

The Spectrophotometric Determination of Antiepileptic Drug in Standard and Pharmaceutical Formulations by Diazotization Coupling Reaction and Some Metals Complexes

¹Khawla Salman Abd-Alrassol¹, ²Outaiba A. Qasim, ²Falah hassan shari, ¹H. N. K. AL-Salman, ¹Hussein H. Hussein

¹Department of pharmaceutical chemistry, College of pharmacy, University of Basrah, Iraq

²Department of Clinical Laboratory Sciences, Collage of pharmacy, University of Basrah, Iraq

Corresponding Author E-mail: hennaserh@yahoo.com

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ABSTRACT

A rapid, sensitive spectrophotometric method has been proposed for the determination of Gabapentin antiepileptic drug in pure and in pharmaceutical preparations was developed. The method is based on the coupling reaction between Gabapentin with 8-hydroxy quinoline in to form an olive colored azo dye which gave maximum absorption at 365nm. The optimum reaction conditions like: pH, Temperature affected and time of reaction were evaluated. The ligand and its complexes were characterized by UV-visible spectroscopy, infrared FT-IR, (C.H.N.) analysis and Molar conductivity. The ratio of (metal: ligand) of all complexes was (1:2) by using molar ratio method and job's method. Beer's law is obeyed for ligand and its complexes with (Cu²⁺, Ni²⁺, Cd²⁺, Co²⁺ and Zn²⁺) in concentration ranges (2 - 20, 1.5 - 25, 1 - 20, 2 - 25 and 2-30 μg m⁻¹) respectively. The molar absorptivity also calculated and it's found to be (1.396×10⁴, 2.0208×10⁴, 2.295×10⁴, 1.684×10⁴ and 1.862×10⁴ L.mol⁻¹.cm⁻¹) for Cu²⁺, Ni²⁺, Cd²⁺, Co²⁺ and Zn²⁺ complexes respectively. The detection of limit and quantification of limits are also calculated. The stability constant of complexes equal to (3.273×10⁶, 1.695×10⁶, 7.859×10⁶, 1.851×10⁵ and 1.588×10² L².mol⁻²) for Cu²⁺, Ni²⁺, Cd²⁺, Co²⁺ and Zn²⁺ complexes respectively. The method is successfully used for the determination of Gabapentin in

pharmaceutical formulations. Analytical parameters like accuracy and precision for the method have been established and evaluated statistically to assess the application of the proposed method. No interferences observed in the proposed method. The complexation with five ions (Cu²⁺, Ni²⁺, Cd²⁺, Co²⁺ and Zn²⁺) were studying. The aim of present work was devoted to investigate the reaction between Gabapentin and 8-hydroxy quinoline to form color Azo dye and use this product in the development of sensitive and simple spectrophotometric method for determination of Gabapentin in its pure and pharmaceutical preparations and spectrophotometric studies of a azo dye formed and it's metal complexes with Cu²⁺, Ni²⁺, Cd²⁺, Co²⁺ and Zn²⁺ ions.

Key words: Azo compound, Diazotization, Gabapentin, Metals complexes.

Correspondence:

Hussein H. Hussein

Department of pharmaceutical chemistry, College of pharmacy

University of Basrah, Iraq

E-mail: hennaserh@yahoo.com

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INTRODUCTION

Gabapentin drug is known chemically as [1-(amino-methyl) cyclohexanecarboxylic acid], it is antiepileptic drug which is a structural analogue of the inhibitory neurotransmitter gamma-aminobutyric acid (GABA) [1]. Gabapentin crosses the blood brain barrier and is used for the treatment of partial seizures. It has demonstrated analgesic effects in patients with chronic neuropathic pain states [2]. Gabapentin anticonvulsant preparation drugs used in both epilepsy treatment and neuropathic pain, as an adjunct therapy for partial seizures in children and adults [3-4]. Many analytical methods have been used for the assessment of Gabapentin drug in pharmaceutical formulations such as (HPLC) high performance liquid chromatography [5-7], voltammetry [8], visible spectrophotometry [9-11], capillary electrophoresis [12], chemiluminometry [13], UV-spectrophotometry [14-16] electrophoresis [17], fluorimetry using sequential injection [18], fluorimetry using sequential injection [19], spectrofluorimetry [20], potentiometric sensor [21] spectrofluorimetry [22] voltammetry [23], using piezoelectric pumping [24]. Many analytical methods for therapeutic monitoring also have been written in the literature explain the quantitative determination of Gabapentin in human serum or plasma using GC [25], CE [26].

EXPERIMENTAL

All absorbance measurements and spectra were carried out by using a Jena Model 1100, UV-Visible spectrophotometer (Germany) in pharmaceutical chemistry department, college of pharmacy, university of Basrah, Iraq. The UV-Visible spectrophotometer was equipped with a quartz cell with a 10mm path length. Electrode meter electrical balance is used for weighting the sample. The pH measurements are performed using Philips PW 9421 pH meter. FTIR-8400 Shimadzu, single beam bath laser spectra were recorded as KBr in the range of (4000-400) cm⁻¹. The CHN analysis measurements for the synthesized compounds were performed by using Euro Vector model EA3000A (Italy), and molar conductivity was measured at 25 °C for 10⁻³M solution of DMSO. Melting points were determined by using Stuart melting point apparatus PH7110.

Reagents

All chemicals used were of analytical grade. Gabapentin pure was purchased from Sigma-Aldrich Co. The commercial drugs used in the present work were taken from commercial markets. Pharmaceutical preparation of Gabapentin-like Gabapentin capsules-100 mg (Al-Debeiky pharmaceutical products for Delta pharma, Egypt), and Gabix capsules (Getz pharma, Karachi, Pakistan), contain 100mg GAB. per capsule. GABATREX capsules (HIKMA) contain 100 mg Gabapentin per capsule.

The 8-hydroxy quinoline and Sodium nitrite (Merck, Germany). Sodium hydroxide and hydrochloric acid (BDH, England).

SOLUTIONS

Gabapentin stock solution, $1000 \mu\text{g}\cdot\text{ml}^{-1}$

A 0.1g amount of Gabapentinis dissolved in distilled water and the volume was completed to 100ml in a volumetric flask. This solution is kept in a brown bottle. Working solution was prepared by diluted.

Sodium nitrite solution 1%

A 1% NaNO_2 was prepared by dissolved by weight 1g of Sodium nitrite in water. Then the volume was completed to 100 ml in a volumetric flask with distilled water.

Diazotized 8-hydroxy quinoline solution, 10 mM

A 0.0145 g of 8-hydroxy quinoline is dissolved with 50 ml distilled water. Then concentrated hydrochloric acid 1.5 ml was added and heated the solution. The mixture was Transferred to a 200ml volumetric flask and cooled to 5°C . The mixture is stirred occasionally for 5 min after added 7 ml of 1 % NaNO_2 and the volume is completed to 200 ml by used cooled water 5°C . The product solution was stored in darkness over ice and used after 15 min. This solution must kept in the refrigerator and it is stable for three days.

Sodium hydroxide solution, 5 M

5M Sodium hydroxide solution was prepared by dissolved 20 g of sodium hydroxide in 100 ml of distilled water in a volumetric flask .The solution transferring to a plastic bottle to storage.

Procedure for Calibration Graph

Aliquot volumes of Gabapentin drug standard solution was transfer and covering the working concentration range from (1 - $30.0 \mu\text{g mL}^{-1}$) in to 25 ml volumetric flasks .A 1.5 ml of 5 mM diazotized 8-hydroxy quinoline reagents are then added. The reaction mixture was allow to stand for 2min, Then 1ml of sodium hydroxide NaOH solution with 5 M concentration was added. Then the volume is completed to 25ml with distilled water. The maximum absorbance of the product color solution was measured and found to be at 365 nm against a reagent blank.

Procedure for Gabapentin capsules

The contents of ten capsules were empty and mix well. In to 100 ml volumetric flask transfer a weighed quantity of the powdered capsules equal to 10 mg of Gabapentin and complete the volume with distilled water to 100ml. stirred the solution for 10 minutes magnetically, then worked under recommended Procedure described.

Absorption spectra

The spectrum of colored product show an absorption band at 365nm. Where there is no absorption band to the reagent blank at this wavelength as show in fig. (1).

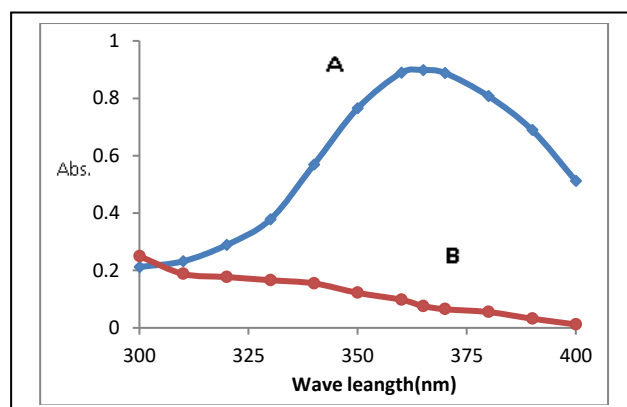


Figure 1: Absorption spectra of A: $20 \mu\text{g ml}^{-1}$ of Gabapentin measured against reagent blank. B: spectra of reagent blank.

OPTIMUM REACTION CONDITIONS

By keeping experimental parameters and the amount of drug constant and varying one .The effect of various variables on the color intensity was studied to establish the optimum conditions for the assessment of Gabapentin.

Effect of Sodium Nitrite Concentration

The effect of 1% NaNO_2 concentration was studies by using different amounts (2-10 ml) of 1% Sodium nitrite solution. The results showed that 7 ml of Sodium nitrite reagent solution is sufficient for production of maximum color intensity (Fig.2).

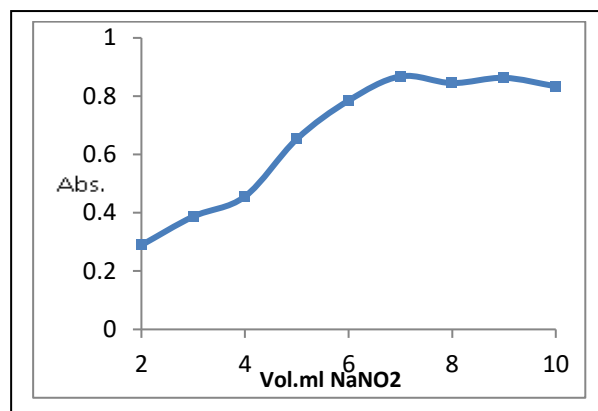


Figure 2: Effect of Sodium nitrite concentration

Effect of Reagent Concentration

The effect of reagent (diazotized 8-hydroxy quinoline) concentration was studied by using different volumes (0.5–

3 ml) of 5mM diazotized 8-hydroxy quinoline solution (fig.3). It was found 1.5 ml of diazotized 8-hydroxy quinoline is required to obtain maximum absorbance.

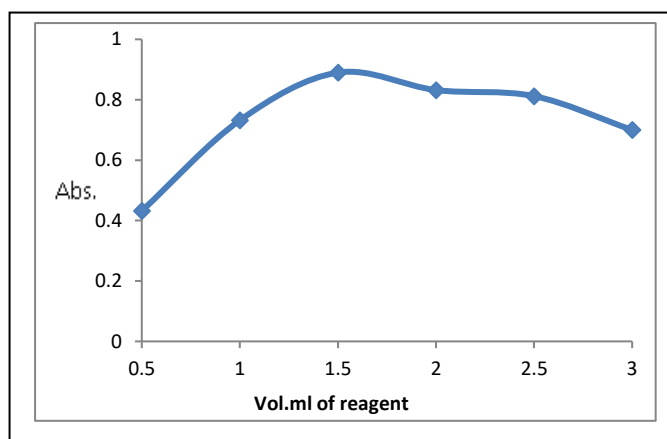


Figure 3: Effect of reagent (diazotized 8-hydroxy quinoline) concentration Effect of the type of acid in diazotization process

Acidic medium is very essential for accomplished the diazotization reaction. For that reason the effect of different prepared acid solutions (1M) were examined such as hydrochloric acid, nitric acid, sulfuric acid and acetic

acid. HCl gave a higher absorbance than other acids; therefore hydrochloric acid was found to be the suitable acidic medium and was used in all experiments (Fig.4).

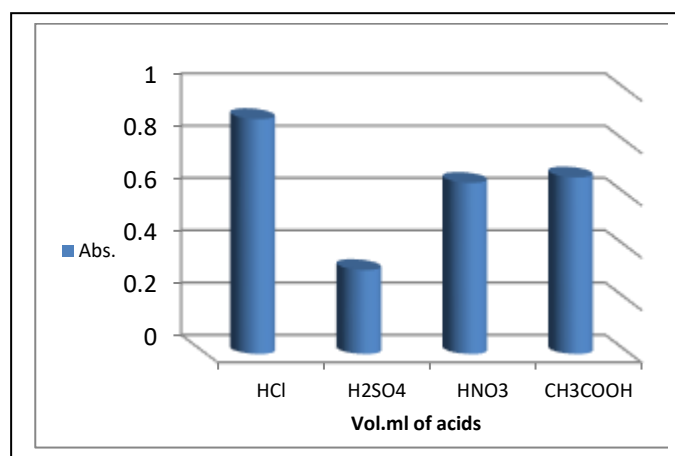


Figure 4: Effect of the type of acid

Effect of acid concentration

The effect of various volumes of hydrochloric acid (1M) was optimized on the absorbance by changeable the amount of HCl in the range (0.5-3mL) and keeping other

parameters constant. The highest absorbance was obtained 1.5 mL of hydrochloric acid and was chosen for use all experiments (Fig. 5).

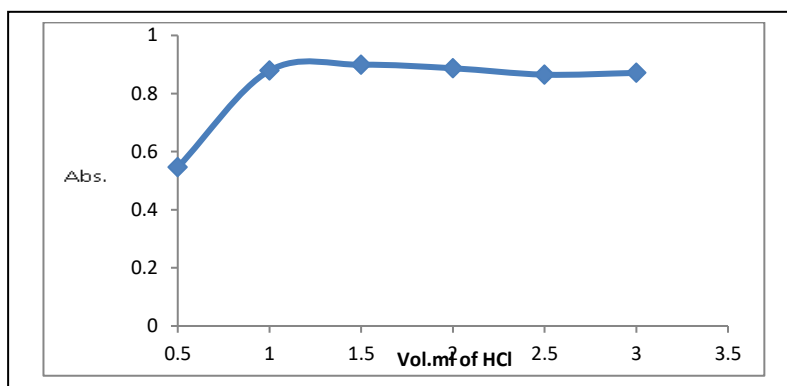


Figure 5: Effect of acid concentration

Effect of the type of Base

Olive colour product was formed just in alkaline medium. The different alkaline solutions effects were tested like sodium carbonate, ammonium hydroxide, potassium

hydroxide and sodium hydroxide. The results show that sodium hydroxide gave a higher absorbance than other alkaline medium (Fig.6).

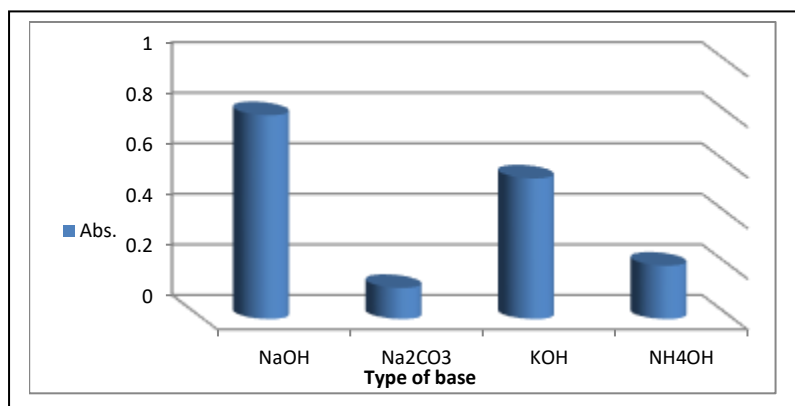


Figure 6: The effect of the type of Base

Effect of Base Concentration

The result indicated that the presence of a base it causes increase the intensity of the product .5M of NaOH was selected which was found that the best volume equal to 1

ml of (0.5-2mL) of NaOH give high sensitivity which selected in subsequent experiments. The figure 7 explained these results.

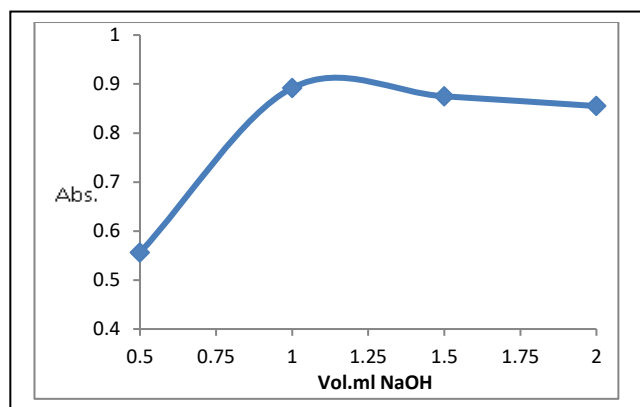


Figure7: Effect of Base Concentration

Effect of reaction time

The reaction was carried out for different times (2 –40 min) and was found to be time dependent. After 15 min

the maximum absorption intensity was obtained (fig.8). It was found that 15 minutes time was sufficient for complete colour development and the colour was stable for 24 hours.

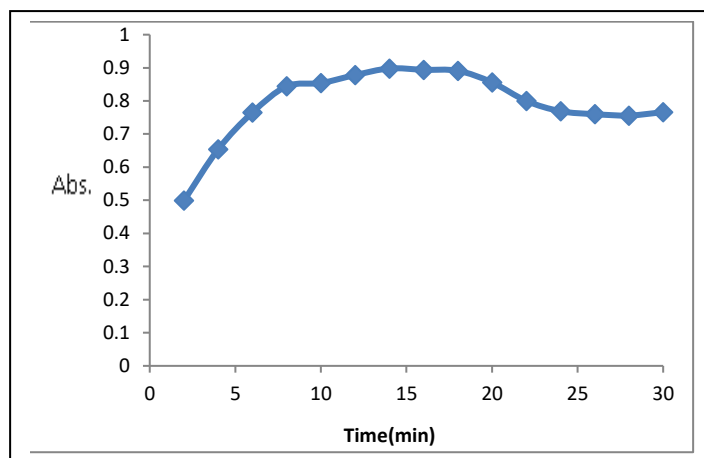


Figure 8: Effect of variation in reaction time

The order of addition of the reagents

Order of addition of the reagents is crucial. Addition of reagents in the order Gabapentin, diazotized 8-hydroxy quinoline reagent, sodium hydroxide and then complete with water gave constant and maximum absorbance.

series of 25ml volumetric flasks are added aliquots of solution containing 1-30 $\mu\text{g ml}^{-1}$ Gabapentin. 1.5 ml of 5 mM diazotized 8-hydroxy quinoline reagent are added, then the mixtures are shaken well. Then 1 ml of 5 M NaOH solution is added and the volume is complete with distilled water, and the absorbance was measured at 365 nm after 15 minutes using 1 cm bath cells against the corresponding reagent blank.

The effect of temperature

The effect of temperature on the absorbance of the colour product Azo dye was studied. The absorbance of the product remains constant in the range 0–40°C and decrease at higher than 40 °C. Therefore, it has been to carry out reaction at room temperature (25°C) and cooling to 0 – 5°C was not necessary.

ANALYTICAL CHARACTERISTICS

Calibration graph was studied by the analytical method described previously and a series of standard solutions were prepared and analyzed in triplicates to study the linearity. Molar absorptivity (ϵ), Sandell sensitivity (S), intercept (a), slope (b), correlation coefficient (R^2), limit of quantification and limit of detection values are shown in Table (1).

CALIBRATION GRAPH

The calibration graphs were dependent on using standard solutions at the optimum condition of experiment. To a

Table 1: analytical parameter

Parameter	Value
$\lambda_{\text{max}}(\text{nm})$	345nm
Linearity range, $\mu\text{g mL}^{-1}$	1 – 30
Correlation coefficient (R^2)	0.9988
ϵ , $\text{L mol}^{-1} \text{cm}^{-1}$	0.449×10^3
S, $\mu\text{g cm}^{-2}$	0.044
Limit of detection (LOD) ($\mu\text{g mL}^{-1}$)	0.2566
Limit of quantification (LOQ) ($\mu\text{g mL}^{-1}$)	0.0683
Slope (b)	0.045
Intercept (a)	0.002

The stoichiometry of the reaction

The stoichiometry of the reaction between Gabapentin and 8-hydroxy quinoline was investigated using

Continuous variation method and mole ratio method [27]; the results obtained figures 9 and 10 show that 1:1 drug to reagent was formed at 365 nm.

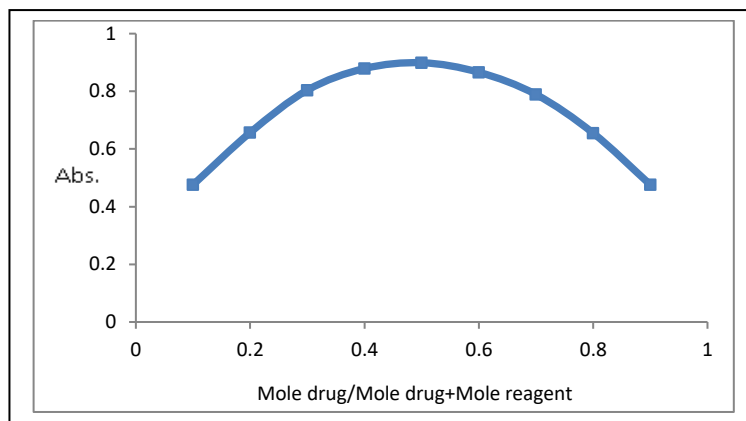


Figure 9: Continuous variation method

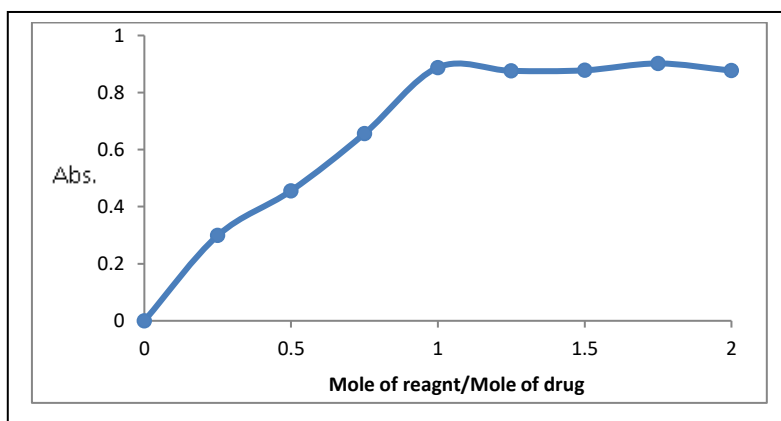


Figure 10: Molar ratio method

Therefore the formation of the product probably follows (Fig.11).

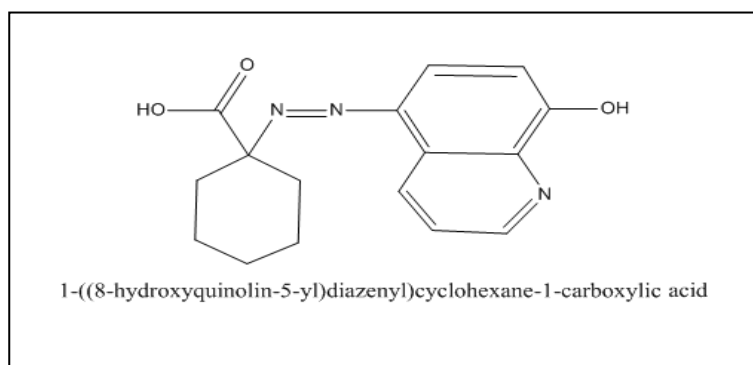


Figure 11: Probable product formation

Precision and Accuracy

The precision and accuracy of the present methods were evaluated through replicate analysis of 5 times for 20µg/ml

and 30µg/ml the results of Recovery, Relative Standard Deviation (RSD %) and Relative Standard error (E %) are shown in Table (2) below.

Table2: Accuracy and precision of the method

Gabapentin Taken µg mL ⁻¹	Gabapentin found µg mL ⁻¹ *	Recovery% *	Relative Standard error %E	Relative Standard Deviation RSD%*
20	20.01	100.20	0.05	1.108
30	29.80	99.80	0.66	1.003

*Average of five determinations

The results in Table (2) prove that satisfactory accuracy and precision could be attained by the current method .The RE (%) and RSD (%) values were title than1.2%which prove the high value of accuracy. The maximum color intensity reached after 15 min from formation of azo dye and the color intensity stable for 24 hours.

The interferences

The selectivity of present method were examined by studies the effect of some common excipients (glucose, starch ,lactose, Sodium chloride Gum Arabic, Talc , glycerin and acacia) on the selectivity. The resulted indicated that the excipients do not effect or interfere with determination of Gabapentin compounds in its pharmaceutical preparation or its dosage forms.

Analytical applications

The present method will be effective for the evaluation of Gabapentin in pharmaceutical preparation.The obtained results were shown in Table 3. The obtained results refers to the Gabapentin content measured by the proposed method was in wonderful agreement with those result by the manual reference British pharmacopoeia method [28]. The results were statistically compared by a t-test for accuracy and a F-test for precision with the standard method at five degrees of freedom and 95 % confidence level, The results indicated that the experimental t-test and F-test were less than the theoretical value.That provide there was no significant difference between the prasente method and standard method.

Table 3: Application of the determination of Gabapentin in pharmaceutical formulations

Methods	Mean**± RSD%	Variance	SE	t-test (2.228)*	F-test (5.1)*
proposed method	99.75± 0.215%	0.047	0.087	0.903	1.40
Reference method ⁽²⁸⁾	99.66± 0.183%	0.034	0.075		

*Theoretical values ** Average of six different experiment

Synthesis of complexes

The reaction of Azo dye (ligand) solution (2mmol) in (10ml) ethanol was added to solution of (1mmol) CuCl₂.2H₂O in (10ml) ethanol. The mixture was stirred for 6 hours at room temperature, the brown solid was collected by filtration, washed with (1:2) mixture of water: ethanol, recrystallized from ethanol and dried in an oven (50°C). A similar method to that mentioned for preparation of CuCl₂.2H₂O complex was used to prepare the complexes of [Ni(II), Cd(II)and Co(II)and Zn(II)] ions

with ligand. Table (4) showed some properties of the prepared complexes and figure (12) as a model of others inons in current study, showed the absorption spectra of complexes they formed a vivid color differ from the ligand color, with a red shitting in the absorption region toward higher wavelength, this may be thought the coordination take part between these ions and the ligand [29]. All complexes are stable in solution and they dissolve in methanol, ethanol, acetone, DMSO and DMF solvents.

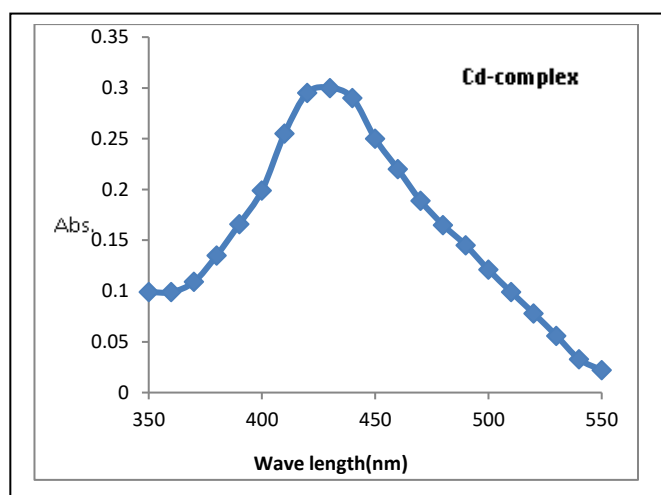


Figure 12: Absorption spectra of Cu, Cd, Co, Ni and Zn-complexes

Optimization of Variables

The different experimental parameters affecting on the intensity of color development were optimized. The conditions were established by changing the parameters one at a time while fixed the other and then notes the absorbance of colored produced effected.

Effect of PH

The effect of PH was studied over the range (3-10) adjusted by mains of diluted HCl and NaOH solutions. Figure (13) shows the relationship between the absorbance and PH for different complexes, where the maximum absorbance

obtained in the range of PH (6-8), therefore the optimum PH was 7, where the absorbance maximum and constant.

Effect of time

The stability of complexes was studied from (0-35min) interval up to 24 hrs. The maximum absorbance was reached at 10 min and remaining constant as show in figure (14).

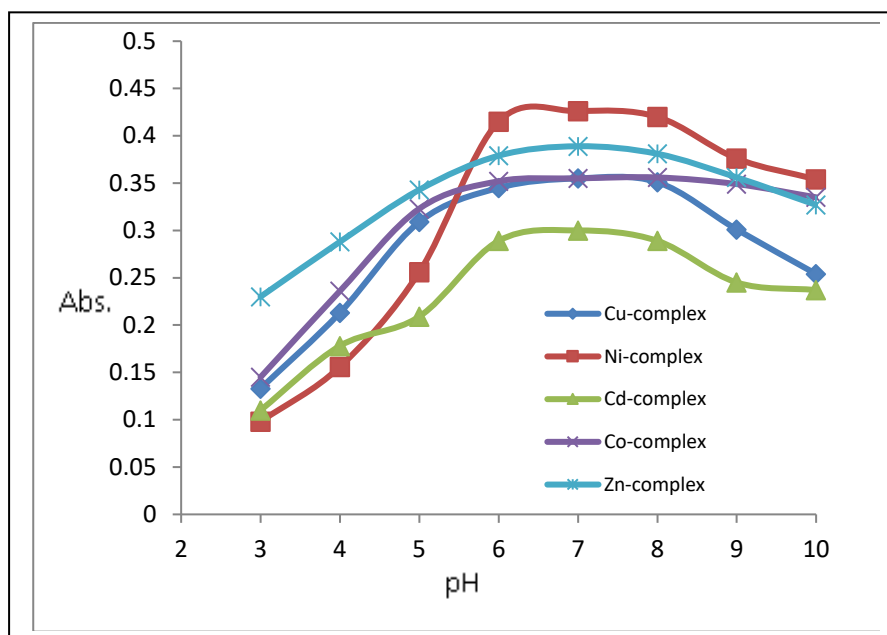


Figure 13: The effect of PH on absorption of complexes (10mg/ml for Cu and Cd, Zn complex 15mg/ml for Ni, Co and concentration)

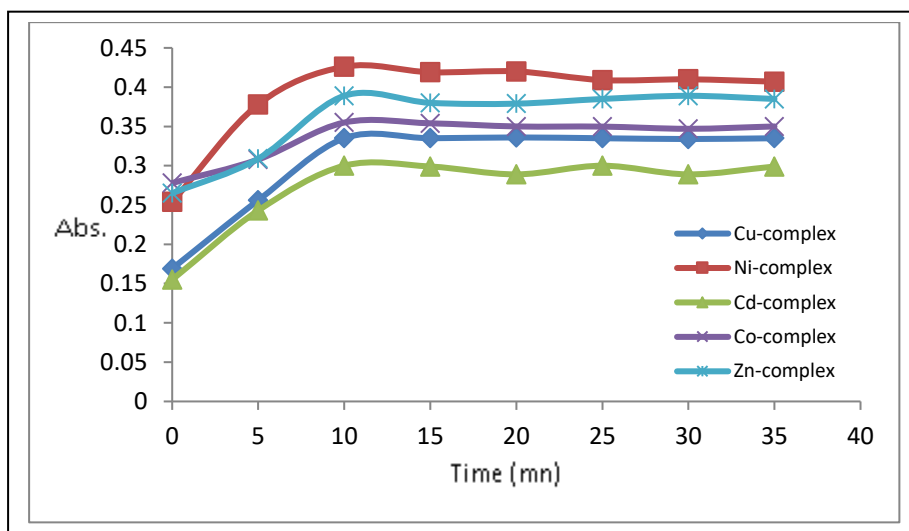


Figure 14: Effect of time on complexes stability

The effect of the temperature
Effect of temperature on the absorbance of complexes was studied. The study was performed at temperature between

5-60°C. The maximum absorbance obtained at 25-40°C, as show in figure (15). At higher than 45°C the complexes suffers dissociation there for the absorbance decrease.

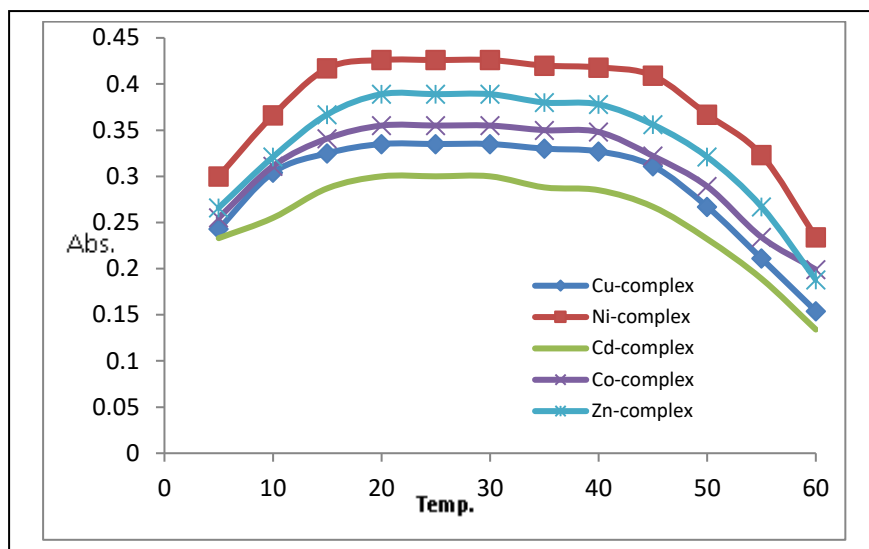


Figure 15: Effect of temperature on absorbance

Measurements of molar conductivity

Electrical molar conductivity measurement results will support us in the suggestion of the geometrical formula of the prepared complexes by the knowledge of the ionic formula of the solid complexes solutions [30], that the conductivity proportionally with the charged species in solution, so it has low values or approached to zero in non-

ionic solutions, our study complexes are measured in two solvents (ethanol and dimethyl formamide) in (1×10^{-3}) M concentration and room temperature condition are non-ionic complexes, agreed with the literature [31]. Table (4) list some properties of ligand and Complexes.

Table 4: Some properties of the ligand and its complexes

Complexes	Chemical formula	M.wt (gm/mole)	Color	M.P(°C)	Yield%	Molar Cond Δm (S.mol ⁻¹ .cm ²)	
						DMF	Ethanol
L		327.40	Olive	>300c°	75	----	----
[Cu(L)2]	C ₃₂ H ₃₄ CuN ₆ O ₆	716.34	Browne	>300c°	78	23	20
[Ni(L)2]	C ₃₂ H ₃₄ NiN ₆ O ₆	711.49	Yellow	>300c°	84	16	21
[Cd(L)2]	C ₃₂ H ₃₄ CdN ₆ O ₆	765.21	Brown	>300c°	76	12	15
[Co(L)2]	C ₃₂ H ₃₄ CoN ₆ O ₆	711.73	Browne	>300c°	78	13	19
[Zn(L)2]	C ₃₂ H ₃₄ ZnN ₆ O ₆	718.21	Black	290c°	80	10	12

Determination of stoichiometry of complexes

The stoichiometry of the reaction between producing azo dye and some metals were investigated by using continuous variation method and molar ratio method. The

results obtained in figure16 as a model for the others metals ion, show that a (1:2) ratio was formed between azo dye and metals.

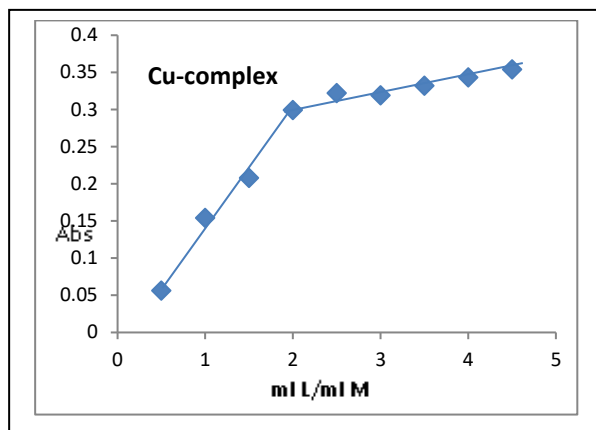


Figure 16: Molar ratio method for Cu-complex

The proposed structural formula of chelate complexes according to the results and discussed could be suggest in Figure (17).

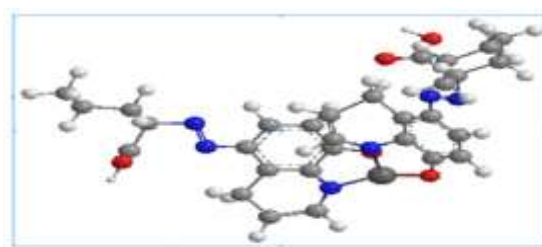


Figure 17: Suggest structural formula of M-complexes

Stability constant calculation

Mole ratio study for the complexes in their solutions tell us in the calculation of stability constant of these complexes, utilizing the absorbencies values of the ligand solution with the ion we want to know its stability constant , this will be done according to the equations:

$$\beta = \frac{[ML_n]}{[M][L]^n}$$

When β = formation constant, when n=2,

$$\beta = \frac{1 - \alpha}{4\alpha^3 c^2}$$

And the β value can determine when α (dissociation constant) are known

$$\alpha = \frac{A_m - A_s}{A_m}$$

From the equations above the stability constant of the complexes can be calculated and found to be 3.273×10^6 , 1.695×10^2 , 7.859×10^6 , 1.851×10^5 and 1.588×10^2 for Cu(II), Ni(II), Cd(II) and Co(II) and Zn(II) complexes respectively. Then, the solid complexes were prepared and the complexes elementary composition has knowledge via (C, H, N) analysis, as shown in the following table (5,6). The calculated and log values for prepared complexes are shown in Table(5). According to the results in table (5) notes the stability constant compatible with Irving-Williams series of stability constant [32].

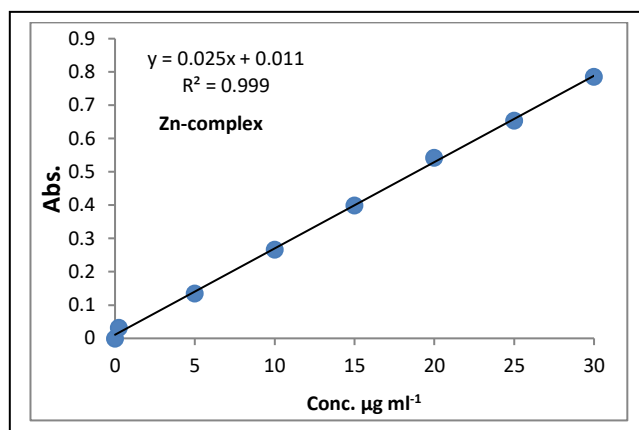
Table5: Complexes stability constants

Stability constant	Complexes				
	CuC ₃ H ₄₆ N ₆ O ₆	NiC ₃ H ₄₆ N ₆ O ₆	CdC ₃ H ₄₆ N ₆ O ₆	CoC ₃ H ₄₆ N ₆ O ₆	ZnC ₃ H ₄₆ N ₆ O ₆
A	0.071	0.032	0.065	0.027	0.015
log (L ² mol ⁻²)	3.273×10 ⁶	1.695×10 ²	7.859×10 ⁶	1.851×10 ⁵	1.588×10 ²
log	6.514	2.229	5.894	5.267	2.198

Analytical characterized

The calibration graphs were created using standard solutions at the optimum conditions of experimented. A linearity was notes between the concentration and the absorbance of metal and complexes from 2-20, 1.5-25, 1-20, 2-25 and 2-30 $\mu\text{g ml}^{-1}$ for Cu-complex, Ni-complex, Cd-complex, Co-complex and Zn-complex respectively. The molar absorptivity 1.396×10^4 , 2.0208×10^4 , 2.295×10^4 , 2.295×10^4 , 1.684×10^4 and 1.862×10^4 $\text{L mol}^{-1} \text{cm}^{-1}$ for Cu-

complex, Ni-complex, Cd-complex, Co-complex and Zn-complex respectively. Sandell's sensitivity for all complexes were fined from beer's law. The limit of quantification (LOQ) and limit of detection (LOD) also accuracy according to United States Pharmacopeia [33] guidelines. Under the optimum conditions of experiment. Table (7) listed parameters and linearity of complexes were show in figure (18) as a model of one of them..



Figures 18: Linearity of complexes

Table6: Elemental analysis

Parameters	Value				
	Cu-complex	Ni-complex	Cd-complex	Co-complex	Zn-complex
wavelength (nm)	435	440	430	420	425
Linear range ($\mu\text{g mL}^{-1}$)	2-20	1.5-25	1-20	2-25	2-30
Intercept	0.011	0.010	0.015	0.009	0.011
Slope	0.033	0.027	0.034	0.024	0.025
Standard deviation	0.0043	0.0032	0.0053	0.0021	0.0044
Correlation coefficient (r^2)	0.997	0.998	0.997	0.999	0.999
Limit of detection, LOD ($\mu\text{g. mL}^{-1}$)	0.430	0.391	0.514	0.288	0.580
Limit of quantification, LOQ ($\mu\text{g.mL}^{-1}$)	1.303	1.185	1.558	0.875	1.760
Molar absorptivity, e ($\text{L mol}^{-1} \text{cm}^{-1}$)	1.396×10^4	2.0208×10^4	2.295×10^4	1.684×10^4	1.862×10^4
Sandels sensitivity($\mu\text{g.cm}^{-2}$)	6.391×10^{-3}	0.104×10^{-3}	0.056×10^{-3}	0.125×10^{-3}	0.1121×10^{-3}

Table 7: Analytical Characterization of Complexes

Compound	C%		H%		N%		O%		M%	
	Calc.	found	Calc.	found	Calc.	found	Calc.	found	Calc.	found
C16H17N3O3	64.20	64.33	5.72	5.88	14.04	14.11	16.03	16.15		
C32H34CuN6O6	58.04	58.21	5.18	5.23	12.69	12.77	14.50	14.66	9.60	9.72
C32H34NiN6O6	58.47	58.54	5.21	5.37	12.78	12.84	14.60	14.79	8.93	8.99
C32H34CdN6O6	54.05	54.18	4.82	4.98	11.82	11.90	13.50	13.63	15.81	15.99
C32H34CoN6O6	58.45	58.59	5.21	5.44	12.78	12.88	14.60	14.77	8.96	8.99
C32H34ZnN6O6	57.88	57.97	5.16	5.25	12.66	12.70	14.46	14.59	9.85	9.95

FTIR Spectra

The most group vibrations of FTIR for the preparation ligand and its metal Complexes were listed in Table(8).The

comparison between ligand spectra with the coordination complexes have revealed certain characteristic differences The spectrum of ligand shows well-defined peaks at

(3448.27 and 3066.82 cm^{-1}) are assigned to the of carboxyl [34]. In the spectra of the all prepared complexes these two peaks a mostly appeared at the same frequency as that of the free ligand, indicating that they don't participate in coordination [35] This band stay in the same region in ligand and in chelate complexes spectra.. Doublet bands

were also noticed at the range characteristic (1690-1683 cm^{-1}) in the spectrum of the free ligand. The FTIR spectra of complexes exhibited new bands at (671-520 and 459-432 cm^{-1}), were attributed to (M-O) and (M-N) respectively [36].

Table 8: The FT-IR spectral ligand and metal complexes

Compounds	V(O-H)	V(N-H)	V(C=O) V(C=C)	V(C=N=N=C)	V(N=N)	V(C-N=N-C)	V(M-O)	V(M-N)
Ligand	3448.72 3066.82 browed	3066.82 Weak	1690.92 1460.37	1462.04 sharp	1388.75 medium	1315.45 1095.57 sharp	-----	-----
Cu-complex	3448.72 3379.29 browed	2930.43 Weak	1647.21 1624.06 sharp	1581.63 1573.02 Sharp	1396.45 doubler	1242.16 1114.86 Weak	593.03 Weak sharp	450.93 Weak sharp
Cd-complex	3448.72 3402.43 browed	2935.66 Sharp	1720.50 1639.49 sharp	1465.89 Sharp	1384.89 browed	1284.59 1041.56 Weak	620.09 Weak	447.49 weak
Co-complex	3414.00 3367.71 browed	2870.50 Weak	1631.78 1577.77 sharp	1460.17 1400.03 Sharp	1300.02 weak	1276.88 1145.72 Weak	520.78 Weak	432.05 weak
Ni-complex	3448.72 3379.29 browed	2924.09 Weak	1674.21 1627.92 weak	1585.49 1570.93 Weak	1384.89	1288.45 1022.27 browed	671.23 Weak	459.06 Weak
Zn-complex	3398.52 3228.84 browed	2924.09 Weak	1651.09 1627.92 weak	1589.99 1559.03 Weak	1388.75 browed	1323.17 1022.27 browed	671.23 Weak	466.17 weak

CONCLUSION

The proposed method was a new method for the spectrophotometric determination of Gabapentin drug in pure and pharmaceutical preparations by using the coupling reaction, which is sensitive and simple with reasonable precision and accuracy. The proposed method was successfully used and applied for the assay of trace quantities commercial Gabapentin drug. The metal complexes with Cu(II), Ni(II), Cd(II), Co (II), and Zn (II) metal ions were spectrophotometrically studied. Stability constants and stoichiometry of complexes were studied. The proposed method has many properties like the procedures do not contain any difficult reaction conditions or tedious sample steps for preparation and can also be considered as a general method for the quantification determination of Gabapentin drug.

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