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Spectrophotometric Determination of sulphadiazine by oxidative coupling reaction with ortho-amino phenol as reagent

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ABSTRACT

A simple, rapid and sensitive spectrophotometric method for determination of sulphadiazine (SDZ) in aqueous solution is described. The method iis based on the oxidation of SDZ by potasium Periodate, and coupling with ortho-amino phenol to give a violet colour of maximum absorbaance at 532 nm. Beer's law is obeyed over the concentration range of 5-40 µg /ml of SDZ with a (R^2=0.9980) and molar absorptivity 5581.6 $L.mol^{-1}.cm^{-1}$ and a relative error in the range of - 0.06 - 2.3 % and a relative standard deviation of not more than 0.31 %. The composition of the resulting product is also investigated and it is found to be1:1. The method is successfully applied for the determinatiion of SDZ in pure and pharmaceutical dosage forms, with recovery of noot less than 101.1%.

Introduction

Sulphadiazine (SDZ), 4-amiino-N-pyrimidin-2-yll-benzensulfonamide[1], its structural formula is shown in Illustration 1

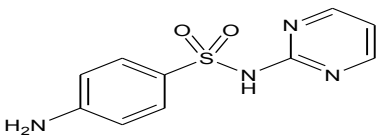


Illustration 1. Composition of sulphadiazine

The molecular formula is $C_{10}H_{10}N_4O_2S$, molecular weight of 250.3 gm/mol [2]. Sulphadiazine is one of the sulfonamide group, which belongs to the antibiotic group and is one of the oldest antibiotics that are still used so far. The sulphadazine has several important applications in pharmaceuticals where it is used in injection molding[2.3].

A number of analytical methods foor the determination of SDZ haas been reported iin the literature. These includes high perforrmance liquid chromotography coupled wiith on- line atmaspheric pressure chimical ionizasion mass spectrametry (HPLC,APCI-MS)[4], clloud poiint extraction /flaw injection-flame otomic absorption (CPE/FI-FAAS) spectrmetry)[5], capillary zone electrophorsis[6], inductively coupled plasma-atamic emission spectroscoppy (ICP-AES)[7], liquid chromatography [8], UV–spectrophotometry [9], immune chromatographic assay [10], flaw injection chemiluminscence[11], ion selective electrode [12]. Many UV-Visibl spectrophotomtric methods for thee determination of SDZ have ben developed. Most of theem included diazotization oof SDZ and then couplling with different couplling reagents, such as: 8- hydroxyquinoline [13], iminodibenzyl [14], histidine[15], γ-resorsolic acid[16], 2,5-dimethoxy aniline[17]. Other spectrophotometric methods are eiither based on th formation of charge, transfer complex wiith alizarin derivatives[18],and with phenosa-phranine[19], or an oxidative coupling reaction of SDZ with 4-amino-N,Ndimethylaniline in the presence oof dichromate [20], N,N-diethyl p-phenylenediamine sulphate and KIO4 [21]. In the present work, a novel sensitive spectrophotometric method is developed for the determination of SDZ based on the oxidation of sulphadiazine by potassium periodate and coupling with ortho-amino phenol which results in the formation of purple product of λ max at 532 nm .

Expermental

Appartus:
All absorption spectraa are carried out by Spectro UV-VIS Doublle Beam Model UVD-3000/UVD-3200 Dhaus with 1.0-cm quartz cells. Sensitive Balance type Sartorius BL 210S and Water bath type of Memmert are also used.

Chemicals

All chemicals usd are of analytical grade.

Sulfadiazin solution (1000 µg / ml): It is prepare by disolving 0.1 gm of SDZ in (1 ml) oof hydrochloric acid (11.8 M) and the voluume is completed to 1 ml with distiled water in a volumtric flask. Working solutions of SDZ is prepared by appropriate dilution of the stoock solution wiith distilled water

Ortho-amino phenol(0.01M) : It is prepared by disolving 0.054 gm of o-amino phenol in (2 ml) of HCl (11.8) and the volume is compllleted to 50 ml with distilled waater in a volumetric flask.

Potassium periodate solutiion (0.01M) : It is prepareed by dissolving 0.230 gm of KIO_4 in distiled water and the volume iis compllleted to 1ml with distiled water in a volumtric flask.

Procedure for assay of sulphadiazine in pharmaceutical preparation

Solution liquid injection veterinary **(**VAPCOTRIM**)**
Each 1ml contains 200 mg sulphadiazine,(100 ml) from this solution 0.5 ml (0.1 gm SDZ) in 100 ml volumetric flask, treated as in the way of SDZ standard solution and then 25 ml of this new solution is diluted by distilled water in a volumetric flask of 100 ml to obtain a solution of 250 µg/ml SDZ .

Results and discussion

Recommended Procedure:
Aliquots of standard solution of sulphadiazine 2 ml of 20 µg/ml are transferred to a 25-ml caliibrated flasks followed by adding 1.5 ml of potassium periodate (with waiting for five minutes), and 0.5 ml of ortho-amino phenol is added. The absorbaance at 532 nm is measured against a reageent blank.

Study of the Optiimum Reaction Conditions:
The effect of various paramters on the absorption intensiity of the formed coloured producted is studied andd the rection conditions are optimized.

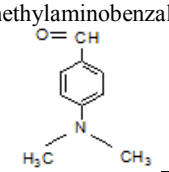
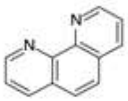
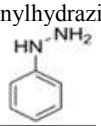
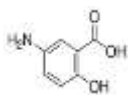
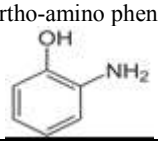
1- Effeect of kind and amount of oxidising agent and time of oxidation:
In this study, 1.5 ml of 1 × 10^{-2} M of different oxidizing agents are investigated, the results are shown in table 1 , it is clear that KIO_4 is the best so it is used in the subsequent experiments. The optimun volume of oxidizing agent is found to be 1.5 ml . The oxidation is completed within five minutes.

Table 1: Effect of type of oxidation agent

Oxidation agent (1×10^{-2}M)	Absorbance
KIO_3	0.143
KIO_4	0.437
$K_2Cr_2O_7$	0.392
$FeCl_3$	0.128

2- Effect of coupling reagent type:
A mong various coupling reagent, Ortho-amino phenol showed the higher value of absorption. In this study 0.5 ml (1 × 10^{-2} M) of reagent, 1.5 ml of (1 × 10^{-2} M) KIO_4 . the results are shown in Table 2

Table 2: The effect of the coupling reagent type

Reagent (1×10^{-2}M)	Colour	Wave length (nm)	Absorbance
1, 4- Dimethylaminobenzaldehyde 	Yellow	452	0.016
1,10-Phenanthroline 	Colourless	313	0.77
Phenylhydrazine 	Colourless	304	0.260
5-aminosalicylic-acid 	Brown	435	0.094
Ortho-amino phenol 	Purple	532	0.440

3- Effect of coupling reagent amount:
This study is carried out by mixing different volumes (0.3 - 3 ml) of (1×10^{-2} M) ortho - amino phenol with constant volume (2ml) of 250 µg/ml SDZ. The absorption when using (0.5 ml) of reagent showed a stability in the absorption value (0.475) while at higher volumes a higher values of absorption are obtained but the reading are not stable, so the volume of (0.5 ml) is chosed..

4- Effect of Temperture: The resulting praduct of the proposed meethod is studied at differeent temperatures. The reisults indicate that the absoorbance values remain constant iin the tempeirature range 25-30 C^0, whereeas, at higher temperatures thee absorbance valae decreases, indicatiing probably foor the dissociation of the prooduct . The coloured prooduct is stable foor more than 1 hors at rom temprature (25 C^0). Therefore thee degree of 25 C^0 is selected as the optimum temperature.

5- Effect of order of addition: The effect of order addition of the reactants are also investigated. The results are shown in table3 ,where the order S+O+R gives the highest value of absorption.

Table 3: order of addition

	order of addition	Absorbance
I	S+O+R	0.475
II	O+S+R	0.437
III	R+O+S	0.298

S is sulphadiazine , O is KIO_4, R is ortho-amino phenol

6- Effect of base
This study is achieved by adding different sizes (0.5 - 2.5 ml) of ammonium hydroxide (0.5 M) to (2ml) of sulphadiazine (250 µg/ml) with (1.5 ml) of potassium periodate (1×10^{-2}M) then coupling with (0.5 ml) of ortho-amino phenol (1×10^{-2}M) , The solubility of the solutions is measured at 532 nm wavelength compared to the solution of each solution & the results are recorided in the table 5

Table 4 : Effeect of base in the reaction of sulfadazine with reagent ortho-amino phenol

ml of 0.5M NaOH	Absorbance
0.0	0.475
0.5	0.468
1	0.459
1.5	0.450
2	0.442
2.5	0.435

The above table shows that the addition of base solution leads to a slight decrease in the absorption of the colored product and therefore it does not used in subsequent experiments

7- Time of stability
After addition the reactants and dilution with distiled water in (25 ml) volumtric flask thee violet product iis directly appeared and no increase in absorption is observed after time of five minutes , and the color is stable for 60 minutes at least (table 8).

Table 5 : Stability of the reaction product sulphadiazne with ortho-amino phenol

Time, minute	Abs
5	0.475
10	0.473
15	0.475
20	0.474
25	0.475
30	0.476
35	0.477
40	0.476
45	0.476
50	0.477
60	0.476

Absorption Spectra
A purple-coloured product of λ max at 532 nm is formed when 2 ml of sulphadiazine (250 µg/ml) is oxidized with 1.5 ml of potassium periodate (1×10^{-2}M) then coupling with 0.5 ml of ortho-amino phenol (1×10^{-2}M). Figure 2 showws the specttra of the formed purple prodact formed and tthe reagent blaank.

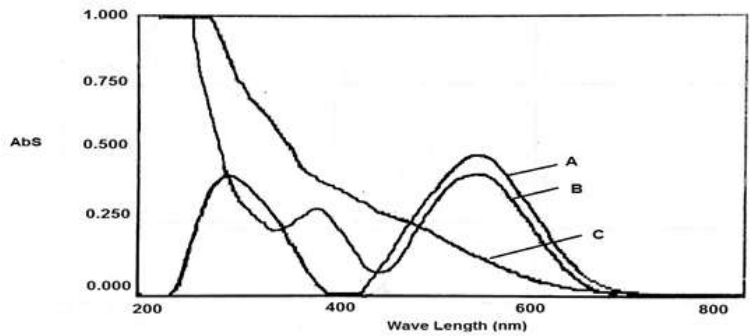


Figure 1. (A) Spectrum oof sample against reaggent blank
(B) Spectrum of sample against distilled water, (c) Spectrum of blank aginst distilled water

Calibration Graph :
Employing the optimum conditions ,in series of volumetric flasks of 25 ml, (0.5-4ml) of sulphadiazine (250 µg/ml) , 1.5 ml (1×10^{-2} M) of potassium periodate and 0.5 ml (1×10^{-2} M) of ortho-amino phenol are added. A liinear calibration graph foor sulphadiazine is obtined (Figure 2), which sows that Ber's law is obeeyed over the concentrtion range of 5-40 µg/ml with R^2 of 0.9989. The molar

absorptivity of the purple product formed is found to be 5581.6 $L.mol^{-1} .cm^{-1}$.

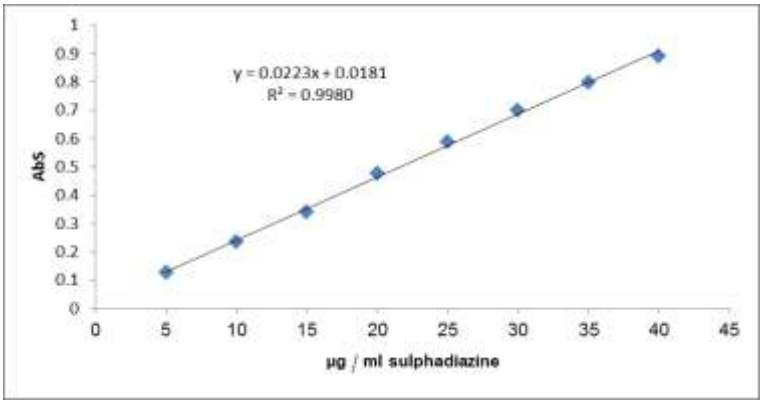


Figure 2. Calibration graph of sulphadiazine

3.4 Precision and Accuracy: sulphadiazine is determined at two different concentrations. The value of relative error,relative standard deviation and recovery are calculated, the reslts are shown Table 6. A satisfactory pricision aand accuracy are obtained.

Table 6. Accurracy and precision oof the proposed meethod.

Taken sulphadiazine (µg/ml)	Found µg\ml	relative error	Recovery %	Average recovery %	RSD %
20	0.475	2.3	102.3	101.1	0.31
35	0.798	-0.06	99.9		0.18

Average of five determinations

Limit of detection: The limit of detection is also calculated. The absorbane of lowest concentration in calibration curve is measured for five times, The results are shown in 7 table.

Table 7. Limit of detection

Amount of sulphadiazine (µg/ml)	Average of absorption value	RSD %	Limit of detection (µg/ml)
5	0.128	0.0015	0.175

Average of five determinations

3.5The stoicheiometry of the color product:
The stoicheiometry of the reaction between sulphadiazine and o-amino phenol is investgated using Job methood and mole raatio methood; the results obtiined (Figure 3, 4) shoow that the ratio is 1:1 drug to reagent.

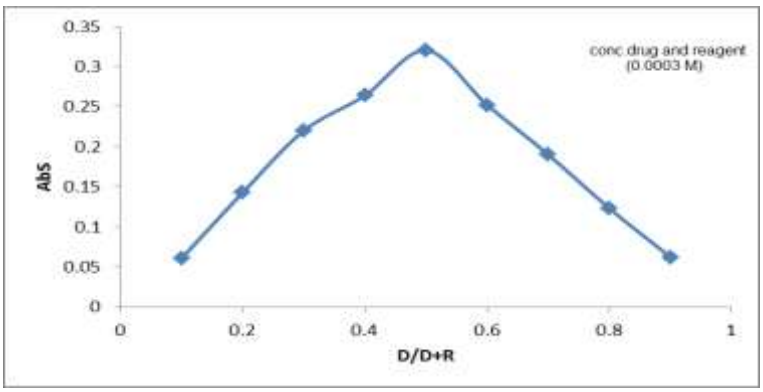


Figure3. Job's method

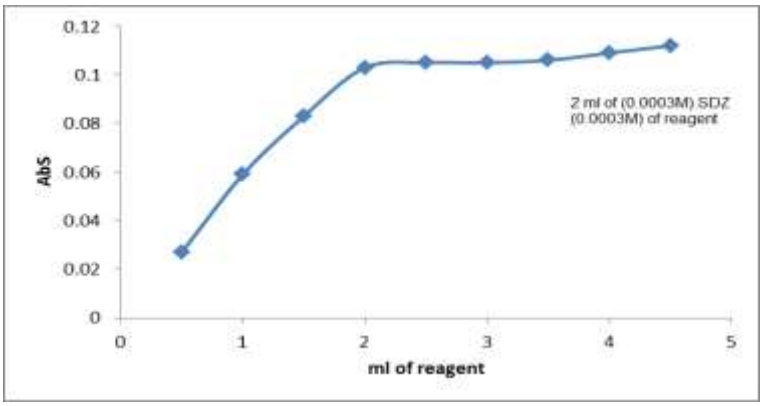
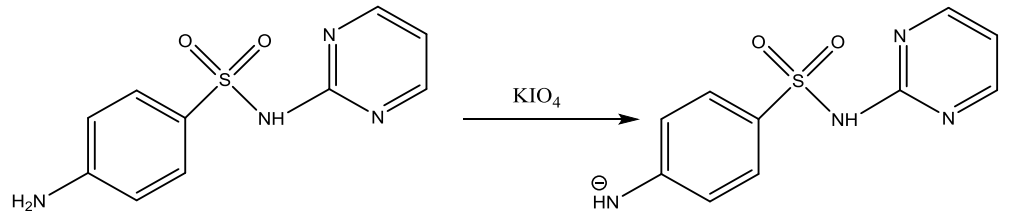


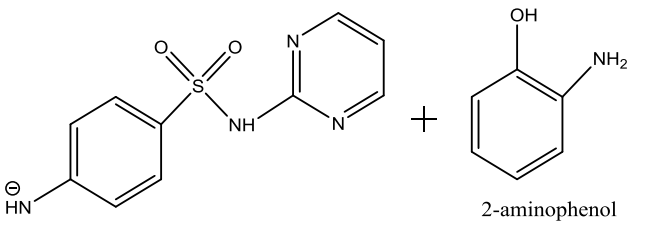
Figure 4 . Mole ratio method

The susgeated mechanis of reaction may be as the following route:



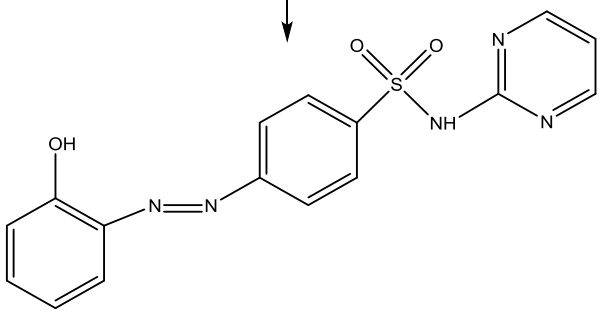
4-amino-*N*-(pyrimidin-2-yl)benzenesulfonamide
(Sulphadiazine)

(4-(*N*-(pyrimidin-2-yl)sulfamoyl)phenyl)amide



(4-(*N*-(pyrimidin-2-yl)sulfamoyl)phenyl)amide

2-aminophenol
(Ortho amino phenol)



(*E*)-4-((2-hydroxyphenyl)diazenyl)-*N*-(pyrimidin-2-yl)benzenesulfonamide

Illustration 2. Probable product formation pathway

3.7 Analytical application :

Direct method

Different sizes (1.5 ml, 2 ml) of sulphadiazine preparation in 25 ml volumetric flask are pipetted and (1.5 ml) of potassium periodate (1×10^{-2} M) (five minutes waiting) (0.5 ml) of ortho-amino phenol (five minutes waiting) are add and dilluted to the marrk with distiled water, Absorption is measured (average of five readings) for every Solution at 532 nm wavelength. The resulte are shown in table 8

Table 8 : Results of sulfadazine determination in the veterinary method by direct method

Veterinary product	Sulphadiazine (µg/ml) Taken	Found	Relative error %	Recovery %	RSD %
VAPCOTRIM	15	0.346	2.06	102	0.43
	20	0.469	-1.2	98,7	0.31

Average of five determinations

Standard additions method

Solution liquid injection veterinary (VAPCOTRIM) containing sulphadiazine have been analyzed. In order to demonstrate the efficiency and accuracy of the proposed method and to show that the developed method is free from interferences', this method is applied. A fixed quantity (0.3 ml , 0.4 ml) of the veterinary solution at a concentration of 250 µg / ml is added in a seriies of 2ml volumetric flaasks, then increasiing volumes (0.5-2.5ml) of the standard sulphadiazine solution at a concentration of 250 µg / ml are added followed by an addition (1.5 ml) of potassium periodate (waiting for 5 minutes) and then (0.5 ml) of ortho-amino phenol is added. The above solutions are treated in the same way as in the calibration curve an absorption is measured for all solutions at 532 nm wavelength. The results are shown in the table 9.

Table 9: The application of proposed meethod foor determination sulphadiazine in VAPCOTRIM pharmaceuticaal preparation

Pharmaceutical Formulation	Drug Amount Present(µg/ml)	Drug Content Found (mg)	Recovery %	Average recovery %
VAPCOTRIM	3	3.03	101	101.1
	4	4.05	101.2	

4. Conclution

A simple, rapiid, precise, and sensitiive spectropphotometric methood haas been developed for the determinaation of sullphadiazine in aqueous sollution baased on its oxidative couplling reactiion with orrtho-amino phenool iin the presence potassium Peeriodate .The proposed methood does not require tempeerature control or solvent extracction step; the method is appliied successfully for the deetermination of SDZ in its phaarmaceutical preparation.

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التقدير الطيفي لعقار السلفادايازين بتفاعل الاقتران التأكسدي مع كاشف اورثو–أمينو فينول.

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قسم الكيمياء ، كلية العلوم ، جامعة تكريت ، تكريت ، العراق

الملخص

تم وصف طريقة طيفية بسيطة، سريعة وحساسة لتقدير عقار السلفادايازين (SDZ) في المحلول المائي. اعتمدت هذه الطريقة على أكسدة SDZ ببيريودات البوتاسيوم والاقتران مع كاشف اورثو–امينو فينول ليعطي ناتج ذو لون بنفسجي يمتص عند λmax 532 nm. مدى الخطية (مطاوعة قانون بير) كان من 5–40 مايكرو غرام/مل ل SDZ بمعامل تحديد 0,9980 ومعامل امتصاص مولاري 5581,6 لتر\ مول سم وخطأ نسبي بمدى من –0,06–2,3 % وانحراف قياسي نسبي ليس اكثر من 0,31% .

تمت دراسة نسبة الاتحاد بين العقار والكاشف و وجدت انها 1:1 وتم تطبيق الطريقة بنجاح لتقدير SDZ بحالته النقية وفي المستحضر الصيدلاني باسترجاعية لا تقل عن 101,1% .