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INDIRECT ESTIMATION OF DIPHENHYDRAMINE.HCL IN WASTEWATER AND PHARMACEUTICAL PREPARATIONS

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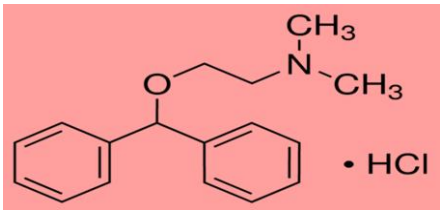
ABSTRACT

A simple, rapid, accurate and sensitive indirect spectrophotometric method for determination of diphenhydramine hydrochloride has been developed. The proposed method is based on the reaction between chloride ion and Mercury(II) thiocyanate (Hg(SCN)2), formation of a colored complex by the reaction between released thiocyanate and ferric ions to form red soluble product with maximum absorption at 462 nm. Beer's law is obeyed over the concentration range of 2-28µg/ml, with molar absorptivity of $0.759x10^4$ l/mol.cm. The present method is considered to be simple because it does not need either heating or hydrolysis or solvent extraction steps. The ingredients often formulated with diphenhydramine hydrochloride have been shown not to interfere, and the proposed method is suitable for the routine determination of diphenhydramine hydrochloride. The method has been successfully applied for the determination of diphenhydramine hydrochloride in pure form, pharmaceutical preparations(Tablets, Syrup and Ampules) and environmental wastewater sample.

KEYWORDS: Diphenhydramine Hydrochloride, Mercury(II) thiocyanate (Hg(SCN)2).

INTRODUCTION

Diphenhydramine hydrochloride (Figure1) is first generation antihistaminic agent is used to treat sneezing, runny nose, watery eyes, hives, skin rash, motion sickness, to induce sleep, itching, etc. Chemically is2-(diphenylmethoxy)-N,N-dimethylethan-1-amine. hydrogen chloride



C17H21NO, HCl==ı291.8

Figure 1: Chemical Structure of Diphenhydramine hydrochloride.

Diphenhydramine Hydrochloride). A mono ethanolamine derivative. A white or almost white, odorless, crystalline powder. Very soluble in water; freely soluble in alcohol. A 5% solution in water has a pH of 4.0 to 6.0.Protect from light. However, when used as ingredient in cold preparations it provokes some undesired ant muscarinic and sedative effects.[1-5] According to the literature, reports that appear analytical techniques for estimation of Diphenhydramine Hydrochloride such as spectrophotometric methods[6], potentiometric titration[7], High performance liquid chromatographic methods[8], spectrofluorimetric method[9], conduct metric titration Method[10], capillary gas chromatography[11], flow injection chemiluminescence[12], FT-Raman spectroscopy[13], LCMS[14], and HPTLC method.[15] The present work describes a new, simple spectrophotometric method for the determination of diphenhydramine hydrochloride in pure form, pharmaceutical formulations and in industrial wastewater samples. The method is based on reaction between chloride ion and Mercury(II) thiocyanate (Hg(SCN)2), formation of a colored complex by the reaction between released thiocyanate and ferric ion.

EXPERIMENTAL

Apparatus

Shimadzu UV- 1700 pharmaspec (double beam) spectrophotometer with 1.0 cm quartz cells was used for absorption measurements.

Reagents

All chemical used were of analytical or pharmaceutical grade and diphenhydramine hydrochloride standard

material was provided from AL-Hokamaa company for pharmaceutical industries (HPI) Mosul-Iraq.

Diphenhydramine hydrochloride standard solution :0.01% (100µg/ml)
This solution was prepared by dissolve 0.01 gm of diphenhydramine hydrochloride in 100 mL of distilled water in volumetric flask.

Ferric ammonium sulfate solution: 5%
5g of ferric ammonium sulfate [FeNH4(SO4)2.12H2O] was dissolved in 50 ml double distilled water and 20ml of concentrated nitric acid was added and diluted with double distilled water to 100ml.

Mercury(II)thiocyanate (Hg(SCN)2) solution: 0.5%
0.5g of Mercury(II) thiocyanate (Hg(SCN)2) was dissolved and diluted to 100 ml with ethanol. Mixed and filtered through filter paper.

General procedure
Different aliquots of standard diphenhydramine hydrochloride solution equivalent 100-700 µg(1-7 mL) were transferred into a series of 25ml volumetric flasks, and 2mL of ferric ammonium sulfate solution were added and2ml of saturated solution of Mercury(II) thiocyanate (Hg(SCN)2) were added to each flask and mixed well with occasional shaking. This was diluted to 25ml with double distilled water. and mixed well . Let stand for 5min, the absorbance of each solution was measured at 462 nm against a reagent blank.

Procedures for pharmaceutical preparations (Tablets)
To minimize a possible variation in the composition of the tablets(containing 25mg of diphenhydramine hydrochloride/tablet were provided from AL-Hokamaa company for pharmaceutical industries (HPI) Mosul-Iraq).). The mixed content of 10 tablets were weighed and grounded, then the powder equivalent to 10 mg of diphenhydramine hydrochloride in about 50 ml of distilled water was stirred well for 30 min and then filtered through whatman No. 42 filter paper and the filtrate solution was diluted to 100ml by distilled water and different volume of this solution was treated as described above under general procedure.

Procedures for pharmaceutical preparations (Ampules)
Ampule containing 10mg of diphenhydramine hydrochloride (were provided from state company of drug industries and medical appliance (NDI) Nineveh-Iraq.) was transferred into 100mL volumetric flask and diluted up to the mark with distilled water, The determination of diphenhydramine hydrochloride was treated as described above under general procedure. and the concentration was calculated by using the calibration curve of this method.

Procedures for pharmaceutical preparations (syrups)
The content of 5 bottles provided from AL-Hokamaa company for pharmaceutical industries (HPI) Mosul-Iraq)[10mg/5ml] were mixed well in 1L dried beaker. Aliquots equivalent to 100 mg of diphenhydramine hydrochloride were transferred into 1L volumetric flasks and diluted with distilled water to the volume. The determination of diphenhydramine hydrochloride proceeded as described under recommended procedure and the concentration was calculated by using the calibration curve of this method.

Procedure for industrial wastewater samples
To demonstrate the practical applicability of the proposed method, real industrial wastewater samples from Al-Hokamaa company for drug industries (HPI) Mosul-Iraq were analyzed by spiked with the concentrations ranging from 2-20 µg /ml of diphenhydramine hydrochloride and aliquot of this solution was treated as described above under general procedure and the concentration was calculated by using the calibration curve of this method.

RESULTS AND DISCUSSIONS

The method depends upon the displacement of thiocyanate ion from mercury(I1) thiocyanate by chloride ion in the Diphenhydramine hydrochloride. The released thiocyanate was found to react with Fe III at room temperature resulting in formation of red colored complex which absorbed at 462nm (Figure. 2).and the intensity of its color is proportional to the original chloride ion.[16]

$$2Cl^- + Hg(SCN)_2 + 2Fe^{3+} \longrightarrow HgCl_2 + 2[Fe(SCN)]_2^+$$

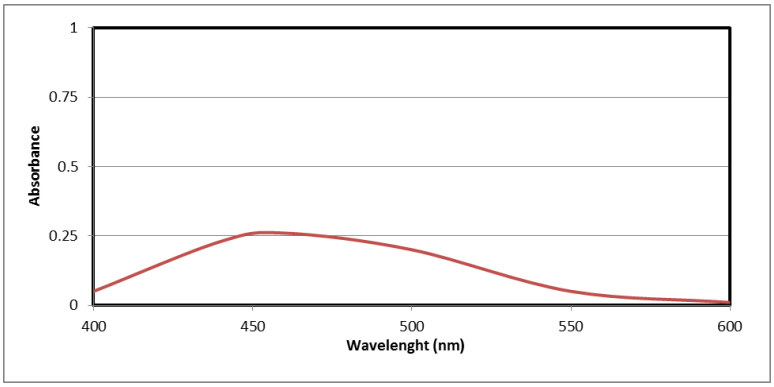


Fig. 2: Absorption spectra of 10µg /ml of Diphenhydramine hydrochloride.

The various experimental affecting the development and stability of the reaction product was optimized by changing each variable in turn while keeping all other variables constant.

Effect of ferric ammonium sulfate solution

The amount of ferric ammonium sulfate solution (5%) for maximal color intensity was examined the maximum constant intensity was reached at 1 ml of reagent solution and remained constant up to 4ml. However 2 ml of the reagent solution was selected for the subsequent work.

Effect of Mercury(II) thiocyanate solution

The amount of Mercury(II) thiocyanate (Hg(SCN)2) solution (0.5%) for maximal color intensity was examined the maximum constant intensity was reached at 1 ml of reagent solution and remained constant up to 4ml. However 2 ml of the reagent solution was selected for the subsequent work.

Effect of temperature and time

The results obtained indicated that complete color formation occurred immediately and not effected by temperature therefore, room temperature was selected as suitable temperature. The absorbance remained constant for 6 hours at least, and 5 min was selected as a suitable time.

Effect of order of addition

To test the effect of order of the addition of the reagents on the absorbance of the product, different order were tested. The selected order was sample solution, ferric ammonium sulfate followed by Mercury(II) thiocyanate (Hg(SCN)2) solution which was gave high absorbance value.

Calibration graph

Employing the conditions described in the general procedure a linear calibration graph of diphenhydramine hydrochloride which obeys Beer's law in the concentration range of 2-28 µg/ml(Figure.3). Linear regression equation: Y= 0.026X+0.0014 (r=0.9997). Where Y is the absorbance and X is concentration in µg/ml. The apparent molar absorptivity was 0.759×10^4 $l.mol^{-1}.cm^{-1}$ and sandal's sensitivity was $0.0385\mu g.cm^{-2}$.The limit of detection and quantification were evaluated as.[17,18]

$$LOD = 3.3\frac{S_0}{b} \text{ and } LOQ = 3LOD$$

Where b is the stop and S_0 is the standard deviation of the regression line. The limit of detection was 0.163 µg $.ml^{-1}$ and the limit of quantification as the lowest standard concentration which could be determine with acceptable accuracy, and precision was $0.489\mu g.ml^{-1}$. The applied method can be used routinely for the estimation of pure drug salts through their chloride concentration.

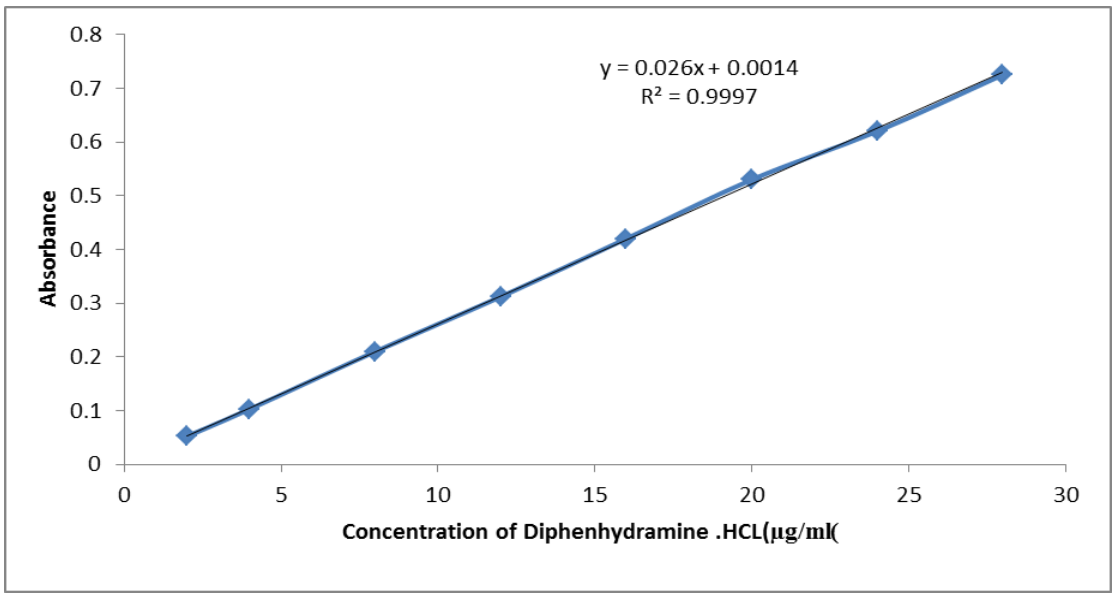


Figure 3: Calibration graph of diphenhydramine hydrochloride.

ACCURACY AND PRECISION

The accuracy and precision of the method were established by analyzing the pure drug solution at three different levels. The average recovery which is a measure of accuracy is 100 ±0.9% revealing high accuracy of the method. The relative standard deviation (RSD), which is an indicator of precision, is less than 1.7%, the result are complied in (Table .1).

Table 1: Optical Characteristics and Statistical Data for Regression Equation of The Proposed Method.

Parameters	Value
λ max (nm)	462
Beer's law limits (µg.ml^{-1})	2-28
Molar absorptivity (L.mol^{-1}.cm^{-1})	0.759×10^{4}
Limit of detection (µg.ml^{-1})	0.163
Limit of quantification (µg.ml^{-1})	0.489
Sandell's sensitivity (µg.cm^{-2})	0.0385
Correlation coefficient (r)	0.9997
Regression equation (Y=C+bX)	
Intercept (C)	0.0014
Slope (b)	0.026
Recovery	100±0.9
Relative standard deviation (%)	< 1.7

Effect of interferences

The interfering effect of foreign species often accompanied with diphenhydramine hydrochloride in the pharmaceutical preparations were studied by adding different amounts of foreign species to 400µg/25ml of diphenhydramine hydrochloride in solution and the recommended procedure for the determination of diphenhydramine hydrochloride was followed. The species are considered to interfere seriously if the cause aching of more than 2% in the absorbance obtained for diphenhydramine hydrochloride a lone.[19] 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 diphenhydramine. HCL in presence of excipients.

Excipients	Amount taken, (µg/ml)	Average recovery, * %
Talc	500 1000	99.98 100.05
Mannitol	600 1000	100.07 99.96
Mg – stearate	600 1000	100.08 100.08
Starch	500 1000	100.08 100.05
Microcrystalline cellulose	500 1000	99.95 99.95

*****Average of five replicate determinations.

Application of the proposed method

The proposed method was successfully applied to the analysis of diphenhydramine hydrochloride in pharmaceutical preparations[tablets, Ampules and Syrups] 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 diphenhydramine hydrochloride in pharmaceutical formulations.

Pharmaceutical formulation supplied by	Amount of diphenhydramine hydrochloride * Proposed method	Label claim	%Recovery
Tablet 25mg/Table [HPI]	24.9 mg	25 mg	99.6
Syrups10mg/5ml [HPI]	10.04	10mg	100.4
Ampules 10mg/Amp [NDI]	9.98	10mg	99.8

*Mean of ten determinations.

Table 4: Determination of diphenhydramine HCL in spiked industrial wastewater sample.

Water samples	Diphenhydramine. HCL (µg/ml) *		%Recovery
	Taken	Found	
Industrial wastewater	4.0	**4.01**	**100**.25
	10	10.05	100.5
	16	16.08	100.5

*Mean of ten determinations

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CONCLUSION

The applied method was simple, rapid, accurate, precise, sensitive and low economical cost. Furthermore, the proposed method doesn't require elaboration of procedures, which are usually associated with chromatographic methods. The proposed method could be applied successfully for determination of diphenhydramine Hydrochloride in environmental water samples, pure form as well as in different pharmaceutical forms.

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