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Spectrophtometric determination of Hydrochlorothiazaide by oxidative coupling with O-Phenylendiamine

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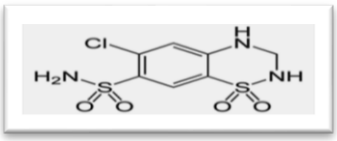
ABSTRACT

This study includes the development of a new sensitive spectrophotometric method for the determination of a hydrochlorothaizide in aqueous solution and pharmaceultical preparations. The method is based on the oxidative coupling reaction of hydrochlorothaizide with O-phenylendiamine reagent in a acidic medium pH 1.5 in the presence of potassium ferricyanide to produce an intense orange color, water soluble and stable product , which exhibits maximum absorption at 450 nm. Beer's law is obeyed over the concentration arange 6 to 48 µg.ml^{-1} of hydrochlorothaizide, with a molar absorptivity of 3602.17 L.mo1^{-1} .cm $^{-1}$, Sandell's sensitivity index of 0.03 µg.cm^{-2} , relative error range not more than 0.215% , and D.L 0.0835µg.ml^{-1} . The method has been successfully applied for the determination of hydrochlorothaizide in tablets.

Introduction

Name is : 2H-1,2,4-Benzothiadiazine-7-sulfonamide, 6-chloro-3,4-dihydro-1,1-dioxide [1]

IUPAC systematic name: 6-Chloro-1,1-dioxo- 3,4-dihydro-2H-1,2,4-benzothiadiazine-7- sulfonamide



Hydrochlorothiazide

Hydrochlorothiazide is a thiazide-type diuretic chiefly used as an antihypertension agent for the control of elevated blood pressure [2]. It is often combined with other agents in the treatment of hypertension, either through separate prescriptions for hydrochlorothiazide and the other agents, or through the use of combination products in which a single tablet contains hydrochlorothiazide plus one other antihypertensive medication (more rarely, two other agents).

In the USA, hydrochlorothiazide is indicated for "the management of hypertension either as the sole therapeutic agent or in combination with other antihypertensives" and is recommended as first-line medication [3]. The European Medicines Agency indication for hydrochlorothiazide is "for treatment of hypertension". Labelling includes use for hypertension and oedema for combination drugs containing hydrochlorothiazide and another diuretic agent. Hydrochlorothiazide is a recommended drug in Europe [4]. A several of analytical methods for the determination of HCTZ has been reported in the literature. These included high performance liquid chromatography coupled with on- line atmospheric pressure chemical ionization mass spectrometry (HPLC, APCI-MS)[5] cloud point extraction /flow injection-flame atomic absorption (CPE/FI-FAAS) spectrometry)[6], liquid chromatography [7], UV–spectrophotometry [8], flow injection chemiluminescence [9], ion selective electrode [10], Many UV-Visible spectrophotometric methods for the determination of HCTZ have been developed. Most of them included an oxidative coupling reaction of HCTZ with different coupling reagents, such as these methods: E.. martin (11) and his group developed three methods for the simultaneous determination of amiloride (AMI) and hydrochlorothiazide (HCT): zero-crossing, derivative quotient spectra with normalized divisor and multiple

linear regression (MULTIC) methods. The two first methods use the derivative spectrophotometry, and the last one uses the absorbance measurement. The three methods were used to determine both compounds in synthetic mixtures and pharmaceutical preparations with errors less than 5% and 15%, respectively.

Sane and Narkar [12] evaluated concentrations of less than 80 µg. ml^{-1} hydrochlorothaizide by its reactor with a 4-amino phenol reagent with an oxidative agent, In a base medium, where a blue-colored complex whose absorption is measured at a wavelength of 640 nanometers.

Experimental

Apparatus

- A UV/VIS spectrophotoeter digital double–beam recording spectrometer/ Shimaduz, Japan, model UV-1650PC which connected has the software UV-Prob version, with 1 cm matched quartz cells were used.
- sencetive balance.
- Water bath.

Materials

All Chemicals used are of the highest purity. A provided from different commercial company.

Table (1) reagent and chemicals that used

Chemicals	Chemical Formula	Company
Hydrochlorothiazide	$C_7H_8ClN_3O_4S_2$	Awamedica-Erbil-Iraq
Potassium ferric cyanide	$K_3[Fe(CN)_6]$	BDH
o-phenylen diamine	$C_6H_8N_2$	BDH

Solutions

Hydrochlorothiazide solution (1000) µg mL-1: prepared by dissolving (0.1000)g of HCTZ in 5 ml of ethanol then completed to (100) mL by distilled water. And other concentrations prepared by dilution.

O-phenylendiamine (0.001) mol mL^{-1}: prepared by dissolving (0.0108)g of O-phenylen diamine in (100)mL ethanol.

Potassium ferricyanide (0.01) mol mL^{-1}: prepared by dissolving (0.3293)g of Potassium ferricyanide (BDH) in (100) mL distilled water.

Hydrochloric acid (1) mol mL^{-1}: prepared by diluting suitable amount of concentrated hydrochloric acid to (25) mL with distilled water.

Procedure:

An aliquot sample containing (0.5-2.5) mL of pure hydrochlorothiazide 300 µg.mL^{-1} was transferd into a series of (25) mL standard volumetric flask. followed by (0.5) mL hydrochloric acid, and (1) mL of Potassium ferricyanide (0.01) mol mL^{-1} were added. The solutions were allowed to stand for (5) min , then (2) mL of o-phenylendiamine was added. The contents are mixed well and diluted to the mark with distilled water. The absorbances are measured After (20) min against the corresponding reagent blank at (450)nm using 1-cm quartz cells.

Procedure for dosage forms

Angizaar-H (contain12.5 mg of HCTZ and 50 mg Losartan potassium): prepared by grinding 6 pills of drug the total weight of pills was 447 Milgram the weightof one pill was74.5 milgram take (0.07) g from drug (containing 12.5 g of HCTZ) after grinding the pills and transferred it into powder then adding distilled water. filtered and diluted up to the mark (100) mL with distilled water. The concentration of HCTZ is obtained by calibration curve already, made and described above.

Results and Discussion

Study of the optimum reaction conditions : The effect of various variables factors on the color development was studied to get the optimum conditions to determine the HCTZ.

1–The Effect of Reagent volume: The effect of reagent (0.001) mol volume (0.1 -4) mL on the intensity of the absorbance, has been studied and (2) mL was found to be optimum.

2- Effect of acid: It was found that the presence of acid caused increase the intensity of the produced color product ; HCl was selected and the effect acid volume (0.05-3) mL on the intensity of the absorbance has been studied and (1)mL was found to be optimum.

3-Effect of potassium ferric cyanide volume : The effect of (0.01) mol mL-1 potassium ferric cyanide volume (0.1- 3) mL on the intensity of the absorbance has been studied and (1.5) mL was found to be optimum.

4-Effect of Reaction Time: The color intensity reached its maximum after (20) min. therefore (20) minutes were selected as optimum in the general procedure.

Table (2) effect of reaction time

Time, minutes	5	10	15	20	25	30	40	45	50	60
Absorbance eeeeee	0.515	0.631	0.682	0.764	0.752	0.731	0.701	0.651	0.525	0.431

5- Effect of Temperature: The effect of temperature on the resulting product was studied. It Was found the coloured product was stable at room temperature (20-30)ºCat higher temperatures the absorbance decrease, and attributed to the dissociation of the product on prolonged heating . (table 3).

Table (3) effect of temperature

Temp C°	**5**	**10**	**15**	**20**	**25**
Absorbance	0.531	0.615	0.731	0.756	0.763
Temp C°	**30**	**35**	**40**	**45**	**60**
Absorbance	0.760	0.752	0.731	0.680	0.601

Absorption spectra

Hydrochlorothiazide was reacted with o-phenylen diamine , under the above-established conditions producing orange colored product with maximum absorption at (450) nm, while the reagent blank shows no absorption at this wavelength. (Fig1) shows the absorption spectra.

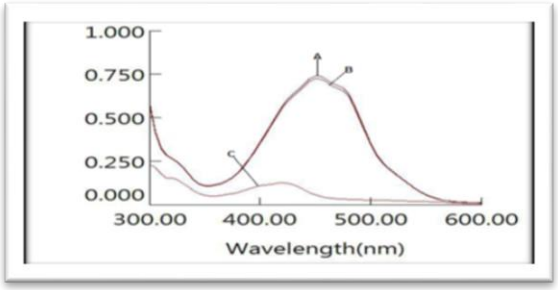


Fig (1) : Absorption spectra : A : hydrochlorothiazide with O-phenylendiamine product versus blank. B: hydrochlorothiazide with O-phenylendiamine versus D.W. C: blank versus D.W.

Calibration curve:

Under the optimum operating conditions, a linear calibration curve (fig2) is obtained over the concentration range of (6-48) µg.mL-1 of HCTZ in a final volume of (25) mL. with a correlation coefficient of (0.9917) and intercept of (0.3532). A negative deviation from Beer's law was observed above (50)µg.ml-1 concentration of HCTZ. The apparent molar absorptivity has been found to be (3602.17) L.mol-1.cm-1.

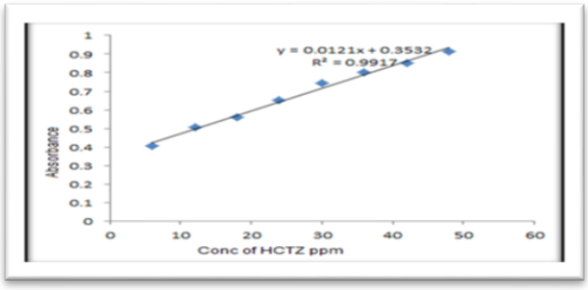


Fig (2) calibration curve of hydrochlorothiazide with reagent O-phinlyendiamine

Accuracy and precision: To calculate the accuracy and precision of the calibration curve, hydrochlorothiazide was determined at two different concentrations. The results shown in Table (1) indicate a satisfactory precision and accuracy.

Table (4): Accuracy and precision of proposed method

Conc.of HCTZ µg /ml	% RE	Recovery, *%	Average of Recovery%	RSD *,%
6	0.24	100.24	100.21	0.397
12	0.19	100.19		0.403

***Average for seven time**

Nature of product and reaction mechanism

The stoichiometry was studied under the established conditions, by applying the continuous variations (Job's method) and mole-ratio methods. The experimental data in both methods (Fig. 3) show that it has been formed by a 1:1 combining ratio of diazotized HCTZ to O-phenylendiamine

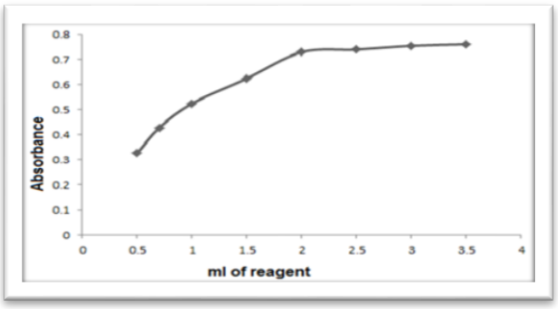


Fig. 3: (a) mole-ratio method

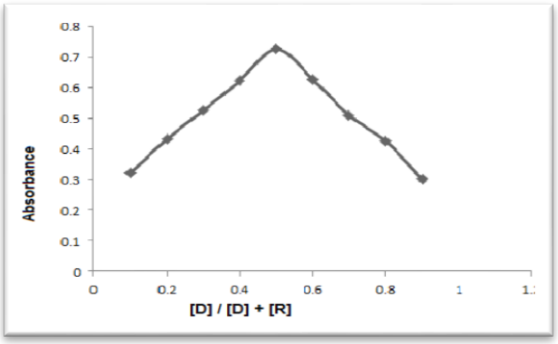
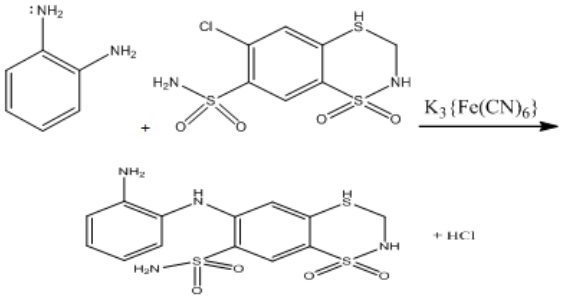


Fig. 3: (b) Continuous variations method

The proposel reaction of the OPD with HCTZ was represent by the following scheme:



Application of the method: The proposed method is applied to the determination of hydrochlorothiazide in the Pharmaceutical preparation (Angizaar-H) (containing 12.5% hydrochlorothiazide):The results which are shown in (Table 5) indicate that a good recoveries were obtained ,the proposed method was compared successfully with the official method.

Table 5: Application of the proposed and standard methods for the determination of Pharmaceutical preparation containing hydrochlorothiazide

Pharmaceutical preparation	Rec.* % proposed method	Rec.* % standard method
Angizaar-H (Iraq)	100.21	103.75

Conclusions

The proposed method was found to be very simple, accurate and sensitive spectrophotometric method, did not require temperature control. The proposed method was applied to determine hydrochlorothiazide

(HCTZ) in both pure and its dosage forms and can be used for the routine analysis.

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دراسة طيفية لتقدير عقار هيدروكلوروثيازيد بتفاعل الإقتران التأكسدي مع أورثو فنيلين ثنائي أمين بوجود سيانيد البوتاسيوم الحديديكي

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الملخص

تم تطوير طريقة طيفية جديدة لتقدير هيدروكلوروثيازيد في الوسط المائي باستخدام تفاعل الاقتران التأكسدي مع الكاشف أورثو فنيلين ثنائي الامين عند الدالة الحامضية 1.5 بوجود العامل المؤكسد سيانيد البوتاسيوم الحديديكي لتكوين ناتج برتقالي اللون ذائب في الماء يعطي أعلى امتصاص عند الطول الموجي 450 نانوميتر . كانت حدود قانون بير في مدى التراكيز 6 - 48 مايكروغرام.مل$^{-1}$ من الهيدروكلوروثيازيد. وكانت الامتصاصية المولارية 3602.17 لتر .مول$^{-1}$.سم$^{-1}$ ودلالة ساندل 0.03 مايكروغرام.سم$^{-2}$, والخطأ النسبي ليس اكثر من 0.215% , وبحد كشف 0.0835 مايكروغرام.مل$^{-1}$. وتم تطبيق الطريقة بنجاح لتقدير للهيدروكلوروثيازيد في مستحضرات صيدلانية على شكل أقراص.