



**DNA BINDING, PHOTO CLEAVAGE, ANTIBACTERIAL AND CYTOTOXICITY
ACTIVITIES OF MONO NUCLEAR METAL COMPLEXES OF AN N, O DONOR
BENZOTHIAZOLE DERIVATIVE SCHIFF BASE LIGAND**

**N. Nageswara Rao, K. Gopichand, E. Kishan, R. Nagaraju, Abdul Majeed Ganai and P.
Venkateswar Rao***

Department of Chemistry, Osmania University, Hyderabad, 500007, Telangana, India

**E-mail: pallapothulavrao@gmail.com*

ABSTRACT

We report the newly Synthesized five mono nuclear **4a** [Cu^{II}(L)(CH₃COO)(H₂O)], **4b** [Co^{II}(L)(CH₃COO)(H₂O)], **4c** [Ni^{II}(L)(CH₃COO)(H₂O)], **4d** [Zn^{II}(L)(CH₃COO)(H₂O)] and **4e** [Cd^{II}(L)(CH₃COO)(H₂O)] complexes formulas derived from Imine base ligand, **HL**¹ 1-((E)-(6-ethoxybenzo[d]thiazol-2-ylimino)methyl)naphthalen-2-ol, were characterized by various spectral techniques such as Proton NMR (¹H-NMR), Carbon NMR (¹³C- NMR) Infrared spectra, Mass spectra, Scanning Electron microscopy (SEM), Energy-dispersive X-ray spectroscopy (EDX or XEDS), Powder XRD, UV absorption spectra and Elemental analysis. Based on analytical results **4a**, **4b** and **4c** complexes are exhibit square planar geometry with four coordinate number and **4d** and **4e** complexes are tetrahedral geometry. The interactions of the five novel synthesized mono nuclear transition metal complexes with calf thymus DNA (CT-DNA) are explored using UV- Visible spectra, Viscosity, Emission spectral methods. The novel Imine base ligand and its mono nuclear metal complexes have DNA photo cleavage affinity by agarose gel electrophoresis technique. The novel synthesized Imine base ligand and mono nuclear metal complexes are screened for antibacterial activities. Among all newly synthesized Imine base ligand and mono nuclear complexes were evaluated HeLa and MCF-7 cell lines by using MMT assay.

KEYWORDS: 2-amino-6-ethoxy benzothiazole; Imine base ligand; Mono nuclear metal complexes; DNA binding; Photo cleavage; Bacterial studies; Cytotoxicity.

1. INTRODUCTION

The Heterocyclic ring contain benzothiazole compounds are biologically active compounds and Research focused on interaction between ligational and biological activities of Imine base ligand and their mono nuclear metal complexes with CT-DNA has obtained much popularity in recent past due to their reality of applications especially treatment of molecular biology and cancer.^{i-vi} The replication of cancer cells stopping by various methods with unnatural

DNA.^{vii-ix} The mono nuclear metal complexes affected DNA by the following of either interaction of DNA binding or affinity of photo cleavage approach.^{x, xi} The binding interaction of mono nuclear metal complexes with CT DNA by various modes such as intercalation, groove and electrostatic binding.^{xii, xiii} The mono nuclear metal complexes used for DNA cleavage affinity by hydrolytic, oxidative and photolytic cleavage methods.^{xvi-xix} Benzothiazole derivative Imine base ligand and their mono nuclear complexes are display a extensive variety of numerous biological activities including anti-malarial, antibacterial, antitumor and antiviral activities.^{xvi-xix} We have focused on synthesis of Imine base and their mono nuclear metal complexes.^{xx-xxii} Furthermore, Imine bases are most broadly studied in medicinal chemistry reason of their wide verity of pharmacological activities such as anticancer^{xxiii}, antioxidant^{xxiv}, antimicrobial^{xxv}, anthelmintic^{xxvi}, anti-inflammatory^{xxvii}, anticonvulsant^{xxviii}, and anti-tuberculosis^{xxix} activities etc. Imine base ligand having nitrogen, oxygen and sulfur as donors and widely studied to their mono nuclear metal complexes.^{xxx-xxxii} Herein, we reported focused on the Synthesis of 1-((E)-(6-ethoxybenzo[d]thiazol-2-ylimino)methyl)naphthalen-2-ol Imine base and their mono nuclear transition metal complexes, and also the biological activities including DNA binding, photo cleavage, antibacterial and cytotoxic activity. Imine base and mono nuclear metal complexes have been characterized by different Spectro chemical studies.

2. EXPERIMENTAL

2.1. CHEMICALS AND MATERIALS

All the chemicals 2-hydroxy-naphthaldehyde and 2-amino-6-ethoxy benzothiazole procured from sigma Aldrich. Solvent's methanol, n-hexane, acetone, chloroform and metal acetate salts were procured from SD fine chemicals. MMT dye procured from sigma Aldrich. The Calf thymus DNA (CT-DNA) was procured from genie company, Bangalore, India and stored at below 5 °C temperature. Preparation of all the buffer solutions with double distilled water and used for CT DNA interaction and affinity of photo cleavage studies.

2.2. GENERAL PHYSICAL MEASUREMENTS

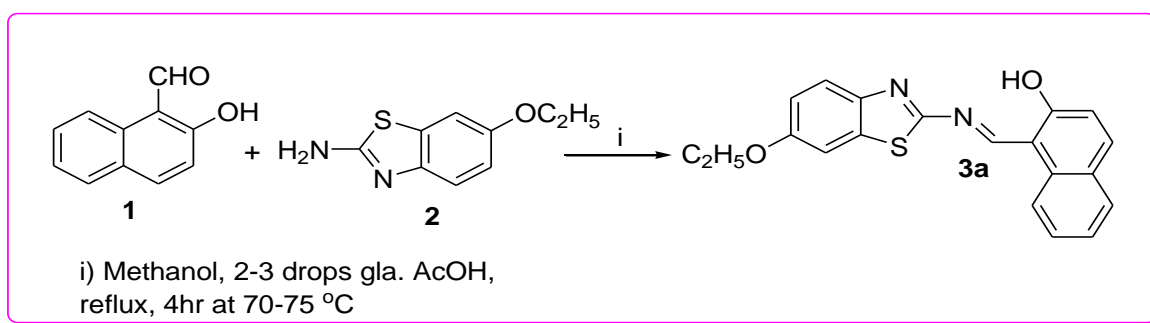
The composition of Carbon, Hydrogen, Nitrogen and Sulphur of the Imine base ligand their mono nuclear metal complexes were carried out by using Perkin Elmer 240C (USA) elemental analyzer. The ¹³C NMR and ¹H NMR spectra's in CDCl₃ solvent of Imine base were recorded on Bruker 400 MHz NMR instrument using TMS as internal reference. FT-IR spectra of the Imine base and mono nuclear metal complexes were recorded in the range of 4000-250 cm⁻¹ using Shimadzu Infrared prestige-21 spectrophotometer using KBr pellets. Mass spectra of Imine base and its mono nuclear metal complexes were recorded on VG AUTOSPEC mass spectrometer. The absorption spectra were recorded on Shimadzu UV-Vis 2600 Spectrophotometer and Fluorescence quenching study was performed on a JASCO FP8500 spectrofluorimeter by using DMSO as a solvent and in the wave length range of 200–800 nm. Melting point of the Imine base and its mono nuclear metal complexes were determined on a Polmon instrument (model MP–96 instruments). The viscosity instrument was using Ostwald capillary viscometer was performed using Ostwald viscometer and temperature setting at 30 ± 0.1 °C in a thermostatic water bath. The elemental analysis determination investigated by Energy Dispersive X-Ray Analysis. The particle size and morphology were recorded on Scanning Electron Microscopy.

2.3. SYNTHESIS OF IMINE BASE LIGAND AND ITS MONO NUCLEAR METAL COMPLEXES (4a-4e)

2.3.1 SYNTHESIS OF IMINE BASE LIGAND (HL¹) (3a)

A mixture of 2-hydroxy-naphthaldehyde (**1**) (1mmol), 2-amino-6-ethoxy benzothiazole (**2**) (1mmol) and 50 ml of methanol poured into a clean 250 ml of 2 Neck round bottom flask then add 2-3 drops of glacial acetic acid and reaction mixture reflux for 4hr at 70-75 °C. After starting material disappears yellow color solid precipitate is obtained. The obtained solid filtration using suction pump washed with cold methanol and dried over under vacuum (**Scheme 1**)

Analytical data: Found (%) for $C_{20}H_{16}N_2O_2S$: C, 68.90; H, 4.59; N, 8.01. Calcd: C, 68.94; H, 4.63; N, 8.04. 1H NMR (400 MHz, $CDCl_3$): δ 1.46-1.49 (m, 3H, CH_3), 4.09-4.14 (m, 2H, OCH_2), 7.08-7.11 (m, 1H, ArH), 7.19-7.26 (m, 1H, ArH), 7.30-7.31 (d, $J=4$ MHz, 1H, ArH), 7.40-7.44 (m, 1H, ArH), 7.59-7.63 (m, 1H, ArH), 7.78-7.80 (d, $J=8$ MHz, 1H, ArH), 7.85-7.87 (d, $J=8$ MHz, 1H, ArH), 7.91-7.93 (d, $J=8$ MHz, 1H, ArH), 8.29-8.31 (d, $J=8$ MHz, 1H, ArH), 10.11 (s, 1H, $CH=N$), 14.42 (s, 1H, OH). ^{13}C NMR (400 MHz, $CDCl_3$): δ 14.83, 64.17, 105.19, 109.55, 115.15, 116.32, 119.88, 120.01, 123.44, 124.27, 126.90, 128, 128.58, 129.45, 133.11, 137.54, 152.57, 157.02, 160.69, and 165.90. IR ν_{max} (KBr/cm^{-1}): $\nu_{(H_2O)}$ 3633, $\nu_{(HC=N)}$ 1637, $\nu_{(C=O)}$ 1199. ESI-MS (m/z): Calcd: 348 Found: 349 $[M+H]^+$, M.P: 228–230 °C, Yield: 83%



Scheme 1. Schematic pathway of Synthesis of Imine base ligand HL^1

2.4 GENERAL PROCEDURES FOR SYNTHESIS OF MONO NUCLEAR METAL COMPLEXES

1-((E)-(6-ethoxybenzo[d]thiazol-2-ylimino)methyl)naphthalen-2-ol (**3a**) (5mmol) and methanol (20ml) taken into a clean 250 ml of 2 neck round bottom flask. The above reaction mixture reflux and add methanolic (20 ml) solution of corresponding metal salts (5mmol) Viz. $[Cu(CH_3COO)_2 \cdot H_2O]$, $[Co(CH_3COO)_2 \cdot 4H_2O]$, $[Ni(CH_3COO)_2 \cdot 4H_2O]$, $[Zn(CH_3COO)_2 \cdot 2H_2O]$ and $[Cd(CH_3COO)_2 \cdot 2H_2O]$ add drop wise using additional funnel at same temperature duration of 20 min. After completion of methanolic solution addition the reaction mixture pH value adjusts with triethylamine (pH=8-9) and the reaction mixture reflux for 4-6hr at 70-75 °C. After starting material disappear various colours solid precipitates obtained. The obtained solids filter using suction pump dried over under vacuum. (**Scheme 2**)

2.4 1. SYNTHESIS OF $[Cu^{II}(L)CH_3COO](H_2O)$ (**4a**)

Analytical data: Found (%) for $C_{22}H_{20}CuN_2O_5S$: C, 54.20; H, 4.10; N, 5.70. Calcd (%): C, 54.14; H, 4.13; N, 5.74. UV-Vis (nm): 277,300. IR ν_{max} (KBr/cm^{-1}): $\nu_{(O-H)}$ 3379, $\nu_{(C=N)}$ 1600, $\nu_{(C-O)}$ 1190, $\nu_{(M-O)}$ 542, $\nu_{(M-N)}$ 449. ESI-MS (m/z): Calcd: 487. Found: 489 $[M+2H]^+$, M.P: 272-274 °C, Yield: 72%

2.4 2. SYNTHESIS OF $[Co^{II}(L)(CH_3COO)(H_2O)]$ (**4b**)

Analytical data: Found (%) for $C_{22}H_{20}CoN_2O_5S$: C, 54.65; H, 4.17; N, 5.76. Calcd (%): C, 54.66; H, 4.14; N, 5.80. UV-Vis (nm): 265, 354, 465. IR ν_{max} (KBr/cm^{-1}): $\nu_{(O-H)}$ 3313,

$\nu(\text{C}=\text{N})$ 1600, $\nu(\text{C}-\text{O})$ 1195, $\nu(\text{M}-\text{O})$ 547, $\nu(\text{M}-\text{N})$ 487. ESI-MS (m/z): Calcd: 483. Found: 484 $[\text{M}+\text{H}]^+$, M.P: 269-271 °C, Yield: 79%.

2.4.3. SYNTHESIS OF $[\text{Ni}^{\text{II}}(\text{L})(\text{CH}_3\text{COO})(\text{H}_2\text{O})]$ (4c)

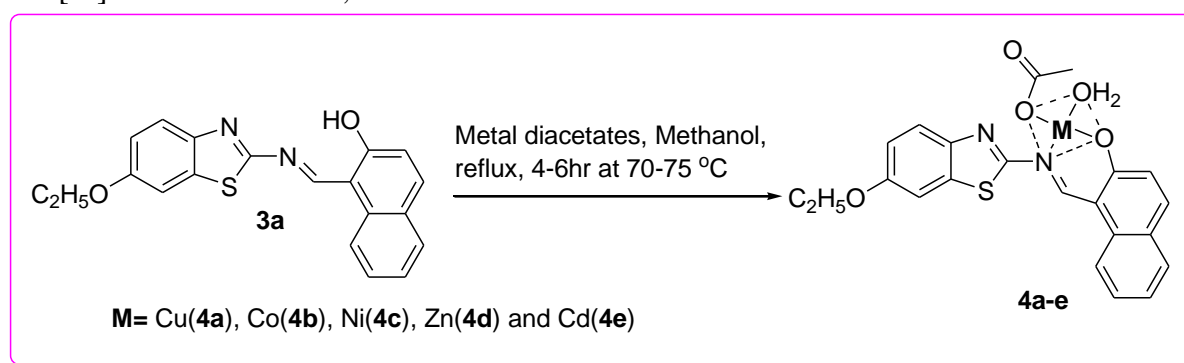
Analytical data: Found (%) for $\text{C}_{22}\text{H}_{20}\text{N}_2\text{NiO}_5\text{S}$: C, 54.77; H, 4.14; N, 5.76. Calcd (%): C, 54.69; H, 4.17; N, 5.80. UV-Vis (nm): 262, 353, 463. IR ν_{max} (KBr/ cm^{-1}): $\nu(\text{O}-\text{H})$ 3323, $\nu(\text{C}=\text{N})$ 1595, $\nu(\text{C}-\text{O})$ 1193, $\nu(\text{M}-\text{O})$ 547, $\nu(\text{M}-\text{N})$ 495. ESI-MS (m/z): Calcd: 482. Found: 484 $[\text{M}+2\text{H}]^+$. M.P: 267-269 °C, Yield: 74%.

2.4.4. SYNTHESIS OF $[\text{Zn}^{\text{II}}(\text{L})(\text{CH}_3\text{COO})(\text{H}_2\text{O})]$ (4d)

Analytical data: Found (%) for $\text{C}_{22}\text{H}_{20}\text{N}_2\text{O}_5\text{SZn}$: C, 53.98; H, 4.08; N, 5.70. Calcd (%): C, 53.94; H, 4.08; N, 5.70. UV-Vis (nm): 257, 360, 485. IR ν_{max} (KBr/ cm^{-1}): $\nu(\text{O}-\text{H})$ 3358, $\nu(\text{C}=\text{N})$ 1600, $\nu(\text{C}-\text{O})$ 1192, $\nu(\text{M}-\text{O})$ 511, $\nu(\text{M}-\text{N})$ 459. ESI-MS (m/z): Calcd: 489. Found: 490 $[\text{M}+\text{H}]^+$. M.P: 270-272 °C, Yield: 68%.

2.4.5. SYNTHESIS OF $[\text{Cd}^{\text{II}}(\text{L})(\text{CH}_3\text{COO})(\text{H}_2\text{O})]$ (4e)

Analytical data: Found (%) for $\text{C}_{22}\text{H}_{20}\text{CdN}_2\text{O}_5\text{S}$: C, 49.25; H, 3.73; N, 5.20. Calcd (%): C, 49.22; H, 3.75; N, 5.22. UV-Vis (nm): 276, 299, 451. IR ν_{max} (KBr/ cm^{-1}): $\nu(\text{O}-\text{H})$ 3442, $\nu(\text{C}=\text{N})$ 1616, $\nu(\text{C}-\text{O})$ 1193, $\nu(\text{M}-\text{O})$ 538, $\nu(\text{M}-\text{N})$ 453. ESI-MS (m/z): Calcd: 536. Found: 536 $[\text{M}]$. M.P: 274-276 °C, Yield: 65%.



Scheme 2. Schematic pathways of Synthesis of mono nuclear metal complexes (4a-4e)

2.5. SPECTRAL METHODS OF DNA INTERACTION ASSAYS

2.5.1 ABSORPTION SPECTRA OF DNA INTERACTION

The DNA interaction studies of the novel synthesized mono nuclear metal complexes have been analysed by using Electronic absorption spectral titration method, recorded at 260 nm and 280 nm and molar extinction coefficient value $66000 \text{ M}^{-1} \text{ cm}^{-1}$. The interaction of the mono nuclear metal complexes of Calf Thymus-DNA was studied in pH= 7.2 value of buffer solution, sodium chloride buffer/50 mM and Tris-HCl. The free of protein and purity of DNA in Tris(hydroxymethyl)aminomethane hydrochloride Buffer solution gave the UV-Vis absorption ratio 1.8 to 1.9 Calf thymus DNA was added to mono nuclear metal complexes solution and reference solution to measure the absorbance of mono nuclear complexes and to eliminate the absorbance of CT DNA. Absorption spectra recorded, incubation 4-5 mins both solutions and calculation UV visible absorption values and binding constant data. All the mono nuclear metal complexes using the following equation (1)

$$[\text{DNA}]/(\epsilon_a - \epsilon_f) = [\text{DNA}]/(\epsilon_b - \epsilon_f) + 1/K_b(\epsilon_b - \epsilon_f). \quad (1)$$

here, $[\text{DNA}]$ is the concentration of DNA base pairs, ϵ_b , ϵ_f and ϵ_a is the extinction coefficients of free, fully and apparent coefficient of the mono nuclear metal complexes, K_b is the intrinsic binding constant.^{xxxiii-xxxv}

2.5.2 EMISSION SPECTRA OF DNA INTERACTION

The emission spectra of all the mono nuclear metal complexes were recorded in the range of 360-800 nm (fixed 350 nm excitation). The emission spectra of all the mono nuclear metal complexes was interaction with CT-DNA in presence of EB (Ethidium bromide). EB solution prepared in pH=7.2 value of Tris(hydroxymethyl)amino methane hydrochloride/Sodium chloride buffer at 25 °C. In the range of mono nuclear metal complexes concentration from 0-60 µM. The CT-DNA interaction with mono nuclear metal complexes was calculated by using Stern-Volmer eq. 2^{xxxvi-xxxix}

$$I_0/I = 1 + K_{sv} r \quad (2)$$

where, K_{sv} Stern–Volmer constant, I_0 and I is fluorescence intensity in the absence and presence of complexes and r is the concentration of mono nuclear complex to that of DNA.

2.5.3. VISCOSITY MEASUREMENT OF DNA INTERACTION STUDIES

The Viscosity titration measurements studies were determined by Ostwald's viscometer at 30±0.1 °C. The concentration of DNA kept constant and concentration of mononuclear metal complexes differed (0-200µM). The viscosity of the mono nuclear metal complexes was calculated by using eq 3.

$$\eta/\eta_0 = t/t_0 \quad (3)$$

Where, η and η_0 is viscosity of DNA with mono nuclear complexes and DNA alone, t and t_0 is flow time observed in the presence of mono nuclear complexes and absence of mono nuclear complexes.^{xxxx-xxxii}

2.6. DNA PHOTO CLEAVAGE STUDIES

The DNA photo cleavage of Imine base ligand and their mono nuclear metal complexes were carried out by agarose gel electrophoresis method at under free oxygen (aerobic) condition with Hydrogen peroxide (H_2O_2) as an oxidant agent by CT-DNA at 37 °C. Each sample contained 40 µM of each mono nuclear complex, 30 µM of CT-DNA in DMSO solvent and 50 µM of H_2O_2 in 50 mM of pH value 7.2 TEA buffer. Then the at room temperatue sample incubated for 2 hrs and under UV light photographed.^{xxxiii-xxxiv}

2.7. ANTIBACTERIAL ASSAY

The novel Imine base ligand and their mono nuclear metal complexes have been investigated by against three gram negative bacterias are *E. coli* (*Escherichia coli*), *K. pneumoniae* (*Klebsiella pneumoniae*) and *P. aeruginosa* (*Pseudomonas aeruginosa*) and two gram positive bacterias are *S. aureus* (*Staphylococcus aureus*) and *S. pyogenes* (*Streptococcus pyogenes*) by the plate diffusion method in presence of nutrient agar medium. The Imine base ligand and mono nuclear complexes concentration range from 1-100 µg/mL. All the tested Imine base ligand and mono nuclear metal complexes well plates were incubated at 37 °C for 24 hrs. The Microbial growth was investigated by diameter zone of inhibition and Minimum inhibitory concentration.^{xxxv-xxxvii}

2.8. IN VITRO CYTOTOXICITY STUDIES

The cytotoxic studies of novel synthesised Imine base ligand and its mono nuclear complexes were screened in cervical cancer cell lines (HeLa) and breast cancer cell lines (MCF-7) was evaluated by MMT assay. The both cell lines were treated with 50, 100, 150 µM three different concentrations. The cancer cells Measure absorbance at 620 nm with Elisa reader. The Inhibitory concentration values (IC_{50}) were calculated from plotted absorbance.^{xxxviii-xxxxx}

3.RESULTS AND DISCUSSION

3.1. INFRARED SPECTROSCOPY

The FT-IR Spectra of Imine base ligand and its mono nuclear metal complexes were recorded using KBr pellets in the range of 4000-250 cm^{-1} . The Imine base ligand showed some

important stretching frequency bands at 3633 cm^{-1} assigned for phenolic O-H group, 1637 cm^{-1} assigned for -HC=N- imine group and 1199 cm^{-1} assigned for phenolic C-O group. The infraed spectra of mono nuclear metal complexes bands at 1595-1637 cm^{-1} assigned for C=N azomithane group, 1190-1199 cm^{-1} assigned for C-O group, M-O and M-N bands present at 511-547 cm^{-1} and 449-495 respectively. The experimental results showed in **Table 1**. Which are at Imine base ligand towards lower frequency in mono nuclear complexes.

Table 1 FT-IR spectral stretching frequency bands (cm^{-1}) of Imine base ligand and its mono nuclear metal complexes

Compounds Code	$\nu(\text{H}_2\text{O}/\text{OH})(\text{cm}^{-1})$	$\nu(\text{HC}=\text{N})(\text{cm}^{-1})$	$\nu(\text{C}-\text{O})(\text{cm}^{-1})$	$\nu(\text{M}-\text{O})(\text{cm}^{-1})$	$\nu(\text{M}-\text{N})(\text{cm}^{-1})$
3a	3633	1637	1199	-	-
4a	3379	1600	1190	542	449
4b	3313	1600	1195	547	487
4c	3323	1595	1193	547	495
4d	3358	1600	1192	511	459
4e	3442	1616	1193	538	453

3.2. MASS SPECTRUM OF COMPOUNDS

The Electrospray ionization Mass spectra of Imine base ligand calculated mass value 348 and obtained molecular ion peak at m/z 349 and its mono nuclear $[\text{Cu}^{\text{II}}(\text{L})(\text{CH}_3\text{COO})(\text{H}_2\text{O})]$ complexes calculated mass value 487 and obtained molecular ion peak at m/z 489, furthermore $[\text{Co}^{\text{II}}(\text{L})(\text{CH}_3\text{COO})(\text{H}_2\text{O})]$ calculated mass value 483 and molecular ion peak at m/z 484, $[\text{Ni}^{\text{II}}(\text{L})(\text{CH}_3\text{COO})(\text{H}_2\text{O})]$ calculated mass value 482 and obtained molecular ion peak at m/z 484, $[\text{Zn}^{\text{II}}(\text{L})(\text{CH}_3\text{COO})(\text{H}_2\text{O})]$ calculated mass value 489 and molecular ion peak at m/z 490 and $[\text{Cd}^{\text{II}}(\text{L})(\text{CH}_3\text{COO})(\text{H}_2\text{O})]$ calculated mass value 536 and molecular ion peak at m/z 536.

3.3. POWDER XRD ANALYSIS

The Imine base ligand and its mono nuclear metal complexes, their crystalline size and structure have been investigated by using X-ray powder diffraction method. The sharp peaks confirmed by crystalline nature of Imine base and their mono nuclear metal complexes. The X-ray diffraction spectra of Imine base and their mono nuclear metal complexes are shown in **Fig. 1**. The calculation of average particle size of compounds was using by Debye-Scherrer's equation 4.

$$D = 0.9\lambda/\beta \cos\theta \quad (4)$$

Here, θ is the Bragg diffraction angle for the hkl plane, β is the FWHM (Full width at half maximum), λ is the wavelength of X-ray diffraction, constant 0.9 is the sharp factor.

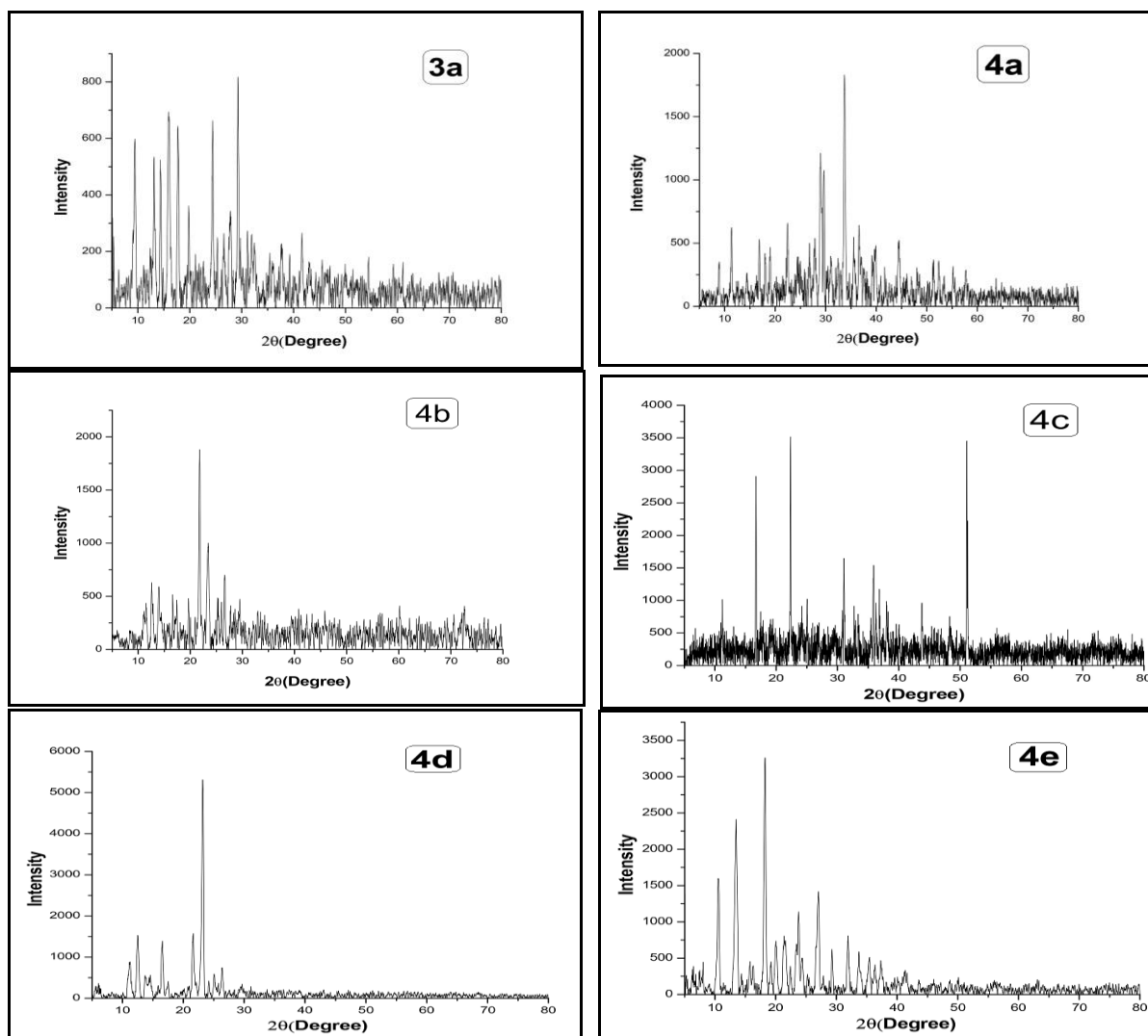
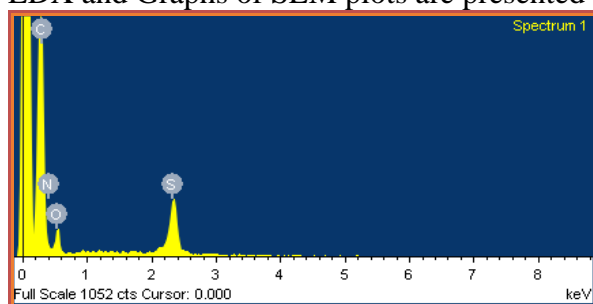


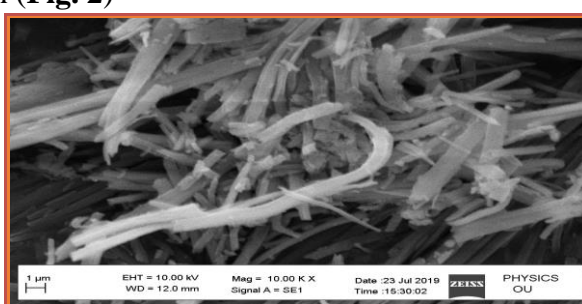
Fig. 1 Powder XRD patterns of **3a**, **4a-4e** mono nuclear metal complexes

3.4 EDX AND SEM

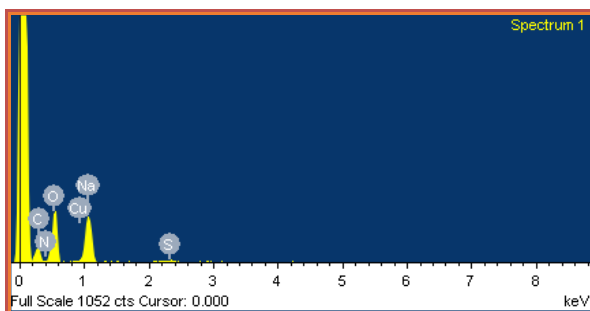
The Imine base ligand and its mono nuclear, metal complexes were composition of elements evaluated by using Energy dispersive X-ray analysis (EDX) and surface morphology explained by using Scanning Electron Microscopy (SEM). The EDX data analysis indicated the elemental composition of all the mono nuclear metal complexes. The SEM micrographs discovered that the surface morphology of mono nuclear metal complexes differ from Imine base ligand and each other due to the complexation and change of metal ion. Photography of EDX and Graphs of SEM plots are presented in (Fig. 2)



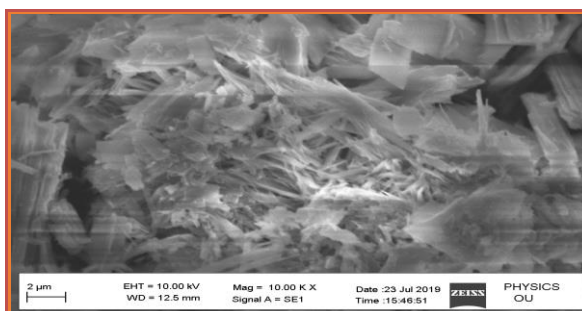
Photography of EDX Ligand (**3a**)



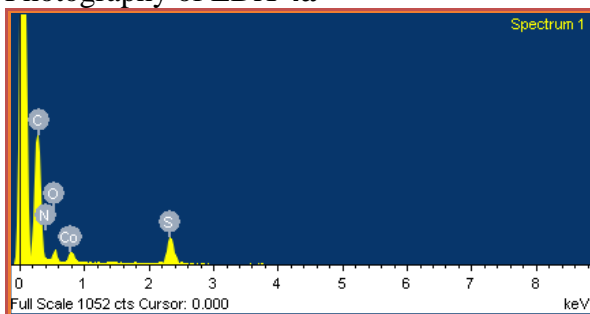
Graph of SEM Ligand (**3a**)



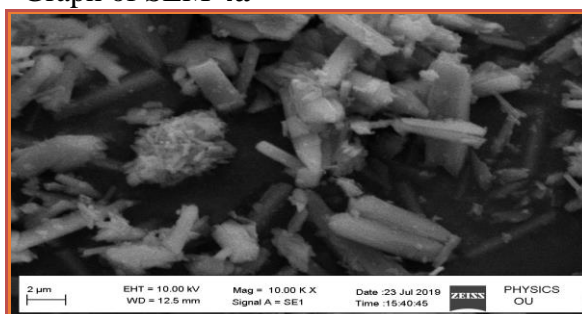
Photography of EDX 4a



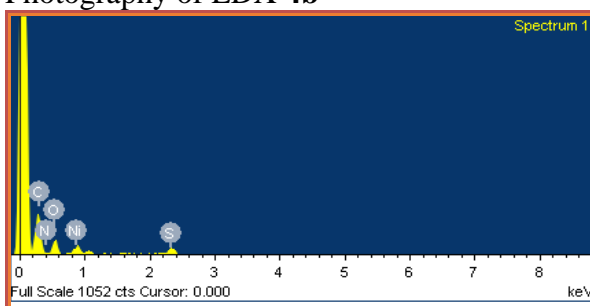
Graph of SEM 4a



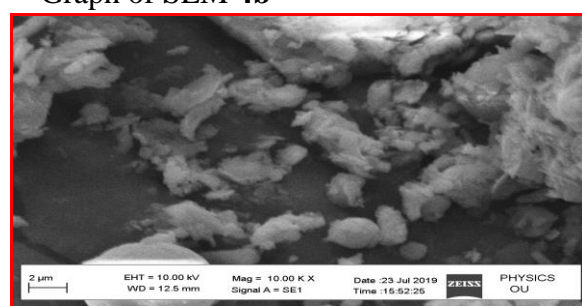
Photography of EDX 4b



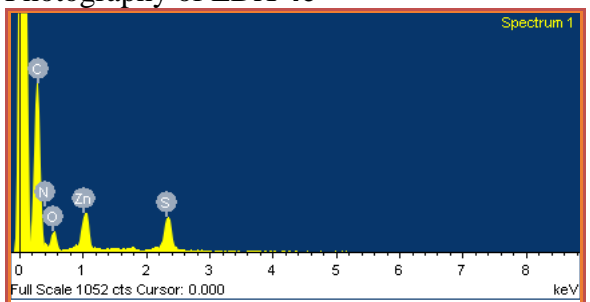
Graph of SEM 4b



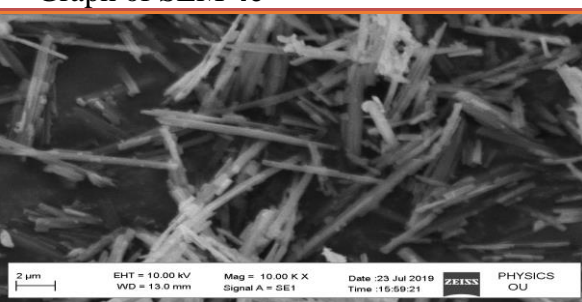
Photography of EDX 4c



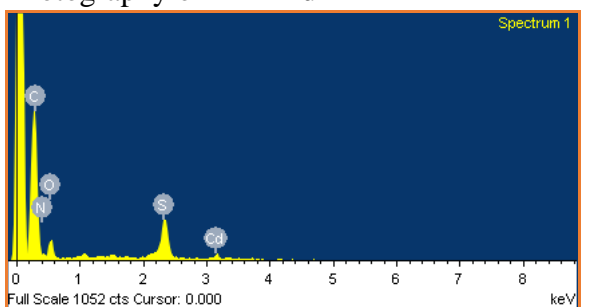
Graph of SEM 4c



Photography of EDX 4d



Graph of SEM 4d



Photography of EDX 4e



Graph of SEM 4e

Fig. 2 Photography's of EDX and Graphs of SEM for **3a**, **4a-4e** mono nuclear metal complexes

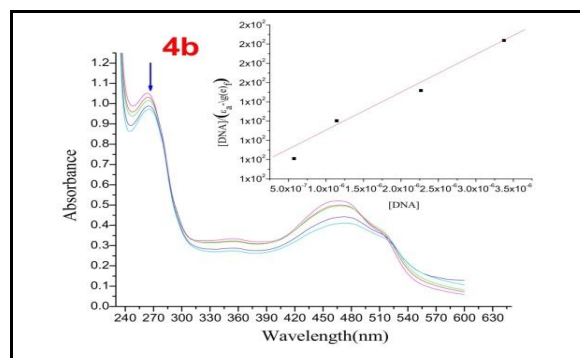
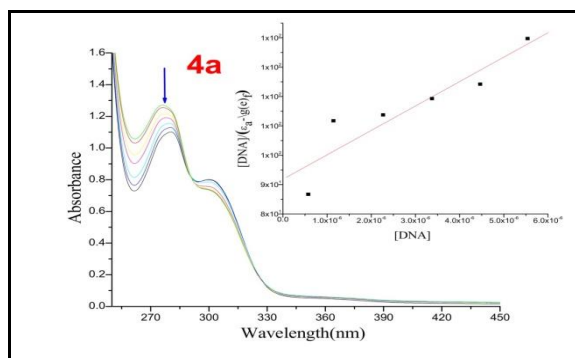
3.5. SPECTRAL STUDIES OF DNA BINDING

3.5.1. ELECTRONIC SPECTROSCOPY OF DNA BINDING

The Electronic spectroscopy was used to measure the binding interaction of mono nuclear metal complexes with base pairs of CT-DNA. The binding interaction of the five mono nuclear metal complexes to the absence and presence of CT DNA was characterized by resulting exhibited hypochromism and shift in the wave length with bathochromic/red shift due to intercalation mode involving a strong stacking interaction between aromatic chromophores in the Imine base ligand and DNA base pairs. The Electronic spectra of the mono nuclear metal complexes in the absence and presence of DNA are shown in (**Fig. 3**). The $[\text{Cu}^{\text{II}}(\text{L})(\text{CH}_3\text{COO})(\text{H}_2\text{O})]$ complex intrinsic binding constant is $9.06 \times 10^5 \text{ M}^{-1}$ and two absorption bands at 277 nm and 300 nm, furthermore $[\text{Co}^{\text{II}}(\text{L})(\text{CH}_3\text{COO})(\text{H}_2\text{O})]$ complex intrinsic binding constant $8.24 \times 10^5 \text{ M}^{-1}$ and three absorption bands at 265 nm, 354 nm and 465 nm, $[\text{Ni}^{\text{II}}(\text{L})(\text{CH}_3\text{COO})(\text{H}_2\text{O})]$ complex intrinsic binding constant $4.05 \times 10^4 \text{ M}^{-1}$ and three absorption bands at 262 nm, 353 nm and 463 nm, $[\text{Zn}^{\text{II}}(\text{L})(\text{CH}_3\text{COO})(\text{H}_2\text{O})]$ complex intrinsic binding constant $1.20 \times 10^4 \text{ M}^{-1}$ and three absorption bands at 257 nm, 360 nm and 485 nm and $[\text{Cd}^{\text{II}}(\text{L})(\text{CH}_3\text{COO})(\text{H}_2\text{O})]$ complex intrinsic binding constant $1.08 \times 10^4 \text{ M}^{-1}$ and three absorption bands at 276 nm, 299 nm and 451 nm. The resulting data indicated that the binding affinity between all the mono nuclear metal complexes potential intercalator like EB (Ethidium bromide). The Cu(II), Co(II) and Ni(II) mono complexes bound strongly to DNA compare to other mono nuclear metal complexes. (**Table 2**)

Table 2 Interactions of mono nuclear Complexes with Calf thymus DNA (CT-DNA) Intrinsic Binding Constant (K_b), Emission Constant (K_{sv}), and R values

Compound codes	CT-DNA		
	K_b	K_{sv}	R
4a	$9.06 \times 10^5 \text{ M}^{-1}$	$8.4 \times 10^4 \text{ M}^{-1}$	0.95
4b	$8.24 \times 10^5 \text{ M}^{-1}$	$6.4 \times 10^4 \text{ M}^{-1}$	0.99
4c	$4.05 \times 10^4 \text{ M}^{-1}$	$1.8 \times 10^4 \text{ M}^{-1}$	0.98
4d	$1.20 \times 10^4 \text{ M}^{-1}$	$1.5 \times 10^4 \text{ M}^{-1}$	0.95
4e	$1.08 \times 10^4 \text{ M}^{-1}$	$4.5 \times 10^3 \text{ M}^{-1}$	0.96



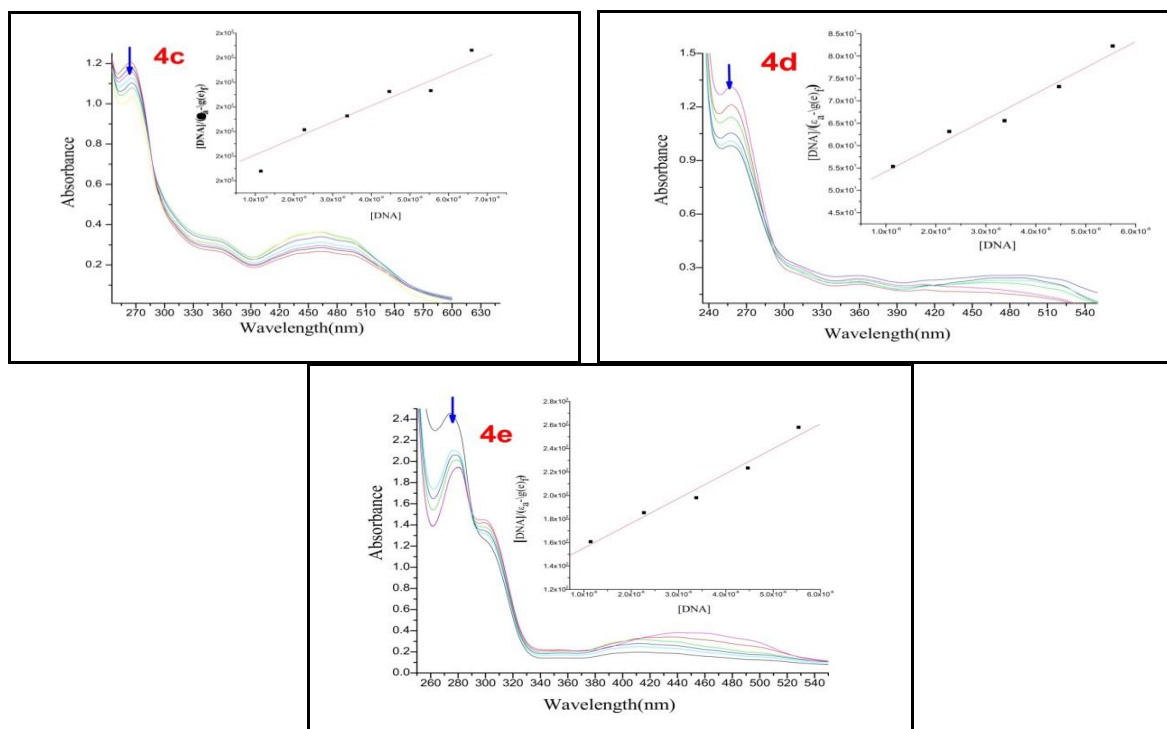
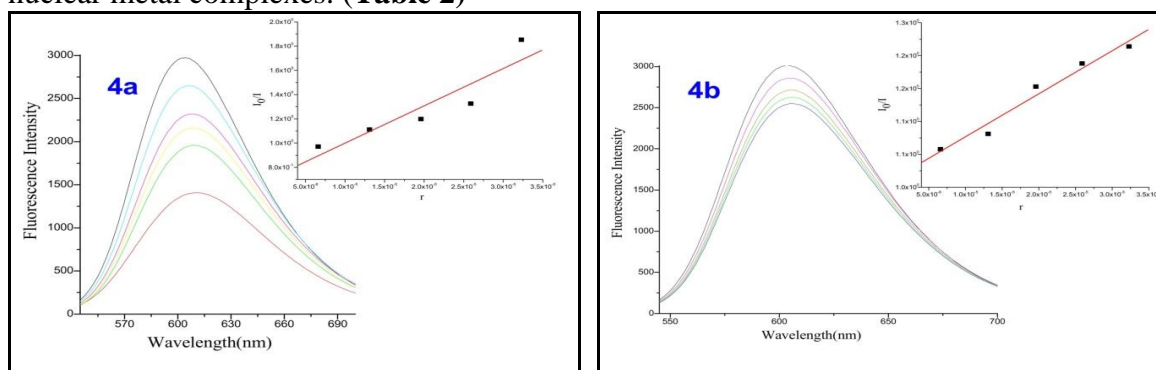


Fig.3 UV-Visible absorption spectra of **4a- 4e** mono nuclear metal complexes in Phosphate buffer pH=7.2. The arrow shows the bathochromic shift and hypochromic upon increasing concentration of Calf thymus DNA (CT-DNA)

3.5.2 FLUORESCENCE QUENCHING OF DNA BINDING

The emission spectroscopy used to binding mode of mono nuclear metal complexes with CT DNA in the presence of ethidium bromide strong fluorescence active substance. The ethidium bromide solution bound CT DNA and fluorescence peaks showed in the range of 580-595 nm. In the presence of DNA, intensity of fluorescence increases due to strong intercalation between ethidium bromide and DNA base pairs. The experimental observations increasing the mono nuclear metal complexes concentration then decreases intensity of EB-DNA due to complex competitive binding to EB bound DNA (**Fig. 4**). The $[\text{Cu}^{\text{II}}(\text{L})(\text{CH}_3\text{COO})(\text{H}_2\text{O})]$ complex binding constant is $6.4 \times 10^4 \text{ M}^{-1}$, Furthermore $[\text{Co}^{\text{II}}(\text{L})(\text{CH}_3\text{COO})(\text{H}_2\text{O})]$ complex binding constant $6.4 \times 10^4 \text{ M}^{-1}$, $[\text{Ni}^{\text{II}}(\text{L})(\text{CH}_3\text{COO})(\text{H}_2\text{O})]$ complex binding constant is $1.8 \times 10^4 \text{ M}^{-1}$, $[\text{Zn}^{\text{II}}(\text{L})(\text{CH}_3\text{COO})(\text{H}_2\text{O})]$ complex binding constant is $1.5 \times 10^4 \text{ M}^{-1}$ and $[\text{Cd}^{\text{II}}(\text{L})(\text{CH}_3\text{COO})(\text{H}_2\text{O})]$ complex binding constant $4.5 \times 10^3 \text{ M}^{-1}$. The mono nuclear metal complexes interacting with Calf thymus DNA through an intercalation mode and it is clear from K_{SV} values that Cu^{II} and Co^{II} complexes bound strongly with DNA than the other mono nuclear metal complexes. (**Table 2**)



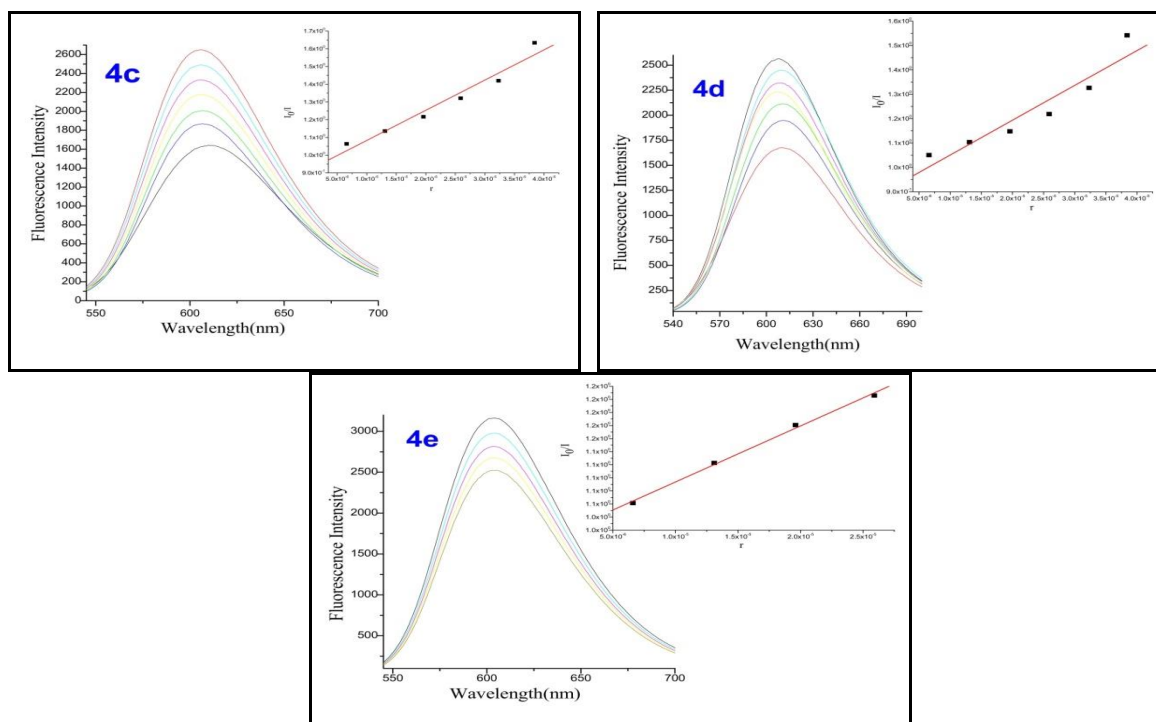


Fig. 4 Emission spectra of **4a-4e** mono nuclear metal complexes. The DNA-EB system in the absence and presence of increasing concentrations of all the mono nuclear metal complexes. Arrows shows changes the emission intensity upon increasing concentrations of all the mono nuclear metal complexes

3.5.3. VISCOSITY TITRATION OF DNA BINDING

The binding interaction between the mono nuclear metal complexes and Calf Thymus DNA (CT-DNA), the Viscosity measurements were evaluated by using CT-DNA with increasing concentrations of the mono nuclear metal complexes. The DNA binding mode can be explained by DNA chain length during the interaction between mono nuclear metal complexes and Calf Thymus DNA. In the Intercalation mode study confirmed that the binding interaction between the mono nuclear metal complexes and base pairs of DNA due to increase in the shape length of DNA. In addition, increasing concentrations of all the mono nuclear metal complexes **4a**, **4b**, **4c**, **4d** and **4e** to DNA show a systematic increase in the viscosity. All the mono nuclear metal complexes viscosity of CT-DNA is shown in **Fig 5**. Increasing order of DNA viscosity of all the mono nuclear metal complexes $4a > 4b > 4c > 4d > 4e$.

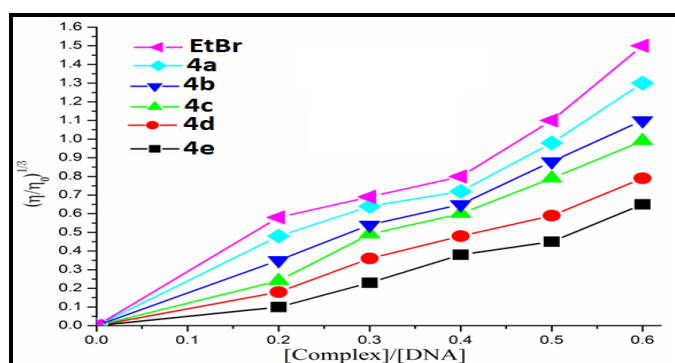


Fig. 5 Viscosity of Ethidium bromide (EB) solution, Imine base ligand and its mono nuclear metal complexes

3.6. DNA PHOTO CLEAVAGE STUDIES

The DNA photo cleavage activity of Imine base ligand and their mono nuclear metal complexes **4a-e** are shown in **Fig. 6**. In this method Lane 1. no DNA Cleavage observed (DNA ladder), lane 2 DNA control, lane 3 DNA+H₂O₂, **3a**. DNA+H₂O₂+Imine bas ligand, **4a**. DNA+H₂O₂+Cu^{II} complex, **4b**. DNA+H₂O₂+Co^{II} complex, **4c**. DNA+H₂O₂+Ni^{II} complex, **4d**. DNA+H₂O₂+Zn^{II} complex and **4e**. DNA+H₂O₂+Cd^{II} complex, Photo cleavage in CT DNA is substantail. Having a base of results it is concluded that the Cu^{II} complexes promote the cleavage DNA more efficiently compare to other mono nuclear metal complexes. Other mono nuclear complexes cleaved in the order of Co^{II}>Ni^{II}>Zn^{II}>Cd^{II}.

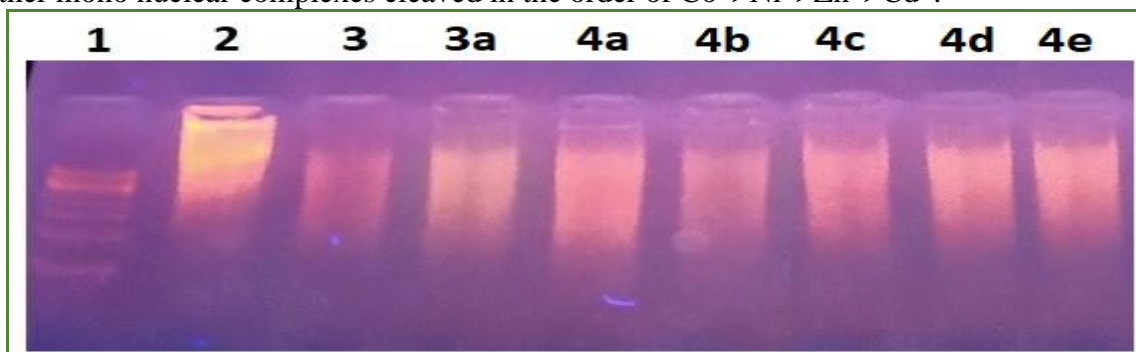


Fig. 6 Photography of Imine base ligand and its mono nuclear complexes by Agarose gel electrophoresis method **1**. DNA ladder **2**. DNA control **3**. DNA+H₂O₂ **3a**. DNA+H₂O₂+Imine base **4a**. DNA+H₂O₂+Cu^{II} complex **4b**. DNA+H₂O₂+Co^{II} complex **4c**. DNA+H₂O₂+Ni^{II} complex **4d**. DNA+H₂O₂+Zn^{II} complex **4e**. DNA+H₂O₂ +Cd^{II} complex

3.7. IN VITRO ANTIBACTERIAL ACTIVITY

The minimum inhibitory concentration (MIC's, µg/mL) of novel synthesized Imine bas ligand their mono nuclear metal complexes was showed very low concentration level was compared with known antibiotic (Ciprofloxacin) against antibiotic susceptible strains of bacteria.

Table 3 Imine base ligand and their mono nuclear metal complexes antibacterial activities MIC values in µg/mL

Compound codes	<i>E. coli</i>	<i>K. pneumoniae</i>	<i>P. aeruginosa</i>	<i>S. aureus</i>	<i>S. pyogenes</i>
3a	11.6±1.36	9.1±0.49	10.8±0.27	10.5±0.09	13.0±1.06
4a	7.9±1.19	7±0.08	8.1±0.20	6.9±0.30	8±0.98
4b	7.7±0.89	7.2±0.58	8±0.76	7.5±1.89	8.6±1.77
4c	9.5±0.20	8.8±0.12	7.4±0.13	7.4±0.10	8.4±0.69
4d	8.3±0.61	6.8±1.51	7.6±1.20	7±0.91	7.8±1.02
4e	9.6±0.18	8±0.84	8.8±0.11	7.7±0.76	8±0.09
Ciprofloxacin	9.8±1.08	4.5±1.34	8.08±0.79	8.12±0.75	9.5±0.11

3.8. IN VITRO CYTOTOXICITY ASSAYS

The newly synthesized Imine base ligand and its mono nuclear metal complexes were screened for their cytotoxic activities against Human cervical cancer cell lines and Human breast adenocarcinoma cell lines using investigating by MTT assay. The Cytotoxicity cells were exposed to three different concentrations. The mono nuclear metal complexes are lower IC₅₀ values compare to Imine base ligand. The screening results indicated that all the mono nuclear metal complexes shown potent anticancer activity listed in **Table 4**. The order of Inhibitory concentration values (IC₅₀) of Imine base ligand and mono nuclear metal complexes against both cell lines as **4a>4b>4c>4d>4e>** Imine base ligand. (**Fig.7**)

Table 4 Imine base ligand and its mono nuclear metal complexes against HeLa and MCF-7 cell lines IC₅₀ values

Compound codes	Inhibitory concentration values (IC ₅₀)	
	HeLa	MCF-7
3a	76.20±2.9µM	81.45±3.5Mm
4e	66.34±2.3µM	72.23±2.7µM
4d	59.65±1.6µM	61.43±1.9µM
4c	53.81±1.7µM	53.61±1.6µM
4b	49.34±1.7µM	46.43±1.9µM
4a	39.25±1.6µM	35.76±1.7µM
Cisplatin	13.10±1.4µM	10.13±2.1µM

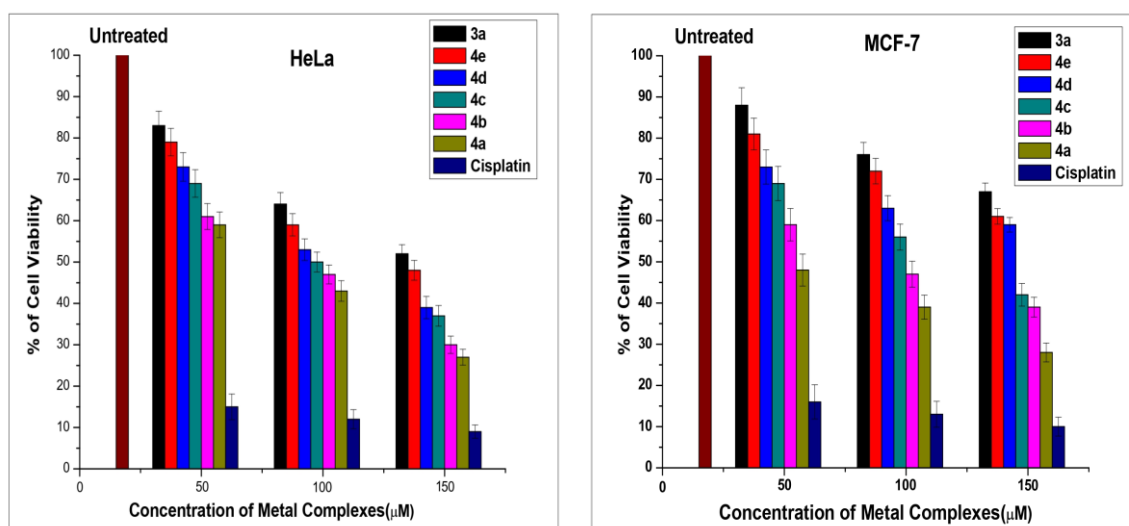


Fig. 7 Cytotoxicity evaluation of **3a**, **4a-4e** on growth and cell viability analysis by HeLa and MCF-7 cell lines was evaluated by MTT assay with 50,100 and 150 three different concentrations

4. CONCLUSION

The Imine base ligand and five mono nuclear metal complexes were synthesized and characterized. The analytical data allow assigning **4a**, **4b**, and **4c** complexes are square planar and **4d** and **4e** complexes are tetrahedral geometry. The binding interactions of the mono nuclear metal complexes with calf thymus have been investigated by electronic, emission spectra titration and viscosity measurements studies. The DNA photo cleavage affinity tendency of all the mono nuclear metal complexes was tested with calf thymus DNA in the presence of UV light and hydrogen peroxide (H₂O₂). In addition, antibacterial and cytotoxic

activities screening results of all the mono nuclear metal complexes are better activity compare to Imine base ligand. The Cu(II) complex exhibit more potent activity compare to other mono nuclear metal complexes

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