ISSN 0036-0236, Russian Journal of Inorganic Chemistry, 2010, Vol. 55, No. 7, pp. 1064–1074. © Pleiades Publishing, Ltd., 2010.

COORDINATION COMPOUNDS

Novel Metal-based Antimicrobial Agents of Copper(II) Complexes: Synthesis, Spectral Characterization and DNA Interaction Study[1]

N. Raman and J. Joseph

Research Department of Chemistry, VHNSN College, Virudhunagar-626 001, India

e-mail: drn_raman@yahoo.co.in

Received July 29, 2008

Abstract—Few novel mixed ligand copper(II) complexes of the type $[Cu(L)(Cl)_2(H_2O)]$, $[Cu(L)_2]Cl_2$, $[Cu(L)L^1]$ and $[Cu(L)(phen)H_2O]Cl_2$ (where L is the ligand obtained from the condensation of *N*-(2-aminoethyl)-1,3-propanediamine with *m*-nitrobenzaldehyde (L_a)/*o*-chlorobenzaldehyde (L_b)/benzaldehyde (L_c)/*p*-methoxybenzaldehyde (L_d)/*p*-hydroxybenzaldehyde (L_e)/furfuraldehyde (L_f)/pyrrole-2-carboxaldehyde (L_g); L^1 is another ligand obtained from the condensation of anthranilic acid with salicyaldehyde; phen = 1,10-phenanthroline) have been synthesized and characterized by the spectral and analytical techniques. From these data, it is found that the ligands adopt distorted octahedral geometry on metalation with Cu(II) ion. The XRD data indicate that the complexes are polycrystalline with nanosized grains. The SEM images of $[Cu(L_a)phen(H_2O)]Cl_2$ and $[Cu(L_f)_2]Cl_2$ complexes show that they have leaf and cauliflower like morphology. The in vitro biological screening effects of the investigated compounds have been tested against the bacteria such as *Escherichia coli, Klebsiella pneumoniae, Salmonella typhi, Pseudomonas aeruginosa* and *Staphylococcus aureus* and fungi such as *Aspergillus niger, Rhizopus stolonifer, Aspergillus flavus, Rhizoctonia bataicola* and *Candida albicans* by the well diffusion method. A comparative study of MIC values of the Schiff base ligands and their complexes indicates that the complexes exhibit higher antimicrobial activity than the free ligands. An electrochemical study of the copper complexes containing electron withdrawing substituted ligands reveals that they prefer to bind to DNA in Cu(II) rather than Cu(I) oxidation state.

DOI: 10.1134/S0036023610070120

INTRODUCTION

With their versatile structures, redox behavior, and physicochemical properties, transition metal complexes are often useful as chemical nucleases [1–5]. The interaction of these complexes with DNA has gained much attention due to their possible applications as new therapeutic agents. The manipulation of the ligands greatly facilitates the interaction between the complexes and DNA [6–17].

The discovery and development of antibiotics are among the most powerful and successful achievements of modern science and technology for the control of infectious diseases. Metal based drugs represent a novel group of antimicrobial agents with potential applications for the control of bacterial and fungal infections. This inspires synthetic chemists to search for new metal complexes for bioactive compounds and copper in particular has attracted the researchers. Probably the most widely studied cation in this respect is Cu(II), since a host of low-molecular-weight copper complexes have been proven beneficial against several diseases such as tuberculosis, rheumatoid, gastric ulcers and cancers [18, 19].

Hence, this work presents the synthesis and characterization of few novel mixed ligands and their Cu(II) complexes. Furthermore, taking into consideration the use of copper complexes in the treatment of some diseases, mentioned above, we have tested the antimicrobial activity of the synthesized ligands and complexes using bacteria such as *Escherichia coli, Klebsiella pneumoniae, Salmonella typhi, Pseudomonas aeruginosa* and *Staphylococcus aureus* and fungi such as *Aspergillus niger, Rhizopus stolonifer, Aspergillus flavus, Rhizoctonia bataicola* and *Candida albicans.*

EXPERIMENTAL

Materials and methods. All reagents were of Merck products and used as supplied. Micro analytical data and FAB Mass spectra of the compounds were recorded at the Sophisticated Analytical Instrument Facility, Central Drug Research Institute (SAIF, CDRI), Lucknow. The FAB mass spectrum of the complex was recorded on a JEOL SX 102/DA-6000 mass spectrometer/data system using argon/xenon (6 kV, 10 mA) as the FAB gas. The accelerating voltage was 10 kV and the spectra were recorded at room temperature using *m*-nitrobenzyl alcohol (NBA) as the matrix. The IR spectra of the samples were recorded on a Shimadzu FTIR-8400S spectrophotometer in 4000–200 cm^{-1} range using pellet with KBr. The UV-Vis. spectra were recorded on a Shimadzu UV-1601

[1] The article is published in the original.

spectrophotometer. Magnetic susceptibility measurements of the complexes were carried out by Gouy balance using copper sulphate as the calibrant. The values were corrected for diamagnetism by applying Pascal's constants. The molar conductance of the complexes was measured using a Systronic conductivity bridge. The X-band EPR spectra of the complex was recorded at 300 and 77 K at IIT, Mumbai using TCNE (tetracyanoethylene) as the g-marker. SEM images were recorded in a Hitachi SEM analyzer. XRD was recorded on a Rigaku Dmax X-ray difrractometer with CuKa radiation ($\lambda = 1.5404$ Å).

Synthesis of Schiff base ligands. The Schiff base was synthesized by mixing an ethanolic solution of *m*-nitrobenzaldehyde(L_a)/*o*-chlorobenzaldehyde(L_b)/ benzaldehydes(L_c)/*p*-methoxy benzaldehyde(L_d)/ *p*-hydroxybenzaldehyde(L_e)/ furfuraldehyde (L_f)/ pyrrole-2-carboxaldehyde(L_g) (10 mM) with *N*-(2-aminoethyl)-1,3-propanediamine (5 mM) followed by reflux for 3 h and the resulting solution was then allowed to stand at room temperature for 8 h. The obtained solid was filtered, washed with ethanol and dried *in vacuo*.

Data of L_a: Yield: 56%; Elemental analysis: Anal. Calc. for $C_{19}H_{21}N_5O_4$: C, 59.52; H, 5.51; N, 18.26. Found: C, 59.55; H, 5.54; N, 18.30%; **Data of L_b:** Yield: 62%; Elemental analysis: Anal. Calc. for $C_{19}H_{21}N_3Cl_2$: C, 62.99; H, 5.83; N, 11.59. Found: C, 63.02; H, 5.85; N, 11.63%; **Data of L_c**: Yield: 42%; Elemental analysis: Anal. Calc. for $C_{19}H_{23}N_3$: C, 77.78; H, 7.89; N, 14.32. Found: C, 77.81 H, 7.92; N, 14.35%; **Data of L_d**: Yield: 36%; Elemental analysis: Anal. Calc. for $C_{20}H_{27}N_3O_2$: C, 70.36; H, 7.96; N, 12.30. Found: C, 70.40; H, 8.01; N, 12.35%. **Data of L_e**: Yield: 75%; Elemental analysis: Anal. Calc. for $C_{19}H_{23}N_3O_2$: C, 70.13; H, 7.12; N, 12.91. Found: C, 70.17; H, 7.16; N, 12.95%; **Data of L_f**: Yield: 60%; Elemental analysis: Anal. Calc. for $C_{15}H_{19}N_3O_2$: C, 65.92; H, 7.00; N, 15.37. Found: C, 65.95; H, 7.05; N, 15.40%; **Data of L_g**: Yield: 48%; Elemental analysis: Anal. Calc. for $C_{15}H_{21}N_5$: C, 66.40; H, 7.79; N, 25.81. Found: C, 66.45; H, 7.83; N, 25.85%.

Molar ratio 1:1/ Molar ratio 1 : 2. A hot ethanolic solution of Schiff base and $CuCl_2 \cdot 2H_2O$ (1 : 1/2 : 1 molar ratio) was refluxed for 4 h. Then the solution was reduced to one-third on a water bath. The solid complex precipitated was filtered and washed with ethanol and dried *in vacuo*.

Molar ratio 1 : 1. Data of $[Cu(L_a)Cl_2(H_2O)]$: Yield: 49%; Elemental analysis: Anal. Calc. for $CuC_{19}H_{23}N_5O_5Cl_2$: Cu, 11.85; C, 42.58; H, 4.32; N, 13.06. Found: Cu, 11.88; C, 42.62; H, 4.35; N, 13.10%; μ_{eff}(BM), 1.86; Λ_m(mhocm^2 mol^{-1}), 25; **Data of $[Cu(L_b)Cl_2(H_2O)]$**: Yield: 58%; Elemental analysis: Anal. Calc. for $CuC_{19}H_{23}N_3Cl_4O$: Cu, 12.35; C, 44.33; H, 4.50; N, 8.16. Found: Cu, 12.38; C, 44.36; H, 4.54; N, 8.20%; μ_{eff}(BM), 1.98; Λ_m(mhocm^2 mol^{-1}), 14; **Data of $[Cu(L_c)Cl_2(H_2O)]$**: Yield: 35%; Elemental analysis: Anal. Calc. for $CuC_{19}H_{25}N_3OCl_2$: Cu, 14.25; C, 51.18; H, 5.64; N, 9.42. Found: Cu, 14.29; C, 51.22; H, 5.68; N, 9.46%; μ_{eff} (BM), 2.06; Λ_m(mhocm^2 mol^{-1}), 18; **Data of $[Cu(L_d)Cl_2(H_2O)]$**: Yield: 40%; Elemental analysis: Anal. Calc. for $CuC_{20}H_{29}N_3O_3Cl_2$]: Cu, 12.87; C, 48.63; H, 5.91; N, 8.51. Found: Cu, 12.90; C, 48.70; H, 5.95; N, 8.55%; μ_{eff}(BM), 1.94; Λ_m(mhocm^2 mol^{-1}), 29**; Data of $[Cu(L_e)Cl_2(H_2O)]$**: Yield: 65%; Elemental analysis: Anal. Calc. for $CuC_{19}H_{25}N_3O_3Cl_2$: Cu, 13.30; C, 68.09; H, 5.26; N, 8.79. Found: Cu, 13.35; C, 68.14; H, 5.31; N, 8.83; μ_{eff}(BM), 2.02; Λ_m(mhocm^2 mol^{-1}), 24; **Data of $[Cu(L_f)Cl_2(H_2O)]$**: Yield: 56%; Elemental analysis: Anal. Calc. for $CuC_{15}H_{21}N_3O_3Cl_2$: Cu, 14.92; C, 42.31; H, 4.97; N, 9.87. Found: Cu, 14.95; C, 42.34; H, 5.05; N, 9.91%; μ_{eff}(BM), 1.94; Λ_m(mhocm^2 mol^{-1}), 26; **Data of $[Cu(L_g)Cl_2(H_2O)]$**: Yield: 60%; Elemental analysis: Anal. Calc. for $CuC_{15}H_{23}N_5OCl_2$: Cu, 14.99; C, 42.51; H, 5.46; N, 16.53. Found: Cu, 15.03; C, 42.54; H, 5.50; N, 16.56%; μ_{eff}(BM) 1.98; Λ_m(mhocm^2 mol^{-1}) = 22.

Molar ratio 1 : 2. Data of $[Cu(L_a)_2]Cl_2$: Yield: 60%; Elemental analysis: Anal. Calc. for $CuC_{38}H_{42}N_{10}O_8Cl_2$: Cu, 7.04; C, 50.53; H, 4.68; N, 15.50. Found: Cu, 7.09; C, 50.56; H, 4.72; N, 15.55%; μ_{eff}(BM), 1.89; Λ_m(mhocm^2 mol^{-1}), 117; **Data of $[Cu(L_b)_2]Cl_2$**: Yield: 45%; Elemental analysis: Anal. Calc. for $CuC_{38}H_{42}N_6Cl_6$: Cu, 7.39; C, 53.13; H, 4.92; N, 9.78. Found: Cu, 7.44; C, 53.16; H, 4.96; N, 9.83%; μ_{eff}(BM), 1.86; Λ_m(mhocm^2 mol^{-1}), 84; **Data of $[Cu(L_c)_2]Cl_2$**: Yield: 30%; Elemental analysis: Anal. Calc. for $CuC_{38}H_{42}N_6Cl_2$: Cu, 8.81; C, 63.28; H, 6.42; N, 11.65. Found: Cu, 8.85; C, 63.35; H, 6.46; N, 11.70%; μ_{eff}(BM), 1.88; Λ_m(mhocm^2 mol^{-1}), 89; **Data of $[Cu(L_d)_2]Cl_2$**: Yield: 35%; Elemental analysis: Anal. Calc. for $CuC_{40}H_{54}N_6O_4Cl_2$: Cu, 7.78; C, 58.78; H, 7.78; N, 10.28. Found: Cu, 7.82; C, 58.83; H, 6.70; N, 10.33%; μ_{eff}(BM), 1.90; Λ_m(mhocm^2 mol^{-1}), 95; **Data of $[Cu(L_e)_2]Cl_2$**: Yield: 50%; Elemental analysis: Anal. Calc. for $CuC_{38}H_{46}N_6O_4Cl_2$: Cu, 8.09; C, 58.13; H, 3.33; N, 10.70. Found: Cu, 8.13; C, 58.16; H, 3.36; N, 10.75%; μ_{eff}(BM), 2.02; Λ_m(mhocm^2 mol^{-1}), 98; **Data of $[Cu(L_f)_2]Cl_2$**: Yield: 30%; Elemental analysis: Anal. Calc. for $CuC_{30}H_{38}N_6O_4Cl_2$: Cu, 9.33; C, 65.91; H, 7.00; N, 15.37. Found: Cu, 9.36; C, 65.95; H, 7.04; N, 15.41%; μ_{eff}(BM), 1.96; Λ_m(mhocm^2 mol^{-1}), 140; **Data of $[Cu(L_g)_2]Cl_2$**: Yield: 56%; Elemental analysis: Anal. Calc. for $CuC_{30}H_{42}N_{10}Cl_2$: Cu, 9.38; C, 53.21; H, 6.25; N, 20.67. Found: Cu, 9.42; C, 53.25; H, 6.30; N, 20.71%; μ_{eff}(BM), 1.86; Λ_m(mhocm^2 mol^{-1}), 135.

Synthesis of Schiff base L^1. The Schiff base L^1 was prepared using the reported method [20].

Mixed ligand complexes of phenanthroline. A hot ethanolic solution of Schiff base and 1, 10-phenanthroline in ethanol was added to an ethanolic solution of $CuCl_2 \cdot 2H_2O$ (1 : 1 : 1 molar ratio) and the mixture was stirred for 1 h. The solid product so formed was separated by filtration and washed with ethanol and dried *in vacuo*.

Data of $[Cu(L_a)phen(H_2O)]Cl_2$: Yield: 45%; Elemental analysis: Anal Calc. for $CuC_{31}H_{30}N_7O_5$: Cu,

8.87; C, 52.00; H, 21.80; N, 13.69. Found: Cu, 8.92; C, 52.05; H, 21.85; N, 13.74%; μ_{eff}(BM), 2.02; Λ_m(mhocm^2 mol^{-1}), 108; **Data of [Cu(L_b)phen(H_2O)]Cl_2**: Yield: 52%; Elemental analysis: Anal. Calc. for $CuC_{31}H_{31}N_5OCl_2$: Cu, 10.18; C, 59.65; H, 5.00; N, 11.23. Found: Cu, 10.21; C, 59.69; H, 5.04; N, 11.27%; μ_{eff}(BM), 1.90; Λ_m(mhocm^2 mol^{-1}), 145. **Data of [Cu(L_c)phen(H_2O)]Cl_2**: Yield: 56%; Elemental analysis: Anal. Calc. for $CuC_{31}H_{33}N_5O$: Cu, 10.15; C, 59.47; H, 5.31; N, 11.19. Found: Cu, 10.19; C, 59.55; H, 5.35; N, 11.22%; μ_{eff}(BM), 1.96; Λ_m(mhocm^2 mol^{-1}), 110; **Data of [Cu(L_d)phen(H_2O)]Cl_2**: Yield: 30%; Elemental analysis: Anal. Calc. for $CuC_{32}H_{37}N_5O_3$: Cu, 9.42; C, 57.02; H, 5.53; N, 10.39. Found: Cu, 9.47; C, 57.06; H, 5.58; N, 10.55%; μ_{eff}(BM), 2.00; Λ_m(mhocm^2 mol^{-1}), 136; **Data of [Cu(L_e)phen(H_2O)]Cl_2**: Yield: 43%; Elemental analysis: Anal. Calc. for $CuC_{31}H_{33}N_5O_3$: Cu, 9,66; C, 56.58; H, 5.05; N, 10.64. Found: Cu, 9.70; C, 56.62; H, 5.10; N, 10.70%; μ_{eff}(BM), 1.92; Λ_m(mhocm^2 mol^{-1}), 126; **Data of [Cu(L_f)phen(H_2O)]Cl_2**: Yield: 45%; Elemental analysis: Anal. Calc. for $CuC_{27}H_{29}N_5O_3$: Cu, 10.47; C, 53.50; H, 4.82; N, 11.55. Found: Cu, 10.51; C, 53.55; H, 4.87; N, 11.61%; μ_{eff}(BM), 1.88; Λ_m(mhocm^2 mol^{-1}), 112; **Data of [Cu(L_g)phen(H_2O)]Cl_2**: Yields: 60%; Elemental analysis: Anal. Calc. for $CuC_{27}H_{31}N_7O$: Cu, 10.52; C, 53.69; H, 5.17; N, 16.23. Found: Cu, 10.55; C, 53.74; H, 5.22; N, 16.26%; μ_{eff}(BM), 1.92; Λ_m(mhocm^2 mol^{-1}), 108.

Mixed ligand complexes of L^1. A hot ethanolic solution of Schiff base and L^1 was added to an ethanolic solution of $CuCl_2 \cdot 2H_2O$ (1 : 1 : 1 molar ratio) and the mixture was refluxed for 1 h and the resulting solution was then allowed to stand at room temperature for 3 h. The solid product so formed was separated by filtration and washed with ethanol and dried *in vacuo*.

Data of [Cu(L_a)L^1]: Yield: 30%; Elemental analysis: Anal. Calc. for $CuC_{33}H_{30}N_6O_7$: Cu, 9.23; C, 57.60; H, 4.68; N, 12.21. Found: Cu, 9.27; C, 57.65; H, 4.72; N, 12.25%; μ_{eff}(BM), 1.93; Λ_m(mhocm^2 mol^{-1}), 12; **Data of [Cu(L_b)L^1]**: Yield: 75%; Elemental analysis: Anal. Calc. for $CuC_{33}H_{30}N_4O_3Cl_2$: Cu, 9.56; C, 59.60; H, 4.54; N, 8.42. Found: Cu, 9.60; C, 9.65; H, 4.60; N, 8.47%; μ_{eff}(BM), 1.90; Λ_m(mhocm^2 mol^{-1}), 05; **Data of [Cu(L_c)L^1]**: Yield: 52%; Elemental analysis: Anal. Calc. for $CuC_{33}H_{32}N_4O_3$: Cu, 10.66; C, 66.49; H, 5.41; N, 9.40. Found: Cu, 10.70; C, 66.52; H, 5.43; N, 9.44%; μ_{eff}(BM), 2.04; Λ_m(mhocm^2 mol^{-1}), 20; **Data of [Cu(L_d)L^1]**: Yield: 50%; Elemental analysis: Anal. Calc. for $CuC_{34}H_{36}N_4O_5$: Cu, 9.86; C, 63.39; H, 5.63; N, 8.70. Found: Cu, 9.91; C, 63.44; H, 5.69; N, 8.75%; μ_{eff}(BM), 1.98; Λ_m(mhocm^2 mol^{-1}), 10; **Data of [Cu(L_e)L^1]**: Yield: 44%; Elemental analysis: Anal. Calc. for $CuC_{33}H_{32}N_4O_5$: Cu, 10.11; C, 63.10; H, 5.13; N, 8.92. Found: Cu, 10.15; C, 63.15; H, 5.17; N, 8.95%; μ_{eff}(BM), 1.90; Λ_m(mhocm^2 mol^{-1}), 12; **Data of [Cu(L_f)L^1]**: Yield: 42%; Elemental analysis: Anal. Calc. for $CuC_{29}H_{27}N_4O_5$: Cu, 11.05; C, 60.57; H, 4.73; N, 9.74. Found: Cu, 11.09; C, 60.61; H, 4.80; N, 9.79%; μ_{eff}(BM), 1.88; Λ_m(mhocm^2 mol^{-1}), 18; **Data of [Cu(L_g)L^1]**: Yield: 56%; Elemental analysis: Anal. Calc. for $CuC_{29}H_{30}N_6O_3$: Cu, 11.06; C, 60.67; H, 5.26; N, 11.64. Found: Cu, 11.11; C, 60.72; H, 5.32; N, 11.68%; μ_{eff}(BM), 2.00; Λ_m(mhocm^2 mol^{-1}), 20.

In vitro antimicrobial activity. In vitro antimicrobial assay was performed by well diffusion method. The complexes and ligands were tested against bacteria such as *Escherichia coli, Klebsiella pneumoniae, Salmonella typhi, Pseudomonas aeruginosa* and *Staphylococcus aureus* by the well diffusion method using nutrient agar as the medium and fungi such as *Aspergillus niger, Rhizopus stolonifer, Aspergillus flavus, Rhizoctonia bataicola* and *Candida albicans*, cultured on potato dextrose agar as medium. In a typical procedure, a well was made on the agar medium inoculated with the microorganisms. The well was filled with the test solution using a micropipette and the plate was incubated at 30°C for 72 h. During this period, the test solution diffused and the growth of the inoculated microorganisms was affected. The inhibition zone developed on the plate was measured. The MIC of the complexes was determined by serial dilution technique [21].

DNA binding experiments. CT-DNA was purchased from Bangalore Genei (India). DNA solution in 5 mM Tris-HCl/50 mM NaCl (pH 7.2) buffer medium gave a ratio of UV- absorbance at 260–280 nm of *ca.* 1.8–1.9 indicating that the DNA was sufficiently free from protein concentration. The DNA concentration per nucleotide was determined by absorption spectroscopy using the molar absorption coefficient (6600 M^{-1} cm^{-1}) at 260 nm [22]. Tris-HCl buffer solution was prepared using deionized, sonicated triply distilled water.

Cyclic voltammetry study was performed on a Bio-Analytical-System CV-50W electrochemical analyzer with three electrode system of a glassy carbon (GC) electrode as the working electrode, a platinum wire as auxiliary electrode and Ag/AgCl as the reference electrode. Solutions were deoxygenated by purging with N_2 prior to measurements. The freshly polished GC electrode was modified by transferring a droplet of 2 μL of 5.75×10^{-3} M of DNA solution on to the surface, followed by air drying. Then the electrode was rinsed with distilled water. Thus, a DNA-modified GC electrode was obtained and both, the peak currents and the peak potentials, were reproducible to better than 10% under experimental conditions [23].

RESULTS AND DISCUSSION

The ligands and their complexes are found to be stable in air. The ligands are soluble in common organic solvents but their complexes are soluble in acetonitrile, DMF and DMSO. The elemental analysis results for the metal complexes agree well with the calculated values. The observed low molar conductance values of the complexes [Cu(L)$(Cl)_2(H_2O)$] and

$[Cu(L)(L^1)]$ in acetonitrile of 10^{-3} M solution at room temperature are consistent with their non-electrolytic nature due to the absence of counter (chloride) ions in the structure of the complexes. However, $[Cu(L)_2]Cl_2$ and $[Cu(L)(phen)(H_2O)]Cl_2$ complexes show higher molar conductance values indicating 1 : 2 electrolytic nature of the complexes due to two counter (chloride) ions in the structure of the complexes [24].

Mass Spectra

The FAB mass spectra of the Schiff base ligands and their copper complexes are used to compare their stoichiometric composition. The Schiff base ligand (L_f) shows a molecular ion peak at 271 *m/z* whereas its copper complex $[Cu(L_f)_2]Cl_2$, exhibits at 677 *m/z*. Further, one of the fragment ions exhibits a peak at 607 *m/z* suggesting the presence of two chloride ions. These two chloride ions are present outside the coordination sphere which is indicated by the test with silver nitrate. These data confirm the stoichiometry of the copper chelates as $[Cu(L_f)_2]Cl_2$. This is also supported by the FAB mass spectra of the other complexes. Similarly, FAB mass spectra confirm the stoichiometry of the other type of copper chelates. The elemental analysis values are also in good agreement with the values calculated for molecular formulae assigned to these complexes.

IR Spectra

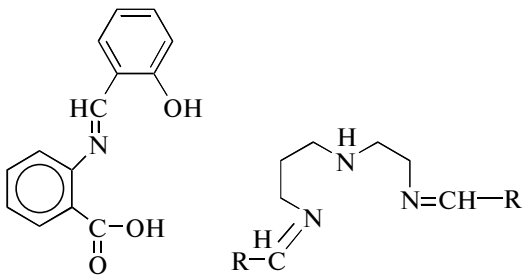
The IR spectra taken in the region 4000–200 cm^{-1} provide some information regarding the mode of coordination in the complexes and were analyzed by a careful comparison with that of the free ligands. The selected IR absorption bands are discussed here. The ligands show characteristic band for ν(N–H) at 3320 cm^{-1}. In all the complexes, the ν(N–H) bands were shifted by 122–140 cm^{-1} to lower frequencies, due to coordination of the NH groups. The formation of the Schiff bases is confirmed by the presence of a band specific for ν(C=N) and the subsequent disappearance of bands due to aldehydic and amino groups. IR spectra of the Schiff bases exhibit a band in 1625–1400 cm^{-1} region attributable to the ν(C=N) groups. On chelation, due to possible drift of the lone pair density towards the metal, the azomethine ν(C=N) bond is expected to absorb at lower frequency in the complex. The bands were also shifted by 19–48 cm^{-1} to lower frequencies, due to participation of the azomethine groups in coordination. The coordination of nitrogen to the metal atom is supported by the appearance of a new band in the region 430–478 cm^{-1} assignable to ν(Cu–N) vibration. The IR spectra exhibit a broad band in the region 3400–3000 cm^{-1}, suggesting the presence of coordinated water molecules. The weak bands around 850 and 710 cm^{-1} are assigned as ν(OH) rocking and wagging vibrations respectively. The two absorption bands occurring near 1595 and 1400 cm^{-1} in the Schiff base corresponding to the asymmetric and symmetric stretching vibration bands of the ionic carboxyl group ν(COO^-) in the complexes are shifted to lower frequencies 1585 and 1390 cm^{-1} respectively. The ν(OH) band originally found in the Schiff base disappeared on complexation indicating deprotonation of the phenolic hydroxyl group and coordination of phenolic oxygen to the metal. This is further supported by the shift in the stretching frequency of the phenolic ν(C–O) at 1530 cm^{-1} to the higher side by 10–20 cm^{-1}. In the low frequency region, the bands observed in the region of 525–535 cm^{-1} are attributed to ν(Cu–N), in the region of 465–480 cm^{-1} to ν(Cu–O) phenolic, and in the region of 415–420 cm^{-1} to ν(Cu–O) carboxyl groups. The sharp bands in the range 750–780 and 1525–1535 cm^{-1} are due to aromatic ν(C–H) and ν(C=C), respectively. A band in the region 310–280 cm^{-1} is also present due to M–Cl bond.

Electronic Absorption Spectra

The electronic absorption spectra of Schiff base ligands and their copper complexes were recorded at 300 K using ethanol and acetonitrile solvents respectively. The absorptions in the ultraviolet region are attributed to transitions within the ligand orbital and those in the visible region are probably due to allowed metal-to-ligand charger transfer transitions (MLCT). The selected electronic absorption bands are discussed here. The Schiff base shows two absorptions, 29560 and 32680 cm^{-1}, which are intra-ligand charger transfer transitions. The UV-Vis., spectrum of the copper complex displays a broad band in the 12260–15460 cm^{-1} region, which is assigned to $^2E_{2g} \longleftarrow {}^2T_{2g}$ transition, attributed to an octahedral geometry around the central metal ion. The broadness of the band can be taken as an indication of Jahn–Teller distortion from the regular symmetry.

EPR Spectra

The EPR spectra of metal chelates provide information about hyperfme and super hyperfme structures which are of importance in studying the metal ion environment in the complexes i.e., the geometry, nature of the coordinating sites of the Schiff base and the metal and the degree of covalency of the metal-ligand bonds. The EPR spectrum of the $[Cu(L_g)_2]Cl_2$ was recorded in CH_3CN at 300 and 77 K. The spectrum of the above copper complex at 300 K shows one intense absorption band in the high-field region, which is isotropic due to the tumbling motion of the molecules. However, this complex in the frozen solution shows four well-resolved peaks with low intensities in the low field region. No band corresponding to the $m_s = \pm 2$ transition was observed in the spectra, ruling out any Cu–Cu interaction.



(L^1) (L)

Fig. 1. Structure of the Schiff base ligands.

The observed $g_\parallel$ and $g_\perp$ values are 2.24 and 2.05 respectively. The g-values of the above copper complex are consistent with tetragonally elongated octahedral geometry ($g_\parallel > g_\perp > 2.0$) and the unpaired electron occupies predominantly in the d_{x2-y2} orbital [25]. In axial spectra, the g-values are related with exchange coupling constant (G) by the expression

$$G = \frac{g_\parallel - 2.0023}{g_\perp - 2.0023}.$$

According to Hathaway [26, 27], if the G is larger than four, exchange interaction is negligible because the local tetragonal axis is misaligned. For the present copper complex, the G value is 4.8, which suggests that the local tetragonal axis is aligned parallel or slightly misaligned and consistent with d_{x2-y2} ground state.

EPR and optical spectra have been used to determine the covalent bonding parameters for the Cu(II) ion in various environments. Since there has been wide interest in the nature of bonding parameters in the system, we adopted the simplified molecular orbital theory [25] to calculate the bonding coefficients such as in-plane π-bonding (β^2) and in-plane σ-bonding (α^2). The in-plane σ-bonding parameter, α^2 is related to $g_\parallel$ and $g_\perp$ according to the following equation:

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

If the α^2 value is 0.5, it indicates a complete covalent bonding, while the value of $\alpha^2 = 1.0$ suggests a complete ionic bonding. The observed value of α^2 (0.85) indicates that the complex has some covalent character. The in-plane π-bonding (β^2) and out-plane π-bonding (γ^2) parameters are calculated from the following equations:

$$\beta^2 = (g_\parallel - 2.0032)(E/-8\lambda\alpha^2), \quad (2)$$

$$\gamma^2 = (g_\perp - 2.0032)(E/-2\lambda\alpha^2), \quad (3)$$

where $\lambda = -828$ cm^{-1} for the free metal ion and E of Eqs. (2) and (3) is 17538 and 16578 cm^{-1} respectively. The observed β^2 (1.05) and γ^2 (0.17) values indicate that there is interaction in the out-plane π-bonding, whereas in-plane π-bonding is completely ionic. This is also confirmed by orbital reduction factors ($K_\parallel$ and $K_\perp$) which are calculated from the following equations:

$$K_\parallel^2 = (g_\parallel - 2.0023)(E/8\lambda), \quad (4)$$

$$K_\perp^2 = (g_\perp - 2.0023)(E/8\lambda), \quad (5)$$

where $\lambda = -828$ cm^{-1} for the free metal ion and E of Eqs. (4) and (5) is 17538 and 16578 cm^{-1} respectively. In the case of pure σ-bonding $K_\parallel = K_\perp$, whereas $K_\parallel < K_\perp$ implies considerable in-plane π-bonding while for out-plane π-bonding $K_\parallel > K_\perp$. For the present complex, the observed order is $K_\parallel$ (0.92) > $K_\perp$(0.39) implying a greater contribution from out-plane π-bonding than from in-plane π-bonding in metal ligand π-bonding.

Based on the above spectral and analytical data, the proposed structures of the Schiff base ligands and their copper complexes are shown in Fig. 1 and Fig. 2 respectively.

XRD Study

The XRD pattern of $[Cu(L_a)phen(H_2O)]Cl_2$ complex (Fig. 3) shows well defined crystalline peaks indicating that the sample is crystalline in nature. It has specific 'd' values which can be used for its characterization. The crystallite size of the complex d_{XRD} could be estimated from XRD patterns using the Scherre's formula (1)

$$d_{XRD} = 0.9\lambda/\beta(\cos\theta), \quad (6)$$

where λ is the wavelength, β is the full width at half maxima and θ is the diffraction angle. The XRD shows that the above complex has the average crystallite size of 53 nm, confirming the nanocrystalline nature of the complex.

The surface morphology of $[Cu(L_a)phen(H_2O)]Cl_2$ and $[Cu(L_f)_2]Cl_2$ complexes are shown in Figs. 4a and 4b. From the SEM images of the complexes, it is inferred that the $[Cu(L_a)phen(H_2O)]Cl_2$ has leaf like morphology, while $[Cu(L_f)_2]Cl_2$ has cauliflower like morphology. The particle size of the above complexes was in the diameter range of few microns. However, particles with sizes less than 100 nm were also observed which groups to form agglomerates of larger size. The smaller grain sizes found from XRD data suggest that these complexes are polycrystalline with nanosized grains.

Antimicrobial Activity

In view of the biological importance of copper(II) complexes, in the present study, the antibacterial and antifungal activities of the copper(II) complexes were tested against the bacteria such as *E. coli, K. pneumo-*

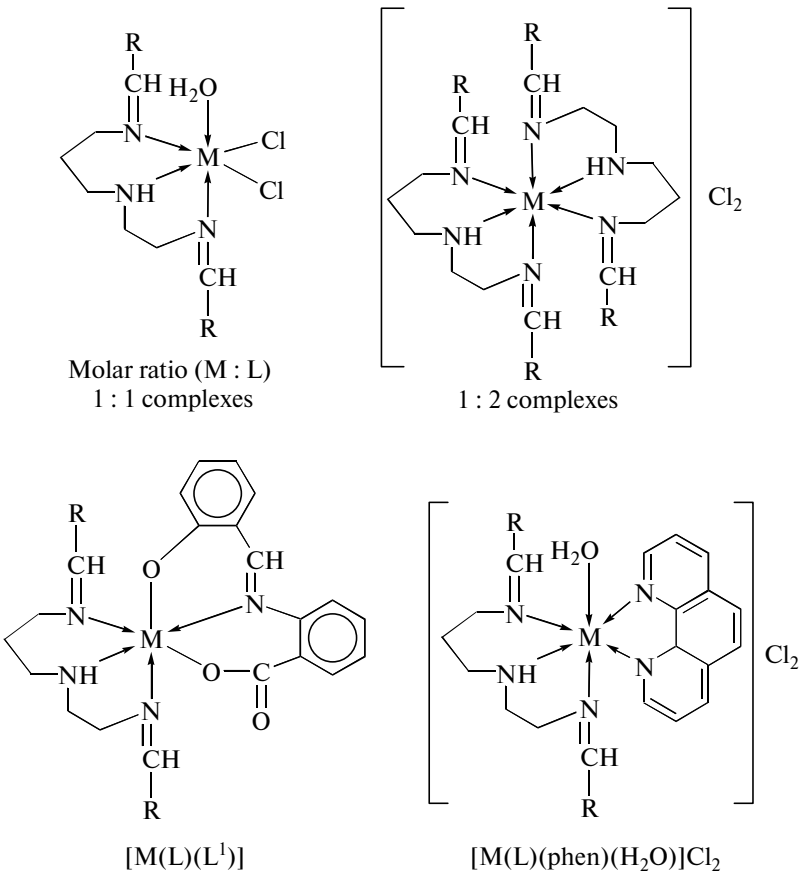


Fig. 2. Structure of the copper(II) complexes.

niae, S. typhi, P. aeruginosa and *S. aureus* and fungi such as *A. niger*, *R. stolonifer*, *A. flavus*, *R. bataicola* and *C. albicans* by the well diffusion method. The minimum inhibitory concentration (MIC) values of the compounds are summarized in Tables 1 and 2. A comparative study of the ligands and their copper complexes (MIC values) indicates that complexes exhibit higher antifungal activity than the free ligands. From the MIC values (Table 1), it was found that the $[Cu(L_g)(phen)H_2O]Cl_2$ was more potent among the other investigated complexes and the standard (nystatin) against *Candida albicans*.

Chelation reduces the polarity of the copper ion mainly because of the partial sharing of its positive charge with the donor groups and possibly the π-electron delocalization within the whole chelate ring system thus formed during coordination. This process of chelation thus increases the lipophilic nature of the copper ion, which in turn favors its permeation through the lipid layer of the membrane. This in turn is responsible for increasing the hydrophobic character and liposolubility of the molecule in crossing cell membrane of the microorganism, and hence enhances the biological utilization ratio and activity of the testing drug/compound. The enhanced activity of the complexes may also be explained on the basis of their solubility, fineness of the particles, size of the metal ion and the presence of bulkier organic moieties.

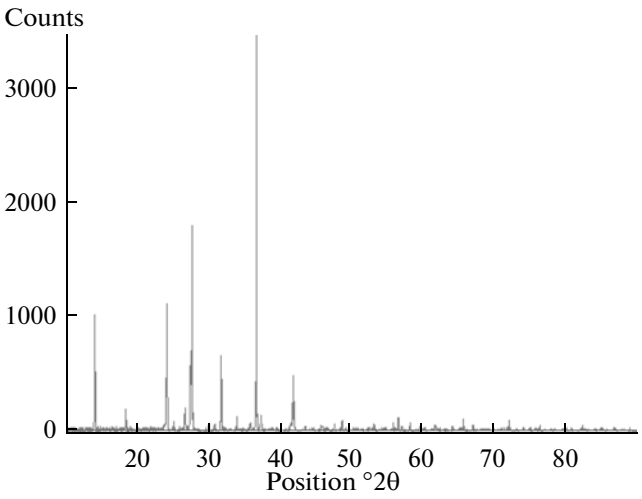


Fig. 3. X-ray diffraction of $[Cu(L_a)phen(H_2O)]Cl_2$ complex.

Molar Ratio 1 : 1 Complexes

Rosenberg's studies demonstrate that the biological activities of metal complexes depend upon the charge, the nature of the counter anion, the geometrical configuration, and the oxidation state of the central metal ion [28]. It is observed from the results (Tables 1 and 2), the higher inhibition of microbial growth is not only due to chelation, heterocyclic moiety, coordinated chloride ions but also due to the presence of azomethine group. The mode of action of the compounds may involve formation of a hydrogen bond through the azomethine group with the active centers of cell constituents, resulting in interferences with the normal cell process [29–31].

Effect of Heterocyclic Moiety

The compounds containing phenyl moiety is replaced by heterocyclic rings such as pyrrole and furan to find out the inhibitory effect due to the presence of heterocyclic moiety. It is observed the heterocyclic moiety enhances the biochemical properties such as antibacterial and antifungal activities of the Schiff base ligands and their complexes (Tables 1 and 2).

Effect of Substituents

Further, inhibitory action gets enhanced with the introduction of electron-withdrawing substituent in the phenyl ring. The complexes, however, with electron-releasing substituents such as methoxy and hydroxyl groups, are lesser active compared to unsubstituted phenyl ring. It is interesting to note that methoxy group of copper complexes showed increased activity than that of hydroxyl group of copper complexes due to the comparatively faster diffusion of copper complex into cell membrane in the presence of methoxy group.

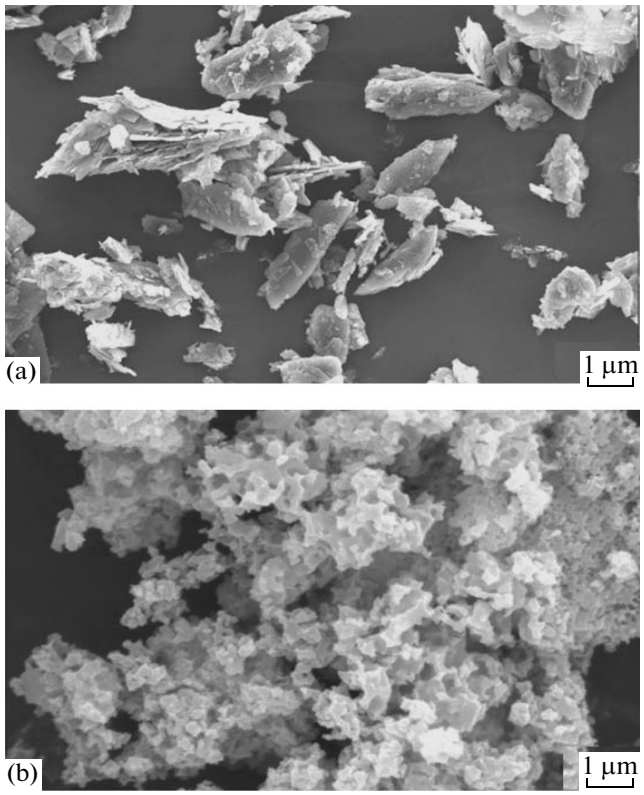


Fig. 4. SEM images of $[Cu(L_a)phen(H_2O)]Cl_2$ (a) and $[Cu(L_f)_2]Cl_2$ complex (b).

Effect of Chloride Ion

Copper(II) complexes of the type $[Cu(L)(Cl)_2(H_2O)]$ possess broad spectrum of antibacterial and antifungal activity in vitro and the greater growth inhibition which may be due to presence of chloride ion in the coordination sphere. From the observation, the order of activity of the synthesized complexes both in bacteria and fungi depends on the nature of the substituents present in the phenyl ring and decreases in the following order:

$$[Cu(L_a)(Cl)_2(H_2O)] > [Cu(L_b)(Cl)_2(H_2O)] > [Cu(L_c)(Cl)_2(H_2O)] > [Cu(L_d)(Cl)_2(H_2O)] > [Cu(L_e)(Cl)_2(H_2O)].$$

Based on the facts, the inhibitory activity of synthesized complexes (*1 : 1 molar ratio*) for both in bacteria and fungi is as follows:

$$[Cu(L_g)(Cl)_2(H_2O)] > [Cu(L_f)(Cl)_2(H_2O)] > [Cu(La)(Cl)_2(H_2O)] > [Cu(L_b)(Cl)_2(H_2O)] > [Cu(L_c)(Cl)_2(H_2O)] > [Cu(L_d)(Cl)_2(H_2O)] > [Cu(L_e)(Cl)_2(H_2O)].$$

Table 1. Minimum inhibitory of concentration of the synthesized compounds against the growth of fungi (μg/mL)

S. No	Compound	*A. niger*	*R. stolinifer*	*A. flavus*	*R. bataicola*	*C. albicans*
1	L_a	58	64	76	80	64
2	L_b	62	68	82	85	68
3	L_c	66	74	85	88	76
4	L_d	70	76	88	90	85
5	L_e	75	80	90	94	92
6	L_f	55	60	74	76	58
7	L_g	48	52	65	69	50
8	$[Cu(L_a)(Cl)_2\ H_2O]$	25	30	34	24	28
9	$[Cu(L_a)L^1]$	16	23	28	22	25
10	$[Cu(L_b)(Cl)_2\ H_2O]$	25	31	35	26	28
11	$[Cu(L_b)L^1]$	15	23	28	24	26
12	$[Cu(L_c)(Cl)_2\ H_2O]$	29	34	38	30	32
13	$[Cu(L_c)L^1]$	18	28	32	30	33
14	$[Cu(L_d)(Cl)_2\ H_2O]$	33	37	42	34	38
15	$[Cu(L_d)L^1]$	24	34	36	32	35
16	$[Cu(L_e)(Cl)_2\ H_2O]$	35	40	44	39	42
17	$[Cu(L_e)L^1]$	28	37	40	35	38
18	$[Cu(L_f)(Cl)_2\ H_2O]$	22	26	30	19	23
19	$[Cu(L_f)L^1]$	13	20	25	18	22
20	$[Cu(Lg)(Cl)_2\ H_2O]$	18	21	26	16	19
21	$[Cu(L_g)L^1]$	11	15	19	14	16
22	$[Cu(L_a)_2]Cl_2$	28	32	35	26	28
23	$[Cu(L_a)(phen)H_2O]Cl_2$	12	16	22	24	19
24	$[Cu(L_b)_2]Cl_2$	32	36	39	30	31
25	$[Cu(L_b)(phen)H_2O]Cl_2$	15	19	23	25	18
26	$[Cu(L_c)_2]Cl_2$	35	41	44	33	36
27	$[Cu(L_c)(phen)H_2O]Cl_2$	18	23	27	30	25
28	$[Cu(L_d)_2]Cl_2$	39	45	50	37	42
29	$[Cu(L_d)(phen)H_2O]Cl_2$	20	26	32	35	28
30	$[Cu(L_e)_2]Cl_2$	44	48	55	41	46
31	$[Cu(L_e)(phen)H_2O]Cl_2$	24	28	34	38	30
32	$[Cu(L_f)_2]Cl_2$	26	30	38	29	40
33	$[Cu(L_f)(phen)\ H_2O]Cl_2$	08	15	16	19	14
34	$[Cu(L_g)_2\ Cl_2$	22	27	32	21	25
35	$[Cu(L_g)(phen)H_2O]Cl_2$	06	10	12	14	09
36	Nystatin	10	16	8	12	14

Molar Ratio 1 : 2 Complexes

The complexes (*molar ratio 1 : 1 complexes*) containing a chloride ion attached directly to the copper ion also showed antimicrobial activity, but the replacement of chloride by one more same ligand moiety (i.e. L in *1 : 2 molar ratio*) enhances the antimicrobial activity. This enhancement in the activity is rationalized on the basis of the structures of 1 : 2 (Cu : L) complexes by possessing an additional azomethine (C=N) linkage which imports in elucidating the mechanism of transamination and resamination reactions in biological system [32, 33], Based on this, the inhibitory activity of synthesized complexes both in bacteria and fungi is as follows:

$$[Cu(L_g)_2]Cl_2 > [Cu(L_f)_2]Cl_2 > [Cu(L_a)_2]Cl_2 > [Cu(L_b)_2]Cl_2 > [Cu(L_c)_2]Cl_2 > [Cu(L_d)_2]Cl_2 > [Cu(L_e)_2]Cl_2.$$

Table 2. Minimum inhibitory of concentration of the synthesized compounds against growth of bacteria (μg/mL)

S. No	Compound	*E. coli*	*K. pneumonia*	*S. typhi*	*P. aeruginosa*	*S. aureus*
1	L_a	52	54	58	60	63
2	L_b	56	56	62	64	68
3	L_c	60	60	66	66	72
4	L_d	66	64	68	70	75
5	L_e	72	68	72	75	78
6	L_f	46	50	54	56	58
7	L_g	42	46	50	48	52
8	$[Cu(L_a)(Cl)_2\ H_2O]$	24	26	28	22	32
9	$[Cu(L_a)L^1]$	18	22	25	24	30
10	$[Cu(L_b)(Cl)_2\ H_2O]$	28	30	32	25	34
11	$[Cu(L_b)L^1]$	20	24	28	28	32
12	$[Cu(L_c)(Cl)_2\ H_2O]$	32	32	35	28	38
13	$[Cu(L_c)L^1]$	24	26	32	30	36
14	$[Cu(L_d)(Cl)_2\ H_2O]$	34	35	38	32	40
15	$[Cu(L_d)L^1]$	26	28	36	34	40
16	$[Cu(L_e)(Cl)_2\ H_2O]$	38	40	42	39	44
17	$[Cu(L_e)L^1]$	28	32	40	38	42
18	$[Cu(L_f)(Cl)_2\ H_2O]$	18	22	25	20	28
19	$[Cu(L_f)L^1]$	15	19	22	18	28
20	$[Cu(Lg)(Cl)_2\ H_2O]$	16	19	22	18	24
21	$[Cu(L_g)L^1]$	12	16	19	15	23
22	$[Cu(L_a)_2]Cl_2$	24	26	31	25	28
23	$[Cu(L_a)(phen)H_2O]Cl_2$	16	24	22	20	28
24	$[Cu(L_b)_2]Cl_2$	28	30	34	29	32
25	$[Cu(L_b)(phen)H_2O]Cl_2$	20	27	25	24	32
26	$[Cu(L_c)_2]Cl_2$	32	34	38	35	36
27	$[Cu(L_c)(phen)H_2O]Cl_2$	24	32	28	30	36
28	$[Cu(L_d)_2]Cl_2$	36	39	44	40	38
29	$[Cu(L_d)(phen)H_2O]Cl_2$	26	35	34	35	38
30	$[Cu(L_e)_2]Cl_2$	38	42	46	44	40
31	$[Cu(L_e)(phen)H_2O]Cl_2$	30	38	36	40	42
32	$[Cu(L_f)_2]Cl_2$	20	24	28	22	25
33	$[Cu(L_f)(phen)\ H_2O]Cl_2$	13	20	21	15	24
34	$[Cu(L_g)_2]Cl_2$	15	18	26	18	24
35	$[Cu(L_g)(phen)H_2O]Cl_2$	14	20	18	13	16
36	Streptomycin	04	08	10	06	12

Mixed-Ligand Complexes of L^1

The replacement of chloride ion from 1 : 1 molar ratio of complexes by another ligand moiety (L^1) enhances the antimicrobial activity due to the presence of phenolic and carboxylic moieties. The results of antimicrobial screening indicate that *o*-aminobenzoic acid-Schiff bases show antimicrobial activity against microorganisms. The activity of these substances may be due to carboxyl group. The ligand containing phenolic and carboxylic moieties shows better inhibition against bacteria and fungi. The alteration in the activity of different molecules against different

organisms depends either on the impermeability of the cells of the microbes or differences in ribosomes of microbial cells [34].

Further, increase of inhibition of microbial growth is due to uncoordinated hetero atoms present in the copper complexes of type [Cu(L)(L^1)]. In the complexes, the ligands have some uncoordinated donor atoms which enhance the activity of the complexes by bonding with trace elements present in microorganisms may combine with the uncoordinated site and may inhibit the growth of fungi.

It has also been suggested [35, 36] that the ligands with nitrogen and oxygen donor systems might inhibit enzyme production, since the enzymes which require these groups for their activity appear to be especially more susceptible to deactivation by the metal ions upon chelation.

Mixed-Ligand Complexes of Phenanthroline

1,10-phenanthroline (phen) and substituted derivatives, both in the metal-free state and as ligands coordinated to transition metals, disturb the functioning of a wide variety of biological systems [37]. From the view of biological relevance, we have chosen this type of metal-phen mixed ligand complexes (1 : 1 : 1 molar ratio, M : L : phen) to study the antimicrobial activity. From the observation, the order of activity of the synthesized compounds in both bacteria and fungi is as follows:

$$[Cu(L_g)(phen)]Cl_2 > [Cu(L_f)(phen)]Cl_2 > [Cu(L_a)(phen)]Cl_2 > [Cu(L_b)(phen)]Cl_2 > [Cu(L_c)(phen)]Cl_2 > [Cu(L_d)(phen)]Cl_2 > [Cu(L_e)(phen)]Cl_2.$$

The compounds (molar ratio 1 : 1 complexes) containing a chloride ion attached directly to the central atom also showed inhibitory activity, but the replacement of chloride ion by another ligand moiety (phen) enhances the inhibition of microbial growth.

Interaction of Copper Complex with DNA by Cyclic Voltammetry Study

Cyclic voltammetric technique is extremely useful in probing the nature and mode of DNA binding of metal complexes. A typical cyclic voltammogram of $[Cu(L_a)phen(H_2O)]Cl_2$ in the absence and in presence of varying amount of [DNA] is shown in Fig. 5.

In the absence of DNA, the cathodic peak appears at −0.107 V for Cu(II) ⟶ Cu(I) couple (Epa = −0.281V, Epc = −0.107 V, ΔEp = 0.174 V and $E_{1/2}$ = −0.194 V. This redox couple ratio of ip_c/ip_a is approximately unity. This indicates that the reaction of the complex on the glassy carbon electrode surface is quasi-reversible redox process. During the incremental addition of DNA to the complex, the redox couple causes a significant shift in $E_{1/2}$ of 17 mV and a decrease in ΔEp of 12 mV. The ip_c/ip_a values also decrease in the presence of DNA. The decrease of the anodic and cathodic peak currents of the complex in the presence of DNA is due to decrease in the apparent diffusion coefficient of the Cu(II) complex upon complexation with the DNA macromolecules. These results show that $[Cu(L_a)phen(H_2O)]Cl_2$ stabilizes the duplex (GC pairs) by intercalating way. The peak potential and current of the Cu(II) complex were changed in the presence of DNA. According to equation,

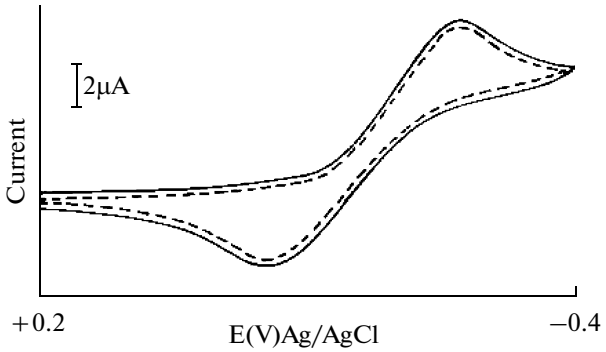


Fig. 5. Cyclic voltammogram of $[Cu(L_a)phen(H_2O)]Cl_2$ complex in the presence (dotted line) and absence of DNA (dark line).

$$E_b^{0'} - E_f^{0'} = 0.059 \log(k_+/k_{2+}),$$

where $E_b^{0'}$ and $E_f^{0'}$ are the formal potentials of the Cu(II)/Cu(I) couple in the binding and free forms, respectively. The ratio of the binding constants (k_+/k_{2+}) is found to be less than unity (Table 3) which indicates that the Cu(II) is displaying higher DNA binding affinity than Cu(I) form. Similarly, the incremental addition of DNA to the complex, the redox couple causes a significant shift in $E_{1/2}$ of 5–40 mV and a decrease in ΔEp of 5–20 mV. The ip_c/ip_a values also decrease in the presence of DNA. The decrease of the anodic and cathodic peak currents of the complex in the presence of DNA is due to decrease in the apparent diffusion coefficient of the Cu(II) complexes upon complexation with the DNA macromolecules. Moreover, the ratio of the binding constants (k_+/k_{2+}) is found to be less than unity (Table 3) which indicates that the Cu(II) is displaying higher DNA binding affinity than Cu(I) form.

CONCLUSIONS

In this work, few mixed ligand copper complexes have been designed and synthesized in 1 : 1 and 1 : 2 molar ratios and they are characterized by analytical and spectral methods. A preliminary study involving the interaction of the synthesized copper complexes with DNA has also been carried out using cyclic voltammetry. From the results, it is found that the synthesized complexes stabilize the duplex (GC pairs) by

Table 3. Electrochemical behaviour of copper complexes containing electron withdrawing substituted ligands on interaction with CT-DNA

SI. No	Complexes	$E_{1/2}$ (V)		ΔEp (V)		K_+/K_{2+}	Ipc/Ipa
		Free	bound	Free	bound		
1	$[Cu(L_a)(Cl)_2\ H_2O]$	–0.180	–0.162	0.108	0.123	0.76	0.84
2	$[Cu(L_a)L^1]$	–0.189	–0.191	0.117	0.129	0.87	0.91
3	$[Cu(L_b)(Cl)_2\ H_2O]$	–0.203	–0.206	0.121	0.131	0.87	0.86
4	$[Cu(L_b)L^1]$	–0.188	–0.196	0.135	0.144	0.74	0.76
5	$[Cu(L_a)_2]Cl_2$	–0.212	–0.207	0.118	0.122	0.95	0.64
6	$[Cu(L_a)(phen)H_2O]Cl_2$	–0.194	–0.236	0.174	0.162	0.80	0.78
7	$[Cu(L_b)_2]Cl_2$	–0.197	–0.188	0.130	0.137	0.91	0.67
8	$[Cu(L_b)(phen)H_2O]Cl_2$	–0.203	–0.175	0.178	0.192	0.83	0.68

intercalating way. The antibacterial and antifungal activities of the ligands and their copper(II) complexes have been done. It is found that these compounds are not only good candidates as antibacterial and antifungal agents, but also a promising addition of new class of compounds as the metal-based drugs. Further studies are required to explore these complexes as drugs.

ACKNOWLEDGMENTS

The authors express their sincere thanks to the Managing Board, Principal and Head of the Department of Chemistry, VHNSN College, Virudhunagar for their constant encouragement and providing research facilities. NR thanks the University Grants Commission (UGC), New Delhi and JJ thanks the Tamilnadu Government for financial assistance.

REFERENCES

1. A. M. Pyle and J. K. Barton, Prog. Inorg. Chem. **38**, 413 (1990).
2. B. Macias, M. V. Villa, B. Gomez, et al., J. Inorg. Biochem. **101**, 444 (2007).
3. C. P. Raptopoulou, S. Paschalidou, A. A. Pantazaki, et al., J. Inorg. Biochem. **71**, 15 (1998).
4. P. Ruíz, R. Ortiz, L. Perelló, et al., J. Inorg. Biochem. **101**, 831 (2007).
5. C. Liu, M. Wang, T. Zhang, and H. Sun, Coord. Chem. Rev. **248**, 147 (2004).
6. M. Dizdaroglu, Free Radical Biol. Med. **10**, 225 (1991).
7. S. Belaid, A. Landreau, S. Djebbar, et al., J. Inorg. Biochem. **102**, 63 (2008).
8. J. Liu, H. Zhang, C. Chen, et al., Dalton Trans., 114 (2003).
9. K. J. Humphreys, K. D. Karlin, and S. E. Rokita, J. Am. Chem. Soc. **124**, 6009 (2002).
10. C. A. Detmer, F. V. Pamatong, and J. R. Bocarsly, Inorg. Chem. **36**, 3676 (1997).
11. K. J. Humphreys, A. E. Johnson, K. D. Karlin, and S. E. Rokita, J. Biol. Inorg. Chem. **7**, 835 (2002).
12. S. T. Frey, H. H. Sun, N. N. Murthy, and K. Karlin, D, Inorg. Chim. Acta **242**, 329 (1996).
13. A. Garc'a-Raso, J. J. Fiol, B. Adrover, et al., J. Inorg. Biochem. **95**, 77 (2003).
14. X. Wang , H. Chao, H. Li, et al., J. Inorg. Biochem. **98**, 423 (2004).
15. A. M. Thomas, M. Nethaji, A. R. Chakravarty, J. Inorg. Biochem. **98**, 1087 (2004).
16. T. Hirohama, Y. Kuranuki, E. Ebina, et al., J. Inorg. Biochem. **99**, 1205 (2005).
17. H. Zhang, C. S. Liu, X. H. Bu, M. Yang, J. Inorg. Biochem. **99**, 1119 (2005).
18. J. R. J. Sorenson, J. Med. Chem. **19**, 135 (1976).
19. D. H. Brown, A. J. Lewis, W. E. Smith, J. W. Teape, J. Med. Chem. **23**, 729 (1980).
20. V. K. Sharma, O. P. Pandey, S. K. Sengupta, Trans. Met. Chem. **12**, 509 (1987).
21. R. Reiner, Antibiotics-an introduction, Roche Scientific Services, Switzerland, **1**, 21 (1982).
22. M. E. Reichmann, S. A. Rice, C. A. Thomas, P. Doty, J. Am. Chem. Soc. **76**, 3047 (1954).
23. N. Raman, A. Sakthivel, K. Rajasekaran, J. Coord. Chem. **62**, 1661, 2009.
24. W. J. Geary, Coord. Chem. Rev. **7**, 81 (1971).
25. R. K. Ray, G. R. Kauffman, Inorg. Chim. Acta **173**, 207 (1990).
26. R. J. Dudley, B. J. Hathaway, J. Chem. Soc. **A**, 2099 (1970).
27. D. E. Billing, B. J. Hathaway, P. Nicholls, J. Chem. Soc. **A**, 1877 (1970).
28. A. K. Das, *Medicinal Aspects of Bioinorganic Chemistry* (CBS, Shahdara, Delhi, Ch. 3, 1990).
29. Y. Anjaneyula, R. P. Rao, Synth. React. Inorg. Met.-Org. Chem., **16**, 257 (1986).
30. L. Mishra, K. K. Upadhyay, V. K. Singh, Synth. React. Inorg. Met.-Org. Chem. **26**, 23 (1996).
31. P. Viswanathamurthi, N. Dharmaraj, K. Natarajan, Synth. React. Inorg. Met.-Org. Chem. **30**, 1273 (2000).
32. J. D. Ming, J. D. Epperson, J. Inorg. Biochem. **91**, 46 (2002).
33. M. Z. Wang, Z. X. Meng, B. L. Liu, et al., Inorg. Chem. Commun. **8,** 368 (2005).
34. N. Raman, A. Kulandaisamy, A. Shunmugasundaram, K. Jeyasubramanian, Trans. Met. Chem. **26**, 131 (2001).
35. Z. H. Chohan, Synth.React. Inorg. Met.-Org. Chem. **34**, 833 (2004).
36. Z. H. Chohan, C. T. Supuran, A. Scozzafava, J. Enzym. Inhib. Med. Chem. **19**, 79 (2004).
37. H. M. Butler, A. Hurse, E. Thursky, A. Shulman, Aust. J. Expt. Biol. Med. Sci. **47**, 541 (1969).