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**EVALUATION OF ANTI-EPILEPTIC AND ANTI-MICROBIAL ACTIVITY OF
Cu(II), Co(II) AND Ni(II) COMPLEXES: SYNTHESIS AND STRUCTURAL
ELUCIDATION**

DHIVYA PRIYA. D¹, AKILA E² AND MAHESWARAN. P^{1*}

1: Department of Chemistry, PGP College of Arts and Science, Namakkal

2: Department of Chemistry, Sri Sarada College for women (Autonomous), Salem-16

3: Principal and Head, PGP College of Arts and Science, Namakkal

***Corresponding Author: E Mail: pm_omk@yahoo.co.in**

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ABSTRACT

The novel Schiff base has been designed and its metal complexes of Co(II), Ni(II) and Cu(II) have been synthesized from their relating metal chlorides utilizing the bioactive ligand acquired from Indole-2,3-dione and 2-(2-aminophenyl)benzimidazole in alcoholic media. Several tools like elemental analyses, magnetic susceptibility, molar conductance, FT-IR, Far IR, UV-Vis, ¹H NMR, Cyclic voltammetry and ESR have been used to obtain the chemical structures of synthesized transition metal complexes. Spectral studies showed that the Schiff base was behaved as Nitrogen and oxygen coordinating chelating agents. Electronic spectra coupled with magnetic susceptibility data suggested that all complexes possess an octahedral geometry. The in vitro biological screening impacts of the explored compounds were tested against the bacterial species (*Bacillus subtilis*, *Salmonella typhi*) and fungal strains (*Aspergillus niger*, *Candida albicans*) by disc diffusion method. A comparative study of inhibition values of the Schiff base ligand and their complexes indicate that the Co-complexes exhibit higher antimicrobial activity than other complexes. The compounds synthesized were screened for anticonvulsant potentialities in *Albino Wistar Rats* by maximal electroshock seizure (MES) and pentylenetetrazole (PTZ) test respectively. The toxicity and hematological properties were inspected for prepared compounds by sub-acute toxicity study. The results revealed that compounds were found to exhibit significant

anticonvulsant property at 10 mg/kg dose level when compared with the reference drug phenytoin in both seizure tests.

Keywords: Schiff base, Isatin, 2-(2-aminophenyl)benzimidazole, Antimicrobial, acute toxicity and Anticonvulsant activity

INTRODUCTION

The discovery of new effective antiepileptic drugs for the treatment of epilepsy still remains a top priority as it affects approximately 1–2 % of the world population [1]. Convulsions or epilepsy is most devastating chronic neurological disorder characterized by recurrent spontaneous seizures, in addition to unpredictable and periodic occurrence of a transient alteration of behavior due to the disordered, synchronous and rhythmic firing of populations of brain neurons. At present, available antiepileptic drugs (AEDs) have proven to be effective in reducing convulsions at the same time their therapeutic efficacy is conquered by some undesirable side effects such as drowsiness, mental dullness, ataxia, hepatotoxicity, megaloblastic anemia [2-4]. Therefore, the development of newer antiepileptic drugs with novel therapeutic targets, enhanced efficacy (increase seizure control, increased tolerability and pharmacokinetic properties) and minimal side-effects become a major goal in epilepsy research [5]. The synthetic chemistry is a major target in the search of new lead drugs to be used for protection against this debilitating neurological disorder. Heterocyclic nucleus namely

indole has gained importance in medicinal chemistry due to its diverse biological activities [6, 7] and numerous indole derivatives are reported to exhibit effective anticonvulsant activity [8, 9].

Schiff base ligands are widely significant and considered generally on the grounds that they can promptly frame stable complexes with most of the metal ions [10, 11]. Metal complexes of these ligands are pervasive due to their facile synthesis, wide applications and also the accessibility of different structural modifications [12]. Their chelating structures, moderate donating of electron and easy tunable electronic and steric impacts additionally make Schiff bases as flexible ligands equipped for setting various metals in different oxidation states with unusual structural features and controlling the performance of metals in an assortment of suitable catalytic transformations [13-16]. Schiff base complexes involving oxygen and nitrogen donor ligands are notable [17] and have empowered unprecedented eagerness among chemists due to their applications in catalysis and their pertinence to bioinorganic system [18].

Benzimidazoles considered being significant class of heterocyclic organic compounds and containing a phenyl ring intertwined to an imidazole ring [19, 20]. In recent years, this class of organic compounds has gathered a great deal of consideration, particularly because of their applications in diverse biological and chemical studies [21]. Schiff bases of benzimidazole have been reported with remarkable antimicrobial [22], antiviral [23] and analgesic [24], anti-inflammatory [25], anti-tumor agents [26], anti-parasitic agents [27], and anti-proliferative [28] activities. To best of our insight, the physiological action and commercial applications of Schiff base metal complexes derived from 2-(2-aminophenyl)-1-H-benzimidazole has scarcely been explored. In this correspondence, we depict the chelation behavior of Schiff base got from the condensation of indole-2, 3-dione and 2-(2-aminophenyl)benzimidazole. Further the metal complexes were acquired utilizing distinctive metal particles like Co(II), Ni(II), and Cu(II) so as to acquire increasingly intense Biological active compounds. To know the geometry of the Schiff base complexes, all the compounds were examined by Physico-chemical and spectral methods. Biocidal and Pharmacological action was carried for every one of the compounds.

EXPERIMENTAL PROTOCOLS

Materials and Physical measurements

The entire chemicals were supplied by sigma Aldrich and used without purification. Melting points were examined by open tube capillary method and are uncorrected. Elemental analyses (C, H and N) were performed by the aid of Perkin-Elmer Elemental analyzer. The molar conductance measurements were carried out at room temperature using Elico model conductivity meter. IR spectra were obtained on a Thermo Nicolet, FT-IR spectrometer (Avatar 370 model) by using KBr pellets. ^1H NMR spectra were recorded on a Bruker Avance III, 400 MHz spectrometer using DMSO with TMS as an internal standard. Electronic spectra were obtained with a Perkin-Elmer Lambda 40(UV-Vis) using DMF in the range 200-800nm. The ESR spectra of powder samples were recorded by E-112 ESR Spectrometer with X-band microwave frequency (9.1 GHz).

Synthesis of Schiff base [(E)-3-((2-(1H-benzo[d]imidazol-2-yl)phenyl)imino)indolin-2-one]

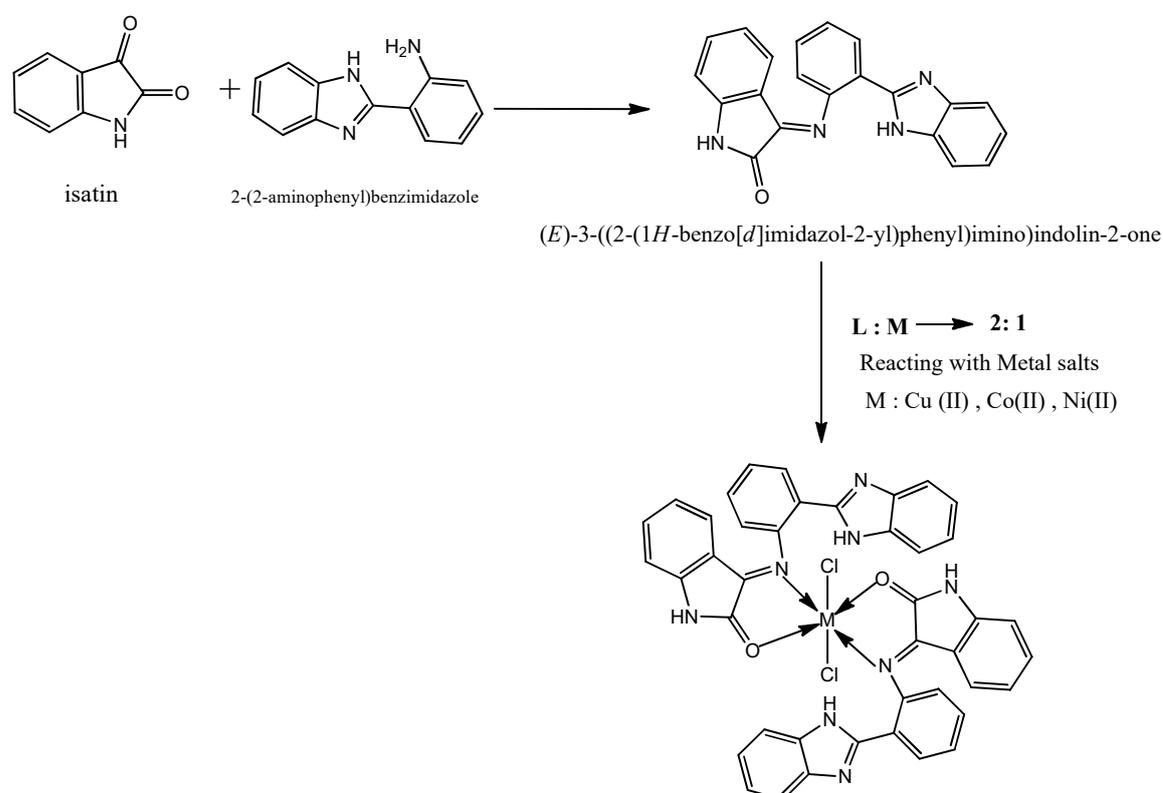
1H-indole-2, 3-dione (1mmol) was dissolved in absolute methanol (20ml) added dropwise to a solution of 2-(2-aminophenyl) benzimidazole (1mmol) in absolute methanol (20 ml) with constant stirring. On stirring the solution turns orange color and the mixture was then

refluxed at 70°C for 3 hrs. The solution was kept for slow evaporation to obtain yellow colored precipitate. The precipitate was washed with ethanol and then dried in air.

Synthesis of metal complexes

The methanolic solution of corresponding salts [CoCl₂.6H₂O, CuCl₂.2H₂O and NiCl₂.6H₂O] was slowly mixed to hot

stirring methanolic solution of ligand L in 2:1 (L: M) molar ratio. The reaction mixture was kept under reflux at 70°C for 3 hrs. Then, the reaction mixture was allowed to cool by slow evaporation and colored precipitates were collected (Scheme 1). The collected precipitates were filtered, washed with cold ethanol and dried in air.



Scheme 1: Preparation of the Schiff base and its Metal complexes

Biological activity

The biological activities of the newly prepared Schiff base and its metal complexes have been screened for their antibacterial and antifungal activities by disc diffusion method [29]. In-vitro antimicrobial activity was screened by using Muller Hinton Agar (MHA) obtained from Hi-media (Mumbai). The antibacterial and antifungal activities were done by

using the following organisms (*Bacillus subtilis*, *salmonella typhi* and *Aspergillus niger*, *Candida albicans*). These bacterial and fungal strains were chosen as they are the known pathogens of human body and used at 25, 50, 75 and 100 µmL⁻¹ concentrations in DMSO. The Petri plates were kept for incubation at 37°C for 24 hrs (bacterial) and at 37°C for 72 hrs (fungal). At the end of incubation, inhibition zones

formed around the disc were measured with transparent ruler in milli-meter. Standard antimicrobial drug (chloramphenicol and Fluconazole) was also screened under similar conditions for comparison.

Pharmacology

The entire compounds incorporated in the present study were screened for their anticonvulsant and acute toxicity activities.

Maximal electroshock seizure (MES) test

Maximal electroshock seizure model was used to evaluate the anticonvulsant activity of various synthetic compounds. Seizures were induced in rats by delivering electroshock of 150 mA for 0.2 sec. by means of an electro-convulsometer through a pair of ear clip electrodes [30]. The test animal (n=6) received 10 mg/kg between various synthetic compounds through intraperitoneally and standard group received phenytoin (25 mg/kg) injected i.p and tested after 30 minutes for MES induced seizure response. All the experimental groups were compared with the control treated with vehicle.

Pentylentetrazole (PTZ) induced seizures

PTZ at the dose of 80 mg/kg was injected i.p. to induce tonic-clonic convulsions in rats. The animal (n=6) received 10 mg/kg various synthetic compounds intraperitoneally and standard group received Phenytoin (25 mg/kg) injected i.p. PTZ was injected i.p. 60 min. after the administration

of drug. Occurrence of HLTE (Hind Limb Tonic Expend) and duration seizure were noted.

Acute toxicity

Male and female Wistar rats weighing 180 ± 10 g are used for the present study. The animals are divided into 6 groups of four animals each. The dose of the preparation is calculated based on the body weight of the animal. The animals in Group I are administered with a single daily dose of 0.5 ml of Tween 80 orally for 20 days. The animals in Group II to VI are administered with 10 mgkg^{-1} between various synthetic drugs once daily for 20 days. The animals are then weighed every five days, from the start of the treatment, to record the weight variation. At the end of the treatment, blood samples are collected by puncturing retro orbital plexus after mild anesthesia for biochemical analysis. The collected blood sample is centrifuged within 5 min of collection at 4000 g for 10 min, which is analyzed for total cholesterol, total triglyceride, HDL-cholesterol levels, LDL-cholesterol, plasma glucose, alanine aminotransferase (ALT), aspartate aminotransferase (AST), creatinine and urea.

Statistical analysis

Data were expressed as percentage (%) protection and mean \pm SEM and were analyzed by one-way ANOVA followed by Dunnett's test for multiple comparisons

using the SPSS version 10. Results were considered significant at $p < 0.05$.

RESULTS AND DISCUSSION

The Schiff base ligand (L) was acquired as a yellow solid precipitate and dissolvable in common organic solvents. The resultant Schiff base complexes are soluble in DMF and DMSO but sparingly soluble in common organic solvents. The analytical data and physical properties of the ligand and its mononuclear complexes are listed in **Table 1**. The analytical data indicate that the metal to ligand proportion is 1:2 for all the complexes. The electrolytic nature of complexes was measured in DMSO using 10^{-3} M solutions at room temperature. From the result, the molar conductance values lies in the range of 17-26 $\text{ohm}^{-1}\text{cm}^2\text{mol}^{-1}$ for the derived mononuclear Schiff base metal complexes. The molar conductance data suggested that no anions are present outside the coordination sphere which indicates that complexes were non-electrolytic in nature [31].

Infrared Spectra

The structure confirmation of metal complexes can be effectively accomplished by contrasting the IR spectra of the free ligands with their metal complexes (**Table 2**). Such comparison exposed that the absorption band showing up in the ligand spectra at $1619 - 1616 \text{ cm}^{-1}$ due to the azomethine group is shifted to higher wavenumbers by $1-3 \text{ cm}^{-1}$ in the complexes

spectra, proposing coordination through the azomethine nitrogen [32, 33]. The band appeared at 1725cm^{-1} is characteristic of C=O group ligand [34] and upon complexation, this band is shifted to higher frequency $1726-1733 \text{ cm}^{-1}$, showing the coordination of carbonyl oxygen to the metal ion which is further bolstered by the appearance of a non-ligand bands in the regions $486-489 \text{ cm}^{-1}$, $521-531 \text{ cm}^{-1}$ and $338-355 \text{ cm}^{-1}$ which are expected to (M-N), (M-O) and (M-Cl) bands [35-38], respectively. Further, the ligand and complexes also display bands at $3174-3361\text{cm}^{-1}$ due to ν (N-H) stretching vibration of isatin and benzimidazole moiety [39].

^1H NMR spectra of the ligand

^1H NMR spectra of the Schiff base were recorded in DMSO and represented in **Figure 1**. The ^1H -NMR spectra of the ligand exhibited a multiple within the range 6.05–7.85 ppm which assigned to aromatic protons. The signals observed as a singlet is due to N-H Protons of Isatin and benzimidazole moieties and appeared at 10.8–11.05 ppm [39, 40]. These signals provide structural arrangement for the synthesized ligand.

Electronic spectra and magnetic moments

The electronic spectra were utilized for assigning the stereochemistry of the metal ions in the complexes reliant on the number

of d–d and charge transfer transitions (Table 3). The electronic spectrum of free Schiff base ligand shows mainly two bands at 270 and 335 nm which is assigned to π – π^* transition of phenyl ring and n – π^* transitions related with in C=N chromophore. On complexation this band was shifted to lower and higher wavelength region proposing the coordination of azomethine nitrogen to the central metal ion. The copper (II) complex shows a broad absorption peak at 560 nm which corresponds to ${}^2E_g \rightarrow {}^2T_{2g}$ transition. The intensity of the bands and the magnetic moment value (1.70 BM) obtained for this complex confirms the octahedral geometry around Cu(II) ion. The spectrum of Co(II) complex are consistent with the formation of an octahedral geometry with the appearance of two absorption bands at 555 nm and 608 nm which may correspond to $4T_{1g}(F) \rightarrow 4T_{2g}(F)$ and $4T_{1g}(F) \rightarrow 4A_{2g}(F)$ transitions, respectively, further supported by the value obtained for magnetic moment 4.29 B.M. The magnetic moment of the Ni(II) complex lies at 3.12 B.M corresponds to two unpaired electrons, the spectrum of reported Ni (II) complexes shows band at 362 nm, 718 nm are ascribed to ${}^3A_{2g}(F) \rightarrow {}^3T_{1g}(F)$ and ${}^3A_{2g}(F) \rightarrow {}^3T_{1g}(P)$ transitions respectively, which is consistent with a formation of octahedral geometry as expected.

ESR spectra of Cu(II) complex

The ESR spectra of $C_{42}H_{28}CuN_8O_2Cl_2$ complex were recorded at 9.1 GHz frequency at room temperature and the figure were shown in Figure 2. The ESR spectral study of Cu(II) complex provides information around the metal ion environment. The ESR spectrum of the mononuclear schiff base Cu(II) complexes exhibits two signals g_{\parallel} at 2.234 and g_{\perp} at 2.012 respectively. The g_{av} ($g_{av} = 1/3(g_{\parallel} + 2g_{\perp})$) value was calculated to be 2.08. The value of $g_{\parallel} < 2.3$ in the present Cu-complex gives a clear indication of covalent character of the metal–ligand bond and delocalisation of the unpaired electron into the ligand. These values follows the same trend $g_{\parallel} > g_{\perp} > g_e$ (2.00276) which suggest that the presence of unpaired electron $dx_{2-}y_2$ orbital giving octahedral geometry [39].

Electrochemical studies

Electroanalytical methods are the most effectual and flexible techniques accessible for the mechanistic study of redox systems. The cyclic voltammogram of Co(II), Ni(II) and Cu(II) complex in DMF solution containing TBAP as supporting electrolyte were recorded in the potential range from 0.5 to 2.0 V. A cyclic voltammogram for metal complexes are conferred in Figure 3.

The cyclic voltammogram of Schiff base complexes contains two peaks and are due to oxidative nature of organic molecule and reductive nature of azomethine group

which is present in Schiff base. The copper $[C_{42}H_{28}CuN_8O_2Cl_2]$ complex shows well-defined redox process and ΔE_p values falls in the range of 160 mV, 230 mV which demonstrates quasi-reversible reduction-oxidation waves. The $E_{1/2}$ values falls in the range of -1.32 V indicates one electron reduction of $Cu(II) \rightarrow Cu(I)$ process whereas 0.96 V indicates the oxidation process of $Cu(I) \rightarrow Cu(II)$. The cobalt $[C_{42}H_{28}CoN_8O_2Cl_2]$ complex exhibit ΔE_p values in the range of 180 mV and 110 mV which corresponds to quasi-reversible reduction-oxidation waves. The $E_{1/2}$ values lies in the range of -0.73 V indicates one electron reduction of $Co(II)/Co(I)$ process whereas 0.89 V indicates the oxidation process. The Nickel $[C_{42}H_{28}NiN_8O_2Cl_2]$ complex shows well-characterized redox process relating to the formation of the quasi-reversible reduction $Ni(II)/Ni(I)$ and oxidation $Ni(I)/Ni(II)$ couple. The both ΔE_p (100/160 mV) and $E_{1/2}$ (-1.03 / 0.46 V) values indicate that each couple corresponds to quasi-reversible one electron transfer process.

Antimicrobial Studies

The bacterial and fungicidal effect of the Schiff base and its metal complexes (Cu, Co, Ni) were determined against microorganisms such as *Bacillus Subtilis*, *Salmonella typhi*, *Aspergillus niger* and *Candida albicans* using the agar diffusion technique under four different concentration. The microbial activity of the

synthesized compounds was also compared with standard antibacterial agent (Chloramphenicol) and antifungal agent (Fluconazole). The results of MIC values and zone of inhibition (in mm) for microbial activity are presented in **Figure 4 & 5**. The MIC values of the ligand (100 μ g/ml) against bacteria (*S.typhi* and *B.subtilis*) are higher to standard drug chloramphenicol though for fungal strains (100 μ g/ml) shows lower action for *Aspergillus niger* and higher activity for *Candida albicans*. A similar investigation of minimum inhibitory concentration (MIC) values indicated that the metal complexes have moderate action when contrasted with the standard but all the complexes are more active than their respective ligand. From the consequence of the antimicrobial, it has been uncovered that cobalt complex shows better activity than other complexes for both bacterial and fungal strains. A possible reason behind the enhanced activity of the metal complexes has been postulated in the light of chelation theory. It was suggested that chelation significantly lessens the charge of the metal ion mainly due to partial sharing of its positive charge with the donor groups and viable p-electron delocalization over the entire chelate ring [41]. Such a chelation could improve the lipophilic character of the central metal atom, which in this way supports its penetration through the lipid

layers of the cell membrane and hindering the metal binding sites on enzymes of microorganism [42, 43]. Besides, the method of activity of the compound may include the formation of a hydrogen bond through the azomethine group with the active centre of the cell, ensuing in interference with the normal cell processes.

Anticonvulsant activity

Antiepileptic activity data of the Schiff base and its metal complexes are presented in **Table 4**. In the present investigation, the synthetic compounds were exposed to a screening anticonvulsant assays including MES and PTZ induced seizure tests in Wister albino rats. The standard medication phenytoin (25 mg/kg) and the various synthetic compounds (10 mg/kg) exhibited significant anticonvulsant action against electroshock induced HLTE. In the MES, protection against HLTE predicts the anticonvulsant activity of the tested agents and furthermore demonstrates the ability of various synthetic drugs to either stop or to slow down the discharge of the seizure within the brain stem substrate [44]. Seizure of MES can be blocked either by hindering the voltage-dependent Na^+ channels or by blocking glutamatergic excitation intervened by the N-methyl-D-aspartate (NMDA) receptors [45]. Since various synthetic drugs showed anti-epileptic activity in the MES, they may act by inhibiting the voltage-dependent

Na^+ channels or by obstructing the glutamatergic neurotransmission intervened by NMDA receptors.

In PTZ test, the outcomes showed that all synthetic compounds possess anticonvulsant activity compared to standard drug. The ability of all synthetic compounds to delay the onset of convulsions and/or shorten the duration of convulsions was considered an indication of anticonvulsant activity. Therefore, the anticonvulsant activities of various synthetic compounds against PTZ seizures might be due to an enhancement on the release of the inhibitory neurotransmitter GABA in the central nervous system, inhibiting T-type Ca^{2+} currents or blocking the glutamatergic neurotransmission mediated by NMDA receptors.

Sub-Acute toxicity

The assessment of sub-chronic and chronic dosing in experimental animals may be more relevant in determining the overall toxicity of the synthetic drug preparation. In the present study, where the acute toxicity study of various synthetic drugs was carried out as per OECD-423 guidelines, no mortality was observed in animals of control group as well as animals treated with synthetic drugs at dose 10 mgkg^{-1} . From the results, we found that there was no significant change in animal behavior due to the absence of toxicity. The animals treated with various synthetic

drugs showed normal growth pattern and body weight compared with control rats treated with normal saline are shown in **Table 5**. So the adjustments in body weight can be utilized as a pointer of antagonistic impacts of medications and synthetic substances [46-48].

The changes in enzymes like ALP, AST and ALT levels show liver impairment, due to toxicity [49]. After 14 days of administration of various synthetic drugs, it was found that at all concentrations drugs do not produce liver damage. The biochemical parameters are shown in **Table 6-8**.

The consequences of hematological parameters are tabulated in **Table 9**. After

14 days of treatment, there were no critical changes in the hematological parameter levels of WBC, RBC among control and test groups following repeated administration of various synthetic drugs. Interestingly, significant increase in the levels of hemoglobin was found in treatment and the possible reason could be that one of the constituents of various synthetic drugs may increase absorption of iron. From the overall toxicity results, it concludes that various synthetic drugs are non-toxic to the hematopoietic and leucopoietic system.

Table 1: Physical properties of ligand and its mononuclear metal complexes

Compound	Molecular Formula	color	Yield	Melting point (°c)	Calculated (found)%						Molar conductance Δ_m ($\text{ohm}^{-1} \text{cm}^2 \text{mol}^{-1}$)
					C	H	N	O	Cl	M	
Ligand	$\text{C}_{21}\text{H}_{14}\text{N}_4\text{O}$	Yellow	85	178	(74.54) 74.55	(4.17) 4.14	(16.56) 16.56	(4.73) 4.73	-	-	-
CuL	$\text{C}_{42}\text{H}_{28}\text{CuN}_8\text{O}_2\text{Cl}_2$	Dark green	80	200	(62.18) 62.2	(3.45) 3.45	(13.81) 13.82	(3.94) 3.95	(8.74) 8.64	(7.84) 7.84	26
CoL	$\text{C}_{42}\text{H}_{28}\text{CoN}_8\text{O}_2\text{Cl}_2$	Light brown	75	195	(62.54) 62.6	(3.47) 3.47	(13.89) 13.91	(3.97) 3.97	(8.79) 8.69	(7.31) 7.32	23
NiL	$\text{C}_{42}\text{H}_{28}\text{NiN}_8\text{OCl}_2$	Dark brown	70	242	(62.56) 62.6	(3.47) 3.47	(13.90) 13.91	(3.97) 3.97	(8.80) 8.80	(7.28) 7.29	17

Table 2: IR Spectroscopic studies of Schiff base ligand and its metal complexes

COMPOUNDS	C=N (ν, cm^{-1})	C=O (ν, cm^{-1})	N-H (ν, cm^{-1})	M-O (ν, cm^{-1})	M-N (ν, cm^{-1})	M-Cl (ν, cm^{-1})
Ligand	1616	1725	3174	-	-	-
CuL	1617	1733	3158	528	487	338
CoL	1619	1726	3168	531	486	355
NiL	1618	1731	3361	521	489	347

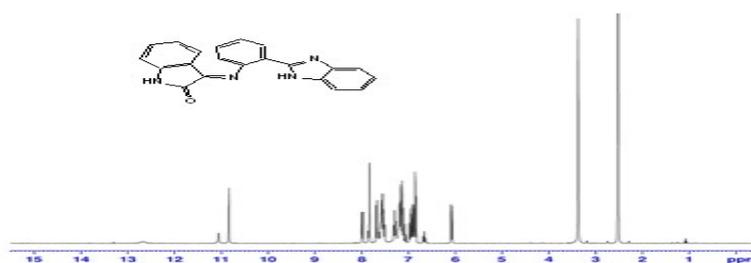


Figure 1: ¹H NMR Spectra for of Schiff base ligand

Table 3: Electronic spectral data of the ligand and their complexes

COMPOUNDS	$\pi-\pi^*$ (nm)	$n-\pi^*$ (nm)	L → M (nm)	d-d (nm)	Magnetic moment value (μ_{eff}) BM
Ligand	270	335	-	-	-
CuL	261	339	361	560	1.70
CoL	284	361	377	555,608	4.29
NiL	259	329	362	718	3.12

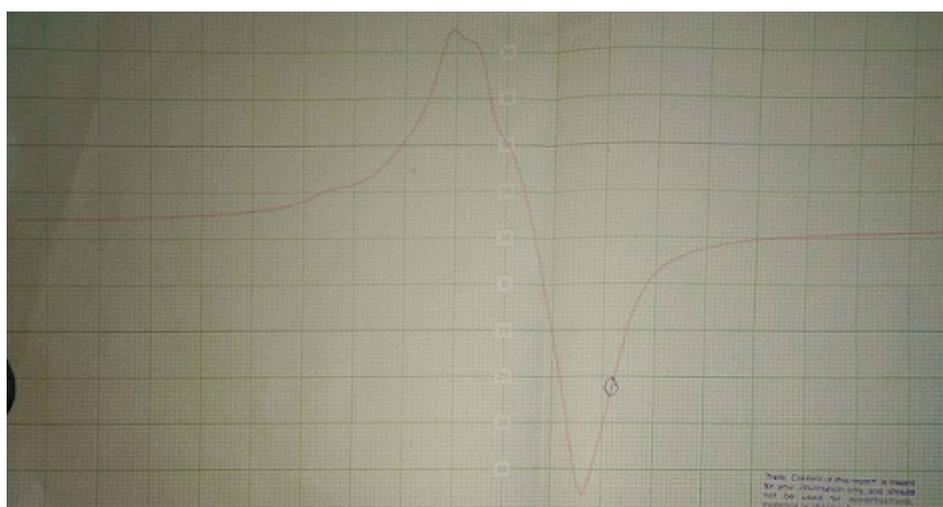


Figure 2: ESR Spectra for Cu complex

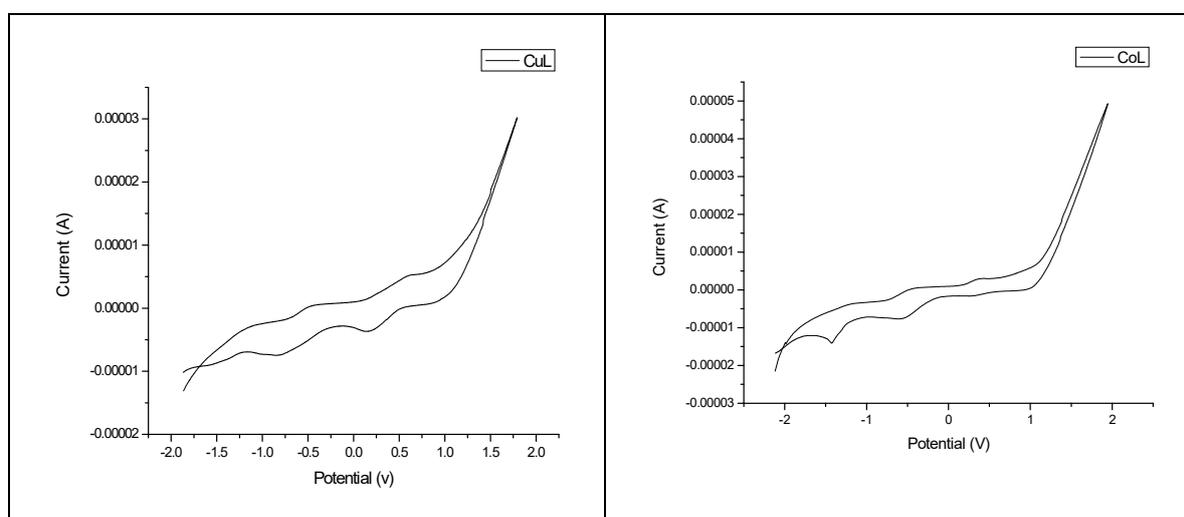


Figure 3: Cyclic voltammogram of CuL and CoL

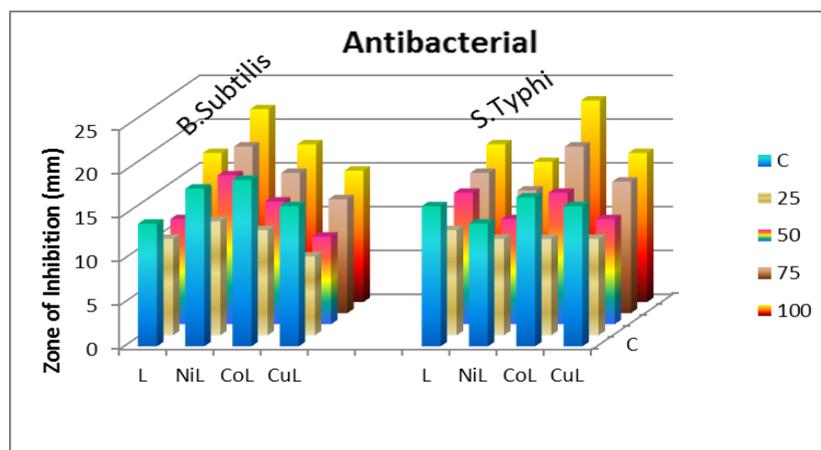


Figure 4: Antibacterial activity of Schiff base and its metal complexes

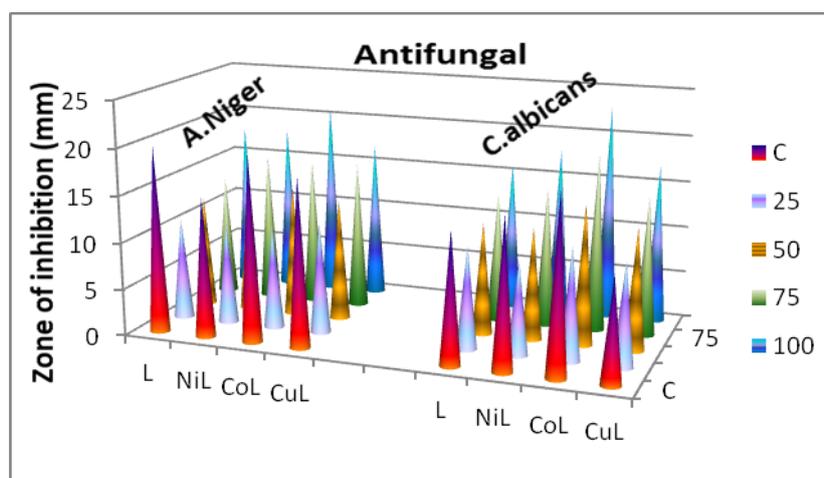


Figure 5: Antifungal activity of Schiff base and its metal complexes

Table 4: Anticonvulsant activity data of Schiff base and metal (II) complexes

Compound	Anticonvulsant activity			
	MES Screen		PTZ Screen	
	Dose ml/mg /kg	HLTE (Sec)	Onset time (sec.)	Duration of HLTE (sec.)
saline	10	13.45± 0.80	53.20± 1.05	34.20± 1.75
phenytoin sodium	25	1.0± 0.25a	0± 00	0± 00
L	10	2.70± 0.65a	54.90± 1.16	22.8± 0.68 a
CuL	10	2.66± 0.58a	56.15± 1.26	24.9± 0.77 a
CoL	10	2.38± 0.42a	55.35± 1.15	25.0± 0.78 a
NiL	10	2.56± 0.52a	55.22± 1.08	23.0± 0.75a

Table 5: Effect of Various synthetic drugs on body weight changes in rats

Compound	Dose (mg/kg)	Day 1	Day 5	Day 10	Day 20
Control	10	189.20±5.6	190.20 ±6.10	198.10 ±6.25	199.6±6.35
L	10	193.65 ±6.4	199.45 ±6.65	197.35 ±6.25	206.28±6.40
CuL	10	192.15 ±5.8	196.50 ±6.20	198.30 ±6.60	203.90±6.50
CoL	10	196.25 ±6.3	200.80±6.45	202.60 ±6.55	207.35±6.80
NiL	10	198.10 ±6.2	199.85 ±6.55	202.60 ±6.75	206.40±6.85

Table 6: Effect of Various synthetic drugs on kidney, heart, liver and brain in rats

Compound	Dose (mg/kg)	Heart (gms)	Kidney (gms)	Liver (gms)	Brain (gms)
Control	10	0.35 ± 0.04	0.72± 0.03	3.32± 0.14	0.72± 0.05
L	10	0.36± 0.05	0.77± 0.02	3.40± 0.18	0.76± 0.20
CuL	10	0.37± 0.06	0.84± 0.04	3.47± 0.21	0.70± 0.06
CoL	10	0.35± 0.03	0.76± 0.02	3.38± 0.20	0.78± 0.10
NiL	10	0.38± 0.05	0.83± 0.05	3.45± 0.19	0.72± 0.05

Table 7: Effect of Various synthetic drugs on biochemical profiles of rats

Compound	Dose (mg/kg)	Glucose (mg.dl ⁻¹)	Cholesterol (mg.dl ⁻¹)	Triglyceride (mg.dl ⁻¹)	HDL (mg.dl ⁻¹)	LDL (mg.dl ⁻¹)
Control	10	94.42± 1.74	39.05± 0.62	33.25± 1.43	143.45± 3.15	90.30±1.85
L	10	97.32±1.45**	41.55± 0.47	22.15± 1.18*	188.25± 3.62*	50.22±1.15
CuL	10	94.18± 1.54	27.90± 0.48*	18.58± 0.92*	172.22±3.35*	73.50±1.25
CoL	10	95.25±1.40**	40.45± 0.42	20.05± 0.96*	190.35± 3.40*	50.45±1.20
Nil	10	93.45± 1.60	26.22± 0.40*	18.40± 0.88*	182.35± 3.70*	75.80±1.40

Table 8: Effect of Various synthetic drugs on biochemical parameters such as AST, ALT, ALP, TP and Albumin in rats

Compound	Dose (mg/kg)	AST (IU.l ⁻¹)	ALT (IU.l ⁻¹)	ALP (IU.l ⁻¹)	TP (g.l ⁻¹)	ALBUMIN (g.l ⁻¹)
Control	10	320.3±11.60	65.4± 3.42	245.35± 8.60	63.36± 3.28	33.30±2.45
L	10	308.8±9.62	57.4±2.48	257.35±8.45	74.84± 3.85	32.88±2.34
CuL	10	308.6±9.45**	61.4± 2.78**	257.40± 8.25**	72.20± 3.86	32.20±2.48
CoL	10	311.7±9.98	56.2± 2.35	256.30± 8.40	73.40± 3.72	33.30±2.42
Nil	10	312.3±10.60**	62.8± 2.85**	256.20± 8.80**	64.22± 3.45	31.85±2.22

Table 9: Effect of Various synthetic drugs on hematological parameters in rats

Compound	Dose (mg/kg)	Hemoglobin (mg.dl ⁻¹)	RBC (10 ⁶ /mm ³)	WBC (10 ⁶ /mm ³)	Calcium (mg.dl ⁻¹)
Control	10	13.56± 1.28	9.24± 0.93	11.55± 0.90	9.44 ±0.60
L	10	12.80±1.15*	8.55± 0.95*	10.15± 1.05*	9.78 ±0.68
CuL	10	13.30± 1.85*	8.60± 1.02*	8.40± 0.85*	9.32 ±0.48
CoL	10	13.05±1.28*	8.30± 0.80*	9.50± 0.90*	9.58 ±0.60
Nil	10	12.40±1.45*	9.25± 1.08*	8.05± 0.80*	9.05 ±0.42

CONCLUSION

In the present work, a series of novel indole ring containing Schiff base has been structured and their relating metal complexes are synthesized by condensation method. The bonding of ligand to Metal ions and the overall geometry of metal complexes have been deduced on the basis of analytical data and various spectroscopic techniques. From the results, the chelation of metal ions to the ligand occurs through the oxygen atom of carbonyl group and the nitrogen atoms of the azomethine group. Electrochemical study indicates that metal complexes exhibit a single electron transfer quasi-reversible nature. The antimicrobial studies proposed that the Schiff bases were found to be biologically active and their metal complexes exhibited significantly

enhanced antibacterial and antifungal activities against microbial strains in comparison to the free ligands. The in-vitro cytotoxicity results showed that the complexes exhibited a significant inhibitory potency towards proliferation of the MCF-7 cell line. The anticonvulsant screening indicated that among the tested compounds, metal complexes exhibited noteworthy activity in both MES and PTZ Seizure test. The results of sub-acute toxicity study show that there was no significant change in animal behavior, hematological parameters due to the absence of toxicity.

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Conflict of interests

The authors declare that they have no conflict of interest

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