

Synthesis, Characterization and Antimicrobial Activities of Schiff Base Complexes Derived from Isoniazid and Diacetylmonoxime

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Abstract

A series of bimetallic Schiff base metal complexes with different transition metal ions such as Cu^{II}, Ni^{II} and Co^{II} has been prepared using isoniazid and diacetylmonoxime. The metal complexes have been characterized on the basis of analytical and spectral data, thermal analysis, magnetic and conductivity measurements and XRD data. Based on the results, tentative structures of the complexes have been proposed. The complexes are found to have good antimicrobial activities against the pathogenic fungus *Aspergillus niger*, *Helminthosporium oryzae* and *Fusarium oxysporium*. The metal complexes are found to possess potent antimicrobial activity in the order Cu > Co > Ni.

Keywords: Bimetallic, Schiff base complex, Thermal analysis, Conductivity measurement, antimicrobial activity.

1. Introduction

Medicinal inorganic chemistry is at the interface between medicine and inorganic chemistry which includes metal-based drugs[1], metal sequestering agents[2] and the medicinal requirement of endogenous metal ions[3]. The number of moderately comprehensive reviews of the topic can still be counted on the fingers of one hand; however the field is growing exponentially[4]. The use of metals in medicinal practice is certainly not anything new. There has always been a curious connection between the discovery of a new precious elements and its quick movement into the medicinal armamentarium[5].

The chemistry of coordination compounds with Schiff base ligand which contain azomethine group R¹HC=N-R², formed by the condensation of primary amines

with aldehydes and ketones[6] extends from mononuclear molecule to polynuclear one. Hydrazones play an important role in coordination chemistry, as they easily form stable complexes with most transition metal ions. Isoniazid is a first line antituberculosis drug[7], manufactured from isonicotinic acid which is produced from 4- methylpyridine[8]. Hydrazine moiety present in the molecule of isoniazid can readily undergo Schiff base condensation with compounds containing carbonyl function to form their corresponding hydrazones. Several authors have carried out the synthesis and structural studies of metal complexes of hydrazones of isoniazid[9, 10]. The bactericide and fungicide properties of such complexes have been well documented[11, 12]. In continuation of our research on this area, the synthesis of a series of complexes of Cu(II), Ni(II) and Co(II) with the ligands derived from isoniazid and diacetylmonoxime have been reported and their structural aspects have been investigated elaborately.

2. Experimental

All the chemicals and solvents used were either of Glaxo or Merck grade. The solvents were purified before use in the reaction. The metal contents of all these complexes were estimated by adopting the standard procedures[13]. The percentage of nitrogen was determined by semi micro Kjeldahl's method. Carbon and Hydrogen were estimated using M. L. W. micro elementary CHN analyzer. The FTIR spectra of the metal complexes were recorded on a Varian Spectrophotometer, Australia, in KBr pellets in the region 4000- 400 cm⁻¹. The electronic spectra of the complexes in DMSO were obtained using a Perkin Elmer-398 Spectrophotometer. The molar conductivities of the complexes were measured with a Philips conductivity bridge (model CLO1- 06, cell

constant 0.5 cm^{-1}) using $1 \times 10^{-3} \text{ M}$ solution of the complexes in DMF. The room temperature magnetic susceptibility values were measured by Gouy method using $\text{Hg}[\text{Co}(\text{SCN})_4]$ as the calibrant. The thermogravimetric analyses of the complexes were carried out on NETZSCH 429 thermal analyzer in nitrogen atmosphere. The measurements were taken using sample weight of 100 mg and rate of temperature increase of $10^\circ\text{C min}^{-1}$ throughout the experiment for all the samples. The ESR spectra of Cu(II) complexes were recorded as powdered sample (poly crystalline) on an E-112 EPR spectrometer with field set at 3200 G, scan range, $2.0 \times 1\text{KG}$, modulation frequency 9.44 GHz, receiver gain 10×10^2 and modulation amplitude $0.63 \times 10\text{G}$. The XRD studies of the powdered samples of the complexes were recorded by a Philips Analytical X-ray B. V, PC-APD diffraction software at IMMT, Bhubaneswar. The XRD data were analyzed using LSUCRIPC software.

2.1 Synthesis of metal complexes with the derivative of isoniazid and diacetylmonoxime(L)

The Schiff base condensation reaction between diacetylmonoxime and isoniazid (INH) produced an oily material of unknown composition. Hence complexes were prepared by *in situ* reaction[14, 15] using metal template method.

2.1.1 Synthesis of Cu(II) complexes:

i. Synthesis of $[\text{Cu}(\text{L})(\text{H}_2\text{O})_2]_2\text{Cl}_2$

1.37g (0.01mol) of isoniazid in 50 ml of ethanol was taken in a round bottom flask. To this ethanolic solution, diacetylmonoxime 1.01g (0.01mol) was added and refluxed for 1 hour. A solution of $\text{CuCl}_2 \cdot 2\text{H}_2\text{O}$ (1.70g or

0.01mol) in ethanol was added to this mixture in drop wise manner. This solution containing the stoichiometric mixture of isoniazid, diacetyl monoxime and $\text{CuCl}_2 \cdot 2\text{H}_2\text{O}$ in 1:1:1 molar ratio was then refluxed at $60\text{-}70^\circ\text{C}$ on a water bath for 5 hours. When a dark greenish solid got separated, it was filtered, washed several times with small volume of ethanol and finally dried over fused calcium chloride.

ii. Synthesis of $[\text{Cu}(\text{L})(\text{H}_2\text{O})_2]_2(\text{NO}_3)_2$

An ethanolic solution of isoniazid (1.37g or 0.01mol) was refluxed with diacetyl monoxime (1.01g or 0.01mol) in a 50 ml round bottom flask for about 1 hour. To this mixture a solution of $\text{Cu}(\text{NO}_3)_2 \cdot 3\text{H}_2\text{O}$ (2.41g or 0.01mol) in ethanol was added slowly and the resulting mixture in 1:1:1 molar ratio was refluxed for 5 hours when a parrot green coloured compound got separated, it was filtered, washed several times with ethanol to achieve the maximum purity and dried over fused calcium chloride.

iii. Synthesis of $[\text{Cu}(\text{L})(\text{H}_2\text{O})_2]_2(\text{CH}_3\text{COO})_2$

A similar method as earlier was adopted for the synthesis of this complex. Here, a stoichiometric mixture of isoniazid (1.37g, 0.01mol), diacetylmonoxime (1.01g or 0.01mol) and $\text{Cu}(\text{CH}_3\text{COO})_2 \cdot \text{H}_2\text{O}$ (1.99g or 0.01mol) in 1:1:1 molar ratio was refluxed in ethanol for 5 hours in a round bottom flask. When a greenish coloured compound got separated out it was filtered, washed with ethanol and dried over fused calcium chloride.

The other binuclear Schiff base complexes of Ni(II) and Co(II) were prepared in a similar manner as described above.

The scheme of reaction is presented in Fig-1.

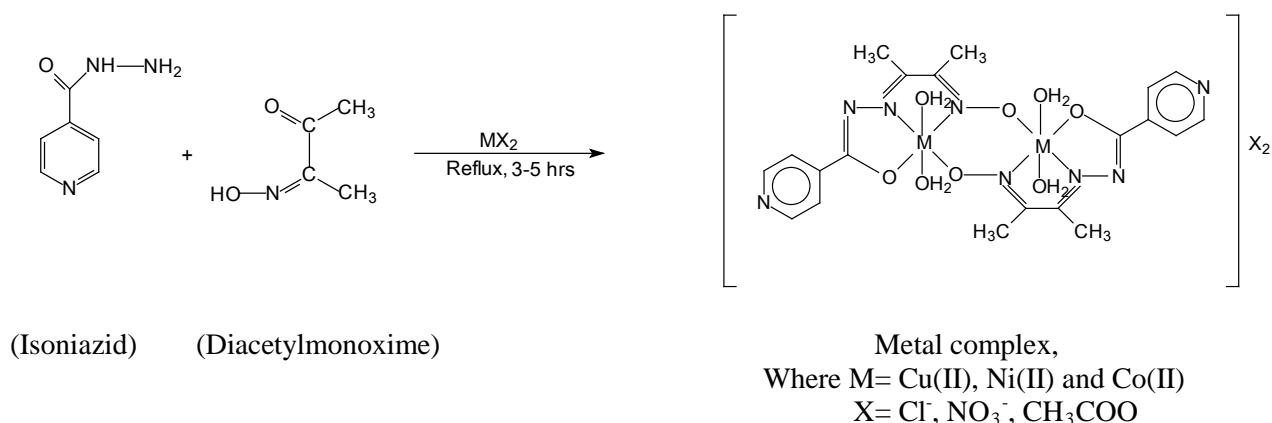


Fig. 1 Synthesis of Metal Complex

3. Results and Discussion

The complexes are highly stable in room temperature and can be stored for long time. They are highly coloured, paramagnetic in nature and have high melting point above 250 °C. They are slowly attacked by alkalis and acids. The complexes are insoluble in water but soluble in DMF/DMSO/dioxane.

High molar conductance values of the complexes in the range 140-160 $\Omega^{-1} \text{ cm}^2 \text{ mol}^{-1}$ suggest them to be electrolyte. The structures of the complexes have been established using different physicochemical methods as discussed below. They have been tested as possible fungicides against some fungal pathogens. The analytical data of the complexes are recorded in Table-1.

Table 1: Analytical and physicochemical data of complexes with diacetylmonoxime derivative of isoniazid

Compounds	Colou	Mol. Wt.	% of Metal Calcd. (Found)	% of C Calcd. (Found)	% of H Calcd. (Found)	% of N* Calcd. (Found)	% of Cl Calcd. (Found)	Λ in $\text{ohm}^{-1} \text{ cm}^2 \text{ mol}^{-1}$	Melting point in °C
$[\text{Cu}(\text{L})(\text{H}_2\text{O})_2]_2\text{Cl}_2$	Dark Green	706	17.98 (18.14)	33.99 (35.45)	3.96 (4.45)	15.86 (16.85)	10.05 (10.90)	148	293
$[\text{Cu}(\text{L})(\text{H}_2\text{O})_2]_2(\text{NO}_3)_2$	Parrot Green	759	16.73 (16.98)	31.62 (35.63)	3.68 (4.05)	18.44 (18.91)	-	144	296
$[\text{Cu}(\text{L})(\text{H}_2\text{O})_2]_2(\text{CH}_3\text{COO})_2$	Green	753	16.86 (17.75)	38.24 (41.47)	4.51 (4.71)	14.87 (15.18)	-	141	295
$[\text{Ni}(\text{L})(\text{H}_2\text{O})_2]_2\text{Cl}_2$	Light Green	696.2	16.83 (16.95)	34.47 (39.05)	4.02 (4.70)	16.08 (16.65)	10.19 (10.97)	154	287
$[\text{Ni}(\text{L})(\text{H}_2\text{O})_2]_2(\text{NO}_3)_2$	Brick Red	749.2	15.64 (16.02)	32.03 (34.73)	3.73 (4.09)	18.68 (19.20)	-	157	284
$[\text{Ni}(\text{L})(\text{H}_2\text{O})_2]_2(\text{CH}_3\text{COO})_2$	Light Brown	743.2	15.76 (16.48)	38.75 (39.01)	4.57 (5.25)	15.06 (15.90)	-	152	286
$[\text{Co}(\text{L})(\text{H}_2\text{O})_2]_2\text{Cl}_2$	Violet	696.8	16.90 (17.05)	34.44 (35.29)	4.01 (4.50)	16.07 (16.75)	10.18 (10.99)	156	282
$[\text{Co}(\text{L})(\text{H}_2\text{O})_2]_2(\text{NO}_3)_2$	Pink	749.8	15.71 (16.07)	32.00 (33.08)	3.73 (4.09)	18.67 (19.09)	-	155	284
$[\text{Co}(\text{L})(\text{H}_2\text{O})_2]_2(\text{CH}_3\text{COO})_2$	Light Violet	743.8	15.83 (16.31)	38.72 (39.26)	4.57 (4.95)	15.05 (15.96)	-	158	279

3.1 IR Spectra

The IR spectra of the metal complexes exhibited several interesting features. Since the ligand could not be isolated in free form, its spectrum could not be recorded. The spectra of the complexes, however, have been compared with those of isoniazid which reveal vital information regarding the structural aspects of the metal complexes. Further,

attempts have been made to identify bands which sufficiently suggest the mode of bonding in the complexes with metals[16], by comparing their spectra with other related reported complexes. The IR spectral data are recorded in the Table- 2.

A strong band in $\sim 3450-3000 \text{ cm}^{-1}$ is assigned to the combined mode of $\nu_{(\text{O-H})}$ of coordinated water[17] and N-H stretching vibrations. The

broadness of the band also suggests strong intermolecular hydrogen bonding. The $\nu_{(C=N)}$ band splits up and appears as a multiplet at 1585- 1600 cm^{-1} which suggests C=N groups to be in different environment[18]. A strong band at 1300-1500 cm^{-1} is assigned to symmetric and antisymmetric $\nu_{(N-O)}$. Similarly a band appearing in the region 1030-1060 cm^{-1} is ascribed to $\nu_{(N-N)}$. The absorption band at $\sim 1680 \text{ cm}^{-1}$ ($\nu_{(C=O)}$) in the spectra of isoniazid is missing in those of the complexes and instead a band appears in the region of 1240 cm^{-1} due to $\nu_{(C-O)}$ which suggests that amido- imidol

tautomerism ($-\text{HN}-\overset{\text{I}}{\text{C}}=\text{O} \rightleftharpoons -\text{N}=\overset{\text{I}}{\text{C}}-\text{OH}$) has taken place before complexation[19]. This is further corroborated by the appearance of bands at $\sim 1590 \text{ cm}^{-1}$ due to $\nu_{(C=N)}$ and a band at $\sim 1050 \text{ cm}^{-1}$ due to $\nu_{(N-N)}$. The band at $\sim 2950\text{-}2850 \text{ cm}^{-1}$ is attributed to $\nu_{(C-H)}$ of the $-\text{CH}_3$ group. The presence of coordinated water in the complexes is further supported by the appearance of another band at $\sim 1025 \text{ cm}^{-1}$ due to $\delta \text{wH}_2\text{O}$ [20, 21]. In the lower frequency region two bands are obtained at $\sim 480\text{-}455 \text{ cm}^{-1}$ and $\sim 440\text{-}420 \text{ cm}^{-1}$ assignable to ν_{M-N} and ν_{M-O} respectively[22, 23].

Table 2: IR data of ligand and metal complexes

Compounds	Band positions in cm^{-1}								
	$\nu_{(O-H)+\nu_{(N-H)}}$	$\nu_{(C-H)}$	$\nu_{(C=O)}$	$\nu_{(C=N)}$	$\nu_{(C-O)}$	$\nu_{(N-O)}$	$\nu_{(N-N)}$	$\nu_{(M-O)}$	$\nu_{(M-N)}$
INH	-	-	1680	-	-	-	-	-	-
$[\text{Cu}(\text{L})(\text{H}_2\text{O})_2]_2\text{Cl}_2$	3200	2935	-	1585	1238	1390	1065	543	436
$[\text{Cu}(\text{L})(\text{H}_2\text{O})_2]_2(\text{NO}_3)_2$	3217	2862	-	1597	1237	1415	1057	531	431
$[\text{Cu}(\text{L})(\text{H}_2\text{O})_2]_2(\text{CH}_3\text{COO})_2$	3230	2881	-	1586	1233	1420	1040	522	420
$[\text{Ni}(\text{L})(\text{H}_2\text{O})_2]_2\text{Cl}_2$	3336	2869	-	1585	1240	1412	1059	541	448
$[\text{Ni}(\text{L})(\text{H}_2\text{O})_2]_2(\text{NO}_3)_2$	3310	2910	-	1591	1224	1398	1038	547	445
$[\text{Ni}(\text{L})(\text{H}_2\text{O})_2]_2(\text{CH}_3\text{COO})_2$	3352	2884	-	1591	1230	1385	1045	543	436
$[\text{Co}(\text{L})(\text{H}_2\text{O})_2]_2\text{Cl}_2$	3420	2950	-	1600	1225	1390	1034	536	448
$[\text{Co}(\text{L})(\text{H}_2\text{O})_2]_2(\text{NO}_3)_2$	3443	2876	-	1593	1239	1345	1058	530	450
$[\text{Co}(\text{L})(\text{H}_2\text{O})_2]_2(\text{CH}_3\text{COO})_2$	3465	2928	-	1588	1240	1387	1051	534	454

The IR spectra of the isoniazid and its binuclear metal complexes are given below in Fig-2(a), 2(b)

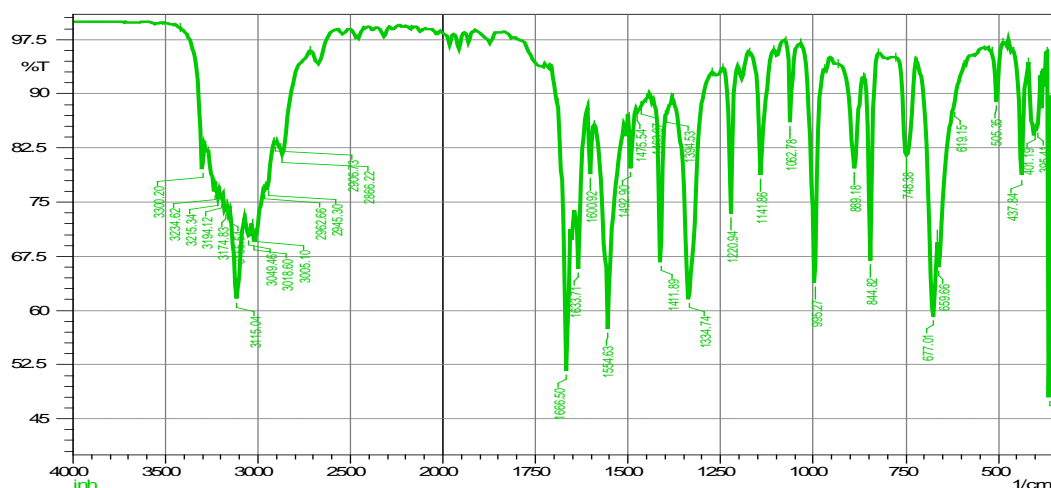
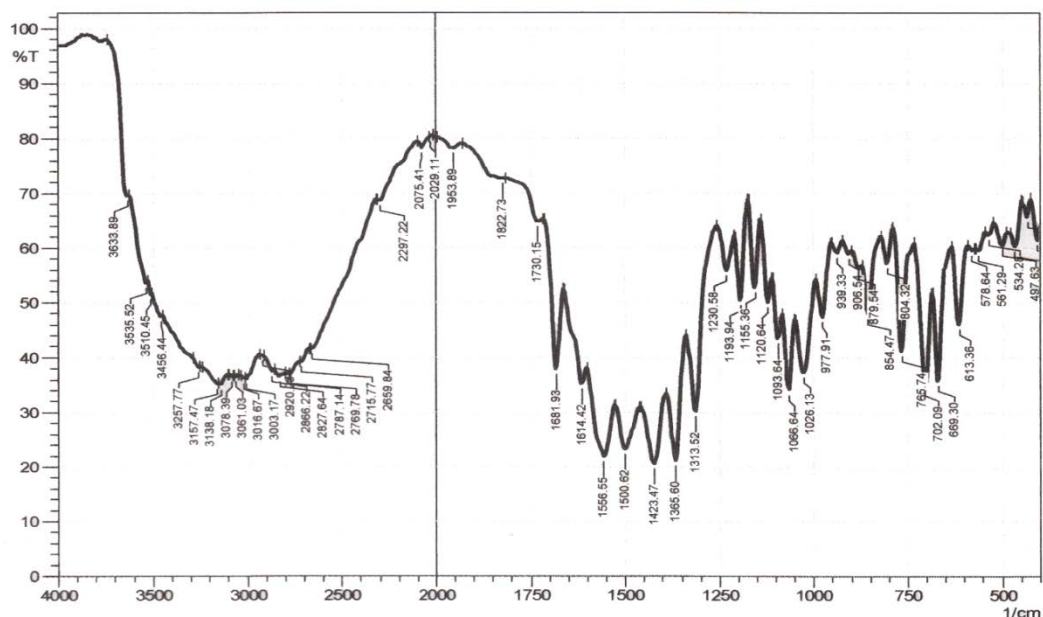


Fig. 2a IR spectrum of Isoniazid


 Fig. 2b IR spectrum of $[\text{Co}(\text{L})(\text{H}_2\text{O})_2]_2(\text{NO}_3)_2$

3.2 Thermal Analysis

The presence of coordinated water in the complexes was reported by the IR spectra which were further ascertained by the thermogravimetric analysis. The thermogram of the chloride complex of copper(II) is recorded in Fig-3. The complex undergoes two step decomposition processes[24]. The first step is observed at around $\sim 200^\circ\text{C}$ which corresponds to the weight loss due to the loss of four molecule of coordinated water. The

second step of decomposition observed at around $\sim 410^\circ\text{C}$ indicates the dissociation of the ligand molecule. The parallel base line corresponds to the formation of copper oxide as the final product. The same thermal behaviour is exhibited by Ni– Ni as well as Co– Co systems. The thermal stabilities of the complexes are in the order of $\text{Cu} - \text{Cu} > \text{Co} - \text{Co} > \text{Ni} - \text{Ni}$.

The thermoanalytical data of the metal complexes are presented in Table-3.

Table 3: Thermoanalytical data of binuclear metal complexes

Metal Complex	Molar Mass	Temp Range ($^\circ\text{C}$)	Peak Temp. ($^\circ\text{C}$)	Mass Loss Found(Calc. %)	Removed Species	Metallic Residue Found(Calc. %)
$[\text{Cu}(\text{L}_1)(\text{H}_2\text{O})_2]_2\text{Cl}_2$	706	150 – 240	210	10.05 (10.20)	$4\text{H}_2\text{O}$	CuO 22.09 (22.52)
		240 – 460	400	67.19 (67.28)	$\text{C}_{20}\text{H}_{20}\text{N}_8\text{O}_2\text{Cl}_2$	
$[\text{Cu}(\text{L})(\text{H}_2\text{O})_2]_2(\text{NO}_3)_2$	759	175 – 245	205	9.08 (9.49)	$4\text{H}_2\text{O}$	CuO 19.45 (20.95)
		245 – 440	395	69.25 (69.57)	$\text{C}_{20}\text{H}_{20}\text{N}_{10}\text{O}_8$	
$[\text{Cu}(\text{L})(\text{H}_2\text{O})_2]_2(\text{CH}_3\text{COO})_2$	753	168 – 235	200	9.03 (9.56)	$4\text{H}_2\text{O}$	CuO 20.79 (21.11)
		235 - 430	385	69.14 (69.32)	$\text{C}_{24}\text{H}_{26}\text{N}_8\text{O}_6$	
$[\text{Ni}(\text{L})(\text{H}_2\text{O})_2]_2\text{Cl}_2$	696.2	152 - 245	192	10.02 (10.34)	$4\text{H}_2\text{O}$	NiO 20.96 (21.43)
		245 – 420	382	68.14 (68.23)	$\text{C}_{20}\text{H}_{20}\text{N}_8\text{O}_2\text{Cl}_2$	
$[\text{Ni}(\text{L})(\text{H}_2\text{O})_2]_2(\text{NO}_3)_2$	749.2	165 – 250	180	9.23 (9.61)	$4\text{H}_2\text{O}$	NiO 19.15 (19.91)
		250 – 450	378	70.30 (70.48)	$\text{C}_{20}\text{H}_{20}\text{N}_{10}\text{O}_8$	

[Ni(L)(H ₂ O) ₂] ₂ (CH ₃ COO) ₂	743.2	155 – 232	188	9.18 (9.69)	4H ₂ O	NiO 19.78 (20.07)
		232 – 425	375	69.98 (70.24)	C ₂₄ H ₂₆ N ₈ O ₆	
[Co(L)(H ₂ O) ₂] ₂ Cl ₂	696.8	160 – 270	204	10.11 (10.33)	4H ₂ O	CoO 21.17 (21.50)
		270 – 465	390	67.85 (68.17)	C ₂₀ H ₂₀ N ₈ O ₂ Cl ₂	
[Co(L)(H ₂ O) ₂] ₂ (NO ₃) ₂	749.8	158 – 249	200	9.26 (9.60)	4H ₂ O	CoO 19.16 (19.98)
		249 – 457	388	70.03 (70.42)	C ₂₀ H ₂₀ N ₁₀ O ₈	
[Co(L)(H ₂ O) ₂] ₂ (CH ₃ COO) ₂	743.8	172 – 260	198	9.14 (9.68)	4H ₂ O	CoO 19.78 (20.14)
		260 – 445	380	69.76 (70.18)	C ₂₄ H ₂₆ N ₈ O ₆	

The TG– DTG curves of Schiff base Cu(II) complex is shown below in Fig-3.

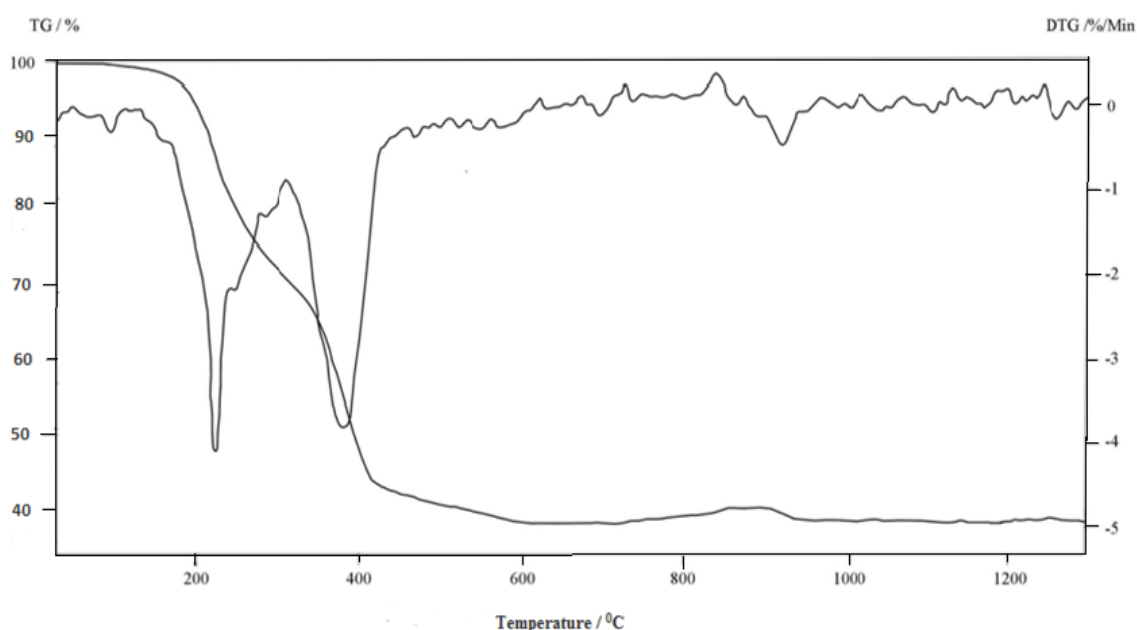


Fig. 3 TG - DTG curves of [Cu(L)(H₂O)₂]₂Cl₂ complex

3.3 Electronic Spectra

The electronic spectral bands occur only in specified positions indicating two metal centres to be equivalent having similar geometry. The magnetic moment value of Ni(II) complexes at the room temperature is in the range 2.88- 3.32 B.M. as expected for six coordinated spin free Ni(II) species. Tetragonal splitting for the excited level ³T_{2g}(F) and ³T_{1g}(F) is observed. The splitting bands for ³T_{2g}(F) appear near 8760 cm⁻¹ and 11180 cm⁻¹. Similarly the splitting band of ³T_{1g}(F) are obtained near 14050 and 17620 cm⁻¹ respectively. These bands are of low intensity than the cobalt complexes. Ni(II) complexes have a higher intensity

for ³B_{1g} → ³T_{1g}(P) transition. The electronic spectral data and the band assignment of Ni(II) complexes are presented in Table-5. The tetragonal parameters such as D_t, D_{qE}, D_{qA} and D_s have been calculated from band positions using standard methods[25] and incorporated in Table-6. The comparison of D_{qE} and D_{qA} values reveals that the ligand in the equatorial position provides a stronger crystal field than the water molecules coordinated at the axial positions around the metal ion..

The copper complexes exhibit normal magnetic moment in the range 1.80 to 1.98 B.M. Broad bands are observed in the region 14000-16500 cm⁻¹ which is the characteristics of distorted octahedral stereochemistry[26]

with D_{4h} symmetry. Besides this another band is developed by a strong charge transfer transition in the region $\sim 26500 \text{ cm}^{-1}$.

The magnetic moment values of Co(II) complexes are in the range 4.76- 4.78 B.M. suggesting the complexes to have the symmetry lower than pure octahedral. The electronic spectra of the ligand field band of the complexes observed at 9380, 19875 and 20980 cm^{-1} are assigned to ${}^4T_{1g}(F) \rightarrow {}^4T_{2g}(F)$, ${}^4T_{1g}(F) \rightarrow {}^4A_{2g}(F)$ and ${}^4T_{1g}(F) \rightarrow {}^4T_{1g}(P)$ transitions respectively[27]. The electronic spectral data, magnetic moment values, bending parameter (C), repulsion parameter (B) and

nephelauxetic parameters (β and β^0) of Cu(II) and Co(II) complexes are compiled in Table- 4. The nitrate salt of the Co(II) complex is found to have a relatively higher degree of covalency than the acetate salt which may be due to the greater delocalization of metal d-electron into the ligand framework resulting from the electron withdrawing nature of nitrate group.

Table 4: Electronic spectral data, magnetic moments, ligand field parameters and nephelauxetic parameters of Cu(II) and Co(II) complexes

Complexes	Band Position in cm^{-1}	Assignment	μ^{eff} in BM	10Dq (cm^{-1})	C (cm^{-1})	B (cm^{-1})	B	$\beta^0(\%)$
$[\text{Cu}(\text{L})(\text{H}_2\text{O})_2]_2 \text{Cl}_2$	15,200(658nm) 26,580(376nm)	${}^2E_g \rightarrow {}^2T_{2g}$ CT	1.89	15,200	-	-	-	-
$[\text{Cu}(\text{L})(\text{H}_2\text{O})_2]_2(\text{CH}_3\text{COO})_2$	14,850(673nm) 26200(382nm)	${}^2E_g \rightarrow {}^2T_{2g}$ CT	1.87	14,850	-	-	-	-
$[\text{Cu}(\text{L})(\text{H}_2\text{O})_2]_2(\text{NO}_3)_2$	15,640(639nm) 26,950(371nm)	${}^2E_g \rightarrow {}^2T_{2g}$ CT	1.85	15,640	-	-	-	-
$[\text{Co}(\text{L})(\text{H}_2\text{O})_2]_2 \text{Cl}_2$	9,380(1066nm) 19,875(503nm) 20,980(477nm)	${}^4T_{1g}(F) \rightarrow {}^4T_{2g}(F)$ ${}^4T_{1g}(F) \rightarrow {}^4A_{2g}(F)$ ${}^4T_{1g}(F) \rightarrow {}^4T_{1g}(P)$	4.81	10,495	980	848	0.874	12.6
$[\text{Co}(\text{L})(\text{H}_2\text{O})_2]_2(\text{CH}_3\text{COO})_2$	9,250(1081nm) 19,650(509nm) 20,925(478nm)	${}^4T_{1g}(F) \rightarrow {}^4T_{2g}(F)$ ${}^4T_{1g}(F) \rightarrow {}^4A_{2g}(F)$ ${}^4T_{1g}(F) \rightarrow {}^4T_{1g}(P)$	4.86	10,400	930	855	0.881	11.9
$[\text{Co}(\text{L})(\text{H}_2\text{O})_2]_2(\text{NO}_3)_2$	9,460(1057nm) 20,100(498nm) 21,000(476nm)	${}^4T_{1g}(F) \rightarrow {}^4T_{2g}(F)$ ${}^4T_{1g}(F) \rightarrow {}^4A_{2g}(F)$ ${}^4T_{1g}(F) \rightarrow {}^4T_{1g}(P)$	4.77	10,640	948	848	0.874	12.6

Table 5: Electronic spectral data (in cm^{-1}) and magnetic moment values of Nickel complexes

Complexes	μ^{eff} in BM*	${}^3B_{1g} \rightarrow {}^3E_g$ (${}^3T_{2g}$)	${}^3B_{1g} \rightarrow {}^3B_{2g}$ (${}^3T_{2g}$)	${}^3B_{1g} \rightarrow {}^3A_{2g}$ (${}^3T_{1g}$)	${}^3B_{1g} \rightarrow {}^3E_g$ (${}^3T_{1g}$)	${}^3B_{1g} \rightarrow {}^3A_{2g}$ (${}^3T_{1g}(P)$)
$[\text{Ni L}(\text{H}_2\text{O})_2]_2 \text{Cl}_2$	2.95	8,760 (1141nm)	11,180 (894nm)	14,050 (712nm)	17,620 (568nm)	25,950 (385nm)
$[\text{Ni L}(\text{H}_2\text{O})_2]_2(\text{CH}_3\text{COO})_2$	3.19	8,600 (1163nm)	10,950 (913nm)	13,800 (725nm)	17,400 (575nm)	25,650 (390nm)
$[\text{Ni L}(\text{H}_2\text{O})_2]_2(\text{NO}_3)_2$	2.91	8,850 (1130nm)	11,350 (881nm)	14,250 (702nm)	17,850 (560nm)	26,300 (380nm)

Table 6: Tetragonal parameters D_t , D_q^E , D_q^A and D_s of Ni(II) complexes

Complexes	D_t (cm^{-1})	D_q^E (cm^{-1})	D_q^A (cm^{-1})	D_s (cm^{-1})
$[\text{Ni L}(\text{H}_2\text{O})_2]_2\text{Cl}_2$	276	876	393(H_2O)	653
$[\text{NiL}(\text{H}_2\text{O})_2]_2(\text{CH}_3\text{COO})_2$	269	860	389 (H_2O)	656
$[\text{NiL}_1(\text{H}_2\text{O})_2]_2(\text{NO}_3)_2$	286	885	386(H_2O)	660

The electronic spectra of the complexes are given below in Fig-4(a), 4(b) and 4(c).

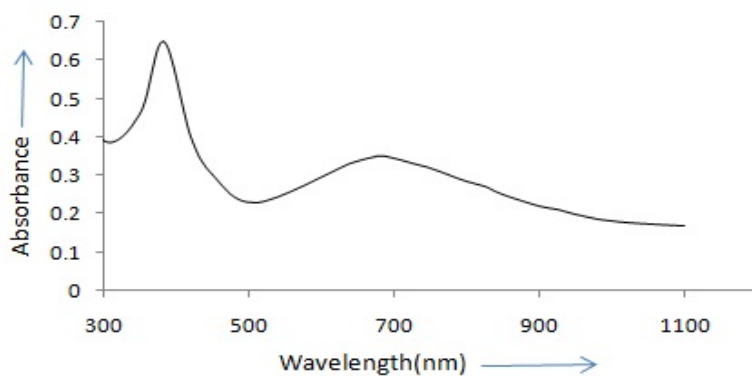


Fig. 4a Electronic spectra of $[\text{Cu}(\text{L})(\text{H}_2\text{O})_2]_2(\text{CH}_3\text{COO})_2$

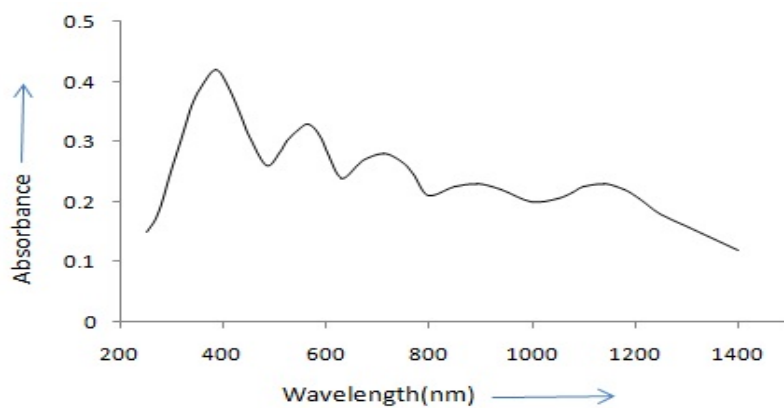


Fig. 4b Electronic spectra of $[\text{Ni}(\text{L})(\text{H}_2\text{O})_2]_2\text{Cl}_2$

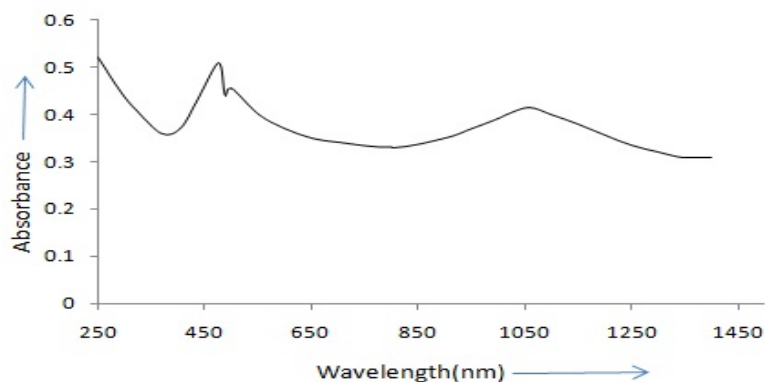


Fig. 4c Electronic spectra of $[\text{Co}(\text{L})(\text{H}_2\text{O})_2]_2(\text{NO}_3)_2$

3.4 ESR Spectra

The ESR parameters g_{\parallel} , g_{\perp} and A_{\parallel} , A_{\perp} corresponding to bimetallic Cu(II) chloride complex are calculated as reported by Goodman and Rayner[28] and recorded in Table- 5. The data show that g_{\parallel} and g_{\perp} values are closer to 2 and $g_{\parallel} > g_{\perp}$ and $A_{\parallel} > A_{\perp}$. The values correspond to copper(II) centre having D_{4h} symmetry[29]. It also suggests that d_z^2 orbital is stabilized by Jahn- Teller effect and the unpaired electron is present in $d_x^2 - y^2$ orbital with major distortions in octahedral environment of copper(II) complex which causes g values to approach to 2. The covalency parameter α^2 is calculated from g_{\parallel} , g_{\perp} and A_{\parallel} values[30] by using the following equation.

$$\alpha^2 = \frac{(g_{\parallel} - 2.0023)}{(A_{\parallel}/0.036)} + \frac{3/7 (g_{\perp} - 2.0023)}{0.04} \quad (1)$$

The α^2 value lie in $\sim 0.875 - 0.911$ indicates that the unpaired electron of copper (II) complexes spends about 12.5 – 8.9% of its time in the ligand donor sites. The complexes under study show $g_{\parallel} > 2.3$ indicating a comparatively anionic or less covalent environment around the metal centre[31]. The values are related by the expression $G = (g_{\parallel} - 2) / (g_{\perp} - 2)$, which measures the exchange interaction between copper centres in polycrystalline solid. If $G > 4$, exchange interaction is negligible and $G < 4$ indicate considerable exchange interaction in the solid complexes. In the present case the axial symmetry parameter G lies in the range 4.00 – 6.00 indicates that the exchange interaction is negligible.

The ESR spectral data of binuclear Cu(II) complexes is given below in Table - 7.

 Table 7: ESR Spectral data of $[\text{Cu}(\text{L})(\text{H}_2\text{O})_2]_2\text{Cl}_2$ complex

Complex	g_{\parallel}	g_{\perp}	g_{av}	$A_{\parallel} \times 10^{-4} \text{ cm}^{-1}$	$A_{\perp} \times 10^{-4} \text{ cm}^{-1}$	$A_{av} \times 10^{-4} \text{ cm}^{-1}$	α^2	$1-\alpha^2$	% of Covalency
$[\text{Cu}(\text{L})(\text{H}_2\text{O})_2]_2\text{Cl}_2$	2.31	2.06	2.14	181	102	141.5	0.875	0.125	12.50

The ESR spectrum of the complex $[\text{Cu}(\text{L})(\text{H}_2\text{O})_2]_2\text{Cl}_2$ is given in Fig- 5.

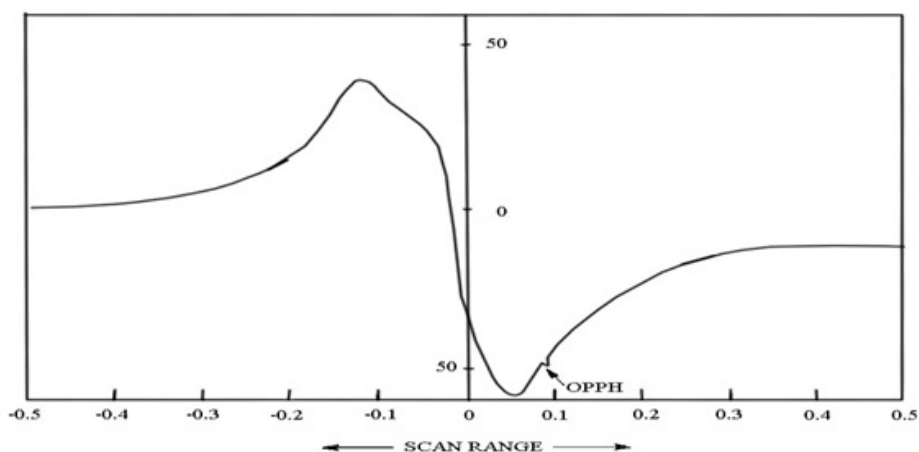


Fig. 5 ESR Spectra of the complex $[\text{Cu}(\text{L})(\text{H}_2\text{O})_2]_2\text{Cl}_2$

3.5 X-ray Diffraction Studies

The powdered XRD data of the chloride complexes of Cu(II), Ni(II) and Co(II) have been analyzed using LSUCRIPC software . Different lattice parameters have been generated by the computer through the

above package. The XRD studies reveal that the unit cell of Cu(II) and Ni(II) complexes are tetragonal while that of Co(II) complex is monoclinic in nature[32]. The edge length (a , b , c), the interfacial angle(α , β , γ) and volume of the corresponding unit cells are presented in Table- 8. The XRD pattern of the chloride complex of Cu(II) is shown in Fig- 6.

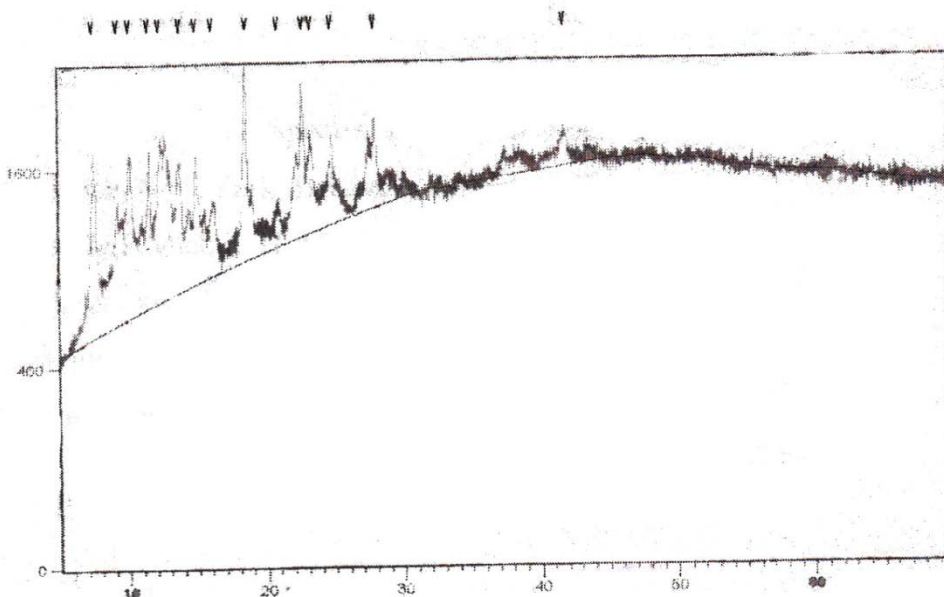


Fig. 6 XRD spectra of $[\text{Cu}(\text{L})(\text{H}_2\text{O})_2]_2\text{Cl}_2$

Table 8: Structural Parameters of the Complexes of Cu(II), Ni(II) and Co(II) as obtained from XRD Data

Sl. No.	Complex	a	b	c	α	β	γ	Vol. Å^3	Crystal Class
1.	$[\text{Cu}(\text{L})(\text{H}_2\text{O})_2]_2\text{Cl}_2$	17.512	22.987	8.237	90°	90°	90°	3325.68	Tetragonal
2.	$[\text{Ni}(\text{L})(\text{H}_2\text{O})_2]_2\text{Cl}_2$	9.425	14.856	9.312	90°	90°	90°	1315.59	Tetragonal
3.	$[\text{Co}(\text{L})(\text{H}_2\text{O})_2]_2\text{Cl}_2$	13.211	13.423	9.209	90°	98.67°	90°	1715.12	Monoclinic

4. Fungicidal Activities

The fungicidal activities of the binuclear metal complexes were carried out. It was observed that isoniazid exhibited toxic behaviour towards fungal pathogens. These activities were further enhanced after the complexation of its derivatives with the metal ions due to an increase in cell permeability.

The lipid membrane which surrounds the cell favours only the passage of lipid soluble materials and it is known that liposolubility is an important factor controlling antifungal activity[33-35]. The observed antifungal activity of the ligand and its metal complexes find support from the literature[36-38] because chelation increases the liposolubility of the complexes which enhances the penetration of

the complexes into the lipid membrane. The organic skeleton of the complexes function as a lipophilic group to drive the compound through the semipermeable membrane of the cell and blocks the metal binding sites in the enzymes of microorganisms. The complexes also disturb the respiration process of the cell blocking the synthesis of proteins which restrict the further growth of the organisms.

The anti-fungal activities of the complexes were tested against the organisms *Aspergillus niger*, *Helminthosporium oryzae* and *Fusarium oxysporium* by the method of Horsfall[39]. The evaluation was carried out at different concentrations of dioxane in ppm. The amount of germination or growth inhibition was determined after inoculation of the fungal spores into Czapek Dox agar-agar media. Spores were also inoculated onto the agar-agar media containing the test sample.

The whole system was kept in an incubator for five days. The percentage of inhibition was calculated as follows:

$$\% \text{ of inhibition} = 100 (P-Q)/P \quad (2)$$

Where P= area of colony growth without test sample, and

Q= area of the colony growth with the test sample. The activity order among the binuclear complexes is found to be $\text{Cu}^{\text{II}} > \text{Co}^{\text{II}} > \text{Ni}^{\text{II}} > \text{INH}$. With respect to the anion, the fungicidal activities of the complexes follow the trend $\text{Cl}^- > \text{NO}_3^- > \text{CH}_3\text{COO}^-$. The statistical calculations adopting two ways ANOVA test[40] have also indicated significant difference with respect to different treatment of complexes (Table- 9) and the relative fungicidal activities of different complexes is displayed in the bar diagram shown in Fig. 7.

Table 9: Antifungal Screening Data of Cu(II), Ni(II) and Co(II) Complexes
Values are expressed as mean \pm S.E.M, (n=3)

Complexes	<i>Aspergillus niger</i>			<i>Helminthosporium oryzae</i>			<i>Fusarium oxysporium</i>		
	25	50	100	25	50	100	25	50	100
INH	12.3 \pm 0.132	13.4 \pm 0.205	15.5 \pm 0.230	14.516 \pm 0.268	14.520 \pm 0.156	18.5 \pm 0.230	15.4 \pm 0.264	16.416 \pm 0.180	19.650 \pm 0.132
[Ni(L)(H ₂ O) ₂] ₂ Cl ₂	22.22 \pm 0.133	23.416 \pm 0.245	25.466 \pm 0.260	23.6 \pm 0.057	25.583 \pm 0.245	29.4 \pm 0.152	24.6 \pm 0.132	26.550 \pm 0.144	31.633 \pm 0.120
[Ni(L)(H ₂ O) ₂] ₂ (NO ₃) ₂	20.17 \pm 0.101	22.606 \pm 0.109	23.566 \pm 0.176	21.607 \pm 0.228	24.466 \pm 0.240	24.466 \pm 0.202	23.816 \pm 0.060	25.616 \pm 0.235	29.66 \pm 0.185
[Ni(L)(H ₂ O) ₂] ₂ (CH ₃ COO) ₂	19.40 \pm 0.168	20.333 \pm 0.176	19.4 \pm 0.251	20.540 \pm 0.121	22.613 \pm 0.12	21.666 \pm 0.120	21.566 \pm 0.088	23.520 \pm 0.102	28.66 \pm 0.088
[Co(L)(H ₂ O) ₂] ₂ Cl ₂	25.31 \pm 0.174	26.493 \pm 0.125	29.366 \pm 0.176	26.503 \pm 0.192	27.520 \pm 0.147	30.5 \pm 0.202	27.693 \pm 0.089	28.650 \pm 0.173	33.43 \pm 0.233
[Co(L)(H ₂ O) ₂] ₂ (NO ₃) ₂	24.53 \pm 0.235	25.316 \pm 0.101	25.433 \pm 0.233	25.466 \pm 0.176	26.700 \pm 0.115	26.5 \pm 0.115	26.850 \pm 0.076	27.190 \pm 0.147	31.6 \pm 0.208
[Co(L)(H ₂ O) ₂] ₂ (CH ₃ COO) ₂	22.37 \pm 0.138	24.423 \pm 0.164	21.5 \pm 0.230	23.5 \pm 0.030	25.640 \pm 0.105	23.433 \pm 0.233	24.6 \pm 0.057	26.726 \pm 0.050	29.6 \pm 0.115
[Cu(L)(H ₂ O) ₂] ₂ Cl ₂	28.46 \pm 0.112	29.623 \pm 0.159	33.7 \pm 0.115	29.590 \pm 0.161	30.516 \pm 0.204	34.366 \pm 0.176	30.350 \pm 0.115	31.333 \pm 0.145	36.46 \pm 0.202
[Cu(L)(H ₂ O) ₂] ₂ (NO ₃) ₂	27.65 \pm 0.163	28.650 \pm 0.144	28.4 \pm 0.208	28.730 \pm 0.141	29.683 \pm 0.101	30.5 \pm 0.230	29.610 \pm 0.149	30.533 \pm 0.202	33.66 \pm 0.120
[Cu(L)(H ₂ O) ₂] ₂ (CH ₃ COO) ₂	26.48 \pm 0.122	27.496 \pm 0.226	24.466 \pm 0.260	27.703 \pm 0.186	28.5 \pm 0.076	27.4 \pm 0.208	28.523 \pm 0.257	29.603 \pm 0.129	30.5 \pm 0.115
Fluconazole	30.44 \pm 0.175	31.316 \pm 0.187	35.666 \pm 0.088	31.333 \pm 0.220	33.6 \pm 0.057	36.433 \pm 0.202	33.770 \pm 0.070	34.630 \pm 0.066	38.46 \pm 0.185

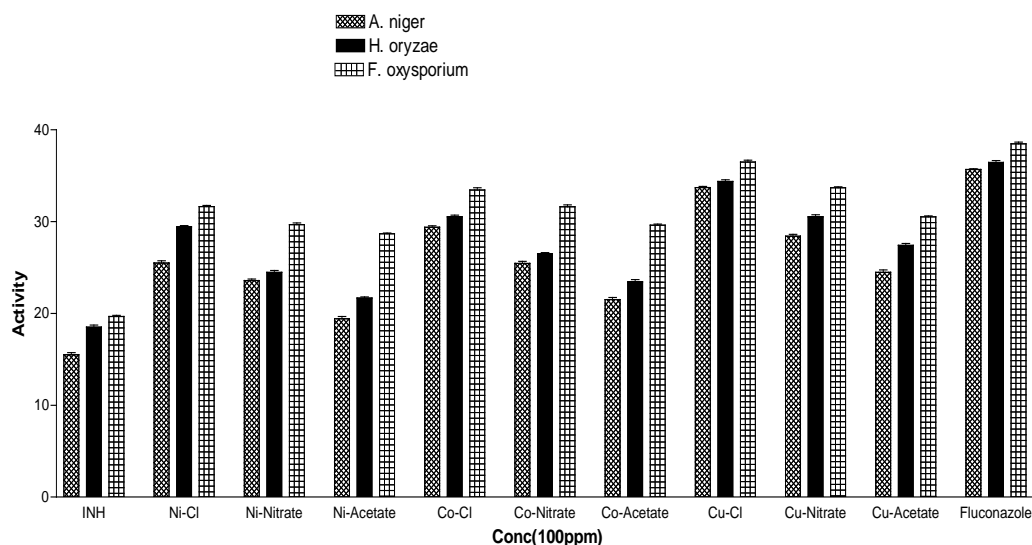


Fig. 7 Fungicidal activities of Cu(II), Ni(II) and Co(II) Complexes

5. Conclusion

i. On the basis of physicochemical studies on the complexes synthesized, they are found to possess nearly octahedral/ tetragonal geometry.

ii. The thermoanalytical investigations reveal that the relative stability of complexes follows the order Cu(II) > Co(II) > Ni(II) for any given anion.

iii. The binuclear nature of the complexes has been evidenced from ESR studies.

iv. The fungicidal screening test indicates all the complexes to be potentially active fungicidal agents. The activity order of different complexes is found to be Cu(II) > Co(II) > Ni(II).

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