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New Analytical Method for Estimation of ferrous in Ferrous Sulfate drug By Preparation and Using 2-(E-(1H_benzo(d) imidozol-2-yl) diazenyl -5-(E-4- dimethyl amino benzaliden amino) phenol as a reagent

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Abstract:

The work covered the synthesis and characterization of a new heterocyclic azo – azo methine ligand and its application of ferrous in some drugs. Azo 2- ((E) – (1H- benzo [d] imidazol-2-yl)diazenyl)-5-(E-4-(dimethyl amino) benzyliden amino) phenol, (BIADMebP) has been synthesized from condensation reaction of 2-[(2-benzimidazolyl) azo] -5-amino phenol with N,N-dimethyl benzaldehyde. The prepared azo and its metal complexes where examined by different spectral technique in terms, C.H.N elemental analyses, metal content, FT-IR, UV-Vis, ^{1}H-NMR and mass spectra studies. Also, the stability constants for these complexes have been calculated spectrally by Ultraviolet-Visible-spectra. All results show that these complexes have high stability. The analytical applications have been done on the drug (ferrous sulfat) for three companies (Actavis 200 mg, Aktiv 158mg, Brawn 150 mg. The results were refer to the accuracy that used by companies by UV-VIS spectroscopy.

Key words: - synthesis of Azo imidazole, metal Complexes identification, synthesis and characterization, estimation of ferrous in drug.

INTRODUCTION:

Iron is the element that play an importance role in formation of hemoglobin and in oxidative operation of living tissues [1]. Divalent iron (Ferrous ion) is essential in the both type of heme and non-heme enzymes. Ferrous ion also is essential part involved O_2 transport in human body [2]. In general iron is a very frequent mineral resource utilized in Pharmaceutical preparations. It is necessary for cells metabolism [3]. Several usage of compounds for assessment of iron in different application were utilized[4-7].Previous studies in this field were focused upon of several techniques for assessment of iron either in an environmental or in pharmaceutical compounds such as graphite furnace atomic absorption, Inductive coupled plasma, atomic absorption spectrometry inductive coupled plasma with optical emission spectrometry were used for more efficient determination of heavy metals [8]. Azo dye compounds are highly important and widely used in several applications involving foodstuffs; rubber; dyes and pigments and medicine since their discovered before in twentieth century [9]. These compounds are used in previous studies as analytical reagent for several elements assessment. Recently substituted imidazole compounds are used a components of providing ionic liquids that used in determination of some traces of metal ions in particular transition elements [10-13].Heterocyclic azo imidazole compounds have an important property in spectral assessment field for determination of trace concentrations of elements in particular transition metals ions owing to high selectivity and selectivity [14,15].The present work aims to synthesis and spectral characterizations of 2-(E-(1H_benzo(d) imidozol-2-yl) diazenyl -5-(E-4- dimethyl amino benzaliden amino) phenol (BIADMebP), and uses as reagent for detection and estimation of ferrous in ferrous sulfate drug.

EXPERIMENTAL:

Chemicals and Methods:

All organic chemicals, solvents and inorganic salts were used in this work are purchased form SIGMA-ALDERICH, B.D.H., Merck and used without further purification. UV-Visb. Spectrophotometer type T80-PG- Spectrophotometerwas used in this study, Infrared Spectrophotometer type Shimadzu FT-IR 8400S spectrophotometer utilized for Innfrared spectra with sample prepared as KBr pellets. ^{1}H-NMR spectra were recorded using a BAMX400 MHZ Spectrophotometer in DMSO-d_6 using TMS as an internal reference.Mass spectra were recorded on a Shimadzu agilent technologies 5975C at 70 and MSD energy using a direct insertion probe (Acq method 10 W energy) at 90-110 °C. Microanalytical data (C.H.N) were collected on EA 300 CHNS Elemental analyzer.

Synthesis of 2-(E-(1H_benzo(d) imidozol-2-yl) diazenyl -5-(E-4-dimethyl amino benzaliden amino) phenol (BIADMebP) and characterization for this ligandare described in our previous work [16].

Recommended Procedure and calibration graph:

Take increasing volumes of working ferrous sulfate salt solution covering the range (25-200 ppm) add to 25- mL volumetric flasks, followed by addition of(2ml) 2- ((E) – (1H- benzo [d] imidazol-2-yl)diazenyl)-5-(E-4-(dimethyl amino) benzyliden amino) phenol, (BIADMebP)(0.01)M and 5ml of sodium per iodate (0.01)M, then add (2mL) of HCl acid (1M) The solutions were left for 20 minutes in a water bath adjusted at 30°C and the absorbance was measured at (442) nm against reagent blank prepared in the same manner but containing no ferrous sulfate salt using 1-cm cells.

Procedure for dosage forms tablets:

Three tablets of ferrous sulfate drugs for different companies (ferrous sulfat) for three companies (Actavis 200 mg, Aktiv 158mg, Brawn 150mg.) were weighed and finely powdered. Aportion of the powder equivalent to 0.05 g of each drug was weighed and dissolved in 1:1 acetone, ethanol solvent, then transferred into 100 mL volumetric flask shaken well and completed to the mark with the solvent. The solution shaken well, filtered and an aliquot of the filtered drug solution was then treated asdonein the recommended procedure. The concentration of all drugs was equal to the exact weight that has been used in drugs by the three companies.

Calibration Curve

By applying the optimum parameters studied above, standard calibration curves for BIADMebP- ferrous color product were constructed in the figure 1, and some analytical parameters of the proposed method are summarized in the table 1.

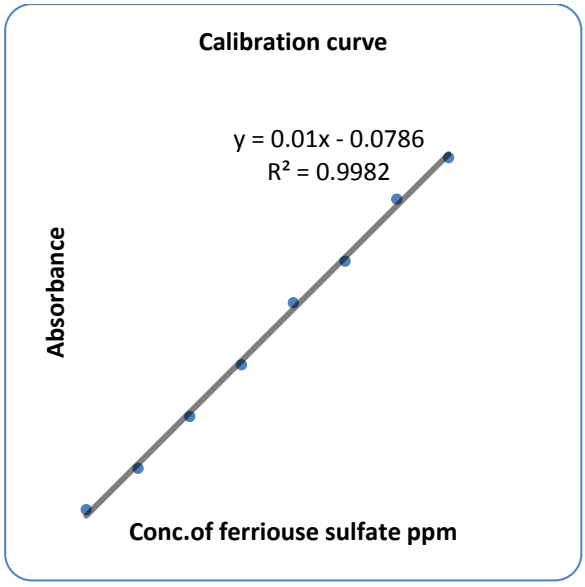

Figure 1: Calibration curve for the complex of BIADMebP-Ferrous

Table 1: Analytical features of the procedure developed for the estimation of BIADMebP- Ferrous:

Analytical parameter	Proposed method
Regression equation	Y=0.0345X-0.0088
Slope	0.00997
Correlation coefficient	0.999107
Linear Range (ppm)	25-200
Limit of detection(LOD)(ppm	5.055
Limit of quantification(LOQ)	16.8505

RESULTS AND DISCUSSION

Absorption spectra

The absorption spectra of ferrous, BIADMebP and BIADMebP-ferrous complex as shown in figure 2. under the optimum conditions.

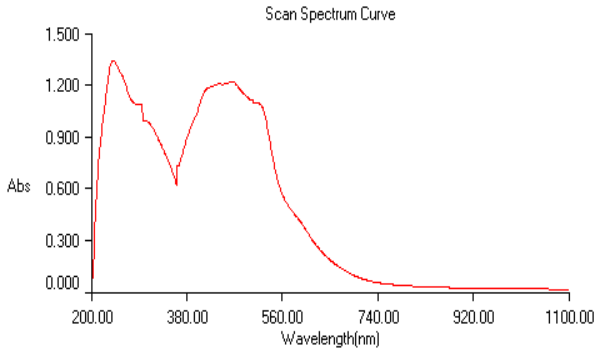

Fig.2: Absorption spectra of ferrous-BIADMebP complex

The electronic spectrum of the complex showed seven characteristics bands. All bands will be illustrate in table 2.

Table 2: Absorption spectra bands of ferrous-BIADMebP complex.

Compound	λmax	Absorption	Transitions
Schiff base(CBAP)	391	25575	n →π*
	241	41494	π →π*
BIACMebp	461	21694	n →π*
	233	42918	π →π*

Precession:

The precision for preparation of complex solutions and measuring their absorbance at λ_{max}=436 was evaluated by calculating the standard deviation(S.D) and relative standard deviation(R.S.D) for seven replicate samples prepared and measured in an identical way. The data and calculations are tabulated 3.

Table 3: Absorption spectra bands of ferrous-BIADMebP complex.

Replicate No.(n)	Absorbance (x_i)
1	0.63
2	0.61
3	0.64
4	0.61
5	0.63
6	0.62
7	0.65
Standard deviation	0.0168
Rel. Standard deviation	2.709 %

Replication Number (n) = 7

Method of The Calculation of Limit of Detection (LOD) and Limit of Quantification (LOQ)

(LOD) and (LOQ) have been determined by using the following equations:

LOD = 3 × S.D/Slope , LOQ = 10 × S.D/Slope

LOD = 3 × 0.0168/0.00997 = 5.055

LOQ = 10 × 0.0168 /0.00997 = 16.8505

Determination of the optimum conditions

Effect of pH

(Figure 3) shows that the absorbance of Ferrous complex measured at λ_{max} change with solution pH. The absorbance of this complex measured at λ_{max} starts low on the acidic side; reaches a maximum at the optimum pH value and then decreases again as pH is increased. The optimum pH values obtained from the plots give pH=7 for Ferrous. The simplest explanation for these observations is probably that the ligand is highly protonated at low pH, making the nonbonding electron-pairs unavailable and therefore diminishing the tendency to form complexes with the metal cations. On the other hand, when the pH is above the optimum value, hydrolysis of Ferrous ion become more significant and reduce the concentration of the complex.

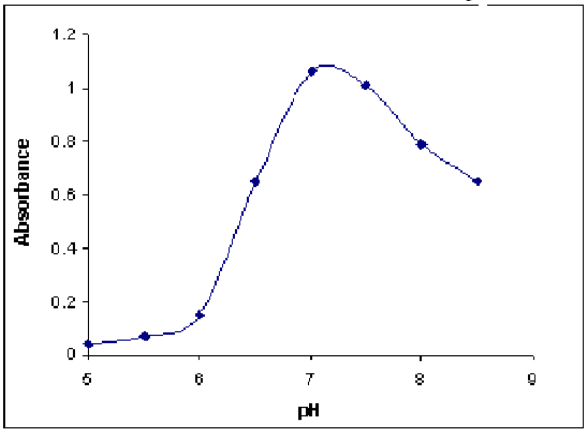

Fig.3 : Effect of pH on absorbance of ferrous-BIADMebP complex.

Effect of time

After mixing the components, the absorbance reaches its maximum within 15 minutes at room temperature and remains stable for at least 200 minutes in acetone-ethanol solution. The

ethanolic-acetone solutions of the chelates of Ferrous is stable for at least 24 hours. The results are shown in figure 4:

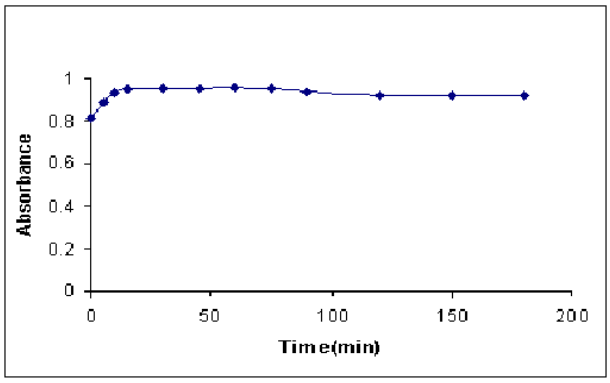

Fig.4 : Effect of Time on absorbance of ferrous-BIADMebP complex.

Effect of Temperature

The effect of temperature on the absorbance of the Ferrous complexe were studied. The study was performed at temperatures between 10℃ and 70℃. The maximum absorption was obtaineded when the temperature was between 20℃ and 30℃. At temperatures higher than 35℃, the absorbance gradually decreases with increasing temperature, which may be attributed to dissociation of the complexes. The results are shown in Figure 5.

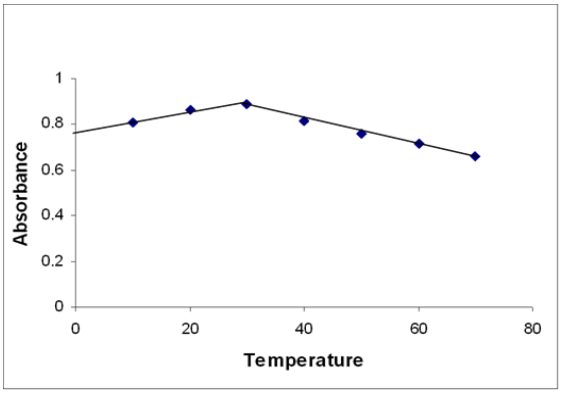

Fig.5 : Effect of Temprature on absorbance of ferrous-BIADMebP complex.

The composition of complexes

The compositions of the complexes were determined by using mole ratio method and Jobe's method:

Mole Ratio Method

This method showed that the mole ratio of Ferrous Sulfate ion to reagentBIADMebPis 1:1 (M: L) as shown in Figure 6:

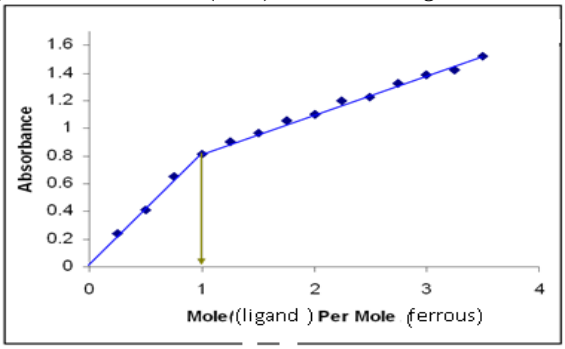

Fig.6 : Mole ratio method for absorbance of ferrous-BIADMebP complex.

Jobe's Method

This method showed that the mole ratio of Ferrouse to reagent BIADMebP is 1:1 (M:L).. The results are plotted in Figure below.

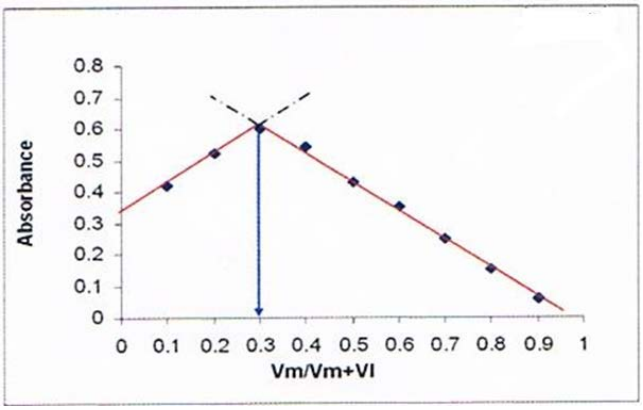

Fig.6 : Job method for absorbance of ferrous-BIADMebP complex.

Interferences:

The effects of some transition metal ions (Ag^{+1},Cu^{+2}, Co^{+2}, Cr^{+3}, Ni^{+2}, Zn^{+2}, and Pb^{+2}) which can form complex with the reagent BIADMebP during its reaction with Ferrous ion (10 ppm) have been studied. On the other hand, suitable masking agent was examined for elimination the effect of the interferences of these ions, the results showed that none of these ions interfered seriously with ferrous sulfate.

Table 4: Effect of feriegn ions on the estimation of ferrous and suitable masking agents

Ferrous	Fereign	Error%	Masking	Error %
10	Ag^{+1}	5.5	tartaric	1.0
10	Cu^{+2}	1.8	5-Sulphosalic	2.5
10	Co^{+2}	6.7	Sodium	3.5
10	Cr^{+3}	3.5	Oxalic acid	0.3
10	Ni^{+2}	3.3	Oxalic acid	0.8
10	Zn^{+2}	1.7	NH4OH at	1.0
10	Pb^{+2}	2.2	Tartaric acid	0.5

CONCLUSIONS:

The analytical application of the tridentate heterocyclic azo reagent2-(E-(1H_benzo(d) imidozol-2-yl) diazenyl -5-(E-4-dimethyl amino benzaliden amino) phenol, derived from thiazole, is reported in this thesis. The reagent forms ethanolic-aecton soluble complexes with ferrous.The chelation and the subsequent spectrophotometric determination of ferrous in various samples with different matrixes, appears to be simple, quick, selective and sensitive. The ferrous complexes under optimum conditions are stable for at least 24 hours.The metal ligand ratio (M:L) in ethanolic-aceton solutions as determined by the "mole ratio" and by Jobe's method, both indicate 1:1 for ferrous complex.The reagent was successfully applied for the determination of ferrous in ferrous sulfate drug for three companies (Actavis 200 mg, Aktiv 158mg, Brawn 150mg.).

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