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Schiff Base–Copper(II) Complexes: Synthesis, Spectral Studies and Anti-tubercular and Antimicrobial Activity

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ABSTRACT

The present study deals with the synthesis, spectral characterization of Schiff base complexes of isoniazid, pyrazinamide an anti-tubercular drug, and benzhydrazide, nicotinohydrazide. Metal selected for complexation is copper. The complexes have been suitably synthesized and isolated in pure powdered form. Analytical data agree with the compositions $[L_2CuClO_4]ClO_4$. Molar conductance values suggesting that they were 1:1 electrolytic nature. The tentative structure assigned to the complexes on the basis of stoichiometry and analytical data were further supported by spectral studies viz.; Fourier transform infrared, magnetic susceptibility, electronic spectra, cyclic votammetry, liquid chromatography-mass spectrometry spectra, and electron paramagnetic resonance studies. A preliminary attempt has also been made to compare the potencies of metal complexes with parent drug. The copper(II) complexes are giving encouraging results.

Key words: *Schiff base, Isoniazid, Pyrazinamide, Benzhydrazide, Nicotinohydrazide, Anti-tubercular activity, Antimicrobial activity.*

1. INTRODUCTION

The heterocyclic hydrazones constitute an important class of biologically active drug molecules which have attracted the attention of medicinal chemists due to their wide-ranging pharmacological properties including iron scavenging and anti-tubercular activities [1,2]. Biological activities of many of these compounds were shown to be related to their metal chelating abilities in the past [3].

Schiff base ligands are excellent coordinating molecules and can exhibit variety in the structure of their metal complexes [4]. The literature reveals that Schiff base complexes have a very special role in the development of inorganic chemistry [5,6]. Schiff base metal complexes have been the subject of intensive research due to their novel properties and their industrial and biological importance. They are found to have a number of pharmacological applications [7,8]. It has been reported that certain Schiff bases exhibit anti-tubercular activities [9]. Thus, looking to the importance of Schiff bases with essential metals in the form of coordination compounds for the successful treatment of various diseases [10-13], we report the synthesis, characterization, anti-tubercular, and antimicrobial activity of the 12 copper(II) complexes, with 12 different NO donor ligands obtained in the reaction of isoniazid (1NH), pyrazinamide, benzhydrazide, and nicotinohydrazide with some dimethoxy benzaldehydes.

2. EXPERIMENTAL

2.1. Materials and Methods

All chemicals employed in the present study were of analytical grade and were used without purification. The purity of compounds were checked routinely by thin layer chromatography (0.5 mm thickness) using silica gel-G coated aluminum plates (Merck), and spots were visualized by exposing the dry plates to iodine vapors or by exposing ultraviolet (UV) light.

Elemental analyzes of the compounds were performed on Vario micro cubes elemental analyzer. Magnetic susceptibility of the copper complexes was measured at room temperature (28±2°C) on a simple Guoy-type balance. Fourier transform infrared (FT-IR) spectra were recorded on Shimadzu FT-IR spectrophotometer using KBr technique in the 4000-400 cm^{-1} range. Electronic spectra of the copper(II) complexes was recorded on a Systronics PC based Double Beam Spectrophotometer 2202 using dimethylformamide (DMF) as the solvent. Electrical conductances of the complexes were made

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on freshly prepared 10^{-3} M solutions in DMF at room temperature on an Equiptronics conductivity meter Model No. EQ-665 with a dip type cell having platinum electrode. Cyclic voltammetric measurements of all the synthesized complexes were carried out on an HCH instruments version 5.01, model 600c series electrochemical analyzer using tetrabutylammonium perchlorate as supporting electrolyte. The three-electrode cell comprised of saturated calomel electrode as a reference electrode, platinum wire as counter electrode, and glassy carbon as working electrode. Dissolved oxygen was removed by purging the solution with pure nitrogen for about 15 min before each experiment. Scanning the cyclic voltammogram for a blank solution was done to check the purity of the supporting electrolyte and the solvent. X-band electron paramagnetic resonance (EPR) spectra of the complexes were recorded in the solid state at LNT and in DMF using Varian E-112 X/Q band spectrophotometer. The g values were calculated taking the diphenylpicrylhydrazyl (DPPH) radical as a reference (g=2.0036).

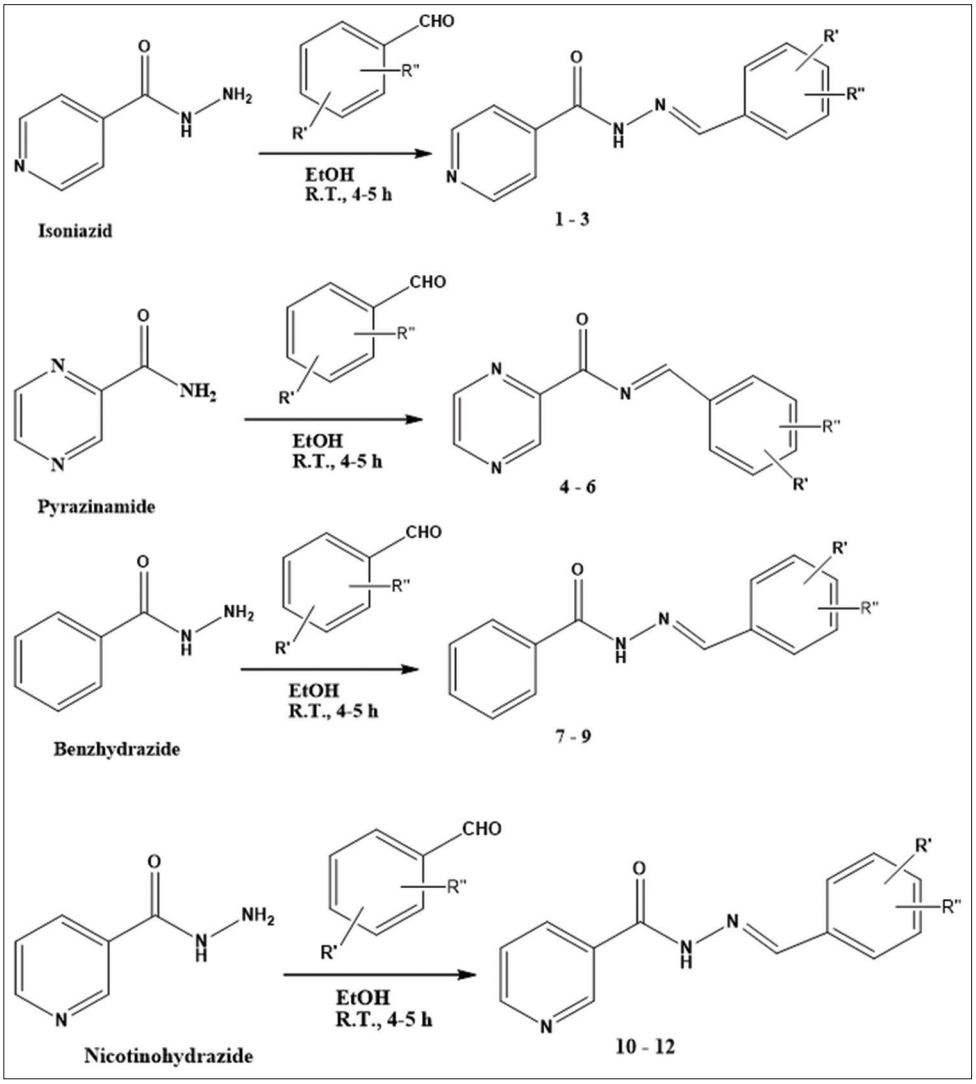
2.2. Synthesis of the Ligands

The ligands were prepared in a similar manner according to the earlier reported procedures (Scheme 1 and Table 1) [14].

2.3. Synthesis of the Copper(II) Complexes

The copper(II) complexes were prepared [15,16] by two methods: (i) By reacting stoichiometric amounts of the Schiff base and the metal salts, (ii) by carrying out the *in situ* reaction of amine, dimethoxy benzaldehyde, and metal salt. However, in both the cases, complexes of the same stoichiometry were isolated. We have adopted the *in situ* reaction in the present investigation as exemplified below.

Hydrazide (2 mmol) and dimethoxy benzaldehyde (2 mmol) were taken together in ethanol (30 ml) and refluxed for 0.5 h after which copper(II) acetate (1 mmol) in ethanol was added, and refluxing was continued for another 3-4 h. Finally, sodium perchlorate (2 mmol) in water was added as a counter ion and



Scheme 1: Synthesis of ligands.

refluxing was continued for some time (Scheme 2). Upon cooling, copper(II) complex precipitated out. It was filtered, washed thoroughly with ethanol and dried. All other complexes were synthesized in an identical manner.

The synthesized complexes were green colored solids and found to be highly stable under laboratory conditions to be stored for a long time.

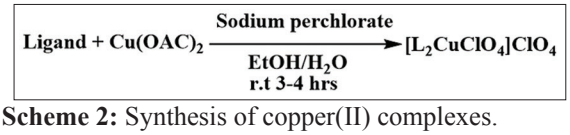
2.4. In-vitro Antibacterial Activity

The antibacterial activity of synthesized copper(II) complexes were evaluated by the agar well diffusion method. Muller Hinton agar medium (20 ml) was poured into each petri plate, and plates were swabbed with 100 µl inocula of the test microorganisms and kept for 15 min for adsorption. Using sterile cork borer of 8 mm diameter, wells were bored into the seeded agar plates, and these were loaded with a 100 µl solution of each compound in dimethylsulfoxide (DMSO) with a concentration of 4.0 mg/mL. All the plates were incubated at 37°C for 24 h. Antibacterial activity of each synthesized complexes were evaluated by measuring the zone of inhibition against the Gram-positive bacteria *Bacillus subtilis* (B.s), *Staphylococcus aureus* (S.a), *Streptococcus pyogenes* (S.p), *Enterobacter faecalis* (E.f), Gram-negative bacteria *Escherichia coli* (E.c), *Klebsiella pneumoniae* (K.p) with zone reader. DMSO was used as a solvent, whereas tetracycline was used as a standard. This procedure was performed in three replicate plates for each organism [17,18].

Table 1: List of chemicals used to prepare ligands.

A	B	Ligand
Isoniazid	Benzaldehyde	1
	2,3-dimethoxy benzaldehyde	2
	3,4-dimethoxy benzaldehyde	3
PZA	Benzaldehyde	4
	2,3-dimethoxy benzaldehyde	5
	3,4-dimethoxy benzaldehyde	6
BZA	Benzaldehyde	7
	2,3-dimethoxy benzaldehyde	8
	3,4-dimethoxy benzaldehyde	9
NCA	Benzaldehyde	10
	2,3-dimethoxy benzaldehyde	11
	3,4-dimethoxy benzaldehyde	12

PZA=Pyrazinamide, BZA=Benzhydrazide, NCA=Nicotinohydrazide



Scheme 2: Synthesis of copper(II) complexes.

2.5. In-vitro Antifungal Activity

The antifungal activity of synthesized copper(II) complexes were evaluated by the agar well diffusion method. Sabouraud dextrose agar (20 ml) was poured into each petri plate, and plates were swabbed with 100 µl inocula of the test microorganisms and kept for 15 min for adsorption. Using sterile cork borer of 8 mm diameter, wells were bored into the seeded agar plates, and these were loaded with a 100 µl solution of each compound in DMSO with a concentration of 4.0 mg/mL. All the plates were incubated at 37°C for 24 h. Antifungal activity of each synthesized complexes were evaluated by measuring the zone of growth inhibition against the fungi such as *Aspergillus fumigatus (A.f), Aspergillus niger (A.n), Candida albicans (C.a)* with zone reader. DMSO was used as a solvent, whereas ketoconazole was used as a standard. This procedure was performed in three replicate plates for each organism [17,18].

2.6. Minimum Inhibitory Concentration (MIC)

MIC of the various synthesized copper(II) complexes were tested against bacterial strains through a macro dilution tube method as recommended by NCCLS. In this method, the various test concentrations of synthesized compounds were made from 100 to 0.25 µg/mL in sterile tubes No.1-10. A 100 µl sterile Muller Hinton broth was poured in each sterile tube followed by addition of 200 µl test compound in tube 1. Two-fold serial dilutions were carried out from tube 1 to the tube 10, and excess broth (100 µl) was discarded from the last tube No. 10. To each tube, 100 µl of standard inoculums (1.5×10^8 cfu/mL) was added. Turbidity was observed after incubating the inoculated tubes at 37°C for 24 h [19].

2.7. Anti-tubercular Activity

The primary screening was conducted at a concentration of 250 µg/mL against *Mycobacterium tuberculosis* H37Rv in the BACTEC 460 radiometric system [20]. The MIC was defined as the lowest concentration inhibiting 99% of the inoculums.

2.8. Statistical Analysis

The results were expressed as mean ± standard error of mean. Statistical analysis of the data was carried out using Student's t-test, and the results were considered significant when $p<0.05$.

3. RESULTS AND DISCUSSION

3.1. Molar Conductivity and Magnetic Susceptibility Measurements

The molar conductance values of the complexes fall in the range 65-93 (Table 2) in DMF suggesting that they were 1:1 electrolytic nature [21]. The room temperature magnetic moment (μ_{eff}) values of the copper(II) complexes were found to be in the range from 1.86 to 2.07 BM indicative of monomeric compounds with square pyramidal geometry (Table 2) [22-26].

Table 2: Magnetic moment values and molar conductance data of the copper (II) complexes.

Complex	Empirical formula	$\chi'_m \times 10^{-6}$	μ_{eff} (BM)	Molar conductance (Ω^{-1} cm^2 mol^{-1})
1	$[(C_{13}H_{11}N_3O)_2CuClO_4]ClO_4$	1478.7	1.88	84
2	$[(C_{15}H_{15}N_3O_3)_2CuClO_4]ClO_4$	1491.5	1.89	78
3	$[(C_{15}H_{15}N_3O_3)_2CuClO_4]ClO_4$	1767.0	2.06	75
4	$[(C_{12}H_9N_3O)_2CuClO_4]ClO_4$	1715.9	2.03	67
5	$[(C_{14}H_{13}N_3O_3)_2CuClO_4]ClO_4$	1789.2	2.07	65
6	$[(C_{14}H_{13}N_3O_3)_2CuClO_4]ClO_4$	1664.6	2.00	68
7	$[(C_{14}H_9N_2O)_2CuClO_4]ClO_4$	1794.0	2.07	68
8	$[(C_{16}H_{13}N_2O_3)_2CuClO_4]ClO_4$	1445.8	1.86	70
9	$[(C_{16}H_{13}N_2O_3)_2CuClO_4]ClO_4$	1345.8	1.79	66
10	$[(C_{13}H_{11}N_3O)_2CuClO_4]ClO_4$	1666.8	2.00	77
11	$[(C_{15}H_{15}N_3O_3)_2CuClO_4]ClO_4$	1745.2	2.04	93
12	$[(C_{15}H_{15}N_3O_3)_2CuClO_4]ClO_4$	1779.0	2.06	82

Magnetic moment value per copper atom in the complex. χ'_m=Corrected molar susceptibility, μ_{eff}=Effective magnetic moment

3.2. IR Spectra

The IR spectra of the complexes, when compared with that of the free ligands, shows remarkable differences. Selected vibrational bands of the free ligands and the copper(II) complexes, useful for determining the mode of coordination of the ligands are given in Table 3. The peak due to C=N mode exhibited a shift to lower frequency suggesting [27,28] participation of exocyclic azomethine nitrogen in the complex formation. The NH stretching absorption of free ligand remained unaffected after complexation. During complexation, the carbonyl bands were shifted to lower frequency indicating the linkage of the metal with a ketonic oxygen atom. In the lower frequency region, the weak bands observed at 619-626 cm^{-1}, 486-495 cm^{-1}, and 447-457 cm^{-1} have been assigned to the υ(Cu-N), υ(Cu-O), and υ(Cu-Cl) vibrations [29,30], respectively. A very strong band present around 1020 cm^{-1}, typical of the perchlorate counter-ion υ(ClO_4^-) [31], was observed. Accordingly, it proved that the ligand binds the metal ion in a bidentate fashion with N, O coordination to copper(II) ion. The bonding sites are the azomethine nitrogen and the carbonyl oxygen atoms.

3.3. Electronic Spectra

The electronic spectra of the copper(II) complexes were recorded in DMF (10^{-3} mol^{-1}). The UV-Visible spectra of all these compounds showed four major absorption bands around 299, 363, 410, and 615 nm. The first band is assigned to π→π* intraligand transitions. On the other hand, the band corresponding to azomethine showed a slight shift to longer wavelength on complexation, indicating coordination of ligands to metal through the azomethine moiety. The band in the wavelength around 615 nm corresponds to d–d transition of this type as expected for square pyramidal copper(II) complexes [32-34].

3.4. EPR Spectra

The solid state EPR spectra of the complexes in the polycrystalline state at 77 K were recorded in the X-band region, using 100 KHz field modulation, and the g factors were quoted relative to the standard marker DPPH (g=2.0036). The EPR spectra of the complexes in the polycrystalline state at LNT (77 K) exhibited an isotropic signal, with g_{iso}=2.07. The g values obtained in the present study when compared to the g value of a free electron, 2.0023, indicates an increase of the covalent nature of the bonding between the metal ion and the ligand molecule [35]. The g_{iso} and A values of the complexes were given in Table 4.

3.5. Cyclic Voltammetry

Cyclic voltammetric studies of the copper(II) complexes were investigated [10] in DMF (10^{-3} mol^{-1}) at a scan rate of 0.01 V in the potential range +1.5 to −1.8 V. The redox potentials are summarized in Table 5. The ΔEp values range from 196 to 3058 mV. In complexes 2, 3, 4, 5, and 6, the i_{pa}/i_{pc} fall in the range 0.20-0.91, which is a clear indication of two one-electron transfer for redox process and for the complexes 1, 7, 8, 9, 10, 11, and 12 the i_{pa}/i_{pc} value fall in around 1.79, which is an indication of one two-electron transfer process. From the above observations, it is well-clear that the mononuclear copper complexes 2, 3, 4, 5, and 6 undergo two one-electron quasi-reversible reductions and the complexes 1, 7, 8, 9, 10, 11, and 12 undergo one two-electron quasi-reversible reduction.

$$Cu(II) \underset{-2e^-}{\overset{+2e^-}{\rightleftharpoons}} Cu(0)$$

$$Cu(II) \underset{-e^-}{\overset{+e^-}{\rightleftharpoons}} Cu(I) \underset{-e^-}{\overset{+e^-}{\rightleftharpoons}} Cu(0)$$

Table 3: IR spectral data (cm^{-1}) of copper(II) complexes.

Compound	υ (cm^{-1})						
	>C=N	>C=O	>N-H	ClO_4-	Cu-O	Cu-N	Cu-Cl
Ligand (1)	1554	1678	3064	-	-	-	-
1	1504	1604	NC	1020	486	624	447
Ligand (2)	1568	1664	3064	-	-	-	-
2	1508	1604	NC	1024	491	619	457
Ligand (3)	1519	1654	3061	-	-	-	-
3	1502	1591	NC	1022	495	626	455
Ligand (4)	1595	1708	-	-	-	-	-
4	1587	1660	-	1049	499	623	445
Ligand (5)	1587	1681	-	-	-	-	-
5	1581	1660	-	1047	493	569	449
Ligand (6)	1585	1680	-	-	-	-	-
6	1516	1662	-	1049	499	623	450
Ligand (7)	1544	1641	3043	-	-	-	-
7	1487	1598	NC	1020	523	623	483
Ligand (8)	1560	1651	3023	-	-	-	-
8	1492	1577	NC	1014	526	619	486
Ligand (9)	1583	1637	3066	-	-	-	-
9	1490	1589	NC	1016	524	623	484
Ligand (10)	1550	1654	3059	-	-	-	-
10	1519	1597	NC	1022	532	624	460
Ligand (11)	1570	1649	3035	-	-	-	-
11	1519	1589	NC	1091	528	624	462
Ligand (12)	1500	1639	3061	-	-	-	-
12	1514	1591	NC	1018	530	626	462

NC=No change, IR=Infrared

Table 4: EPR spectral parameters of the copper (II) complexes in polycrystalline state at 77 K.

Complex	Parameters	
	A	G
2	314	2.07
5	315	2.06
8	315	2.05
11	309	2.10

EPR=Electron paramagnetic resonance

3.6. Liquid Chromatography-mass Spectrometry (LC/MS) Spectra

LC/MS spectrums of complexes have shown a cationic and an anionic spectrum. The major signal of complex 1, around at m/z 733.7, was obtained from the cationic complex. Another signal assigned around at m/z 98.9 was attributed to the perchlorate counter anion ClO_4^-. The calculated molecular ions were in perfect agreement with the expected structures.

3.7. Antibacterial Activity

Among the copper(II) complexes (Table 6), the complexes 1 (11.4-17.0 mm), 5 (15.4-22.0 mm), 8 (13.0-18.0 mm), and 10 (10.0-20.5 mm) showed the higher activity against all the tested bacterial strains compared to copper salt.

3.8. MIC

Among the copper(II) complexes (Table 7), 8 (1.6 µg/mL) showed the lowest MIC against B.s. The complex 4 (3.9 µg/mL) was found to be lowest MIC against S.a. In the case of S.p, the complex 7 (3.8 µg/mL) showed the lowest MIC. The complex 8 (3.2 µg/mL) was found to be lowest MIC against E.f. In the case of E.c, complex 10 (1.6 µg/mL) showed the lowest MIC. The complex 11 (1.05 µg/mL) was found to be highly effective as they exhibit the lowest MIC against K.p. The antimicrobial studies suggested that all the copper(II) complexes showed significantly enhanced antibacterial activity against microbial

Table 5: Redox potentials for copper(II) complexes in DMF solution at 298 K.

Complex	Epc (mV)	Epa (mV)	ΔEp (mV)	i_{pc} (µA)	i_{pa} (µA)	i_{pa}/i_{pc}
1	−1419	1639	3058	45.34	80.99	1.79
2	−1073	950	2023	49.74	18.98	0.38
	72	542	470	7.06	6.45	0.91
3	−883	−687	196	35.84	8.26	0.23
	−674	−400	274	35.01	7.09	0.20
4	−1517	1201	2718	41.88	21.67	0.51
	−994	456	1450	34.79	10.21	0.29
5	−1413	1208	2621	39.79	21.25	0.53
	−968	482	1450	31.67	9.78	0.31
6	−978	1086	2064	34.05	17.69	0.52
	−589	−745	156	1.46	1.03	0.70
7	46	291	245	5.00	6.90	1.38
8	−962	1652	2614	36.50	58.75	1.61
9	−1145	1409	2554	17.44	36.52	2.09
10	−515	1266	1781	15.98	23.63	1.47
11	−981	1606	2587	38.44	64.38	1.67
12	298	642	344	4.05	7.28	1.79

Epa=Anodic peak potential, Epc=Cathodic peak potential, i_{pa}=Anodic peak current, i_{pc}=Cathodic peak current, i_{pa}/i_{pc}=Number of electrons, ΔEp=Epa−Epc, Scan rate (V/s)=0.1, DMF=Dimethylformamide

Table 6: Antibacterial activity of copper(II) complexes.

Copper(II) complexes	Zone of inhibition (mm)±SD					
	Gram-positive			Gram-negative		
	B.s	S.a	S.p	E.f	E.c	K.p
1	15.0±0.63	15.0±0.27	11.4±1.60	17.0±3.10	16.2±2.00	13.0±0.18
2	13.0±0.18	14.0±0.44	12.0±0.18	14.0±2.00	16.0±1.40	16.5±1.02
3	14.0±0.66	12.0±1.88	14.0±0.50	18.0±2.11	10.0±2.44	17.0±0.11
4	15.3±2.70	13.0±1.64	15.0±0.30	18.0±2.40	13.0±0.10	18.0±3.20
5	16.0±1.77	19.0±2.90	22.0±0.42	15.4±2.40	19.0±1.03	16.0±2.90
6	10.0±1.60	16.0±1.95	14.0±0.54	18.0±1.30	15.4±3.00	17.0±2.40
7	15.0±0.29	14.3±0.30	15.5±1.50	18.0±1.32	18.0±0.16	18.0±0.10
8	14.0±0.82	18.0±0.16	13.0±0.10	16.4±1.39	15.5±1.30	16.5±1.30
9	11.0±0.38	15.0±0.52	15.0±2.50	17.0±0.10	14.0±0.13	16.0±1.30
10	19.0±0.02	20.0±0.33	20.5±2.60	10.0±1.22	15.0±0.22	20.5±2.60
11	13.0±0.18	12.0±0.62	14.4±0.20	18.5±1.20	17.0±0.98	15.3±1.20
12	10.0±0.24	10.5±0.50	13.0±0.21	15.3±1.25	16.0±0.27	18.0±0.10
Cu salt	12.0±1.62	16.0±1.12	11.0±0.31	17.0±0.10	16.0±1.30	11.0±0.31
Tetracycline	20.0±0.01	20.0±1.0	18.0±2.9	18.0±2.1	19.5±1.33	18.0±2.1

SD=Standard deviation, B.s=*Bacillus subtilis*, S.a=*Staphylococcus aureus*, S.p=*Streptococcus pyogenes*, E.f=*Enterobacter faecalis*, E.c=*Escherichia coli*, K.p=*Klebsiella pneumoniae*

strains in comparison to the free ligands. Previous studies elsewhere suggested that chelation tended to make the ligands act as more powerful and potent bactereostatic agents [36], thus inhibited the growth of bacteria more than the parent ligands did and it is similar with that of this study. It was suspected that factors such as solubility, conductivity, dipole moment, and cell permeability mechanism influenced by the presence of metal ion might be the possible reason for the increase in activity.

Table 7: MIC of copper(II) complexes.

Copper(II) complexes	MIC (µg/mL)±SD					
	Gram-positive			Gram-negative		
	B.s	S.a	S.p	E.f	E.c	K.p
1	3.4±0.05	8.0±0.55	9.6±0.11	10±0.82	4.6±0.10	4.6±0.04
2	4.6±0.25	9.7±0.41	5.9±2.9	5.8±0.19	7.3±0.12	1.0±0.80
3	7.3±0.22	8.5±0.10	6.4±0.22	9.4±0.14	9.9±0.10	2.8±0.19
4	2.8±0.33	3.9±0.14	5.7±0.55	6.8±0.9	11.9±0.10	1.6±0.91
5	2.3±0.22	9.5±0.68	8.4±0.29	4.6±0.41	6.8±0.10	1.4±0.51
6	2.4±0.15	10.0±0.92	6.3±0.81	8.6±0.12	9.4±1.0	2.8±0.10
7	7.6±1.0	7.3±0.91	3.8±0.82	3.4±1.02	6.5±1.7	4.6±0.02
8	1.6±1.5	12.0±0.62	14.4±0.2	3.2±1.50	17.0±0.98	15.3±1.2
9	11.0±0.21	9.46±0.23	10±0.62	18.5±1.2	10.0±1.3	6.8±0.29
10	8.3±1.0	7.0±0.23	6.0±0.91	7.6±0.22	1.6±2.0	7.4±0.20
11	6.8±0.39	13.8±1.42	6.8±0.11	1.94±0.9	19.0±2.1	1.05±0.81
12	9.4±0.91	9.8±1.92	9.0±0.30	7.0±0.22	2.8±1.4	6.6±0.76

MIC=Minimum inhibitory concentration, SD=Standard deviation, B.s=*Bacillus subtilis*, S.a=*Staphylococcus aureus*, S.p=*Streptococcus pyogenes*, E.f=*Enterobacter faecalis*, E.c=*Escherichia coli*, K.p=*Klebsiella pneumoniae*

Table 8: *In-vitro* anti-tubercular activity of copper(II) complexes against *M. tuberculosis*.

Compound	MIC (µg/mL)	% Inhibition
2	250	93
5	250	68
8	250	49
11	250	79

M. tuberculosis=Mycobacterium tuberculosis,
MIC=Minimum inhibitory concentration

3.9. Antifungal Activity

The *in-vitro* antifungal activity of synthesized copper(II) complexes against the fungal strains *viz*.; *A.f, A.n, C.a,* showed <10 mm of zone of inhibition. Since the zone of inhibition was found to be <10 mm, the synthesized compounds produced no observable inhibitory effect against any of the tested fungal strains.

3.10. Anti-tubercular Activity

In copper(II) complexes, complex 2 (Table 8) exhibited the highest efficacy with 93% inhibition.

From the structure-activity relationship, we observed that the complexes 2 and 11, reinforcing the pharmacophoric contribution of isoniazid moiety to the mechanism of action against the *M. tuberculosis*.

4. CONCLUSION

The molecular formulae of the complexes were calculated from the elemental analyzes data. The magnetic moment values and cyclic voltammetric data substantiate a mononuclear structure for all the complexes. The EPR spectral data also favors the mononuclear structure with square pyramidal geometry. Although no problem was encountered in this work, perchlorate salts containing organic ligands are potentially explosive. They should be prepared in small quantities and handled with care.

The antimicrobial activities copper(II) complexes were observed by the formation of zone of inhibition and MIC against selected bacterial and fungal strains. The antibacterial studies suggested that all the copper(II) complexes showed significantly enhanced antibacterial activity against microbial strains in comparison to the free ligands and <10 mm of zone of inhibition against selected antifungal strains. Anti-tubercular activity copper(II) complexes were observed by MIC, showed that the complex 2 exhibited the highest efficacy and exhibited >70% inhibition. The complexes 2 and 11 reinforcing the pharmacophoric contribution of isoniazid moiety to the mechanism of action against the *M. tuberculosis*. The antibacterial study indicates that the synthesized copper(II) complexes showed appreciable activity with that of the standard. Whereas, the anti-tubercular activity was found to be relatively less than that of the standard used. Nevertheless, this research work could be a good start point to further studies, as well as to synthesize new lead compounds with a different framework.

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