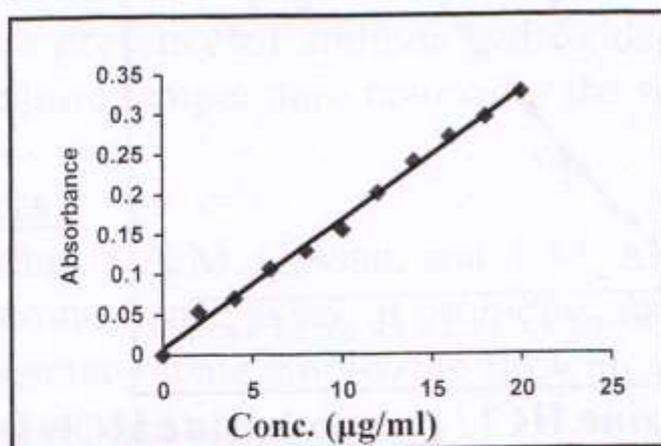


Figure 2: Calibration graph of promethazine hydrochloride.

### Precision

Promethazine HCl was determined at three different concentrations. The results shown in Table 1.

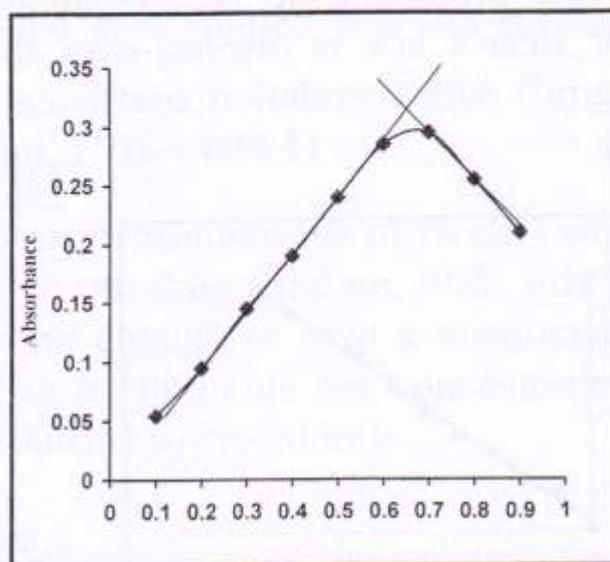
Table 1: Precision of the method

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

### Structure of the Dye:

The stoichiometry 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 nm.



**Job's [promethazine.HCl / promethazine.HCl+In (III)]**

**Figure 3: Job's plot method of promethazine. HCl –In (III) in sodium hydroxide medium.**

Therefore the formation of the product probably occurs as follows (Illustration 2):

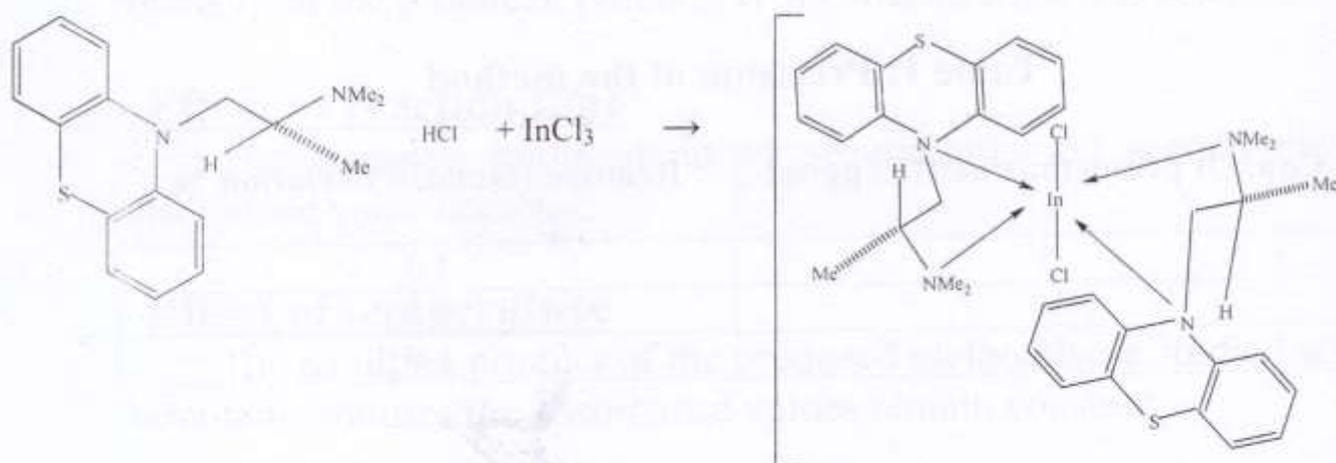


Illustration 2. Probable product formation pathway.

The product formed was water soluble, the stability constant was calculated by comparing the absorbance of a solution containing stoichiometric amount of promethazine HCl and In

III with that of solution containing the optimum amount of In 111) (0.25 ml of  $4.35 \times 10^{-4} \text{M}$  .

## **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 111 in the presence of sodium hydroxide.-the proposed method does not require temperature control or the solvent extraction step.**

## **References**

- 1. S.M. Sultan, Y.A.M. Hassan, and A.M. Abukibash, chemiluminescence assay of promethazine hydrochloride using acidic permanganate employing flow injection mode operated with syringe and peristaltic pumps, Talanta, Vol.59,(2003),pp1073-1080.**
- 2. R.I.Baxter, G.Svehla, B.Kem and A.D.Woolfson, Determination of promethazine by anodic differential pulse voltammetry, Anal.Chim.Acta, Vol.164,(1984),pp171-181.**
- 3. Ni Yongnian, Li Wang, and Skokot, Voltammetric determination of chlorpromazine hydrochloride and promethazine hydrochloride with the use of multivariate calibration, Analchim Acta, Vol.439,(2001),pp159-168.**
- 4. G.-Taylor and J.B.Houston, Simultaneous determination of promethazine and two of its circulating metabolites by high performance liquid chromatography, J.Chromatogr.B, Vol.230,(1982),pp194-198.**
- 5. P.G.H.M. Muijselaar, H.A. Claessens and C.A. Crommels, Determination of structurally related phenothiazines by**

capillary zone electrophoresis and micellar electrokinetic chromatography, *J.Chromatogr.A*,Vo1.735, (1996), pp395-402.

6. F.J.Lara, A.M. Garcia- Campana F.Ales- Barrero and J.M.

bosquesendea, *Anal.chim.Acta*, Determination of thiazinamium, promazine and promethazine in pharmaceutical formulations using a CZE method, Vo1.535,(2005),pp101-108.

7. L.D.L.Pena, A. Gomez-Hens, and D.Perez- Bendito, Kinetic

fluorimetric determination of promethazine by a stepped-flow I i mixing technique, *J. Pharm. Biomed. Ana1*.Vo1.1 1,(1993).pp893-896.

8. J.M. Calatayud, S.N. Sarrion, A.S. Snmpedro, and C.G. Benito,

Determination of promrthazine hydrochloride with bromophenol blue by a turbidimetric method and flow injection analysis, *Microchem. J.*,Vo1.45,(1992),pp129-136.

9. S.M.Golabi, and M.showkati-shishevan, potentiometric titration of phenothiazine compounds in chloroform and its use.

in pharmaceutical analysis, *Talanta*,vol. 38,(1991), pp1253-'1256.

10. A.S.1ssa, and M.S. Mahrous, Titrimetric determination of some phenothiazine derivatives, with ferricyanide, *Talanta*, V01.31,41984),pp287-288.

11. E.A.Ibrahim, A.S. Issa, M.A. Abdel salad, and M.s.Maitrous, The ues of chloranil for spectrophotometric determination of some tvanquillizers and antidepressants, *Talanta*, V01.30,(1983),pp531-533.

- 12. K.Basavaiah, Determination of some psychotrop phenothiazine drugs by charge-transfer complication reaction with chloranilic acid, IIF|armaco, Vo1.59,(2004),pp315-321.**
- 13. E.Regulska,M. Tarasiewicz, and H.puzanowska Tarasiewicz  
Extractive-spectrophotometric determination of some phenothiazines with dipicrylamine and picnic acid, J.pharm.Biomed.Anal .,Vo1.27, (2002), pp335-340.**
- 14. S.M.Sultan, and F.suliman, Application of super modified simplex optimization to the flow-injection spectrophotometric determination of promethazine hydrochloride in drug formulations, anal sci V01.8,41992),pp841-843.**
- 15. J.M.catatayud and T.G. Sancho, Spectrophotometric determination of promethazine by flow-injection analysis and oxidation by Ce IV, J. Pharm.Biomed .Anal.,Vol.10,(1992),pp37-42.**
- 16. D.Daniel and I.G.R. Gutz,Flow-injection spectroelectroanalytical method for the determination of promethazine hydrochloride in pharmaceutical preparations, Ana1.Chim.Acta.,Vo1.494,(2003),pp215-224.**
- 17. A.S.Najim,R.A.Nief and I.I.Mona,spectrophotometric determination of promethazine hydrochloride VIA oxidative coupling reaction with sulfanilic acid, App.Sci.,Vol.3,(2006),pp1-12.**
- 18. S.Y.Zhou, Z.Jun, Z.Da-pengand and C.L.Yun, electrochemical determination of trace promethazine hydrochloride by a procreated Glassy carbon electrode modified with DNA,Anal.Sci.,Vol.23,(2007),pp569-572.**

# طريقة طيفية لتقدير البروميثازين بواسطة الانديوم الثلاثي

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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 هيدروكلورايد مع الانديوم (III) بوجود هيدروكسيد الصوديوم لتكوين ناتج ذائب في الماء ويمتلك اقصى امتصاص عند الطول الموجي 304 نانومتر. وجد ان قانون بير ينطبق ضمن التراكيز (2-20) مايكروغرام / مللتر وبلغت قيمته الامتصاصية المولارية (5.001 x 10 لتر /مول . سم) . تم دراسة الظروف المثلى لتكوين المعقد وطبقت الطريقة بنجاح في تقدير البروميثازين هيدروكلورايد في حالته النقية.