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spectrophotometric Determination of zinc in pharmaceutical preparations by using a new synthesized reagent [4,5-diphenyl-2-((1E)-(4-(1-(2-phenylhydrazono)ethyl)phenyl)diazenyl)-4H-imidazole]

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Abstract

A simple , rapid, sensitive and new spectrophotometric method to estimate zinc in pharmaceutical preparations is described. The method depends on the reaction between zinc and the new synthesized reagent [4,5-diphenyl-2-((1E)-(4-(1-(2-phenylhydrazono)ethyl)phenyl)diazenyl)-4H-imidazole] (**DPHEDPI**) to form a reddish-pink complex at pH 7.5 with a mole ratio (M:L)of (1:2), the complex exhibits a maximum absorbance at 520 nm with molar absorptivity coefficient (Ɛ) of $4.4*10^2$ $L.mol^{-1}$ cm^{-1}. Beer's law is obeyed in the range of (0.5–27) ppm for zinc with correlation coefficient of (0.9996) ,and the stability constant was found to be $1*10^{12}$ $L.mol^{-1}$. The relative standard deviation for seven replicate measurements, relative error and recovery values of this method were found to be 0.0015 % , -0.778%, and 99.22% respectively. Finally, this proposed method was applied for the determination of zinc in the zinc sulphate capsules drug and the results were compared with atomic absorption method.

Introduction:-

Schiff bases are compounds which dervied from condensation reaction of aromatic aldehydes with aromatic or aliphatic primary amine in methanoic or ethanoic media [1, 2]. The complexes of schiff base involve significant part in the

development of inorganic chemistry and used as biochemical, analytical, and antimicrobial reagents. Also they have been used as antibacterial, antifungal, anticancer, antitubercular, hypertensive, and hypothermic reagents[3-6]. Furthermore, they are significant intermediates in the synthesis of bioactive compounds such as β-lactams[7]. The heterocyclic azo compounds are considered very active toward metal ions because they have active donor group and contain atoms such as oxygen, nitrogen and sulfur, to form chelatic coordination complexes and make it important in the biological field [8-11]. The azo dye are used in the electronic industry, like nonlinear optical (NLO) devices , colorimetric sensors, and liquid crystalline displays (LCDs)[12]. The nitrogen atom in the imidazol ring has biological activities such as antibacterial[13], anti-inflammatory, antimycotic[14], antitumor[15], and powerful antifungal agents[16]. Azo compounds show a highly pharmacological activity, whereas the drug become very active when administered as metal complexes [17, 18]. Azo compound include some biological reactions like inhibition of RNA, DNA,and protein synthesis, carcinogenesis and nitrogen fixation[19]. Metal complexs of hetrocyclic azo compounds are useful in the redox responsive, and pH-sensitive through azo group[20]. In this paper, a simple and sensitive spectrophotometric method for the determination of trace amounts of zinc (II) is explained based on the formation of the complex between zinc metal and the azo-linked schiff base reagent (DPHEPDI). The reagent and it's complex were characterized by Elemental analysis and infrared , UV–Vis , atomic absorption spectra .The effect of some analytical parameters like pH and reagent amounts, etc. on the complex formation were studied.

Experimental Apparatus

(FTIR) Spectra (4000-400 cm^{-1}) in KBr disk were recorded on a SHIMADZU IR Affinity-1. Elemental analyses were carried out on a EURO EA3000 single elemental analyzer(Europe). UV- Vis Absorption spectra were measured on a UV-1610 pc double beam spectrophotometer SHIMADZU (japan) using 1cm quartz cells. Atomic absorption measurements was made using SHIMADZU AA-6300 S Atomic absorption spectrophotometer, A WTW model multi 740 pH – meter was used for the pH measurements.

Reagents

All chemicals used are obtained from commercial sources were of super pure grade.

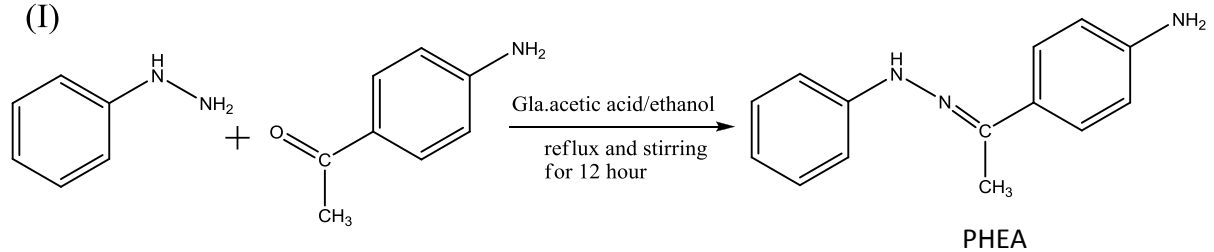
(I) Synthesis of (E)-4-(1-(2-phenylhydrazono)ethyl)aniline (PHEA) [21]

Schiff base has been synthesized by condensing the ethanoic solution of p-amino acetophenone (1.35 g, 0.01 mole) with the ethanoic solution of Phenylhydrazine (0.98 ml, 0.01 mole) with a five drops of glacial acetic acid as a catalyst. The mixture was refluxed with stirring for 12 hours , The brown product was seperated , dried at room temperature then recrystallized with ethanol.

(II)Synthesis of the reagent [4,5-diphenyl-2-((1E)-(4-(1-(2-phenylhydrazono)ethyl)phenyl)diazenyl)-4Himidazole][22](DPHEDPA)

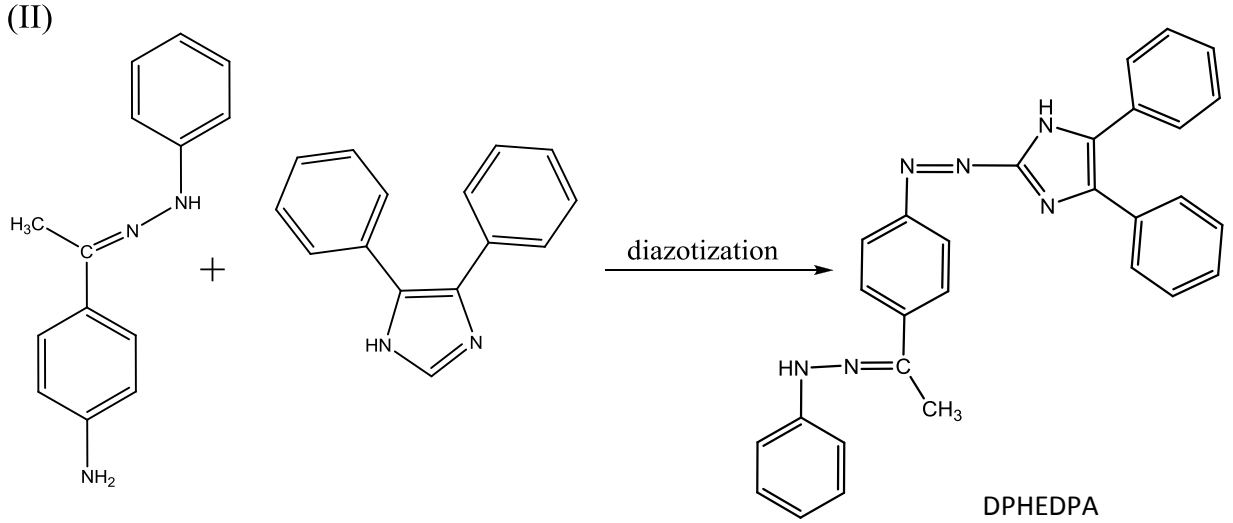
2.25 gm (0.01 mole) of PHEA was dissolved in the mixture of 30 mL ethanol and 3 mL concentrated HCl (37%), the mixture was cooled to 0 ^{o}C, then the solution of sodium nitrite prepared from dissolving 0.8 gm in 15mL distilled water was added to the mixture, then the solution was let for 15 minutes to complete diazotization process. After that the diazonium salt solution was added slowly (drop by drop) with stirring to the basic solution of 4,5-diphenyl imidazol prepared from dissolving (2.20 g , 0.01 mole) 4,5-diphenyl imidazol in 50 mL ethanol and 1g sodium hydroxide (NaOH) in 10 mL distilled water, a red color was formed, then 100 mL of cold distilled water was added and the solution was neutralized (pH=7) and left to stirring for 30 min, after that the precepitate was left for 24 hours and then washed several times with distilled water and dried , the percentage yield gained was (83%).

(I)



PHEA

(II)



DPHEDPA

Standard solution of zinc

A solution of 500 ppm zinc (II) was prepared by dissolving 0.026 g of $ZnCl_2$ in (25mL) of distilled water, the working solutions were prepared by appropriate dilution of the stock solution.

Standard solution of reagent DPHEDPA ($5*10^{-5}$ M)

0.0114 g of the reagent was dissolved with ethanol in volumetric flask(25mL), then 1.25mL of this solution was transfered to a 25 mL volumetric flask and diluted to the mark with absolute ethanol.

General procedure

Into a 10mL volumetric flask , transfer 1mL of sample solution containing 15 ppm of zinc(II) and 2mLof 5×10^{-5} M of reagent solution ,dilute to the mark with distilled water, adjust pH to 7.5, mix well and after 5 minutes measure the absorbance of solution at 520nm at room temperature against a reagent blank prepared in the same conditions .

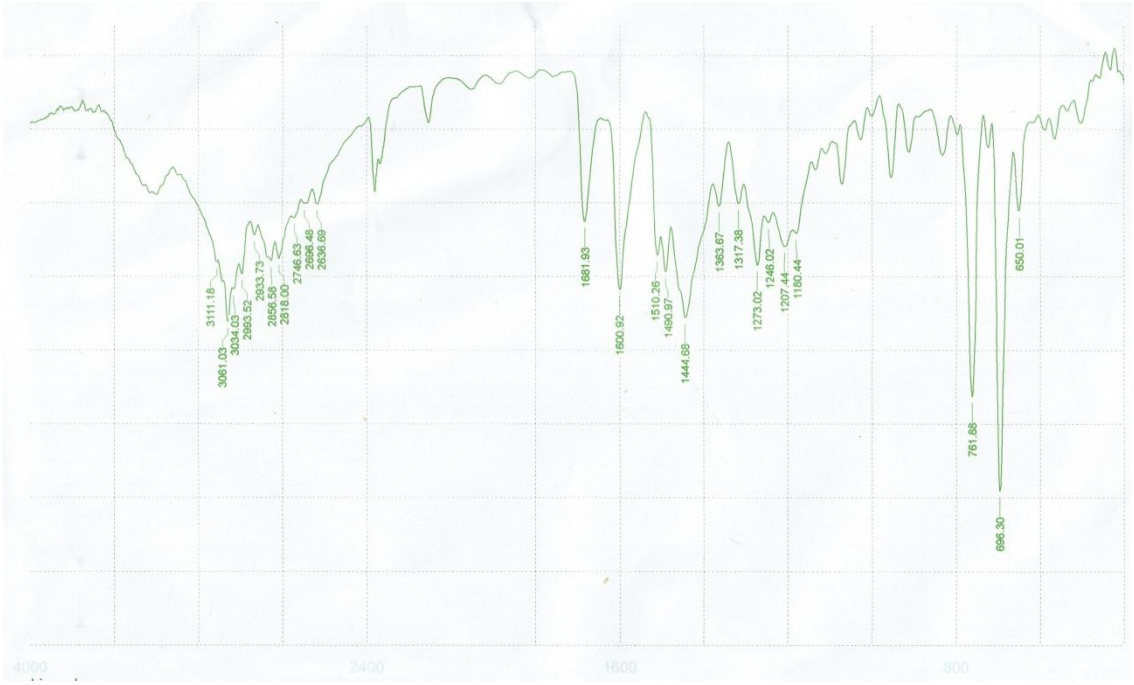
Applications

The method was applied for the determination of zinc (II) in zinc sulphate pentahydrate capsules drug produced by (Nutravalue LLC) USA .The powder content of ten capsules were mixed, then 0.1313 g of the powder was dissolved with distilled water acidified by 2 M HCl in a beaker , quantitatively transferred to a 100 mL volumetric flask and completed to the mark with the same solution, then 1 mL of this solution was transferred to a 5mL volumetric flask, 2mL of reagent were added, the solution was diluted to the mark with distilled water and the pH of solution was adjusted to 7.5, after 5 minutes the absorbance of solution was measured at 520nm at room temperature against a reagent blank which is prepared in the same conditions .

Results and discussion

FT-IR Spectrum of the Reagent (DPHEPDI)

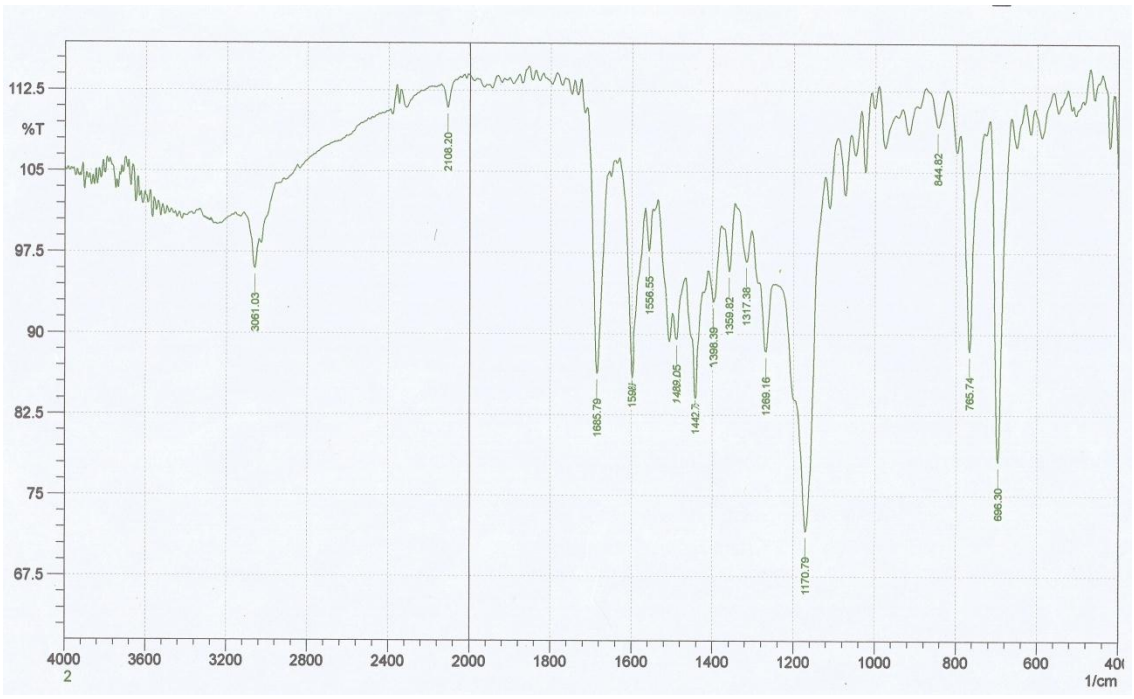
The FT-IR spectrum (4000-400 cm^{-1}) of reagent fig(1) exhibit absorption band at 3482 υ(N-H), 3061 υ(C-H), 1600 $\upsilon(C=N)_{imd}$, 1681 $\upsilon(C=N)_{shf}$, 1490 υ(CH=CH), 1092 υ(C-N), 1444 υ(N=N).



Fig(1) FT-IR Spectrum of the Reagent (DPHEPDI)

FT-IR Spectrum of zinc complex (Zn- DPHEPDI)

The FT-IR spectrum (4000-400 cm^{-1}) of zinc complex fig(2) exhibits absorption bands at 3478 υ(N-H), 3061 υ(C-H), 1598 $υ(C=N)_{imd}$, 1685 $υ(C=N)_{schif}$, 1489 υ(CH=CH), 1114 υ(C-N), 1442 υ(N=N), 434 υ(M-O).



Fig(3) FT-IR Spectrum of the zinc complex

Absorption Spectra

The absorption spectra of the reagent (DPHEPDI) and it's zinc complex under the optimum conditions are shown in fig (4):-

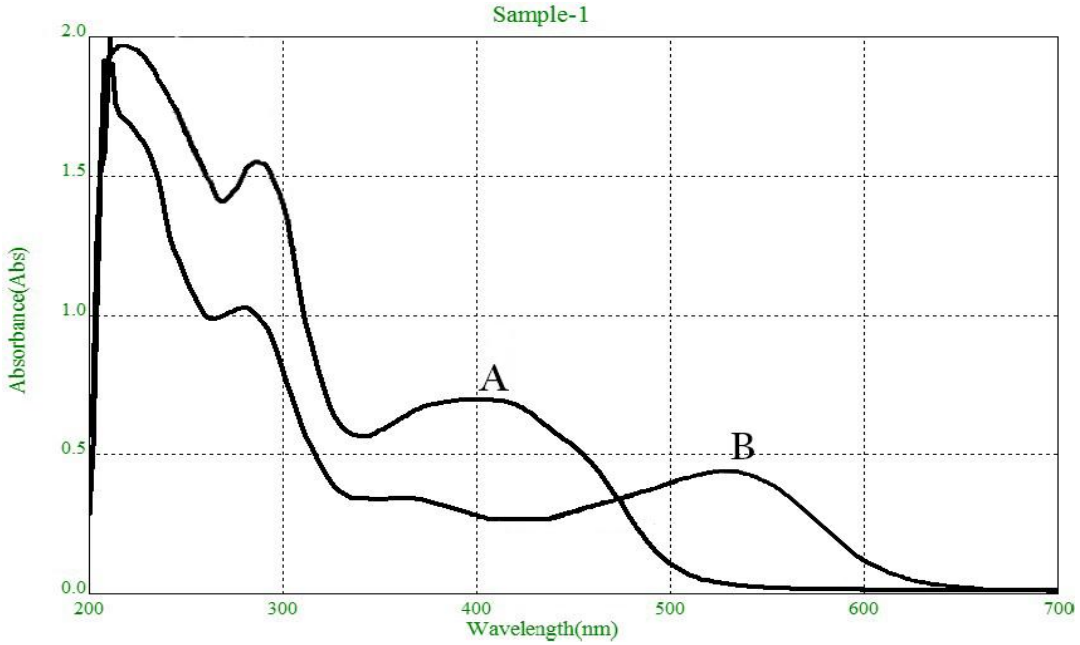


Fig.(4):-Absorption spectra of A: DPHEPDI reagent ($5*10^{-5}$M), B: Zn-DPHEPDI complex at pH=7.5

The electronic spectrum of the reagent shows three bands, the first two bands at (216,286) nm is related to the ($\pi \rightarrow \pi^*$) transition of the aromatic ring , wherease the third band at (412)nm is related to the ($n \rightarrow \pi^*$) transition of the non bonding electron pairs of the nitrogen atom . The zinc complex with this reagent exhibits a maximum absorbance wavelength(λ_{max}) at 520nm which differs from that for the reagent (DPHEPDI), this indicates that a reaction take place between Zn (II) and the reagent and the complex Zn-DPHEPI is formed.

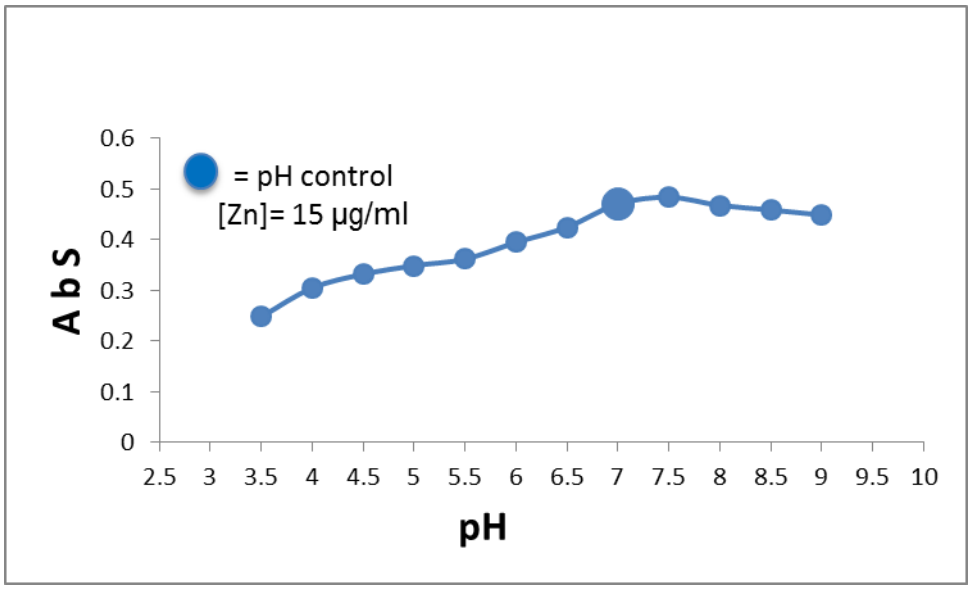
Effect of reagent concentration

The concentration of zinc (II) solution is remained constant for all conditions optimization,The concentration of reagent DPHEPI was studied at the range ($1*10^{-6}$-$1*10^{-3}$)M, on mixing with zinc solution , the reagent concentration range ($5*10^{-4}$-$1*10^{-3}$)M gives the metal complex as a precipitate, while the reagent concentrations ($8*10^{-5}$-$3*10^{-4}$)M show a high absorbance value,wherase for the reagent concentration ($1*10^{-6}$-$9*10^{-9}$)M exhibits a very

low absorbance which are insufficient for measurement ,and the concentration between ($1*10^{-5}$-$5*10^{-5}$) M give the best absorbance, therefore the reagent concentration of $5*10^{-5}$M was chosen as the optimum value.

Effect of pH

The optimum pH range for the complex formation was examined fig (5), At the pH lower than 3.5 there is no complex formation takes place may be due to the protonation of the electrons pair of nitrogen atoms that prevent the zinc cations from coordination with the reagent. On increasing the pH, the zinc ions will compete with the hydrogen ions to occupy the electrons pair and form a coordination complex, showing a good absorbance value for the range (3.5 – 9), while for the pH value more than (9), the precipitate of zinc hydroxide $Zn(OH)_2$ will be formed. The optimum pH value chosen is 7.5 .
The pH was adjusted by addition of 0.2M NH_4OH and 0.2M HCl.



Fig(5):-Effect of pH on the absorbance of zinc complex ,[zn]=15 µg/mL.

Effect of time and temperature on the zinc(II) complex formation

The minimum time required to achieve the complex formation is 5 minutes which absorbance remains stable for 24 hours fig(6). The optimum temperature of complex formation was also examined and the absorbance is shown to be stable in the range (5-50) ^{o}C fig (7) , while decreased for the temperature higher than 50 ^{o}C, which may be due to the dissociation of the complex,Therefore the room temperature (25 ^{o}C) is chosen as the optimum temperature for the complex formation .

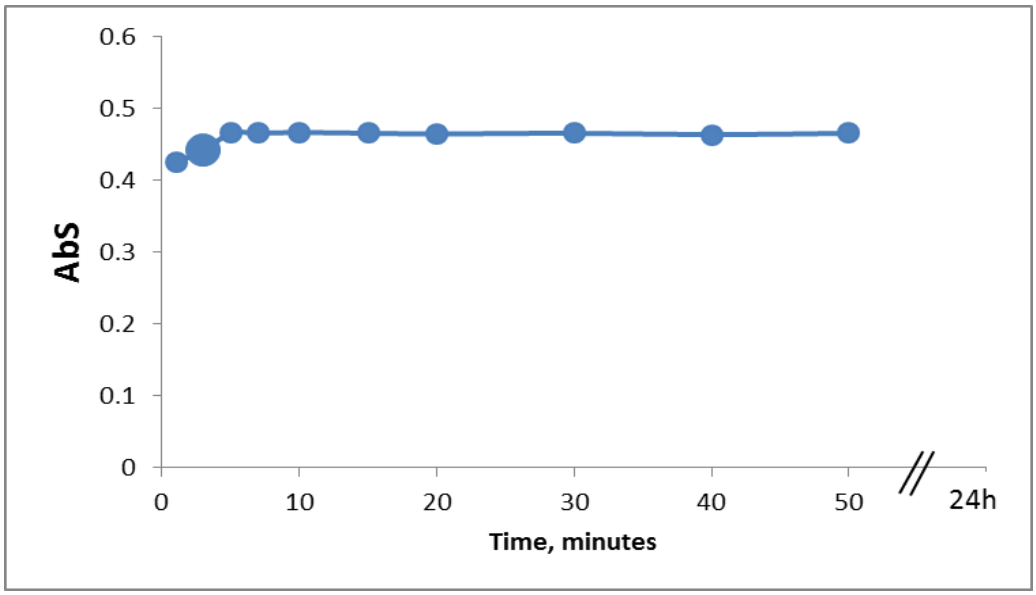


Fig (6) effect of time on the complex of formation

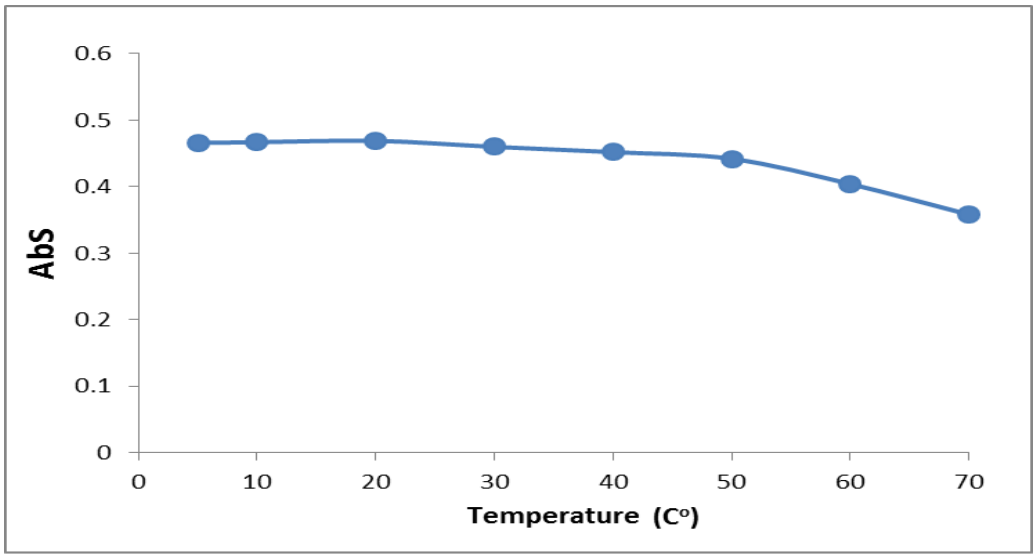


Fig (7) effect of temperature on the complex formation

Composition and stability constant of complex.

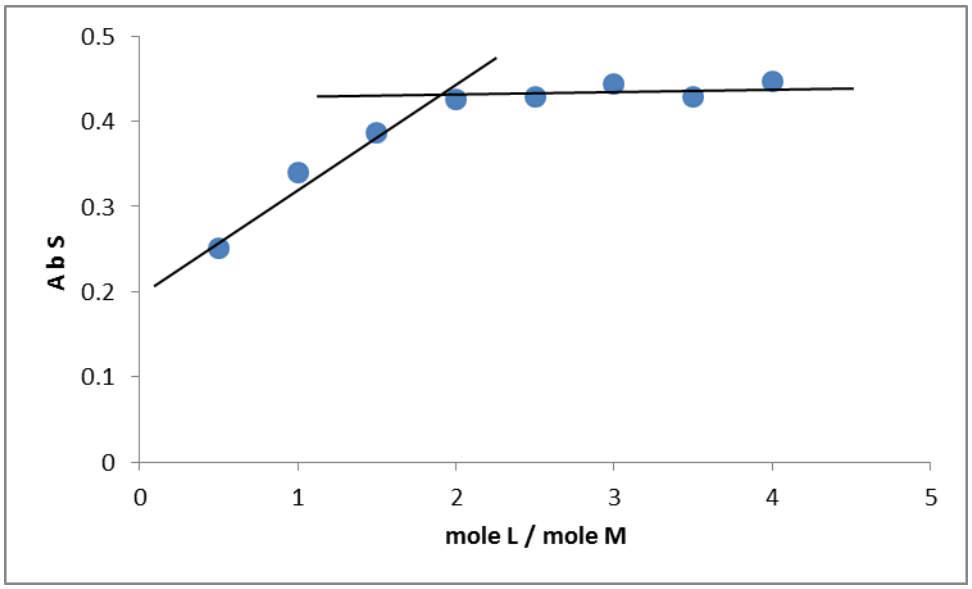
The composition of the complex was determined by mole-ratio and job's methods [fig (8,9)] ,the two methods show that the complex has a molar ratio of (1:2) (M:L) at pH 7.5, the dissociation constant (α) and stability constant (K_{st}) of complex were found to be (0.044) and ($1*10^{12}$ $L.mol^{-1}$) respectively by using the following equations[23]:

M + n L _____ $M L_n$ ----------(1)

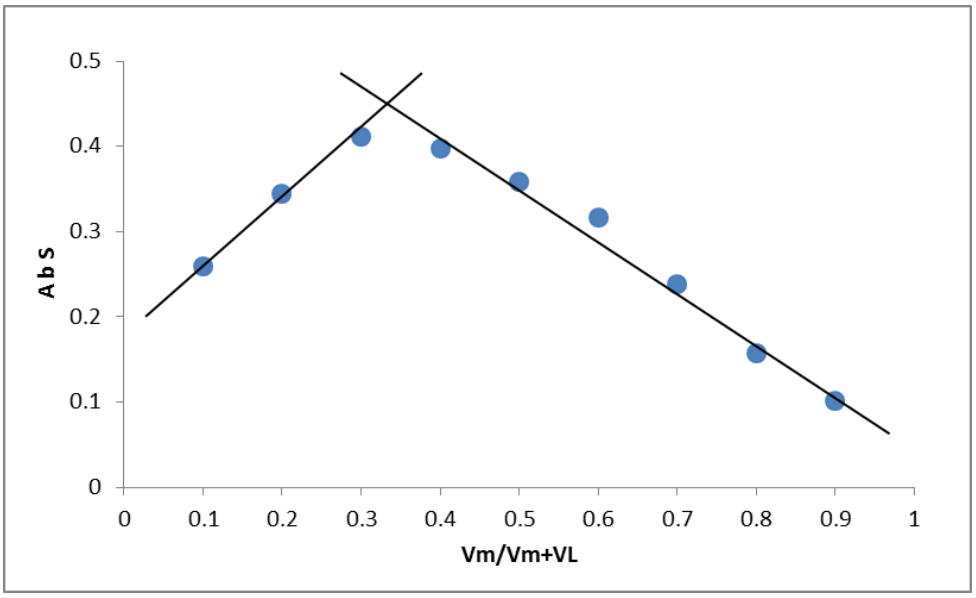
$$k_{st} = \frac{c(1-\alpha)}{(\alpha c).(n\alpha c)^n} \quad \text{----------(2)}$$

$$\alpha = \frac{A_m - A_s}{A_m} \quad \text{---------- (3)}$$

Where (n) represents the mole ratio (number of moles of reagent that associated to metal ion)and equal to two, C represents the concentration of complex which is equivalent to the concentration of the metal ions, A_s represents the absorbance value for the chosen mole ratio of complex, A_m represents the absorbance value when there are excess amount of reagent,



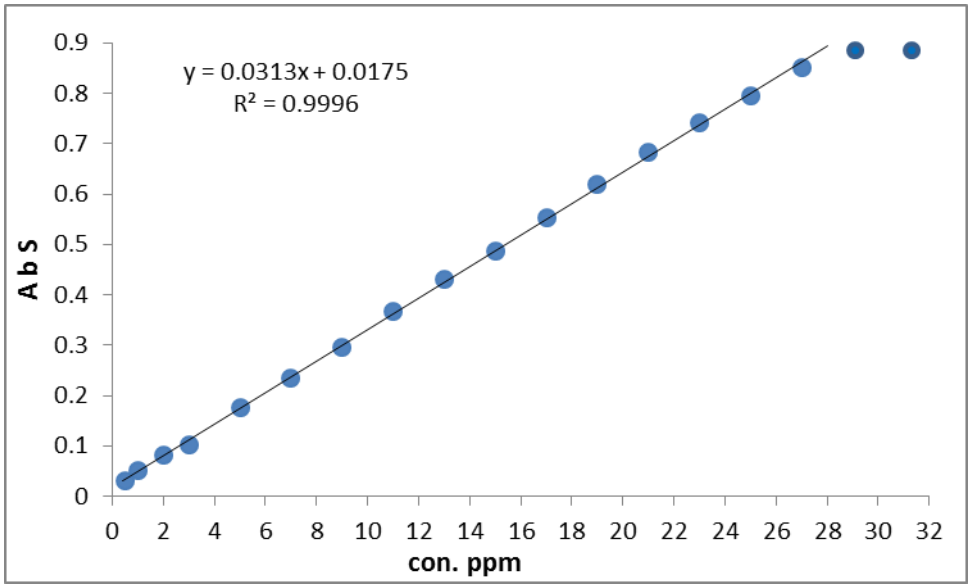
Fig(8):- Mole ratio method for zinc complex at pH=7.5



Fig(9):-Continuous variation method for zinc complex at pH=7.5

Calibration graphs and the some analytical parameters

A calibration curve fig(10) was constructed for zinc where Beers Law was obeyed in the range of 0.5-27 µg/mL of zinc at 520 nm. The analytical parameters were summarized in table (1)



Fig(10):-Calibration curve of zinc

Table (1) : Analytical parameters of the proposed procedure
(N =number of determinations)

analytical parameter	value
Molar absorptivity (Ɛ)	$4.4*10^2$
Correlation coefficient(r^2)	0.9996
Sandell's Sensitivity	0.0148 µg.cm^{-2}
Detection Limit(D.L)	0.12 ppm
Relative .Standard .Deviation (R.S.D)	0.402% (N=7)
Standard deviation	0.0013
Percentage Relative error	-0.181%
Percentage Recovery	99.812%

Analysis of samples

In order to illustrate the utility of the proposed method, it was used for the spectrophotometric determination of zinc in the pharmaceutical samples. The zinc concentration was determined by the proposed method and the results are compared with that obtained by atomic absorption Analysis method. The results are shown in Table (2).

Table (2) : comparison of the proposed method and the atomic absorption results

Drug Sample & Origin	The Original concentration (ppm)	Concentration measured by Atomic Absorption (ppm)	Concentration measured by the proposed method (ppm)	S.D	R.S.D% (N=5)	Rec%
Zinc sulphate (NUTRAVALUE LLC, USA)	5.000	4. 940	4.894	0.001	0.680	97.880

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