



PREPARATION AND IDENTIFICATION OF NEW DERIVATIVE OF ACETAMINOPHEN AND STUDY ITS APPLICATION IN THE DETERMINATION OF CU (II) USING SPECTROPHOTOMETRIC METHOD

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Abstract

This paper includes the preparation and diagnosis of the new organic reagent for acetaminophen by available spectral methods such as infrared spectroscopy, ultraviolet-visual radiation, C.H.N elements and H1NMR techniques. New derivative used in a simple and sensitive spectrophotometric methods for the determination of copper(II) ion is based on the complex formation by new reagent in acid medium which shows maximum absorbance at 504nm. Under the optimum experimental conditions such as the pH of the medium, reagent concentration, reagent volume, addition order, time effect and temperature. At the best conditions, the copper (II) quantitatively be determined in the range of (0.05-10) mg/l, The limit of detection (LOD) and limit of quantification (LOQ) were found to be 0.0353 μ g/ml and 0.1176 μ g/ml, respectively and Sandal sensitivity is 0.025 μ g.cm⁻². The percentage recovery of the drug and preparation samples for the proposed method ranged from 100-102.3%.

Keywords: Copper Ion (II), Determination, UV-VIS Spectroscopy, Acetaminophen.

Introduction

Many chemical reagents are of great interest by researchers (Flagg, 1948), this compounds always characterized by the containing group (N=N) and are used in a wide range including cosmetics and food additives (Hassan, Taha and Other, 2018), the pharmaceutical industry emerged at the beginning of the 20th century where there was a revolution in it, i.e. an era of chemotherapy and its manufacture was more than plant extracts (Rang, Dale and Other, 2012). Acetaminophen is an important pain-relieving and antipyretic drug (Ali and Muslim, 2019 A), it is using as an effective alternative to aspirin treatment and is given after surgery to relieve pain (Shi, Xue and Other, 2017) but at over-the-top overdoses leads to cirrhosis of the liver and kidney failure if it exceeds its concentration in serum (150 μ g mL⁻¹) after four Hours (Khair and Al-Shwaiyat, 2013), has been estimated in several ways, including spectral (Abdul- Raheem, Alsamarrai and Other, 2016), bead injection flow spectrophotometric (Ali and Muslim, 2019B) HPLC (Al-Abachi, Al-Safi and Other, 2015). Copper is present in nature in the form of a free state in several forms of chlorides, sulfides and carbonates (Ali and Ziyed, 2015). Human blood serum contains 0.7-1.4 mg/l Cu (Ali, Ali and Other, 2014) as well as cancer (Bonham, Connor and other, 2002). Appreciated in many techniques, including the technique of the flow injecting (Raheem, 2017), Flame Atomic Absorption Spectroscopy (Bagherian, Chamjangali and other, 2019), ETAAS and Potentiometric (Prkic, Mitar and other, 2018), Novel Micro Extraction Cloud Point and UV-Vis Spectrophotometry (Ghasemi and Kaykhahi, 2017), the Turbidity Method (Saeed, Khudhair and Other, 2019).

Materials and Methods

All chemicals used were of analytical reagent grade. Chloride Copper (II) dihydrate (purity of 98%) was obtained from B.D.H Germany company. Acetaminophen (purity of 100%) was obtained from Samarra; m-acetyl aniline. hydrochloric

acid (36.5–38%) was obtained from BGG. Pharmaceuticals were purchased from the market.

Preparation of Azoreagent N-(3-((3-acetylphenyl) diazenyl)-4- hydroxyphenyl)acetamide (ADHA)

An amount of (0.01 mol, 1.3517g) of amine (3-acetyl aniline) was dissolved in a mixture of 5ml concentrated hydrochloric acid and 5ml of distilled water cools the mixture to a (0-5)^oC and then add a solution (0.01mol, 0.7g) of sodium nitrite dissolved in 20ml distilled water only drop with continuous stirring with no note of over 5 ^oC, then let the solution settle for half an hour to complete the coupling process, then add the diazonium chloride solution prepared with a drop with constant stirring to a solution (0.01mol, 1.5117g) of acetaminophen dissolved in 50ml of ethanol with 50ml of 10% solution of NaOH observed in color reddish orange, leave for the next day, the dark orange crystals were deposited in addition to the distilled water with the solution equation with ammonium hydroxide solution, filtered sediment and washed many times with distilled water and recrystallized it with a solution 1:1 water: ethanol. Figure 1 shows the mechanical preparation of the reagent.

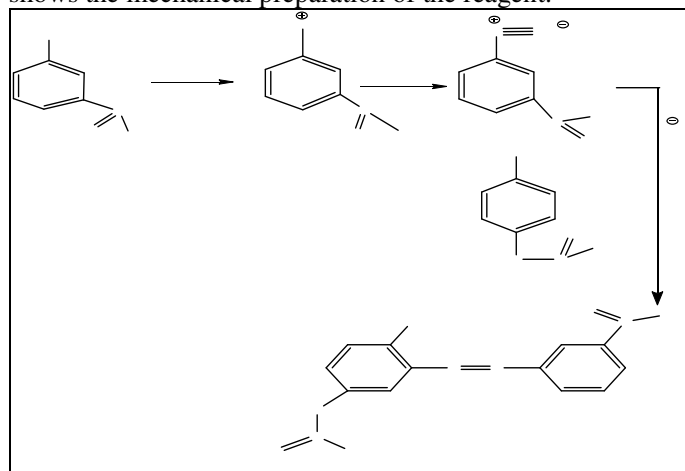


Fig. 1 : Mechanical preparation of the reagent

Preparation of standard stock solution :

A- Copper(II) solution 100 mg l^{-1} : A stock solution was prepared by dissolving 0.0268 g of copper chloride in 100 ml of distilled water and additional dilution was performed to obtain working solutions.

B- New organic reagent ADHA solution $1 \times 10^{-2} \text{ M}$: A stock solution was prepared by dissolving 0.2971 g of the organic reagent in 100 ml of ethanol.

C- Potassium chloride solution 100 mg l^{-1} : A stock solution was prepared by dissolving 0.01 g of KCl in 100 ml water.

D- Sodium acetate solution 0.1 M : A stock solution was prepared by dissolved by 0.4102 g of it with distilled water 25 ml and after the completion of the dissolving

process transfer the solution to a volumetric flask 50 ml and diluted with distilled water to the mark.

Results and Discussion**1- Identification of the new N-(3-((3-acetylphenyl) diazenyl)-4-hydroxyphenyl) acetamide reagent (ADHA) :**

1-1- When comparing the analytical data obtained in practice with the theoretically calculated data listed in the Table 1, the great convergence between them is clearly evident, confirming the validity of the composition of the solid organic reagent.

Table 1: Results of careful analysis of elements (C.H.N) of the solid reagent

Compound	C %		H %		N %	
	Practical	theoretical	Practical	Theoretical	Practical	Theoretical
New reagent ADHA	64.64	64.30	5.09	4.98	14.13	13.80

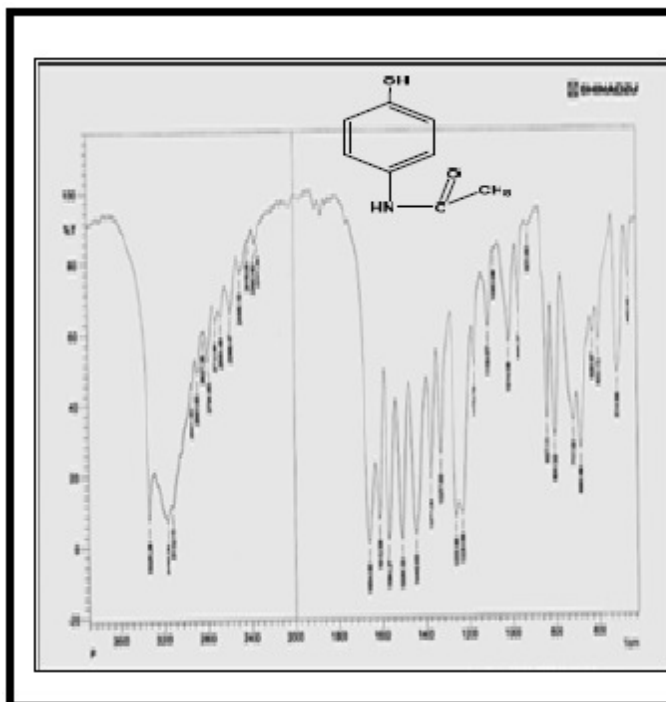
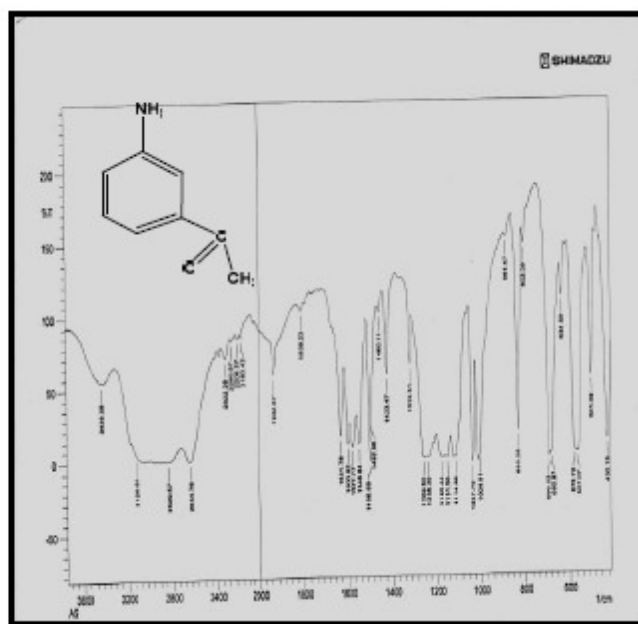
1.2 Infrared spectrum

In order to clarify the mode of bonding and the effect of the metal ion on the reagent, the IR spectra of the reagent and the starting materials are studied and assigned based on careful comparison of their spectra with that of the reagent in

Table 2, where the infrared spectrum was recorded in the most important totals ($400\text{--}4000$) cm^{-1} as shown in Figures 2,3,4, acetaminophen, m-acetyl aniline, the reagent respectively.

Table 2: Characteristic FTIR absorption bands of the form the reagent and reagent

Compound	ν (N=N-)	ν (O-H)	ν (C=O)	ν (HN-CO)	ν (C-N)	ν (H-N)
Acetaminophen	—	3325.28	—	1654.92	1014	3163.26
m-acetyl aniline	—	—	1631.78	—	1004	3126.61, 3439.08
New reagent ADHA	1504.41-1560.41	3417.86	1664.57	—	10037	3327.21

**Fig. 2:** FTIR spectrum of acetaminophen.**Fig. 3 :** FTIR spectrum of 3-acetyl aniline.

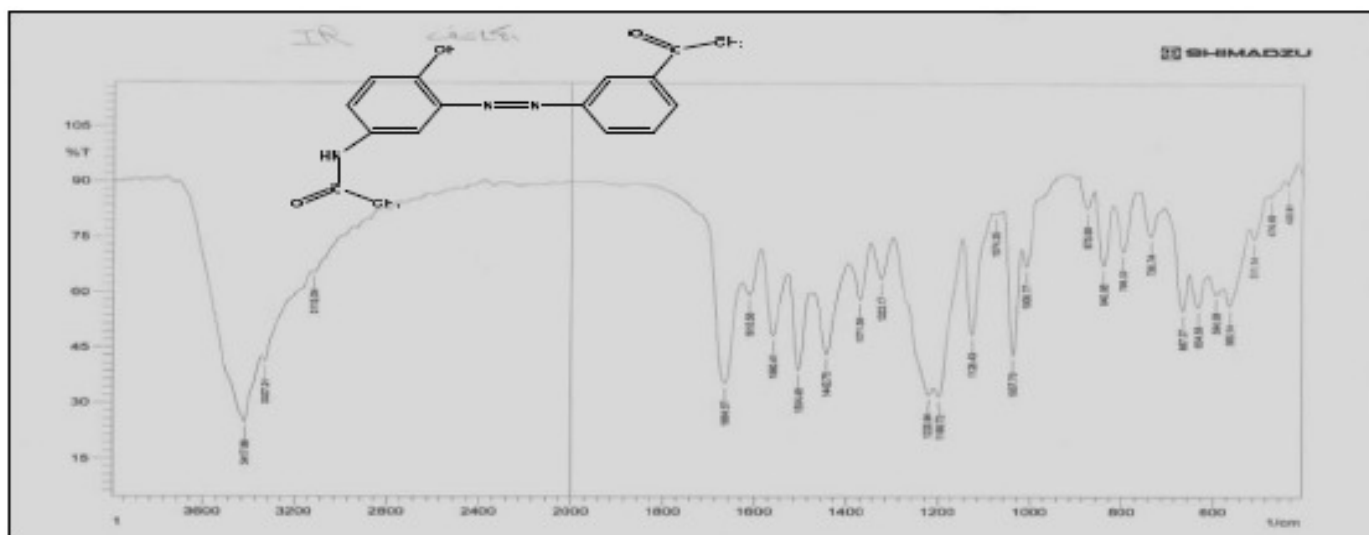


Fig. 4 : FTIR spectrum of N-(3-((3-acetylphenyl)diazenyl)-4-hydroxyphenyl)acetamide reagent (ADHA)

1.3 ¹HNMR of the organic reagent:

The ¹HNMR Spectra of the reagent was recorded in DMSO-d₆. The ¹HNMR spectrum of the reagent shows the following signals: phenyl multiples at (6.69-8) δ range, -NH at 10 δ, N -CO-CH₃ at 2.1 δ, Ar-O=C-CH₃ at 1.7 δ and OH at 9.75 δ, as shown in Figure 5.

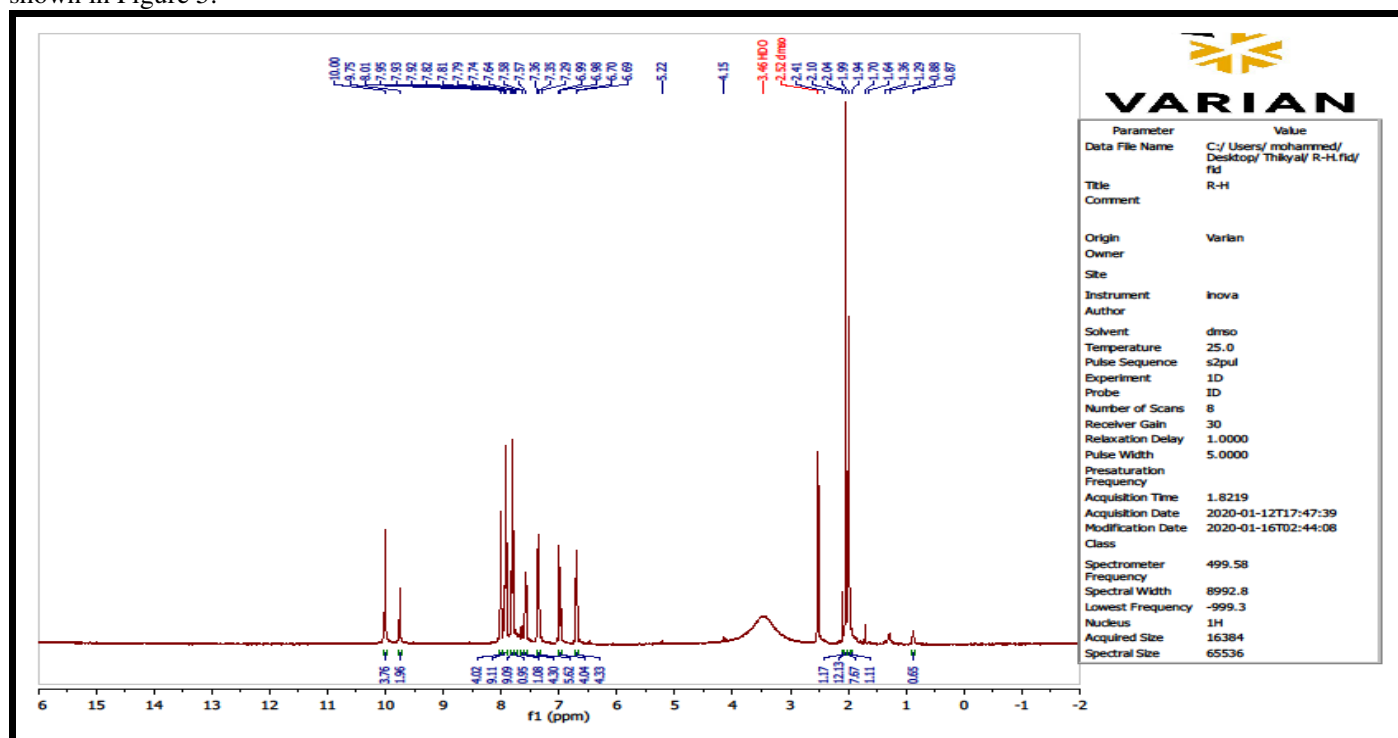


Fig. 5 : The ¹HNMR spectrum of new reagent.

1.4 The Best solvent Reagent

The effected the solvent study using four solvents (water, ethanol, methanol and chloroform) were used, showing that the optimal solvent for the reagent was ethanol 96% as shown at Figure 6.

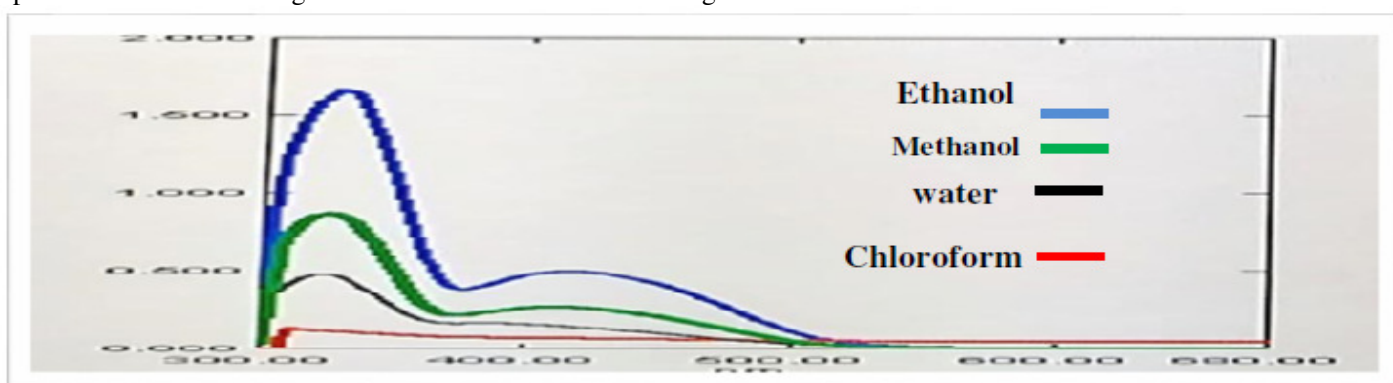


Fig. 6 : Absorption spectrum of the new reagent into different solvents.

1.5. Identification of the isosbestic point of ADHA

Prepared the concentration of 1×10^{-4} M of organic reagent in different pH of medium (3-11) and the electronic spectroscopic study to determine the point of isosbestic point as shown in Figure 7, from the result shown that compound

has two dissociation constant as it has stable chemical formula at rang 3-9 pH then it begins with a clear color change, this indicates a change in its structure in high medium of 9 pH.

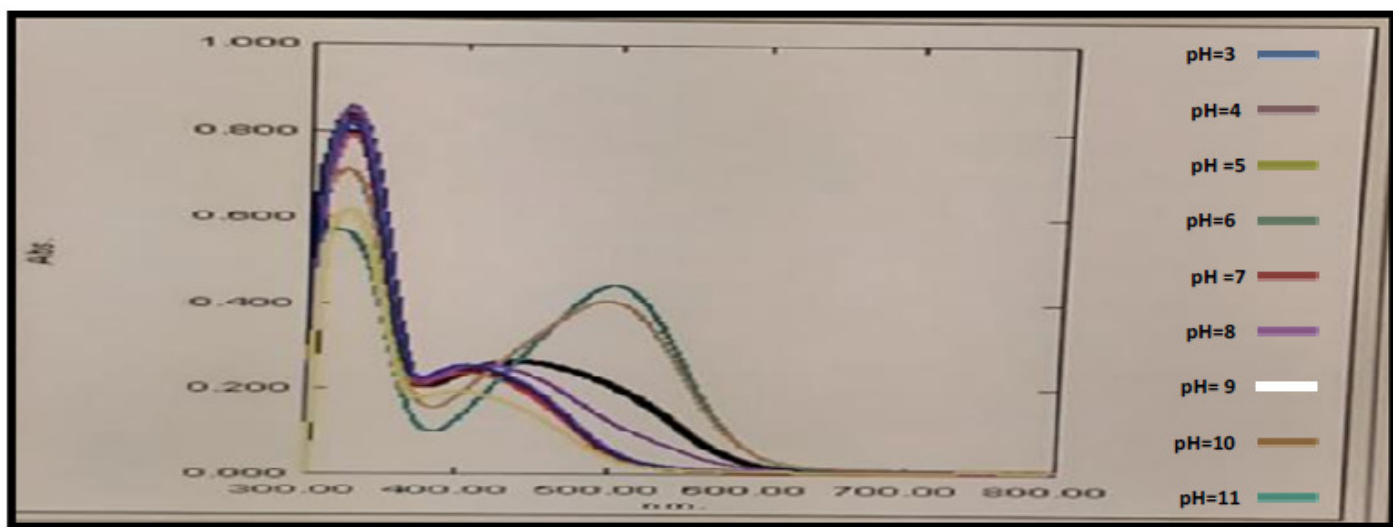


Fig. 7 : The isosbestic point of the new reagent ADHA

2. Wavelength Determination at maximum absorption

The wavelength of the maximum absorbance was identified by scanning for ADHA and its complex over the range 300-800 nm with a Shimadzu UV-1700 spectrophotometer. A wavelength of 504 nm for the complex and 400 nm for reagent as in the following Figure(8).

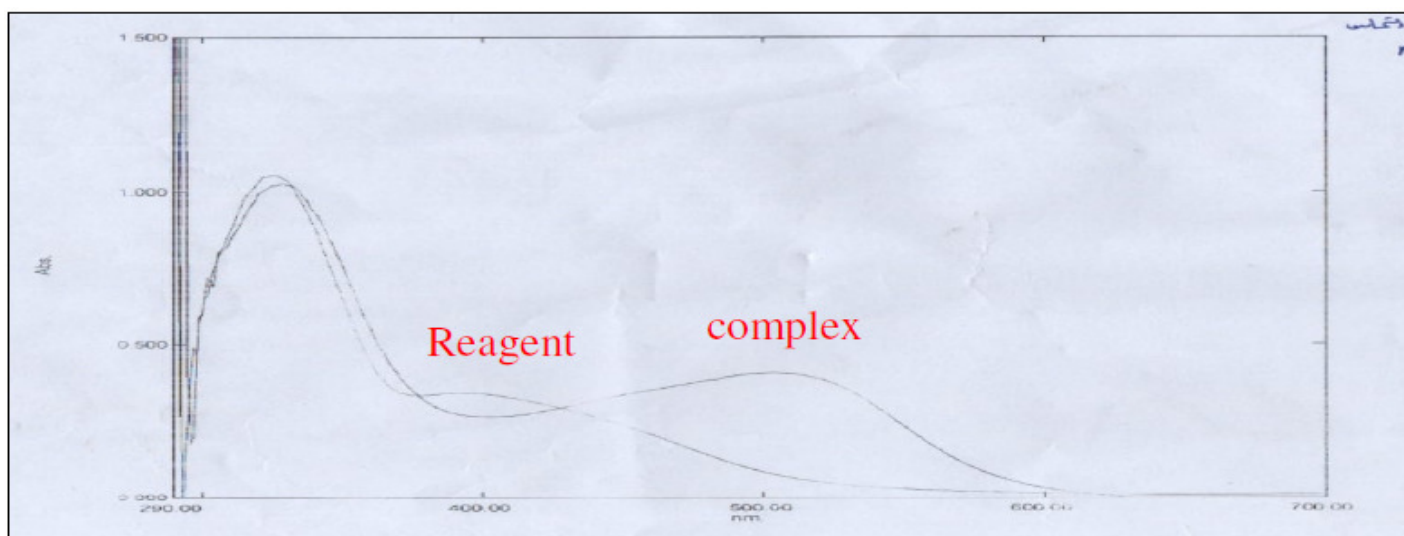


Fig. 8 : The absorption spectrum of both the new reagent and the copper(II) complex

2.1 Optimal conditions for complex formation Cu (II)

Influence of Acid function on the Cu(II) complex formation : The pH of medium was varied in the range 4-11 using NaOH and HCl to determine the optimum pH of complexity. It is evident that pH 5 favors the complex formation; this value was selected as the working value. The results are shown in Figure(9).

Influence of reagent concentration on the Cu(II) complex formation : Under the optimum pH value the effect of reagent concentration on the absorbance profile is illustrated in Figure 10. The reagent concentration range 0.0001-0.005 M, the values of best absorption at addition of 0.001M of ADHA solution due to the better reaction between Cu (II)

and the ADHA and giving the spectrum of color intensity high.

Influence of time on the Cu(II) complex formation : Under the optimized conditions, although the color developed almost instantaneous, 3 min was allowed to obtain the maximum and constant absorbance. The color derivative was stable up to 90 min then absorbance varied by $\pm 2\%$ in a day.

Influence of volume reagent on the Cu(II) complex formation : The influence of the various reagent volume 2.5-0.25 ml on the absorbance using 2 ml from Cu(II) solution. The reagent volume that exhibited the greatest absorbance was found to be 2 ml and was chosen as the optimum as in Figure (12).

Influence of Temperature on the complex formation : The effect of temperature change on the complex formation has been studied, Figure (13) shows that the value of complex absorption value and gives the best color intensity at temperatures (15-30) and then decreases the absorption value because decrease in complex stability.

Study stoichiometric to Cu(II) complex composition of the complex determined by molar ratio method and the stoichiometric was found to be 1:2 (Metal: reagent).the results are shown in the Figure(14).

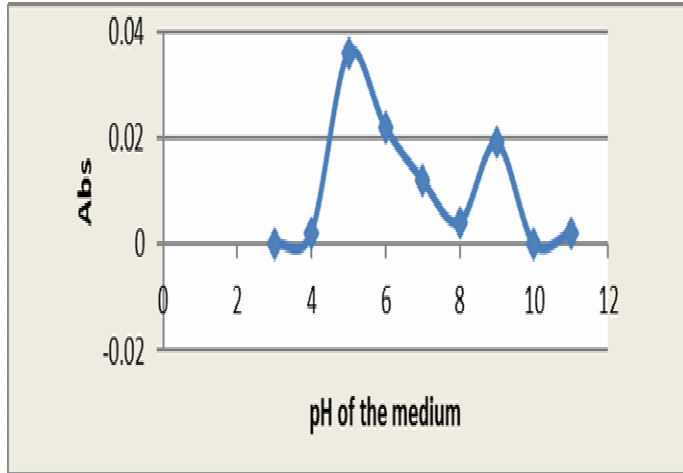


Fig. 9 : Influence of acid function on the complex formation

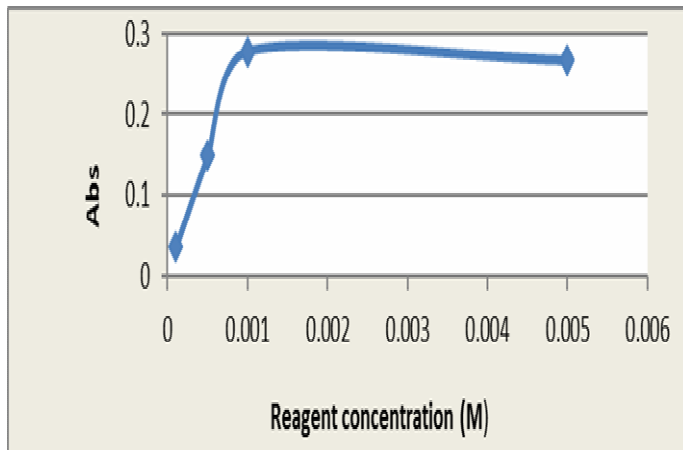


Fig. 10 : Influence of reagent concentration on the complex formation Cu(II)

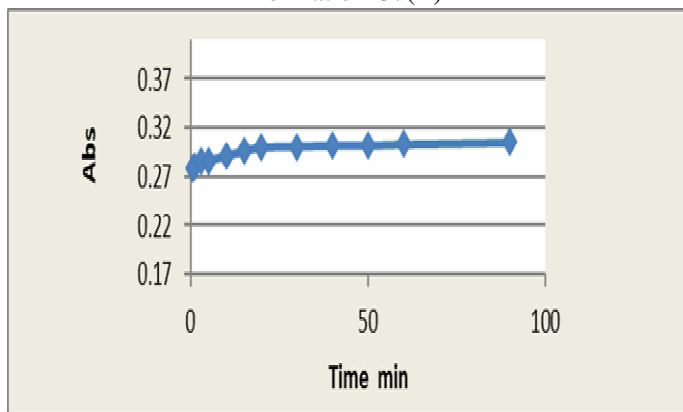


Fig. 11 : Influence of time on the Cu(II) complex formation

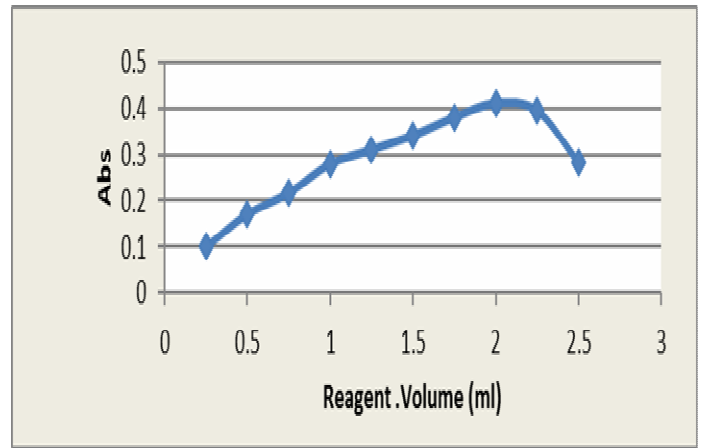


Fig. 12 : Influence of Volume reagent on the complex formation

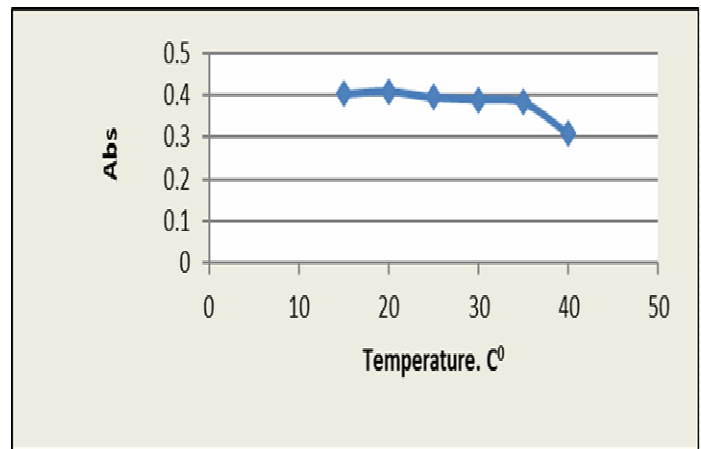


Fig. 13 : Influence of temperature on the complex formation

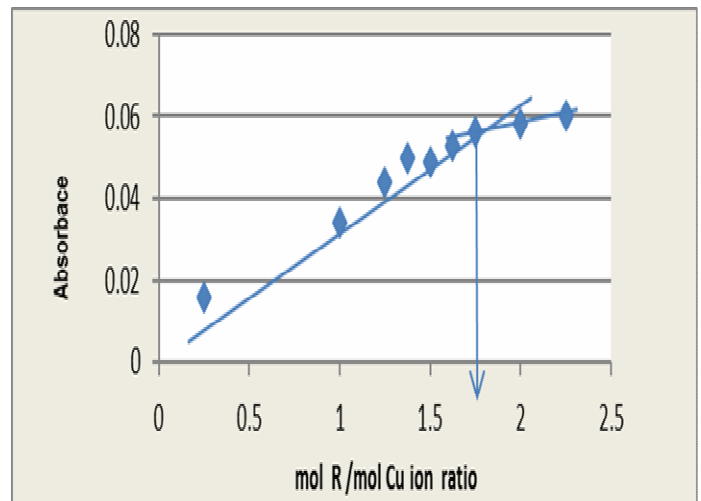


Fig. 14 : Mole ratio method to Study stoichiometric for Cu(II) complex

2.2 Calibration curve for Cu(II) complex

A series of Cu(II) ion solutions of the range (0.05-15) mg/l were prepared from stock solutions and under the optimum conditions, the result show in Figure (15). The calibration curve was linear in the range of (0.05-10)mg/l. The detection limit was 0.0353 mg/l .

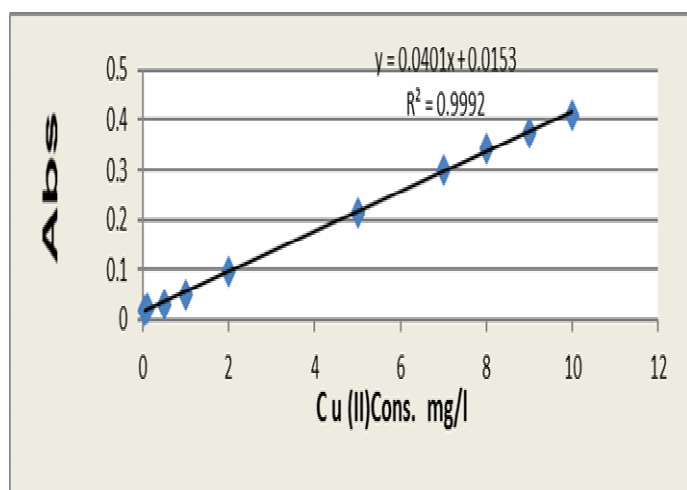


Fig. 15 : Calibration curve for Cu(II) complex

2.3 Study the influence of Interference

A study of interference effects was carried out for cations and anions, in amounts ranging up to 10 and 50 mg/l

Table 4: Applicable different models of appreciation of Cu (II) ion

Samples	Take value (mg/L)	found value (mg/L)	Er %	Rec%
tap water	0.5	0.5	0.0	100
Pregnacar, London, England	6	6.14	2.3	102.3
Ferromera, Belgium	5	5	0.0	100
laboratory-prepared solutions				
1	7	7	0.0	100
2	3	3.10	0.03	100.03
3	2	2.0	0.0	100

The optical characteristics of the spectrophotometric determination of Cu(II) ion by new reagent as shown in Table 5

Table 5: Optical characteristics Spectrophotometric.

Optical characteristics	Spectrophotometric method
The linearity	0.05-10 mg/l
maximum absorbance	504nm
sensitivity	0.025 $\mu\text{g}\cdot\text{cm}^{-2}$
LOD	0.0353 mg/l
LOQ	0.1176 mg/l
RSD% determination for 5mgL^{-1} , n=10	0.4651
Correlation coefficient	0.9992
Ratio(Ion: Reagent)	1:2
Recovery(%)	100-102.3

Conclusions

The preparation method for the new derivative of acetaminophen, N-(3-((3-acetylphenyl)diazonyl) - 4 - hydroxyphenyl) acetamide (ADHA) was simple. New derivative used in a simple and sensitive spectrophotometric methods for the determination of copper(II) ion. The method has good sensitivity, compared with other spectrophotometric determination methods. Finally, the developed method can be considerably declared for the determination of Cu(II) in pharmaceutical and aqueous solution.

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with 10 mg/ l of Cu(II), through the study that all positive ions (Cd^{+2} , Ni^{+2} , Zn^{+2} , Pb^{+2}) overlap except Fe^{+3} and were used KCL(A.F. Hussein and N.M. Mahdi, 2014) as masking agent for (Cd^{+2} , Ni^{+2} , Zn^{+2} , Pb^{+2} at 10mg/ l) ions and Rochelle salt to masking Pb^{+2} at 50mg/l. For the interference of negative ions ($\text{C}_4\text{H}_4\text{O}_6^{-2}$, CO_3^{-2} , Cl^- , F^- , SO_4^{-} , CH_3COO^-), they all do not interference except carbonate, titrate and sulfate with high concentration.

2.5.4 Application

The proposed method has been applied to the determination of Cu (II) in pharmaceutical Samples preparation according to the Reference method (D.C. Garratt, 2012), laboratory-prepared solutions and tap water, To check the accuracy of the proposed method in copper analysis in different samples, a recovery study was carried out in the samples mentioned in Table 4.

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