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SPECTROPHOTOMETRIC ESTIMATION OF PROMETHAZINE HYDROCHLORIDE IN PHARMACEUTICAL PREPARATIONS

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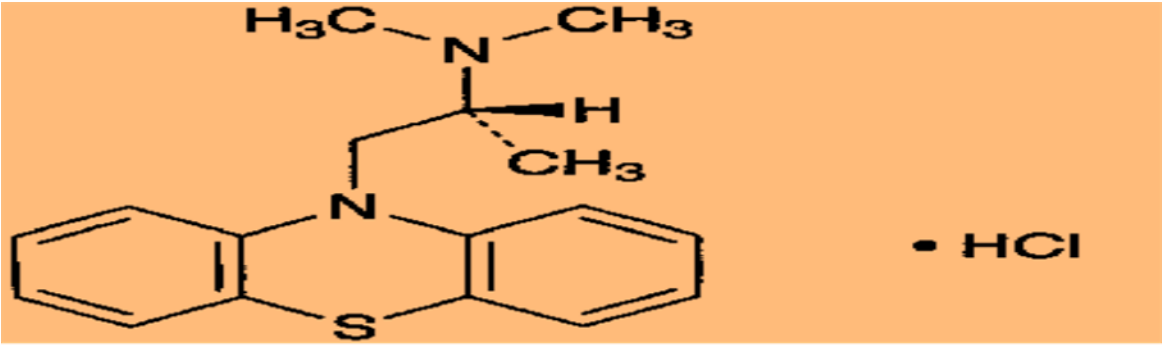
ABSTRACT
A simple, accurate, and rapid visible spectrophotometric method has been developed for the determination of Promethazine Hydrochloride in pure form, pharmaceutical preparations and environmental water samples. The method is based on the oxidation of Promethazine hydrochloride by sodium hypochlorite in a Sulfuric acid medium to form a pinkish red colored product with an absorption maximum at 518 nm. Beer's Law was obeyed in the range of 2-28 µg/ml with molar absorptivity of 0.978×10^4 L.mol.-1.cm-1. The relative standard deviation of the method was less than 2% and accuracy (average recovery) was 100±0.98%. The optimum conditions for all color development are described and the proposed method has been successfully applied for the determination of Promethazine Hydrochloride in pharmaceutical preparations and water samples. The common excipients and additives did not interfere in the proposed method.

KEYWORDS: Promethazine Hydrochloride, Sodium hypochlorite, spectrophotometric.

INTRODUCTION
Promethazine hydrochloride chemically is [(*RS*)-*N*,*N*-dimethyl-1-(10*H*-phenothiazine-10-yl)propan-2-amine hydrochloride] is a phenothiazine derivative (Figure 1) and is commonly prescribed for its antihistaminic action. Now a days, it is often used after minor operations as an emetic, analgesic, sedative and hypnotic drug.[1-3]



C17H20N2S.HCl: 320.88
Figure 1: Chemical structure of Promethazine Hydrochloride.

Recently promethazine hydrochloride used as a chromogenic reagent for the spectrophotometric determination of hypochlorite and iodate ions.[4,5] The literature survey reveals that various methods has been reported for estimation of some anti-psychotic drug by Indirect Titrimetric.[6] Spectrophotometric[7-9] Spectrofluorometric[10], Turbid metric[11] Chemiluminescence.[12] Volta metric[13], RP-HPLC.[14-17] In the view of the need in the industry for routine analysis of promethazine, attempts are being made to develop simple and accurate instrumental methods for quantitative estimation of promethazine. Thus there is need for the development of new, simple, sensitive and accurate analytical method for the quantitative estimation of promethazine as an active pharmaceutical ingredient. The present study describes simple, sensitive, accurate, rapid and economical spectrophotometric methods for the estimation of Promethazine Hydrochloride in bulk and its tablet dosage forms.

MATERIAL AND METHODS

Apparatus

A spectra scan 50 UV visible spectrophotometer with 1.0 cm quartz cells was used.

Reagents

All chemicals used were of analytical grade and the promethazine hydrochloride standard material was provided from (HPI) Mosul-Iraq. AL-Hokamaa company for pharmaceutical industries.

Promethazine hydrochloride stock solution (1000 ppm) was prepared by dissolving 0.1g of promethazine hydrochloride in 100 ml distilled water in a volumetric flask **Promethazine hydrochloride standard solution (100 ppm)** was prepared by diluting10 ml of stock solution to 100 ml by distilled water in a volumetric flask.

Sodium hypochlorite solution (0.1%) was prepared by dilution 1.25 ml of 8% sodium hypochlorite to 100 ml by distilled water, this solution was standardized every 4-5 days and stored in a dark bottle.[18]

Sulfuric acid 1M, this solution was prepared by diluting 14 ml of 18 M H_2SO_4 solution to 250 ml by distilled water in a volumetric flask.

Recommended procedure

Aliquots of standard solution of promethazine hydrochloride (50-700µg) were transferred into a series of 25 ml calibrated flasks, added 1 ml of 1M Sulfuric acid solution and 1 ml of 0.1% sodium hypochlorite solution, dilute the solution to the mark with distilled water. The absorbance of the pinkish red-colored product was measured at 518 nm against a reagent blank.

Procedure for pharmaceutical preparations(tablets)

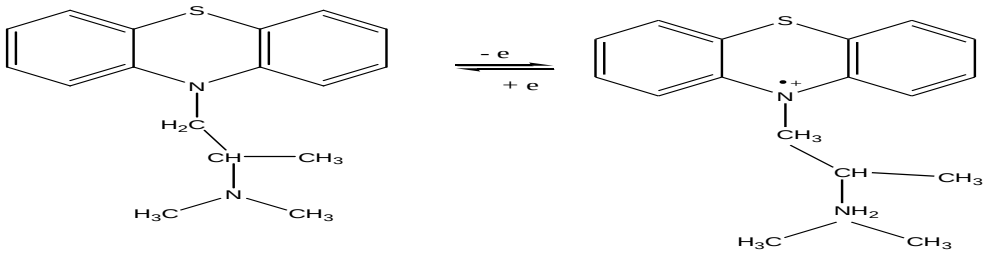
To minimize a possible variation in the composition of the tablet, the mixed content of 10 tablets were weighed and grounded, then the powder equivalent to 10 mg of promethazine hydrochloride was accurately weighed and transferred in about 100ml distilled water and mixed for 20 mint and then filtered using a what man No.42 filter paper. The filtrate was mad up to 100 ml with distilled water. Different volume of this solution was treated as mentioned under recommended procedure.

Procedure for industrial waste water

To demonstrate the practical applicability of the proposed method, industrial waste water sample from AL-Hokamaa company for pharmaceutical industries (HPI) Mosul-Iraq. were analyzed, by spiked with the concentrations ranging from 2-28 µg.ml^{-1} of promethazine hydrochloride and treated as described above for recommended procedures.

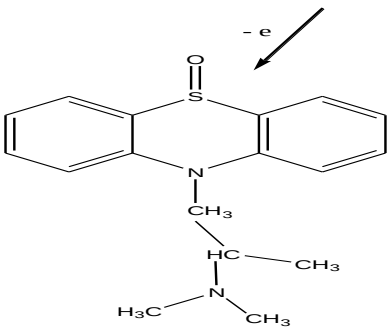
RESULTS AND DISCUSSION

Promethazine hydrochloride is oxidized in sulfuric acid medium with sodium hypochlorite solution instantaneously at room temperature to form a pinkish red colored product which is believed to be a radical cat ion, and is irreversibly oxidized to a colorless sulfoxide with loss of electron[19], as shown below.



Promethazine

Red species(radical cat ion)



Colorless sulfoxide

The pinkish red–colored radical cat ion shows maximum absorbance at 518nm, where the blank does not absorb appreciably, as shown in (Figure 2).

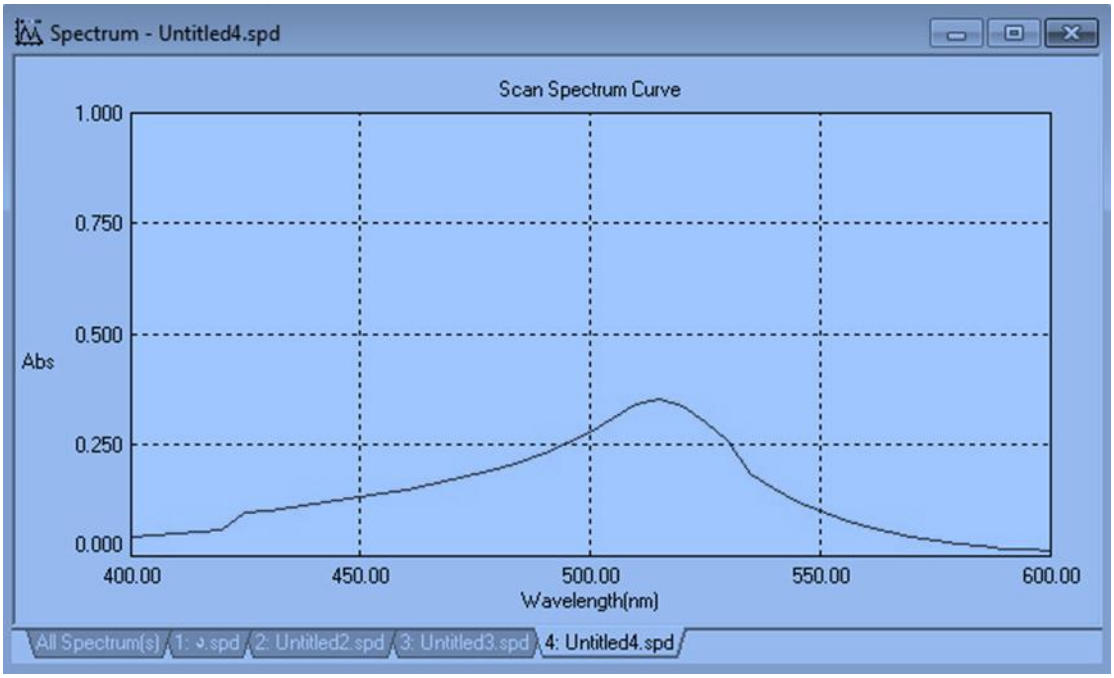


Figure 2: Absorption spectra of 12µg/ml of Promethazine. HCL product against distilled water.

The reaction variables were optimized by varying each variable while keeping others constant for obtaining maximum absorbance. The oxidation reaction was found to be quantitative in sulfuric acid medium. It was found that 1 ml of 1M sulfuric acid solution give high sensitivity and this amount has been used for subsequent experiments. The effect of the amount of sodium hypochlorite on the absorbance was investigated. A maximum and constant absorbance was found with 1 to 2 ml of 0.1% sodium hypochlorite solution and 1.0 ml has been used for subsequent experiments. The color reaction occurred at room temperature immediately and remained stable for at least 24h. and a reaction time of 5 min was selected for reproducible results. under the experimental conditions described, Beer 's law is obeyed over the concentration range 2-28 µg /ml (Figure 3).

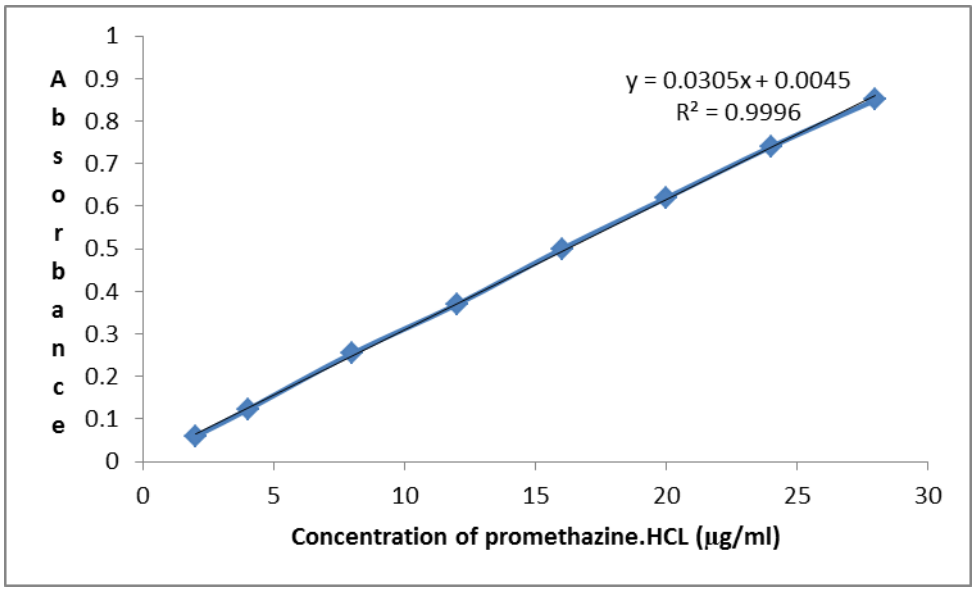


Figure 3: Calibration graph of Promethazine. HCL.

A regression analysis of Beer 's law plot at 518 nm revealed a good correlation (r=0.9996, n=8) the graph of the absorbance versus the concentration of promethazine hydrochloride showed a low intercept (0.0045) and slope (0.0305) and is described by a regression equation Y = ax + b (where x is the concentration ofpromethazine hydrochloride in µg /ml, Y is the absorbance, a is the slope and b is the intercept. The apparent molar absorptivity was 0.978×10^{4} l. mol^{-1}. cm^{-1} and sandell's sensitivity was $0.0328\mu g.cm^{-2}$. The limit of detection and quantification were evaluated as The limit of detection and quantification were evaluated as:

LOD = Intercept / Slopex10
And LOQ = 3.3LOD

The limit of detection was 0.0147µg/ml and the limit of quantification 0.0486µg/ml as the lowest standard concentration which could be determine with acceptable accuracy.

Accuracy and precision

The accuracy and precision of the method was established by analyzing the pure drug solution at three different levels. The average recovery which is a measure of accuracy is 100 ± 0.98 revealing high accuracy of the method. The relative standard deviation (RSD), which is an indicator of precision is better than ±2%. The results are compiled in Table[1].

Table [1]: Optical characteristics and statistical data for regression equation of the proposed method.

Parameters	Value
λ max (nm)	518
Beer´s law limits (µg .ml^{-1})	2 – 28
Molar absorpitivity (1.mol^{-1}.cm^{-1})	0.978×10^{4}
Determination coefficient (r^2)	0.9996
Regression equation (Y= a × + b)	
Slope (a)	0.0305
Intercept (b)	0.0045
Recovery %	100 ± 0.98
Relative standard deviation (%)	< 2

Effect of interferences

The interfering effect of foreign species often accompanied with promethazine hydrochloride in the pharmaceutical preparations were studied by adding different amounts of foreign species to 300µg/25ml of promethazine hydrochloride in solution and the recommended procedure for the determination of promethazine hydrochloride was followed. The species are considered to interfere seriously if the cause aching of more than 2% in the absorbance obtained for tetracycline hydrochloride a lone.[20] Results of the recovery analysis are presented in Table[2]. Excipients at the concentration show in Table[2] do not interfere with the assay. In addition recoveries in most cases were around 100%.

Table [2]: Determination of promethazine hydrochloride in presence of excipients.

Excipients	Amount taken, (µg/ml)	Average recovery, * %
Talc	700	99.96
	1000	100.09
Mannitol	800	100.08
	1000	99.97
Mg – stearate	600	100.06
	1000	100.08
Starch	500	100.09
	1000	100.04
Microcrystalline cellulose	500	99.97
	1000	99.96

***** Average of five replicate determinations.

Application of the proposed method

The proposed method was successfully applied to the analysis of promethazine hydrochloride in tablets and industrial waste water sample. The result of analysis for pharmaceutical formulations revels that there is close agreement between the results obtained by the proposed method and the label claim table[3], And the results of water samples table [4] show that the recovery values obtained were close to 100%.

Table [3]: Assay of promethazine hydrochloride in pharmaceutical formulations.

Pharmaceutical formulation supplied by HPI	Amount of promethazine hydrochloride * Proposed method	Label claim	%Recovery
Tablet 5mg	5.008mg	5 mg	100.16

*Mean of ten determinations.

Table [4]: Determination of promethazine. HCL in spiked industrial wastewater sample.

Water samples	Promethazine. HCL (µg/ml) * Taken Found	%Recovery
Industrial wastewater	44.0 10 9.95 20 20.02	100 99.5 100.1

*Mean of ten determinations.

Application of the proposed method to content uniformity[21,22]

Content uniformity or the Uniformity of dosage unit was defined as the degree of uniformity in the amount of active substance among dosage units. The risk assessment strategy underlying content uniformity testing is the assumption that some pre-specified limits exist where safety and efficacy outcomes may change if content uniformity fails. The proposed method proved to be suitable for the content uniformity test, where a great number of assays on individual tablets are required. Data presented in table [5] indicate that the proposed method cans accurately and precisely quantitative promethazine hydrochloride in its commercially available tablets. The mean percentage (with RSD) of the labeled claim found in ten tablets was 100.1 (0.68%) which fall within the content uniformity limits specified by the USP Pharmacopoeia.[23]

Table [5]: Content uniformity testing of promethazine hydrochloride tablets using the Proposed method.

Parameter	% of the label claim
Tablet No.1	100.4
Tablet No.2	99.9
Tablet No.3	100.5
Tablet No.4	100.3
Tablet No.5	99.5
Tablet No.6	100.2
Tablet No.7	99.8
Tablet No.8	100.2
Tablet No.9	100.4
Tablet N0.10	99.8
Mean(X)	100.1
%RSD	0.68
Max. allowed unit value[23]	±15%

CONCLUSION

In this work, a simple, rapid, precise and accurate spectrophotometric method was developed and validated for the determination of promethazine hydrochloride in pharmaceutical preparations and industrial waste water samples. The method free from such experimental variables as heating or solvent extraction step. The method rely on the use of simple and cheap chemicals and techniques and can be used for rapid routine determination and quality control of promethazine hydrochloride in pure form, bulk sample, pharmaceutical preparations and real industrial waste water sample.

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