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Anti-Tuberculosis, Cytotoxic, Antimicrobial and DNA Cleavage Evaluation of Mononuclear Metal Complexes of Quinoline Schiff Base: Synthesis and Spectral Approach

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ABSTRACT

The condensation of 2-hydrazino-4-phenyl thiazole and 3-formyl-2-hydroxyquinoline has led to the synthesis of a new Schiff base (L) and its series of mononuclear Co(II), Ni(II) and Cu(II) complexes have also been synthesized. The synthesized Schiff base and its metal complexes were characterized by elemental analyses, spectral techniques (FT-IR, ^{1}H-NMR, ^{13}C-NMR, GC-MS, ESI-MS, UV-Vis, etc;) and magnetic studies. Elemental analyses reveals the $[M(L)_2.(H_2O)_2]$ stoichiometry, where M= Co(II), Ni(II) and Cu(II); "L"= doubly deprotonated ligand. The synthesized metal complexes are completely soluble in DMF and DMSO. The molar conductivity values indicate that, the metal complexes are non-electrolytic in nature. The newly synthesized compounds are good anti-tuberculosis and cytotoxic agents. They have been screened for *in-vitro* antibacterial and antifungal activities by MIC method. The DNA cleavage activity is studied by agarose gel electrophoresis method using pBR322 Plasmid DNA.

Keywords: Quinoline Schiff base, Mononuclear metal complexes, Electronic spectral studies, Anti-tubercular activity, Cytotoxicity, DNA Cleavage studies.

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INTRODUCTION

Nitrogen containing heterocyclic compounds have been widely used in pharmaceutical industries; as they show diverse biological activities [1-3]. Quinoline and its derivatives represent the major class of heterocyclic compounds and are considered as the backbone for most of the natural products. Many quinoline based synthetic compounds having diverse pharmacological applications such as antioxidant [4], anti-proliferation [5]**,** anti-inflammatory [6]**,** antimalarial [7], antiplasmodial [8], cytotoxic [9], antihypertensive [10] and anti-cancer [11,12] activities.

Such a wide spectrum of biological applications of quinoline, forced us to synthesize the transition metal complexes with quinoline Schiff base. Further, many investigations have shown that, the binding of a drug to a metalloelement enhances its activity and in some cases, the metal complex possesses even more healing properties than its respective Schiff base [13].

Thiazole is a heterocyclic compound constituting nitrogen and sulphur in its five membered ring, which are well known for their vitality in the coordination of mononuclear metal ions at active sites of numerous metallobiomolecules [14]. Thiazole and many substituted thiazoles possess the interesting biological activities, probably conferred to them by the strong aromaticity of their ring system [15]. Since last decade, thiazole-containing chelating agents and their metal derivatives have gained the interest due to their potency towards anticancer [16-18], anti-inflammatory [19], anti-degenerative [20], anti-HIV [21] and antimicrobial [22] activities. The mononuclear metal complexes of thiazole derivatives are known to exhibit cytotoxic effect against melanoma MW-115 cell lines [23].

Hence, in the light of wide applications of coordination compounds and paucity of literature in various fields encouraged us to undertake the present investigation.

MATERIALS AND METHOD

Reagents

All chemicals used in the present investigation for the synthesis of Schiff base and its metal complexes were of reagent grade and used without further purification. Thin Layer Chromatography (TLC) used was 0.20mm Aluchrosep Silica Gel 60/UV 254 TLC on silica gel coated plates (Merck, Mumbai)

Physical measurements

Carbon, hydrogen and nitrogen were estimated by using Elemental Analyzer Carlo Erba EA1108 analyzer. The IR spectra of the Schiff base and its Co(II), Ni(II) and Cu(II) metal complexes were recorded on a HITACHI-270 IR spectrophotometer in the 4000-400 cm^{-1} region in KBr disc. The electronic spectra of the complexes were recorded in HPLC grade DMSO on a VARIAN CARY

50-BIO UV-spectrophotometer in the region of 200-1000 nm. The ^{1}H-NMR and ^{13}C-NMR spectra of the Schiff base were recorded in d$_6$-DMSO on a BRUKER 400 MHz spectrometer at room temperature using TMS as an internal reference. The mass spectra of Schiff base and metal complexes were recorded in GCMS and ESI-MS respectively. Molar conductivity measurements were recorded on ELICO-CM-82 T Conductivity Bridge with a cell constant of 0.5 and magnetic moment measurement was carried out by using Faraday balance.

Synthesis

Preparation of 3-formyl-2-hydroxyquinoline [24,25]**:**

9.6 mL of DMF was taken in round bottom flask and kept at 0 ^{0}C, with constant stirring 32.2 mL of $POCl_3$ was added drop wise to prepare Vilsmeier-Haack reagent. To the above reagent, 6.75g of acetanilide was added and stirred again for another 15-20 min. at room temperature. The resulting solution was heated on a water bath for 16h, cooled and poured on to crushed ice. The separated pale yellow solid was filtered and recrystallized using ethyl acetate to get 2-chloro-3-formylquinoline. The obtained compound was refluxed with 4M HCl for 10h and then quenched in ice cold water to obtain the desired compound and recrystallized with aqueous CH_3COOH.

Preparation of 2-Hydrazino-4-phenylthiazole [26,27] **:**

Potassium acetate (12.5 mmoles) was dissolved in 40 mL of aqueous ethanol (1:1) with stirring then thiosemicarbazide (12.5 mmoles) and phenacyl bromide (12.5 mmoles) were introduced; stirring was continued. After 3 hours of stirring at room temperature the separated solid was filtered, washed with cold alcohol and dried. The compound was recrystallized from alcohol. Yield: 82%; M.P: 162-163 ^{0}C.

Synthesis of Schiff base (L)

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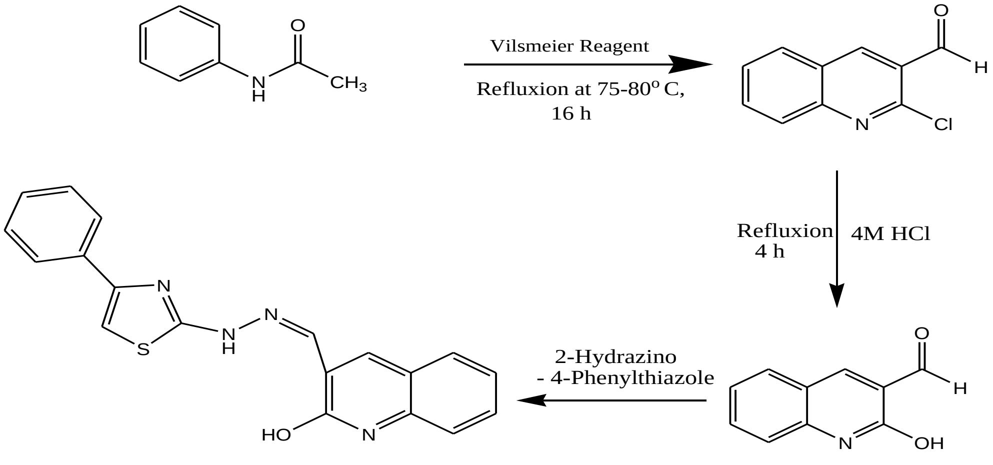


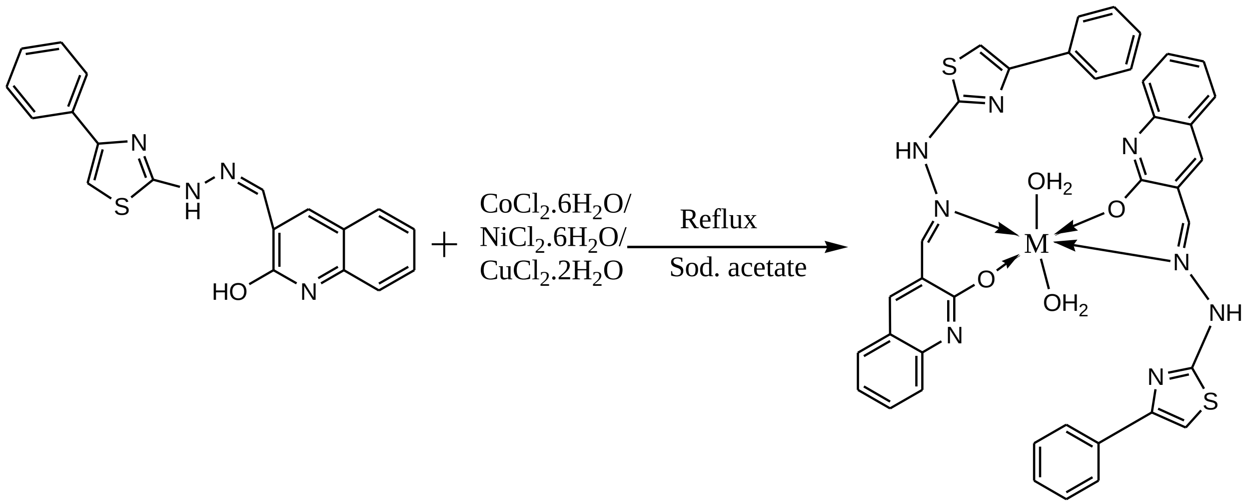
Scheme 1: Synthesis of Schiff Base

2-Hydrazino-4-phenylthiazole(2.6 mmoles) was dissolved in ethanol with stirring, then an ethanolic solution of 3-formyl-2-hydroxyquinoline (2.6 mmoles) was gradually added to it. The reaction mixture was refluxed for about 5-6 hours; progress of the reaction was monitored by TLC at regular intervals. The reaction mixture was filtered to collect the yellow colored solid formed, dried and recrystallized in methanol. Synthesis of the Schiff base (L) is shown in **Scheme 1**

Synthesis of Metal Complexes

General procedure for the synthesis of metal complexes (Scheme-2)

An alcoholic solution of Schiff base (L) (2 mmoles) was refluxed with 1 mmole of $CoCl_2.6H_2O/NiCl_2.6H_2O/CuCl_2.2H_2O$ in ethanol on water bath for 1h. Then, sodium acetate (2 mmoles) was added to the reaction mixture and was continued to reflux for 3h. The separated metal complexes were filtered and washed thoroughly with water, ethanol and ether. Finally, the metal complexes were dried in vacuum over fused $CaCl_2$.



Scheme 2: **Synthesis of Metal Complexes (1-3).**

Pharmacology

Anti-Tuberculosis Activity

The anti-tuberculosis activity of the newly synthesized compounds was assessed against M. tuberculosis ATCC 27294 using microplate Alamar Blueassay (MABA). This methodology is non-toxic, utilizes a thermally stable reagent and shows good correlation with proportional and BACTEC radiometric method. Briefly, 200 mL of sterile deionized water was added to all outer perimeter wells of sterile 96 wells plate to minimize the evaporation of medium in the test wells during incubation. The 96 wells plate received 100 mL of the Middlebrook7H9 broth and serial dilution of compounds were made directly on plate. The final drug concentrations tested were 100 to 0.2 mg/mL. Plates were covered and sealed with parafilm and incubated at 37 ^{0}C for five days. After this time, 25 mL of freshly prepared 1:1 mixture of Almar Blue reagent and 10% tween 80 were added to the plate and incubated for 24 h. A blue color in the well was interpreted as no bacterial growth, and pink color was scored as growth. The MIC was defined as lowest drug concentration which prevented the color change from blue to pink.

Cytotoxic Activity

Assays for in vitro cytotoxicity against Vero Cells

To obtain an insight into the potential toxicities of the synthesized compounds, they were further tested for their cytotoxicity against Vero Cells at the concentration 10 times their actual MIC value. The cytotoxicity of compounds with MIC ≤ 6.25 mg/mL was evaluated in Vero cells, which were cultured in Dulbecco Modified Eagle Medium (DMEM) containing 2 mM Na_2CO_3 supplemented with 10% (v/v) Fetal Bovine Serum (FBS). The cells were incubated at 37 ^{0}C under 5% CO_2 and 95% air in a humidified atmosphere until confluent and then diluted with phosphate-buffered saline to106 cells/mL. Stock solutions were prepared in dimethyl sulfoxide (DMSO) and further dilutions were made with fresh culture medium. The medium was removed and replaced by 180 mL of fresh medium containing the test compounds at concentration 10 folds their actual MIC values. After incubation at 37 ^{0}C for 72 h, medium was removed and monolayer was washed twice with 100 mL of warm Hanks' balanced salt solution (HBSS). One hundred microliters of warm medium and 20 mL of freshly made MTS-PMS[3-(4,5-dimethylthiazol-2-yl)-5-(3-carboxymethoxyphenyl)-2-(4-sulfophenyl)-2H-tetrazolium and phenylmethasulfazone] (100:20) (Promega) were added to each well; plates were incubated for 3 h, and absorbance was determined at 570 nm using a microplate reader. Percentage of cell survival was calculated considering the control wells (cells incubated in DMSO-containing medium).

DNA Cleavage Activity

For the gel electrophoresis experiments, solutions of the complexes in DMSO (1 mg/mL) were prepared and these test samples (100 µM) were added to the pBR322 plasmid DNA and incubated for 2 h at 37 ^{0}C. Agarose gel was prepared in TAE buffer (4.84 g Tris base, pH 8.0, 0.5 MEDTA/l pH 7.3), the solidified gel obtained at 55 ^{0}C was placed in an electrophoresis chamber flooded with TAE buffer. Then, each of the incubated complex-DNA mixtures (mixed with bromophenol blue dye at a 1:1 ratio) was loaded on the gel along with the standard DNA marker, and the electrophoresis was carried out under the TAE buffer system at 100 V for 2 h. At the end of electrophoresis, the gel was carefully stained with EtBr (ethidium bromide) solution (10 lg/mL) for10–15 min and visualized under UV light using a Bio-Rad Geldoc gel imaging system.

Antimicrobial Activity

Microbial strains *Staphylococcus aureus*, *Escherichia coli*, *Aspergillus fumigates* and *Candida albicans* were used in the present study. MIC was determined by the micro dilution method using a 96 well plate according to the NCCLS (National Committee on Clinical Laboratory Standards). First, 100 µL of Mueller-Hinton broth (for bacterial strains) or Sabouraud dextrose broth (for fungal strains) was placed in each well. The stock solutions of the extracts were diluted and transferred into the first well and serial dilutions were performed; so that, concentrations in the range of 100-0.781µg/mL were obtained. The inoculums were adjusted to contain approximately 10^5 CFU/mL of bacteria and 10^4 CFU/mL of fungi. One hundred micro liters of the inoculums were added to all the wells and the plates were incubated at 37 ^{0}C for 24 h for bacteria and at 30 ^{0}C for 48 h for fungi. Antimicrobial activity was detected by adding 20 µL of 0.5% TTC aqueous solution. The MIC value taken was the lowest concentration of the extract that inhibited any visible bacterial or fungal growth, as indicated by TTC staining after incubation. Nystatin and Gentamycin were used as the reference antibiotic controls.

RESULTS AND DISCUSSION

The synthesized Schiff base and its Co(II), Ni(II) and Cu(II) complexes are non-hygroscopic coloured solids, stable at room temperature and completely soluble in DMF and DMSO. Carbon, hydrogen and nitrogen were estimated by using a C, H, N analyzer. The low conductance values confirm the non-electrolytic nature of all the synthesized metal complexes. Elemental analyses, molar conductance and magnetic moment values are listed in Table 1.

Table 1: Elemental Analyses of Schiff Base and its Metal Complexes along with Molar Conductance and Magnetic Moment Data.

Compound Name	**Empirical Formula**	**Colour / Yield %**	**M%**		**C%**		**H%**		**N%**		**Molar Cond.(Ohm^{-1} cm^{-2} mole^{-1})**	**μ_{eff} (BM)**
			Obsd.	**Calcd.**	**Obsd.**	**Calcd.**	**Obsd.**	**Calcd.**	**Obsd.**	**Calcd.**		
Schiff Base	$C_{19}H_{14}N_4OS$	Yellow/ 68%	-	-	65.76	65.88	3.97	4.07	16.23	16.17	-	-
Co(II)$L_2.(H_2O)_2$	$Co(C_{19}H_{14}N_4OS)_2.(H_2O)_2$	Light Brown / 65%	7.49	7.51	58.08	58.13	3.32	3.34	14.20	14.27	20.22	4.85
Ni(II)$L_2.(H_2O)_2$	$Ni(C_{19}H_{14}N_4OS)_2.(H_2O)_2$	Dark Brown/ 63%	7.45	7.48	58.11	58.15	3.29	3.34	14.25	14.28	17.26	3.20
Cu(II)$L_2.(H_2O)_2$	$Cu(C_{19}H_{14}N_4OS)_2.(H_2O)_2$	Dark Brown / 66%	7.98	8.05	57.73	57.79	3.28	3.32	14.12	14.19	22.57	1.80

NMR Spectral Studies

The ^{1}H and ^{13}C NMR spectra were recorded in d_6-DMSO for the synthesized Schiff base. ^{1}H NMR spectrum revealed that, the singlet peaks at 12.34, 12.00 and 8.28 ppm are respectively assigned to the protons of –NH, –OH and –HC=N [Figure. 1]. The resonance of remaining protons was observed in the aromatic region. In ^{13}C NMR spectrum [Figure 2] the peaks of C-OH, C-NH, C=N and C-S are observed at 167, 164, 160 and 103 ppm respectively and rest are in the aromatic region.

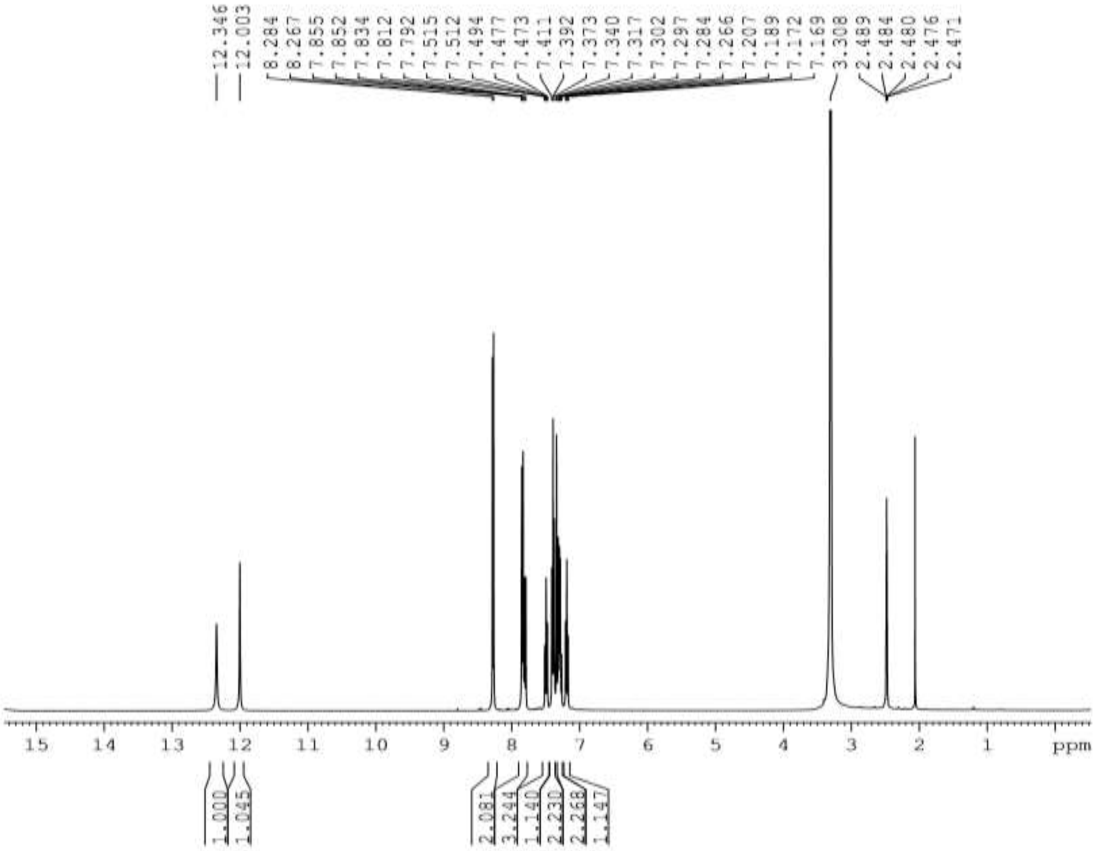


Figure 1: ^{1}H NMR Spectrum of Schiff Base (L).

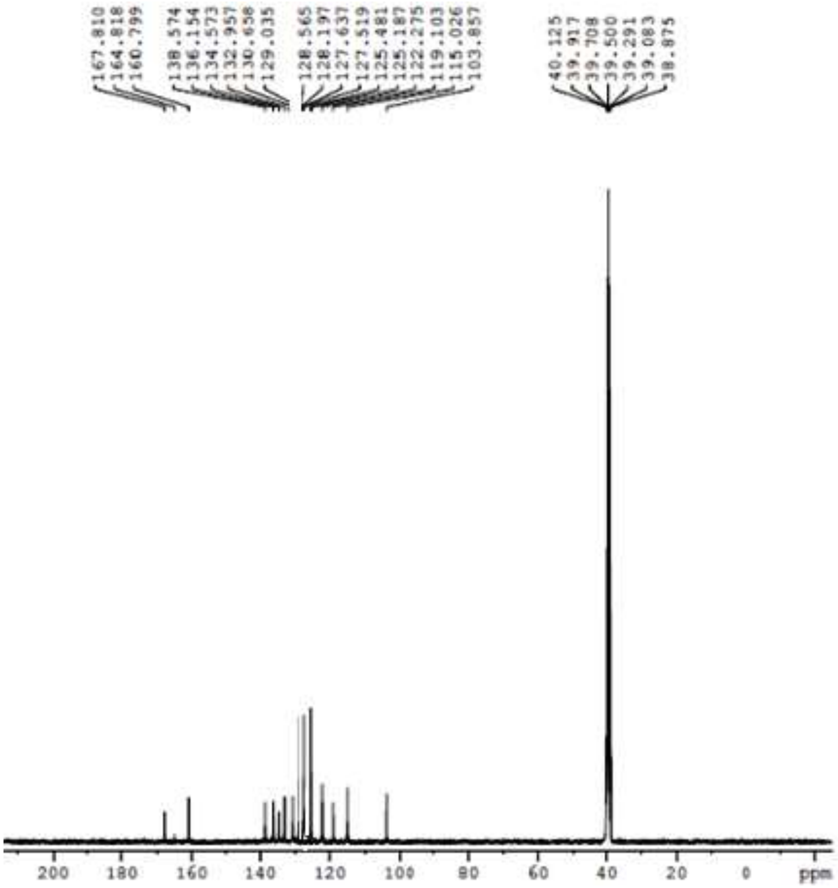


Figure 2: ^{13}C NMR Spectrum of Schiff Base (L).

Mass Spectral Study

The formation of Schiff base was confirmed by its mass spectrum analysis. The mass spectrum of Schiff base exhibited a molecular ion peak at m/z 346; which is equivalent to its molecular weight. The fragmentation peak at m/z 329 is due to cleavage of -OH group and the peak at m/z 176 is due to the cleavage of Schiff base at N-N [Figure. 3].

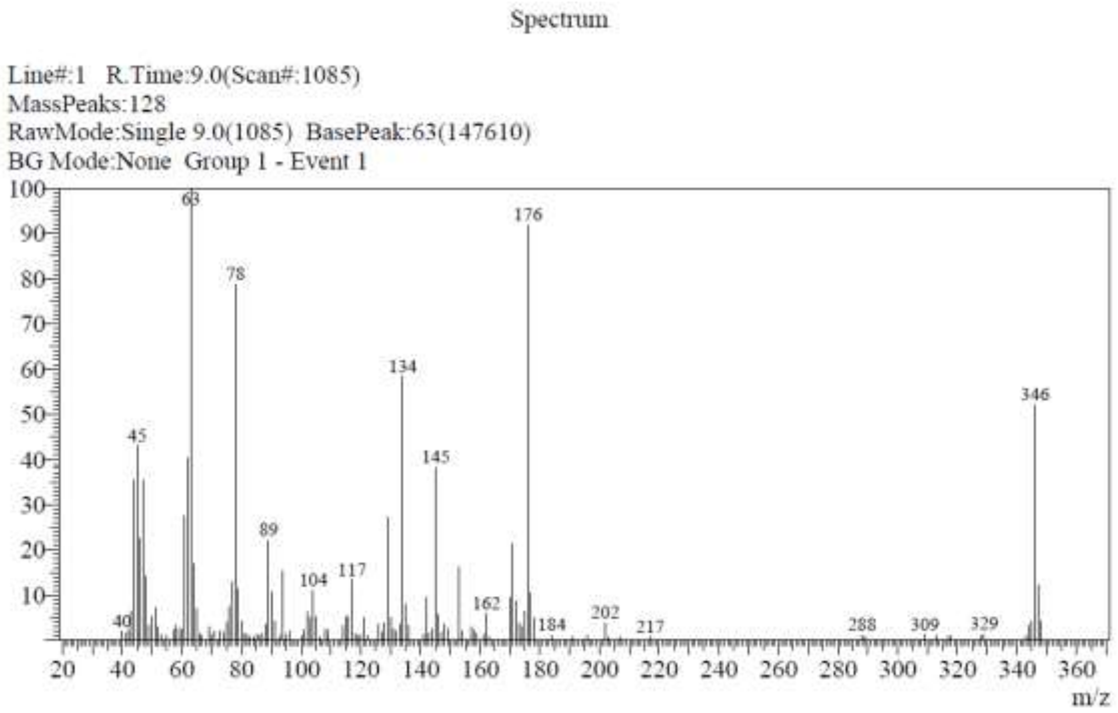


Figure 3: Mass Spectrum of Schiff Base (L).

Infrared Studies

IR spectrum of Schiff base (L) and its metal complexes are recorded in order to confirm the coordination mode of Schiff base. The band at 1657 cm^{-1} is attributed to the ν(C=N) vibration. The Schiff base showed a characteristic bands due to *ν*(NH) and *ν*(OH) for hydrogen bonded O-H peak in the region 3180 and 3441 cm^{-1} respectively. In addition, a C-O stretching band has appeared at 1261 cm^{-1}. The bands observed at 1571 cm^{-1} and 751 cm^{-1} are respectively assigned to the ν(C=N), and ν(C-S-C) of thiazole.

The shift in the azomethine stretching frequency of the Schiff base was observed in the synthesized metal complexes and this confirmed the formation of the complexes. The shifting values of ν(C=N); are 1644, 1644 and 1635 cm^{-1} which are attributed to the complexes of Co(II), Ni(II) and Cu(II) respectively. The band due to hydrogen- bonded (-OH) at 3441 cm^{-1} in the Schiff base is disappeared and a broad band of high intensity is appeared around 3446 cm^{-1} and which has been ascribed to the water molecules in the metal complexes. The shift observed in the stretching frequency of ν(C-O) of the Schiff base from 1261 cm^{-1} to 1239 cm^{-1}, 1238 cm^{-1} and 1240 cm^{-1} in the spectra of Co(II), Ni(II) and Cu(II) complexes respectively supports the coordination through oxygen atom via deprotonation. The bands observed at 420 cm^{-1}, 473 cm^{-1} and 471 cm^{-1} are assigned to ν(M-N) bonds and the bands at 553 cm^{-1}, 556 cm^{-1} and 540 cm^{-1} to ν(M-O) bonds of Co(II), Ni(II) and Cu(II) complexes respectively.

ESI-Mass Studies

The ESI-mass spectra of Co(II), Ni(II) and Cu(II) complexes showed the molecular ion peaks at m/z 785, 784 and 790 respectively corresponding to their molecular weights. Figure 4 represents the spectrum of Cu(II) complex.

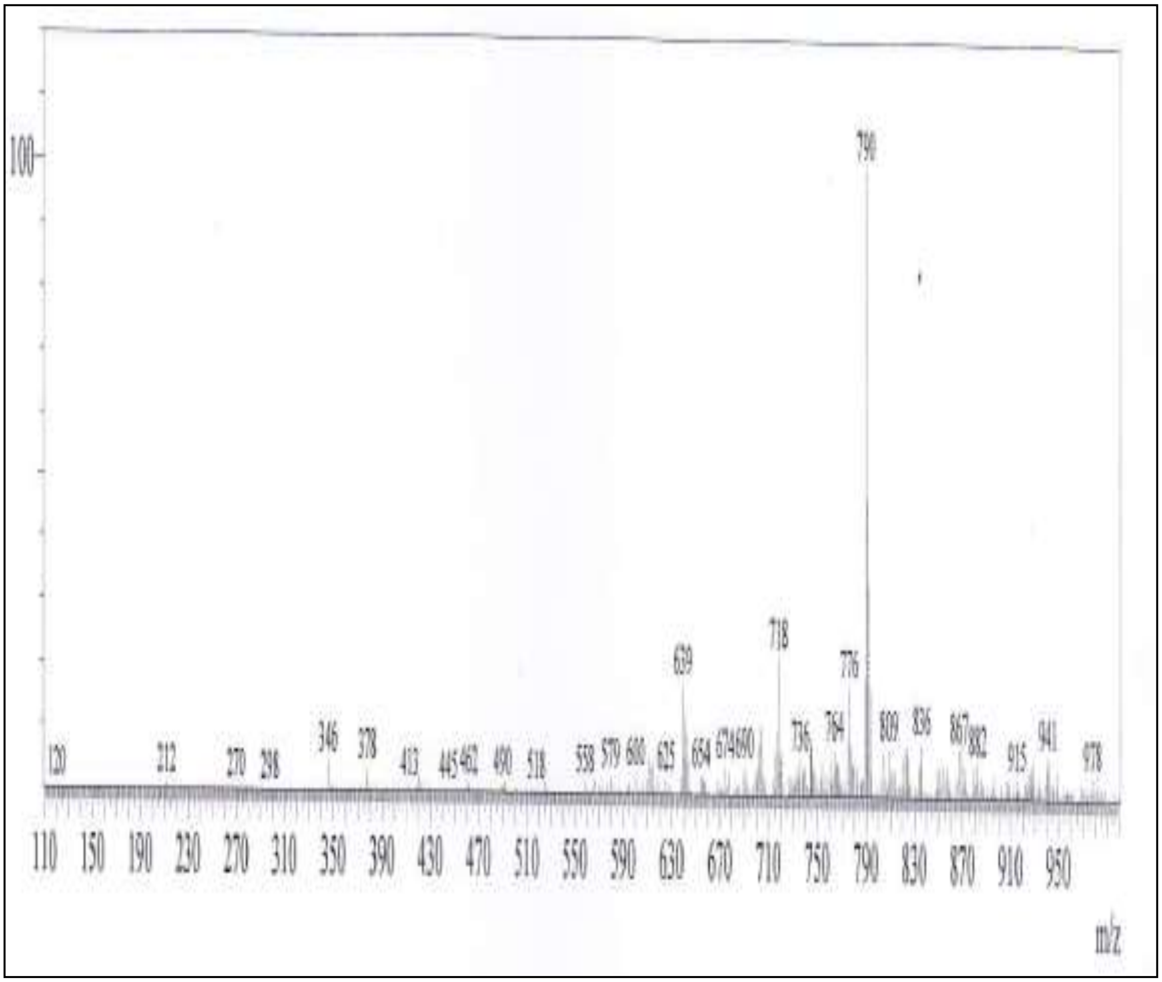


Figure 4: **ESI-MS of Cu(II) Complex.**

Electronic Absorption Spectra and Magnetic Studies

The information concerned to the stereochemistry of the metal ions can be obtained with the help of UV Visible spectra. The electronic spectra of all the synthesized compounds are recorded in DMF. The strong absorptions in the spectra of free ligand around 263-291 nm are due to the intra-ligand π-π* transitions, which remain unchanged even upon complexation. The band observed at 398 nm is due to n-π* transition associated with non-bonding electrons on nitrogen of azomethine group in Schiff base, the bathochromic shift of this band is due to the donation of lone pair of electrons to the metal ion. This change indicates the coordination of azomethine nitrogen to the metal ion. The electronic spectral values are depicted in Table 2.

Table 2: Electronic Spectral Data.

Compound	λ_{max} in cm^{-1} (nm)	Band Assigned	Geometry
$Co(C_{19}H_{14}N_4OS)_2.(H_2O)_2$	10256 (975)	${}^4T_{1g}(F)\rightarrow {}^4T_{2g}(F)$ (ν_1)	Octahedral
	17857 (560)	${}^4T_{1g}(F)\rightarrow {}^4T_{1g}(P)(\nu_3)$	
$Ni(C_{19}H_{14}N_4OS)_2.(H_2O)_2$	10152(985)	${}^3A_{2g}(F)\rightarrow {}^3T_{2g}(F)$ (ν_1)	Octahedral
	14925 (670)	${}^3A_{2g}(F)\rightarrow {}^3T_{1g}(F)$ (ν_2)	
	27624 (362)	${}^3A_{2g}(F)\rightarrow {}^3T_{1g}(P)$ (ν_3)	
$Cu(C_{19}H_{14}N_4OS)_2.(H_2O)_2$	14705 (680)	${}^2T_{2g}\leftarrow {}^2E_{2g}$	Distorted Octahedral
	25906 (386)	L→ M	

Electronic spectra of the synthesized metal complexes are recorded in DMF. The electronic spectrum of Co(II) complex exhibited the absorption bands in the region 560 and 975 nm corresponding to ${}^4T_{1g}(F)\rightarrow {}^4T_{2g}(F)$ (ν_1) and ${}^4T_{1g}(F)\rightarrow {}^4T_{1g}(P)$ (ν_3) transitions respectively. Observed magnetic moment of Co(II) complex was 4.85 BM, both the above facts are in good agreement with the octahedral geometry for the synthesized Co(II) complex.

In case of Ni(II) complex, three bands were observed in the region 985, 670 and 362 nm are due to the ${}^3A_{2g}(F)\rightarrow {}^3T_{2g}(F)$ (ν_1), ${}^3A_{2g}(F)\rightarrow {}^3T_{1g}(F)$ (ν_2) and ${}^3A_{2g}(F)\rightarrow {}^3T_{1g}(P)$ (ν_3) transitions respectively, this observation supports octahedral geometry around Ni(II) ion. The magnetic moment value of 3.20 BM also is in good agreement for octahedral geometry for Ni(II) complex. The absorption spectrum of Ni(II) complex is reproduced in Figure 5.

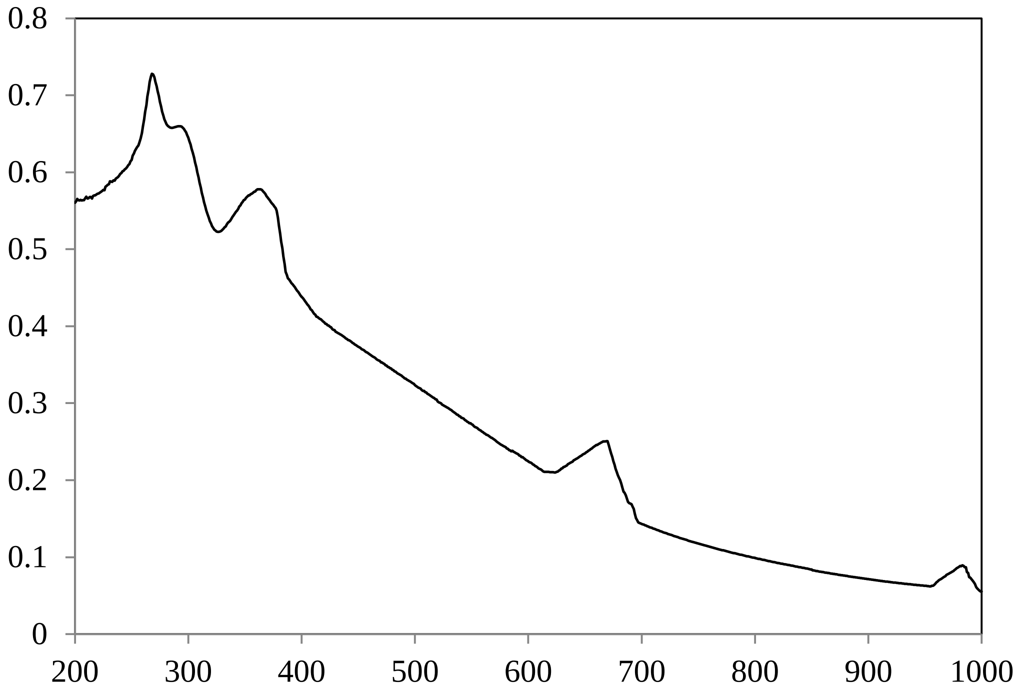


Figure 5: Electronic Absorption Spectrum of Ni(II) Complex

Two absorption bands were observed in the spectrum of Cu(II) complex at 680 and 386 nm. A low intense band at 680 nm is assigned to $^2E_g \rightarrow {}^2T_{2g}$ transition which supports the distorted octahedral geometry to the metal ion. The other band at 386 nm is due to symmetry forbidden ligand → metal charge transfer. The obtained magnetic moment value of 1.80 BM also suggests the octahedral environment around the metal ion.

Electrochemistry

The redox behavior of the newly synthesized Cu(II) complex was investigated in DMSO by cyclic voltammetric studies using a glassy carbon working electrode. Figure 6 illustrates the cyclic voltammogram of Cu(II) complex. It shows an oxidation peak at 0.1V (Epa) with a corresponding reduction peak at 0.54V (Epc). The difference between these peak potentials (0.44V) suggested that, Cu(II) complex undergoes quasi reversible redox behavior. This also confirmed by a large separation between the cathodic and anodic peaks with increased scan rates.

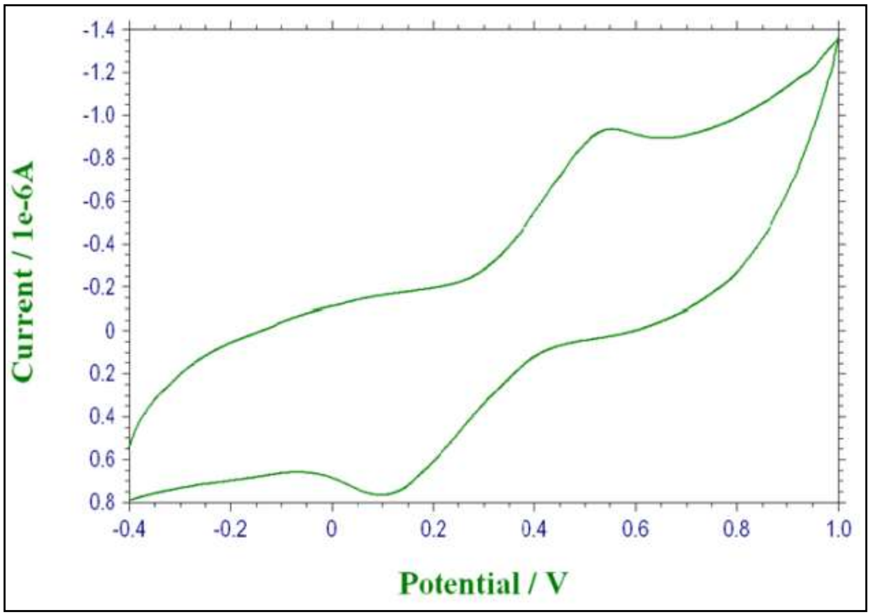
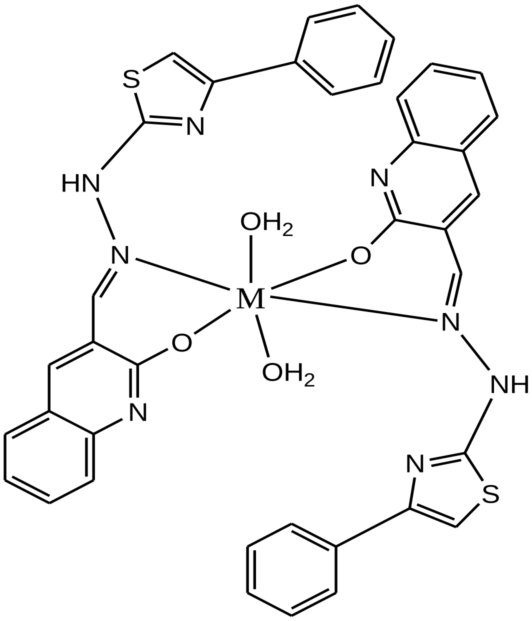


Figure 6: Cyclic voltammogram of Cu(II) complex.

Based on the above experimental evidences the tentative structure to the synthesised metal complexes has been depicted in Figure 8.



M= Co(II), Ni(II) and Cu(II).

Figure 8: Proposed Structure for the Metal Complexes.

Bio-Assay Investigations

Anti-Tuberculosis

All the newly synthesized metal complexes were evaluated for their anti-tuberculosis activity against M. tuberculosis using microplate Alamar Blue assay (MABA). The results are tabulated in Table 3; which indicate that, the synthesized metal complexes act as good anti- tubercular agents when compared to Schiff Base. Cu(II) complex exhibited the moderate activity than other metal complexes.

Cytotoxicity

These results clearly indicate that, most of the tested compounds have shown good safety profile except Schiff Base. The Co(II), Ni(II) and Cu(II) complexes exhibited the good safety profile; out of which Cu(II) complex showed the highest safety profile with 95% survival rate of Vero Cells which indicates a good selectivity. The results are tabulated in Table 3.

Table 3: *In-vitro* Anti-Tubercular Screening against M.tb ATCC 27294 and Cytotoxicity Assay against Vero Cells

Compound	**%Inhibition at concentration 6.25 -µg/mL**	**MIC[a] µg/mL**	**% Survival of Vero Cells at Conn. (10 x MIC)[b]**
Schiff Base	88	ND	ND
$Co(C_{19}H_{14}N_4OS)_2.(H_2O)_2$	94	0.097	88
$Ni(C_{19}H_{14}N_4OS)_2.(H_2O)_2$	90	0.781	73
$Cu(C_{19}H_{14}N_4OS)_2.(H_2O)_2$	98	0.04	95
Isoniazid	100	0.02	100

ND- Not Determined.

[a] Minimum inhibitory concentration against M. tuberculosis ATCC 27294 (μg/mL).

[b] Compound is considered toxic if it causes over 50% inhibition of normal cells at concentration 10 fold higher than its MIC value

In-vitro Antibacterial and Antifungal Activity

The results obtained for antimicrobial studies of Schiff bases and their metal complexes are systematized in Table 4. Synthesized compounds were screened for their *in-vitro* antibacterial activity against *Staphylococcus aureus* and *Escherichia coli*. Metal complexes showed a good inhibiting action against few species. Co(II) and Ni(II) complexes exhibited highest antibacterial activity against all the bacterial species used. The antifungal assay was carried out against fungal (*Candida albicans* and *Aspergillus fumigatus)* species. In this case, Co(II) and Cu(II) complexes showed the moderate activity.

Table 4: Antimicrobial Studies of Schiff Base and its Metal Complexes.

Sl. No.	Compound	*Staphylococcus aureus*	*Escherichia coli*	*Candida albicans*	*Aspergillus fumigatus*
1	Schiff Base	6.25	12.5	25	12.5
2	$Co.L_2.(H_2O)_2$	3.125	1.562	3.125	6.25
3	$Ni.L_2.(H_2O)_2$	3.125	1.562	12.5	50
4	$Cu.L_2.(H_2O)_2$	6.25	3.125	3.125	6.25
	Gentamycin(Standard)	6.25	3.165		
	Nystatin(Standard)			3.125	6.25

DNA Cleavage Study

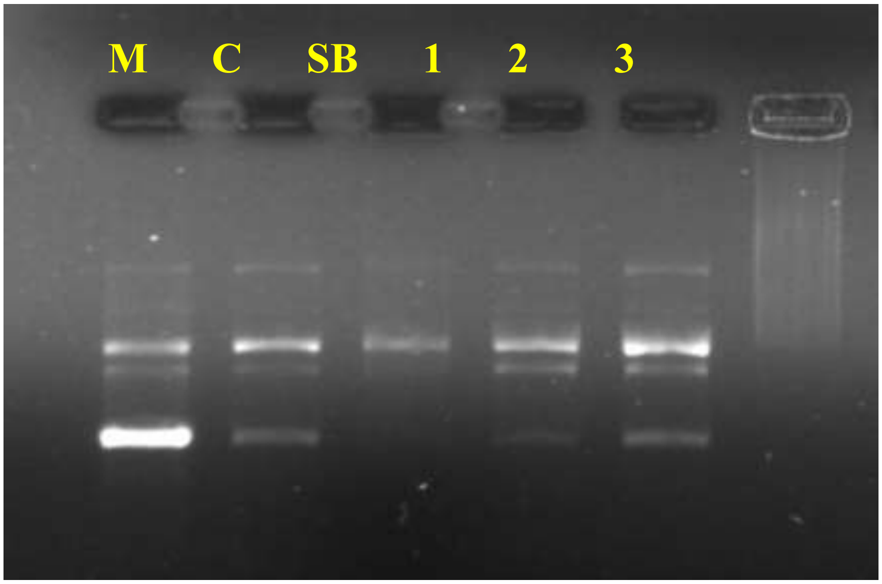


Figure 7: DNA Cleavage Activity of Schiff Base and its Metal Complexes.

(‘M’–is standard DNA molecular weight marker, ‘C’–control DNA i.e. untreated pBR322 Plasmid DNA and lanes SB and 1-3 are pBR322 treated with different Schiff base and metal complexes respectively).

The DNA cleavage activity of Schiff base and its metal complexes were studied by agarose gel electrophoresis method using pBR322 Plasmid DNA. The cleavage activity of Schiff base and its complexes are reproduced in Figure 7. Gel electrophoresis works on, migration of DNA under the influence of electric potential. In the present case, ligand along with the Co(II) and Ni(II) complexes shows the partial cleavage; whereas, the Cu(II) complex cleaves the DNA completely.

CONCLUSION

The newly synthesized Schiff base acts as a bidentate ligand which is coordinated to metal ions through azomethine nitrogen and oxygen atoms via deprotonation. The elemental analyses confirmed that, the synthesized metal complexes have the stoichiometry of the type $[M(L)_2.(H_2O)_2]$ where, [M= Co(II), Ni(II) and Cu(II)] and ‘L’ is a doubly deprotonated ligand. The molar conductivity study shows that, all the synthesized metal complexes have low conductivity values. Cyclic Voltammetry study ensures that, the Copper(II) complex had a large separation between the cathodic and anodic peak and it increases with scan rate, indicating a quasi-reversible character. These various spectro-analytical techniques performed help in assigning the following tentative structure for the synthesized metal complexes. The newly synthesized Schiff base and its metal complexes have been screened for their *in-vitro* antitubercular, cytotoxicity, antimicrobial and DNA cleavage activities. Among the tested compounds Cu(II) complex was proved to be a good antitubercular agent with high cytotoxic safety profile. Whereas, antimicrobial assays show the increased activity of Schiff Base upon coordination. The DNA cleavage activity of Schiff base and its metal complexes were studied by agarose gel electrophoresis method using pBR322 Plasmid DNA, in which the Cu(II) complex showed the effective cleavage than any other synthesized compounds.

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