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Research Article

Structural Elucidation of newly synthesized Potentially active Mononuclear Schiff Base Cu(II) & Ni(II) Complexes using Physicochemical methods derived from o-phenylenediammine

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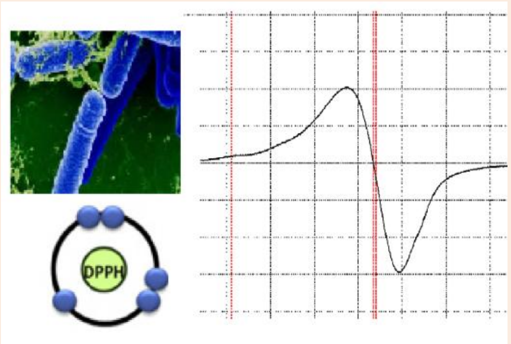
Abstract

A new Cu(II) and Ni(II) metalloinsertors have been synthesized by using a Schiff base, formed by the condensation reaction of o-phenylenediammine, 2-amino 4-cholorophenol with 1,10-phenanthroline. They have been structurally characterized by IR, ^{1}H NMR, UV–vis, EPR, elemental analyses, magnetic susceptibility and molar conductivity studies. The molar conductance data of the complexes indicate that they are non-electrolytes. The spectral and analytical data reveal that the complexes adopt distorted octahedral geometry. They have been examined for their antibacterial and antifungal activities against few pathogens. The data reveal that the complexes exhibit better biocidal activities against bacteria and fungi than the free Schiff base ligand. Additionally, the Cu(II) complex exhibited potential antioxidant properties in *in vitro* studies.



Keywords: 1,10-phenanthroline, antimicrobial assay, antioxidant properties

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Introduction

Schiff bases form an important division of organic compounds in chemistry due to their constructive physical and chemical properties and large number of reactions that they undergo. Schiff bases, derived from aliphatic amines and aromatic aldehydes, have a wide variety of applications in many fields, e.g. biological, inorganic and analytical chemistry. Schiff bases and their coordination compounds have gained importance recently because of their application as models in biological, biochemical, antimicrobial, anticancer, antibacterial and antifungal activities [1]. Studies of new kinds of chemotherapeutic Schiff bases now fascinated the attention of biochemists. Metal complexes of Schiff bases are extensively studied due to their synthetic flexibility and sensitivity toward a variety of metal atoms. They are found useful in catalysis, in medicine as antibiotics and anti-inflammatory agents and in the industry as corrosion inhibitors. It has been found that few of the complexes are antimicrobially active and show higher activity than the free ligand. Metal chelation affects significantly the antimicrobial/ bioactive behavior of organic ligands. We are especially interested in the coordination chemistry of electron rich first row transition metals. In contrast to most metals from the left and center of the transition metal row, which are mostly six coordinate and more or less octahedral, complexes of metals such as Cu and Ni show a much richer structural diversity. For the Cu(II) ion the d^{9} configuration is Jahn–Teller active: a single unpaired d-electron occupies one of the d-orbitals which gives rise to structural flexibility with coordination numbers varying between 4 and 6 with often severely distorted coordination geometries. Copper is an attractive prospect, being an essential trace element which is required for normal cellular activity as a cofactor for many enzymes However, role of copper is much more complex because it can also promote nucleic acid cleavage and therefore has been utilized as metallodrug to cause DNA damage. In Ni(II) no odd unpaired electron is present and its metal complexes are less likely to be distorted, but they still show a diversity of coordination geometries rarely found for other transition metal complexes, with square planar and octahedral being the most common.

In the present research article we wish to report the synthesis, structure, anti-biogram, and anti-oxidant studies of transition metal complexes derived from condensation of o-phenylenediammine, 2-amino 4-cholorophenol and 1, 10-phenanthroline with the metal salts of Cu(II) and Ni(II) acetates.

Experimental

Materials and physical measurements

All the chemicals used were chemically pure and AR grade. Solvents were purified and dried according to standard procedures. Metal salts were purchased from Merck. o-phenylenediammine, 2-amino 4-cholorophenol and 1, 10-phenanthroline were obtained from Aldrich. Ethanol, DMSO and DMF were used as solvents purchased from Merck and Loba Chemie Pvt. Ltd. The purity of metal complexes was tested by TLC.

The elemental analysis were carried out with a Carlo- Erba 1106-model 240 Perkin Elmer analyzer. The solution conductivity measurements were performed to establish the charge type of the complexes. The complexes were dissolved in DMF and molar conductivities of 10^{-3}M of their solutions at 29 ^{0}C were measured with ELICO CM 185 conductivity Bridge. Infrared spectra were recorded on the Perkin Elmer FT-IR- 8300 model spectrometer using KBr disc in the range of 4000-400 cm^{-1}. Electronic absorption spectra in the UV-Visible range were recorded on Perkin Elmer Lambda -25 between 200-800 nm by using DMF as the solvent. EPR spectra were recorded on a Varian JEOL-JES-TE100 ESR spectrophotometer at X-band microwave frequencies for powdered samples.

Synthesis of Schiff base (H_2L^1)

The Schiff base ligand was prepared according to the literature method. To an ethanolic solution of 2-amino 4-cholorophenol (2 mmol) and ethanolic solution of o-phenylenediamine (1 mmol) was added in drop wise. The reaction mixture was kept on water bath for refluxion. It was stirred for 2 hours. Yellow colour solid was separated and were filtered off, washed with 5 ml of cold ethanol and then dried in air.

Yield: 78 %. M.p: 156-158°C. *Anal. Calc. For* $C_{20}H_{14}N_2O_2Cl_2$: C, 62.50; H, 3.64; N, 7.29. Found: C, 62.49; H, 3.65; N, 7.28. (%). IR (KBr pellet, cm^{-1}): 3355 ν(-OH); 1612 ν(-CH=N) ; 1286 (-C-O). UV–Vis λ_{max} (nm), 320, 348 ($\pi\rightarrow\pi^*$, $n\rightarrow\pi^*$). H^1 NMR (DMSO-d$_6$, δ ppm): 6.8-7.9 ppm (m, Ar-H), 8.10 ppm (s, CH=N), 9.8 ppm (Ph-OH).

Synthesis of metal complexes [2]

An ethanolic solution (20 mL) containing L^1 (o-phenylenediammine and 2-amino 4-cholorophenol) (1 mM) and L^2 (1, 10-phenanthroline) (1 mM) were added to a solution of Metal(II) acetates of Cu(II) and Ni(II) (1 mM) in 20 ml of ethanol. The solution was refluxed for 3 hrs and then allowed to stand at room temperature for 24 hrs. The resulting powder was filtered and dried in vacuum.

$Cu(C_{42}H_{20}N_4O_2Cl_2)$: Yield: 72 %. M.p: 210-222°C. *Anal. Calc. For* $Cu(C_{42}H_{20}N_4O_2Cl_2)$: C, 67.60; H, 2.68; N, 7.51; Cu, 8.51. Found: C, 67.62; H, 2.66; N, 7.52; Cu, 8.50 (%). IR (KBr pellet, cm^{-1}): 1606 ν(-CH=N) ; 1282 ν(-C-O) ; 485ν(-M-N) ; 547 ν(-M-O). UV–Vis λ_{max} (nm), 280, 375, 430 ($\pi\rightarrow\pi^*$, $n\rightarrow\pi^*$, L→MCT); 510, 565, 630 (d→d). Molar conductance x 10^{-3} (Ω^{-1} cm^2 mol^{-1}): 12.63; μ_{eff} (BM): 1.72.

$Ni(C_{42}H_{34}N_4O_6)$: Yield: 75 %. M.p: 212–214°C. *Anal. Calc. For* $Ni(C_{42}H_{20}N_4O_2Cl_2)$: C, 68.04; H, 2.70; N, 7.56; Ni, 7.92. Found: C, 68.02; H, 2.71; N, 7.55; Ni, 7.93 (%). IR (KBr pellet, cm^{-1}): 1601 ν(-CH=N) ; 1277 ν(-C-O) ; 468 ν(-

M-N) ; 541 ν(-M-O). UV–Vis λ_{max} (nm), 272, 377, 451 ($\pi \rightarrow \pi^*$, $n \rightarrow \pi^*$, L→MCT); 511, 558, 608 (d→d). Molar conductance x 10^{-3} (Ω^{-1} cm^2 mol^{-1}): 9.63; μ_{eff} (BM): 3.12.

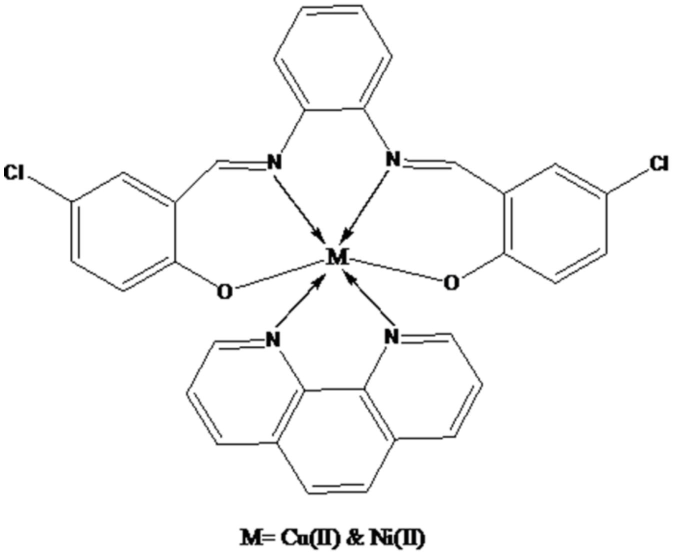

Figure 1 Supposed structure of Schiff Base metal(II) Complexes

In vitro antibacterial assay

The microbial activities of the synthesized Schiff bases and its Cu(II) and Ni(II) complexes were screened for their antibacterial and antifungal properties in DMF solvent against *Staphylococcus aureus*, *Bacillus subtilis* (Gram-positive bacteria) and *Escherichia coli* and *Klebsilla pneumonia* (Gram-negative bacteria), whereas against *Fusarium oxysporum* and *Aspergillus fumigates* fungal strains. The antibiotic *Streptomycine* was used as standard reference in the case bacteria and *Clotrimazole* was used as standard anti-fungal reference. The tested compounds were dissolved in DMF to get concentration of 100 µg/ mL. The test was performed on medium potato dextrose agar contains infusion of 200 g potatoes, 6 g dextrose and 15 g agar. Uniform size filter paper discs (three disks per compound) were impregnated by equal volume from the specific concentration of dissolved tested compounds and carefully placed on incubated agar surface. After incubation for 36 h at 27°C in the case of bacteria and for 48 h at 24°C in the case of fungus, inhibition of the organism which evidenced by clear zone surround each disk was measured and used to calculate mean of inhibition zones [3].

Antioxidant Activity

Spectrophotometric determination of DPPH (1, 1-diphenyl-2- picryhydrazyl radical)-scavenging activity

To establish the antioxidant activity, DMF was used as a solvent [4], due to the low solubility of synthesized compounds in ethanol and methanol. The free radical scavenging effects were evaluated with various concentrations (200, 400, 600, 800, 1000 µg/ mL) of the test compound in 1mL DMSO were added to a 3 mL of 0.003 %(w/v) methanol solution of DPPH. After 30 min the absorbance was taken at 517 nm. Ascorbic acid (AA) was used as a reference compound.

$$\text{DPPH}^{o} \text{ scavenging effect (\%)} = \left[\frac{A_0\text{-}A_1}{A_0} \right] \text{ X } 100$$

Where A_0 is the absorbance of the control solution and A_1 is the absorbance in the presence of sample solutions or standards for positive control.

Hydrogen peroxide assay

Hydroxyl radicals were generated in aqueous media through the Fenton-type reaction. The solution of reaction mixture (3 mL) contained 1.0 mL of 0.10 mmol aqueous safranin, 1 mL of 1.0 mmol aqueous EDTA–Fe(II), 1 mL of 3 % aqueous H_2O_2, and a series of quantitative microadditions of solutions of the test compound. A sample without the tested compound was used as the control. The reaction mixtures were incubated at 37°C for 30 min in a water bath [5]. The absorbance (A_i, A_o, A_c) was then measured at 520 nm. The scavenging effect for OH° was calculated from the following expression:

$$\text{Scavenging ratio (\%)} = [A_i\text{-}A_o/\ A_c\text{-}A_o] \text{ X } 100$$

Where A_i = absorbance in the presence of the test compound; A_0 = absorbance of the blank in the absence of the test compound; A_c = absorbance in the absence of the test compound, EDTA-Fe(II) and H_2O_2.

Results and Discussion

The solubility of the ligand and its complexes were studied in various organic solvents. The ligand was found to be soluble in ethanol, insoluble in water whereas the complexes were soluble in DMF and DMSO.

EPR studies

The EPR-spectra of Copper(II) complex were measured at X-band frequencies at 9.862117 GHZ. The EPR-spectra of Cu(II) complex provides information about the coordination environment around Cu(II) ion. ESR measurement has been made for copper complex using powder sample at room temperature, which could provide only value of g_{iso} and does not give hint about the individual g perpendicular and g parallel. The g_{iso} value of the complex is 2.107. The value of g_{iso} shows that the copper (II) complex is in octahedral environment [6].

Antibacterial activity

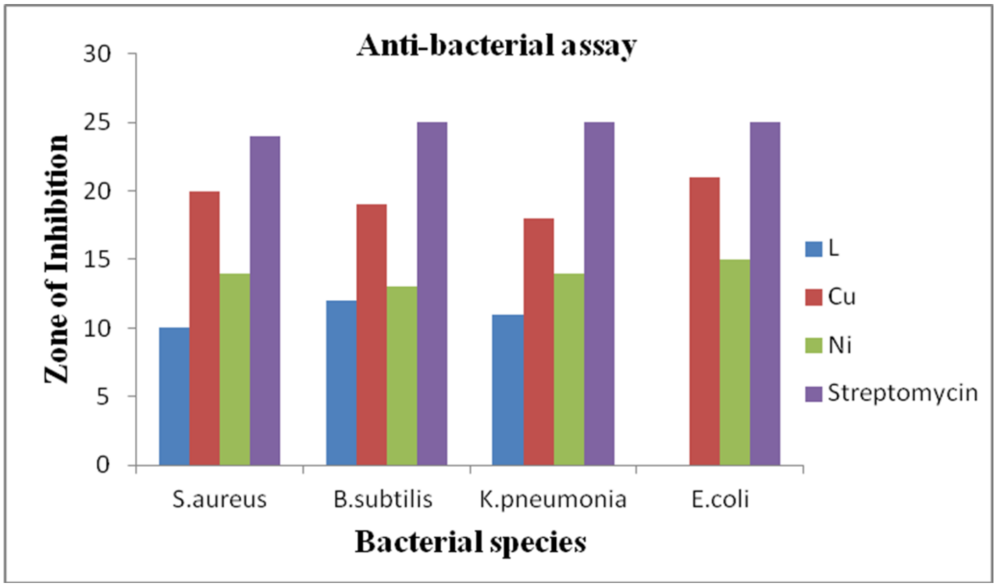

Figure 2 Difference between the Anti-Bacterial Activities of the Schiff Base and Its Binuclear Metal Complexes against Gram-Positive and Gram-Negative Bacteria. Standard = *Streptomycin*, Inhibition Zone in mm, Concentration 100 µg/mL

The antibacterial activities of metal complexes are shown in **Figure 2**. Among the synthesized compounds the Cu(II) complex possess highly active against *Staphylococcus aureus*, *Bacillus subtilis*, *Escherichia coli* and *Klebsilla* *pneumonia* bacteria species. The improved activity of Cu(II) complexes can be explained on the basis of chelation theory [7]. *Streptomycin* was used as standard antibiotics.

In case of antifungal activity, the results were compared with the standard drug *Clotrimazole*. All Schiff bases were show high activity against fungal species. Cu($C_{42}H_{20}N_4O_2Cl_2$) complex showed significantly enhanced antifungal activity than their SB- ligands. The metal complexes of the Schiff base showed much enhanced activity as compared to the uncoordinated compounds (**Figure 3**). It was evident from the data that, this activity significantly increased on coordination.

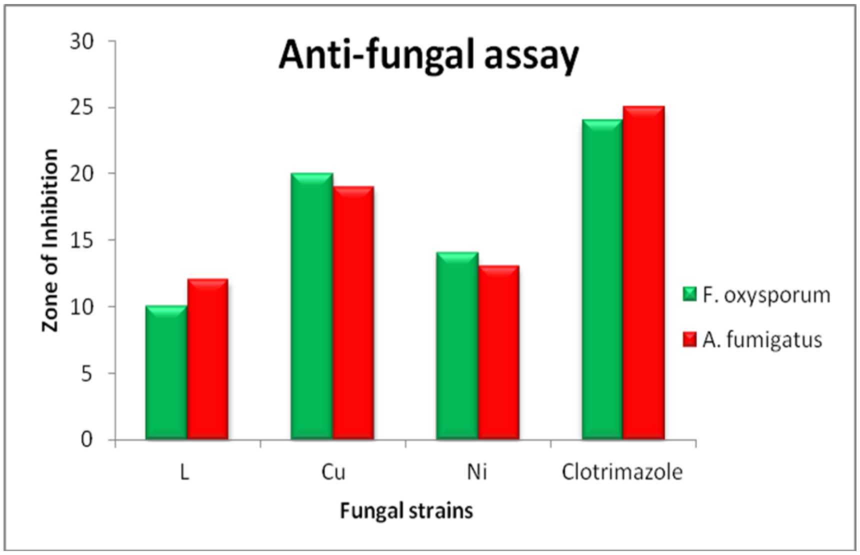

Figure 3 Differences between the Anti-Fungal Activities of the Schiff Base and Its Mononuclear Metal Complexes against Fungi. Standard = *Clotrimazole*. Inhibition Zone in mm, Concentration 100 µg/mL

DPPH Radical Scavenging Activity [8]

The scavenging activity was increased by increasing the concentration of the compounds. DPPH antioxidant assay is based on ability of decolourization of DPPH (a stable free radical) in the presence of antioxidants. This radical contains an odd electron responsible for absorbance at 517 nm. When DPPH accepts an electron donated by an antioxidant compound, the DPPH is decolorized which can be quantitatively measured by changes in absorbance. In the present study, based on the IC_{50} values, the scavenging activities of ligands and their complexes are calculated. From the results, it was found that the IC_{50} values of Cu($C_{42}H_{20}N_4O_2Cl_2$) is 7.82 mg/ml show good activity compared to remaining complexes and ligand. Ascorbic acid is used as standard.

The order of the scavenging activity of all the complexes according to their IC_{50} values is given below.

Ascorbic acid > Cu($C_{42}H_{20}N_4O_2Cl_2$) > Ni($C_{42}H_{34}N_4O_6$) > $C_{20}H_{14}N_2O_2Cl_2$

Hydrogen Peroxide Scavenging Activity

The result shows the plots of hydroxyl radical scavenging effect (%) for ligand and their complexes, respectively, which are concentration- dependant. The values of IC_{50} of ligand and complexes for hydroxyl radical scavenging effect are 4.7–7.9 mg/ml with the order of Ascorbic acid > Cu($C_{42}H_{20}N_4O_2Cl_2$) > Ni($C_{42}H_{34}N_4O_6$) > $C_{20}H_{14}N_2O_2Cl_2$.

These orders of IC_{50} are opposite to the abilities of scavenging effects for hydroxyl radicals. It is marked that the hydroxyl radical scavenging effects of Cu(II) complex are much higher than those of their ligands [9].

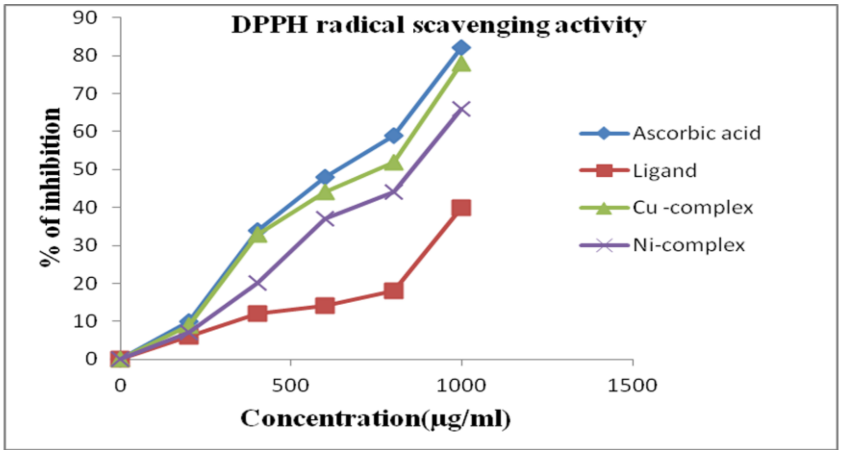

Figure 4 DPPH Radical Scavenging Activity Spectrophotometric Assay of Various Concentrations of Metal Complexes

Conclusion

Single crystals of the complexes could not be isolated from any common solvent. However, the analytical, spectroscopic and magnetic data enabled the prediction of the possible structures. In addition, all the complexes show potent biological activity.

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