Novel method for determination of Zinc in some pharmaceutics using new prepared reagent of methyl phenol

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Abstract

This work studied the amalgamation and portrayal of another Azo-Schiff base ligand and its utilization of zinc in certain medications. Azo 2-(E)- (1H-benzo[d]Imidazol-2-yl)diazenyl)- 5-((E)- (4-Chlorophenylimino)methyl)phenol (BIACMebp) has been incorporated after the closely resembling system and Al-Adilee et.al., with some adjustment in a two-venture measure, in the initial step, 2-Amino benzimidazole (1.33 g) was blended in with hydrochloric corrosive 3ml In (thirty mL) refined water and diazotized under 5 °C with sodium nitrite NaNO2 (0.75 gm, 0.01mol, broke up in 20 ml refined water) was included drops, and in the next step the diazonium chloride compound is then combined with 3-(4-Chlorobenzylideneamino)phenol (CBAP) (2.31 gm, 0.01 mol), disintegrated in combination from 60 ml ethanol and 18 ml sodium hydroxide(5%) Pour the blend for 1 hour at a temperature of 5-0 m. The readied azo where inspected by various phantom procedure in wording, C.H.N natural investigations, metal substance, FT-IR, UV-Vis, 1H-NMR and mass spectra contemplates. The metal ligand proportion (M:L) in alcoholic watery arrangements controlled by mole proportion methodand it demonstrates 1:1 for the complex. Additionally, the strength constants for the complex with zinc has been determined frightfully by UV-Vis technique. All outcomes show this complex has high strength. The systematic applications have been achieved in medication (zinc sulfat) for several companies (zincodin (Aktive) 25 mg, Zinc (Kontam) 35 mg, Zinc Sulfate (Jink.) 20 mg.

Key words: - Azo compounds, phenol derivative as reagents, estimation of zinc, determination of Zinc in drug, zincodin drug

1. Introduction:

Azo schiff bases intensifies got from the response between azo mixes and the schiff base [1], this mixes are critical because of their broad uses as against corrosion[2], Inhibiting the development of microbes [3,4]and natural reagents to distinguish a ton of metal particles, regardless of whether momentary or non-temporary, and great extraction reagents for some temporary component particles of fluid arrangements [5]. Shiff base buildings with metals particle it got intrigued after use of these edifices in a few examinations particularly as a reagent in explanatory techniques for recognition a few kinds of metal particles [6, 7]. Imidazole mixes have wide applications in pharmaceutics since the atom of imidazole ring happens in a progression of mixes, for example, in histidine, in Vitamin B12 and biotin just as
numerous chemotherapeutic specialists [8,9]. Zinc considers as the most fundamental of minor components that required for our bodies. This component go about as practical and underlying cofactor for some intracellular proteins. A few of this metal edifices display high antitumor movement against a ton of human tumors cell which causes harm in DNA [9,10]. This component entomb in a few kinds of medication. A few strategies have been followed to decide the components utilizing legands as a reagent to shape edifices, for example, subbed imidazole mixes [11, 12]. The venture of this work is to combination and otherworldly portrayal of a novel reagent 2-(e-(1h_benzo(d) imidozol-2-y) diazenyl - 5-(e-4-chlorophenylimino) methyl) phenol and utilizing as a reagent for discovery of Zinc metal in zincodin drug.

**Synthesis of azo-Schiff base ligand (BIACMebp).**

Azo schiff bases intensifies got from the response between azo mixes and the schiff Azo-Schiff base ligand was orchestrated after the comparable to method [13] and Al-Adilee et.al., [14] with some adjustment in a two-venture measure as portrayed underneath. In the initial step, 2-Amino benzimidazole (0.01 mol) was blended in with hydrochloric corrosive 3ml In (30 mL) refined water and diazotized under 5 °C with sodium nitrite NaNO2 (0.75 gm, 0.01mol, disintegrated in 20 ml refined water) was included drops [15,16]. In the second step the diazonium chloride compound was then combined with 3-(4-Chlorobenzylideneamino)phenol(CBAP) (2.31 gm, 0.01 mol, broken up in combination from 60 ml ethanol and 18 ml sodium hydroxide(5%) Pour the blend for 1 hour at a temperature of 5-0 m [17, 18]. Formula the arrangement and wash the accelerate with refined water a few times and afterward re-take shape with ethanol arrangement and dry the encourage utilizing 50 ° C for a couple of hours [19]. (schem-1) shows the arrangement cycle. The current work means to combination and phantom portrayals of 2-(E-(1H_benzo(d) imidozol-2-y) diazenyl - 5-(E-4-chlorophenylimino) methyl) phenol, and utilizations as reagent for identification and assessment of zinc in zincodin drug [20, 21].

(Schem-1) Synthesis of zo-Schiff base ligand (BIACMebp)
Procedure and calibration curve

Several volumes of zinc sulfate arrangement in range(25-200 ppm) added to 25-mL glassy volumetric cups, trailed by option of (2ml) (BIACMebp) (0.01)M and 5ml of sodium periodate (0.01)M, at that point a (2mL) of HCl acid (1M) was added. The arrangements were left for 20 minutes in awater shower changed at 30°C and the absorbance was estimated at (460) nm using 1cm container of sample.

Dosage forms tablets procedure's

Three kinds of zinc medicament for various organizations (zinc sulfate) for three organizations (zincodin (Aktive) 25 mg, Zinc (Kontam) 35 mg, Zinc Sulfate (Jink.) 20 mg, were gauged and accurately crushed. Aportion of the crushed tablets identical to 0.05g of eachdrug was weighed and dissolved in 1:1 CH3)2CO, ethanol dissolvable, at that point moved into 100 mL volumetric shaken carefully and finished to the imprint with the dissolvable. The arrangement shaken carefully, sifed and analiquot of the separated medication arrangement was handled as done in the suggested system. The grouping of each medications were equivalent to the specific weight that have been utilized in medications by the three organizations.

2. Results and discussion

Electronic Spectra

The electronic assimilation spectra of zo-Schiff base ligand (BIACMebp) show two retention groups at 460 nm (21692 cm-1) because of n →π* of (HC=N and – N=N-) transitions and 233nm (42918 cm-1) because of a π →π* progress in phenyl rings, UV-Vis. spectra of the ligand are appeared in figure (1).

![Scan Spectrum Curve](image)

Figure (1). UV-Vis. spectra of Azo-Schiff base ligand (BIACMebp)

1H-NMR Spectra

The 1H-NMR spectra of ligand (figures 1) was estimated in DMSO-d6 as dissolvable with TMS as an inside reference (400MHz). This mixes as appeared in Figure (2) and table (1)

| Table (1): 1H-NMR spectrum of Azo-Schiff base ligandBIACMebp |
Figure (2): $^1$H-NMR spectrum of Azo-Schiff base ligand (BIACMebp)

Infrared spectra of azo-schiff base ligand

IR spectra noticed two sharp tops in the area (1496) cm$^{-1}$ and (1620) cm$^{-1}$ are because of azo and azomethine(- N=N-, - C=N-).

The IR range displays band at district (3348) cm$^{-1}$ which can be ascribed to (OH) phenolic gathering, the infrared ghastly are appeared in figure (3).
Standardization Curve

Via submitting the ideal boundaries concentrated up, criterion adjustment bends for (BIACMebp)- Zinc shading item were developed in the figure 4, and comparatively logical boundaries of the offered strategy are summed up in the table 2.

Table (2):- Analytical parameters of the proposed method for estimation of zinc

| Analytical parameter          | Proposed value          |
|------------------------------|-------------------------|
| Regression equation          | Y=0.0345X-0.0088        |
| Slope                        | 0.04                    |
| Linear Range (ppm)           | 10-45                   |
| Correlation coefficient      | 0.998771                |
| Limit of detection (LOD) (ppm)| 3                      |
| Limit of quantification (LOQ) (ppm) | 10                  |
Precession

The precession for arranging of complex courses of action and assessing their A value at maximum wavelength = 460 nm was surveyed by registering S.D and R.S.D for seven recurrent tests masterminded and assessed randomly. Table 3 illustrates all the data and tallies.

Table (3):-Calculation and data for precession profile

| Replicate No.(n) | Absorbance ($x_i$) |
|------------------|---------------------|
| 1                | 0.45                |
| 2                | 0.47                |
| 3                | 0.51                |
| 4                | 0.46                |
| 5                | 0.45                |
| 6                | 0.51                |
| 7                | 0.40                |

S. D. = 0.04

S.D. = Standard deviation

R.S.D. = Relative Slandered Deviation

LOD and LOQ

Limit of detection and Limit of quantification were calculated by the equations 1 and 2:

\[
\text{LOD} = \frac{3 \times \text{S.D}}{\text{Slope}} \quad \ldots \ldots(1)
\]

\[
\text{LOQ} = \frac{10 \times \text{S.D}}{\text{Slope}} \quad \ldots \ldots(2)
\]

\[
\text{LOD} = \frac{3 \times 0.04}{0.04} = 3
\]

\[
\text{LOQ} = \frac{10 \times 0.04}{0.04} = 10
\]

Examination of the optimum Circumstances
**pH Affect**

The absorbance of the chelating complexes assessed at $\lambda_{max}$ appears low on the acidic media; shows up at a generally outrageous in ideal pH worth and there after lowring again as pH is extended. Figure 5, illustrates the perfect media at pH=8 for Zn$^{2+}$, this may be attributed to the protonation in legend in low value of pH. As a result for this behavior the non bonding electron is likely make blocked off and subsequently decreasing the affinity to shape structures with the metal cation.

![Figure 5: optimum value of pH](image)

**Time Affection**

Subsequent to blending the parts, the absorbance arrives at its most extreme inside 15 min at standard condition and stays strait for in any event 200 min in watery arrangement (term of analysis). The ethanolic aqueous solutions of the chelate of Zn(II) are stable for at least 24 hours, figure 6, shows the effect of time for matching zinc with legand. Figure 6, demonstrate the effect of time.
Temperature Affection

The impact of temperature on the absorbance of the Zn(II) complex was contemplated. The examination was performed at temperatures somewhere in the range of 10°C and 70 °C. The most extreme ingestion was obtained when the temperature was between 20°C and 30°C. At more than 35°C temperature, the absorbance bit by bit diminishes with expanding temperature, which might be credited to separation of the complex, figure 7 shows effect of temperature on formation of complex.

Figure (6):- effect of time on chelating

Figure (7):- optimum value of temperature for formation of complex
The combination of chelating compounds

The combination of chelating compounds were fixed by using mole ratio as shown in figures 8, shows the mole ratio of BIACMebp)-Zn is 1:1 (M: L)

Figure (8):-mole ratio to determine the ratio between ligand and metal

Molar Conductivity Measurements

Table 3, indicates molar conductivity of the complexes. Estimations were achieved in ethyl alcohol as solvent for complex centralization of 200 ppm, at room temperature. The molar conductivity was equivalent to 13.16S.cm2.mol-1. The low estimations of molar conductivity demonstrate that the complex of Zn(II), are non-electrolytes or extremely feeble electrolytes ordinarily, and that no anions are available external the coordination circles.

Stability constant (β) of the examined metal complexes

Stability consistent of chelating compounds were achieved spectrophptpmeter by estimating the A of arrangements of metals and reagent particle at measured maximum wavelength, and measured pH value. The level of development of the edifices were gotten from the association offered by Vosburgh and Copper, equation 3.

\[ \beta = \frac{1-\alpha}{\alpha 2c} \]  \( \text{equation 3} \)

\( \alpha \) was calculated according to equation 4.

\[ \alpha = \frac{A_m-A_s}{A_m} \]  \( \text{equation 4} \)

where Am and As are the absorbance of completely and somewhat framed complex separately at ideal focus. The worth is β=6.87×1011. The higher solidness of the reagent (BIACMebp) towards Zn (II) demonstrates to the higher liking of the ligand to divalent cations.
Study of interference

The impacts of several transition metal particles (Cu$^{+2}$, Ni$^{+2}$, Co$^{+2}$, Fe$^{+2}$, Pb$^{+2}$, Cr$^{+3}$, and Ag$^{+1}$) which can chelate with the reagent (BIACMebp)- during its response with zinc particle (10 ppm) have been examined. Then again, appropriate concealing specialist was analyzed for elimentation the impact of the interferences of this particles, the outcomes demonstrated that none of these particles meddled earnestly with zinc sulfate.

3.Conclusion:

The use of (BIACMebp) legand for recognition of zinc in zincodin drug demonstrated that the readied ligand is proficient for this reason with high security for this complex by means of count of buildings dependability steady. The ideal conditions for recognition zinc were: the best estimation of pH =8, the ideal temperature was 30 °C and the development of complex not need in excess of 15 min. The proportion of metal to ligand was 1:1. Other diagnostic boundaries demonstrated that the constraint of location =3, while the restriction of quantitation was 10.

4.References:

[1] Arshed A.Ali Shihad, Khamis A.Abedalrazaq2 , Faiq F. Karam3 , Haider M. Hessoon3 , Khalid J. Al-Adilee4 , Ayad F. Alkaim5, 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. Journal of Pharmaceutical Science and Research, Vol. 10(9), 2018, 2179-2182.

[2] Al-Khateeb, Ziyad T., Karam, Faiq F., Al-Adilee, Khalid. Synthesis and characterization of some metals complexes with new heterocyclic azo dye ligand 2- [2. - (5- Nitro thiazolyl) azo]-4- methyl -5- nitro phenol and their biological activities, Journal of Physics Conference Series, 10.1088/1742-6596/1294/5/052043.

[3] Ziyad T Al-Khateeb, Faiq F. Karam, Khalid Al-Adilee, Synthesis and characterization of some metals complexes with new heterocyclic azo dye ligand 2- [2. - (5- Nitro thiazolyl) azo]-4- methyl -5- nitro phenol and their biological activities, Journal of Physics: Conference Series, 2019 , 1294 052043.

[4] FAIQ F. KARAM , Ziyad T. Al-Khateeb, Preparation of a novel cartridge of SPE column using a new surface of heterocyclic azo ligand with modified activated carbon, Journal of Global Pharma Technology 11(3):30-44 · October 2019.

[5] H. H. Eissa; Int. J. Curr.Res.Chem.Pharma.Sci., (2015),2(1),84–94.

[6] Saima Akhter, Hilal Ul Zaman, Shafia Mir, Ayaz Mahmood Dar and Sarita Shrivastava.(2017). Synthesis of schiff base metal complexes: a concise review.

[7] Eur. Chem. Bull., 2017, 6(10), 475-483.

[8] Khalid J.AJ-Adilee. (2015). Preparation and Characterization of Some Transition Metal Complexes with NovelAzo-Schiff base Ligand Derived from 2(E)-(1H- benzo[d] imidazole-2-yly diazenyl)-5-((E)-benzylideneimino)phenol (BIADPI). RIPBCS 6(5) Page No. 1297
[9] Maria de F.V. de Mouraa, Ótom A. de Oliveira, Robson F. de Farias (2003), Synthesis, characterization and thermogravimetric study of zinc group halides adducts with imidazole. Thermochimica Acta 405 (2003) 219–224.

[10] Zhijian Che, Shaoxiang Wang, Shenggui Liu, Guobi Li, Qiting Wu, Chunyu Lin, Linglang Kong, Sheng Wang (2015). Synthesis, structure, photoluminescence and antitumour activity of zinc complex based on 2-(2-(1H-benzo-[d]imidazol-2-yl)benzyl)- 1H-benzo-[d]imidazole. Spectrochimica Acta Part A: Molecular and Biomolecular Spectroscopy 135 (2015) 878–882.

[11] Arshed A. Ali Shihad, Khamis A.Abedalrazaq, Faiq F. Karam, Haider M. Hessoon, Khalid J. Al-Adilee, Ayad F. Alkaim, (2018). 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. J. Pharm. Sci. & Res. Vol. 10(9), 2018, 2179-2182

[12] A.Z. El-Sonbati, M.A. Diab, A.A. El-Bindary, A.F. Shoair, N.M. Beshry, Journal of Molecular Liquids, 218 (2016) 400–420.

[13] Khalid J. Al-Adilee and ShaimaaAdnan, Orienta Journal of chemistry,33(4),(2017), 1-13.

[14] F. I. Abdullah, M.M. Elajaily, R. A. Ockasha, M. S. Suliman and A. A. Maihub; IJAPBC., (2014) Vol. 3(2), 256-265.

[15] A. A. S. AL-Hamdani and S. Shaker; Orient. J. Chem., (2011) Vol. 27(3), 835-845 .

[16] Z. J. Mohammed, A. H. Al-Khafagy and A. M. Ali; International Journal of Current Research., (2013), Vol. 5, Issue, 12, pp.3705-3710.

[17] J. Al-Adilee, Khalid & A. Jaber, Sudad. (2018). Synthesis, Characterization and Biological Activities of Some Metal Complexes Derived from Azo Dye Ligand 2-[2’-(5- Methyl thiazoly)]azo]-5-dimethylamino Benzoic Acid. Asian Journal of Chemistry. 30. 1537-1545. 10.14233/ajchem.2018.21222.

[18] Maradiya, H. R., & Patel, V. S. (2001). Synthesis and dyeing performance of some novel heterocyclicazo disperse dyes. Journal of the Brazilian Chemical Society, 12(6), 710-714

[19] AL-Adilee, K. J., & Fanfon, D. Y. (2012). Preparation, Spectral Identification and Analytical Studies of Some Transition Metal Complexes with New Thiazolylazo Ligand and Their Biological Activity Study. Journal of Chemistry and Chemical Engineering, 6(11), 1016.

[20] K.J. Al-Adilee, Res. J. Pharm. Chem. Sci. 6 (5) (2015) 1297e1308. 19.

[21] A. Skooge, D.M. West and F.J. Holler, Fundamentals of Analytical Chemistry, Saunders College Publishing, New York, edn. 5 (1988).

[22] Irving, H., & Williams, R. J. P. (1953). The stability series for complexes of divalent ions. J Chem Soc, 1953, 3192-3205.