



Novel Metal-based Pharmacologically Dynamic Agents of Transition Metal(II) Complexes: Designing, Synthesis, Structural Elucidation, Efficient Nuclease Activity, In Vitro Antibacterial and In Vitro Antioxidant Assay

KEYWORDS

NOON donors, Cleavage activity, Antioxidant property

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ABSTRACT A new tetradentate Schiff base metal(II) complexes $[Cu_2(C_{52}H_{34}N_4O_4)]$, $[Ni_2(C_{52}H_{34}N_4O_4)]$ and $[VO_2(C_{52}H_{34}N_4O_4)]$ derived from Schiff base H2L(L= 4,4 - Bis- [2-(2-hydroxy-phenylimino)-1,2-diphenyl-ethylideneamino]-biphenyl-3,3 -diol, 1:2:2 condensation of 3, 3'-dihydroxybenzidine, Benzil and 2-aminophenol) are reported here and have been characterized by various physico-chemical techniques like elemental analyses, IR, UV-visible, ¹H NMR and ESR as well as magnetic. Gel electrophoresis assay demonstrated the ability of the complexes to cleave the pUC18DNA in the presence of H₂O₂. The Schiff bases and their complexes have been screened for their antibacterial activity against four bacterial strains (Staphylococcus aureus, Escherichia coli, Bacillus subtilis and Klebsilla pneumonia) by disc diffusion method. Additionally, the Cu(II) complex exhibited potential antioxidant properties in in vitro studies.

INTRODUCTION

Presently, there is a growing interest in the coordination chemistry of structurally modified bio-ligands. Schiff bases have been often used as chelating ligands in coordination chemistry, in catalysis, anti-oxidative activity, medicine as antibiotics, anti-inflammatory agents and in industry for anti-corrosion properties (Bibhesh et al., 2012). Transition metal complexes of Schiff base compounds are used as growth inhibiting agents for most of bacteria and fungi also they are widely used as potential therapeutics; they are useful in health and skin care. The complexes of this type are also used as catalysts in organic redox and electrochemical reduction reactions for various chemical reactions. Tetradentate Schiff base metal complexes involving N,O donor sites possess many advantages such as facile approach for synthesis, relative tolerance, readily adjusted ancillary ligands, and tunable steric and electronic coordination environments on the metal centre (Keypour et al., 2013).

In the present research article we wish to report the synthesis, structure, anti-biogram, anti-oxidant and cleavage studies of transition metal complexes derived from condensation of 3, 3'-dihydroxybenzidine, Benzil and 2-aminophenol. The results should be beneficial in designing novel agents for targeting DNA as well as setting the stage for the synthesis of chemical antibacterial and antioxidant drugs.

EXPERIMENTAL

Material:

All chemicals were obtained from Sigma-Aldrich Chemical & Co, Merck and Loba chemicals, India. They included Metal salts, 3, 3'-dihydroxybenzidine, Benzil and 2-aminophenol. The solvents Ethanol, Methanol, DMSO and DMF were used after purification.

Methodology:

Elemental analysis was carried out on a Carlo Erba Model 1106 elemental analyzer. IR spectra were recorded on a SHIMADZU model spectrophotometer on KBr disc in the range 4000– 400 cm⁻¹. Molar conductivity was measured by using an ELICO CM 185 conductivity bridge using freshly prepared solution of the complexes in DMF solution. Electronic spectral studies were carried out on a Perkin Elmer Lambda-25 spectrophotometer in the range 200– 800 nm. The magnetic studies were carried out at room temperature on a Gouy balance calibrated with Hg[Co(SCN)₄]. EPR spectra were recorded on a Varian JEOL-JES-TE100 ESR spectrophotometer at

X-band microwave frequencies for powdered samples.

Preparation of 4, 4'-Bis-[2-(2-hydroxy-phenylimino)-1, 2-diphenyl-ethylideneamino]-biphenyl-3, 3'-diol:

The binucleating tetradentate Schiff base was prepared by condensation of 3, 3'-dihydroxybenzidine (1 mM) in 10 mL of ethanol, benzil (2 mM) and 2-aminophenol (2 mM) in 20 mL of ethanol were mixed and heated at reflux for 2 h as shown in Figure 1. The resulting yellow solid was separated and dried in vacuum. Yield: 80%.

Ultraviolet-visible spectroscopy and magnetic study:

The electronic spectra of the ligands and their metal complexes were recorded in DMF at room temperature are given in Table 2. The bands of the ligands and complexes in the region 280–290 and 384–397 nm are attributed to a benzene $\pi-\pi^*$ and $n-\pi^*$ transitions. Cu(II) complex shows very intense absorption bands in the UV region, attributed to ²B_g→²A_g transitions at 593 nm respectively, which indicates the possibility of square planar geometry of Cu(II) complex. The Cu(II) complex has magnetic moment 1.72 B.M. reveals square planar geometry around the metal ion. The Ni(II) complex exhibited absorption bands at 564 and 642 nm which may be assigned to two spin allowed transitions, ¹A_{1g}→¹A_{2g}, ¹A_{1g}→¹B_{1g}, respectively characteristic of square planar geometry around Ni(II) ion (Fierro et al, 2011) and the Ni(II) is diamagnetic in nature due to square planar geometry. For VO(II) complex, three absorption bands were observed at 520, 580 and 620 nm, assigned to d_{xy}→d_{xz}, d_{yz}, d_{xy}→d_{x²-y²} and d_{xy}→d_{z²} transitions indicate that the present oxovanadium(IV) complexes are square-pyramidal geometry and μ_{eff} of VO(II) is 1.70 B.M.

Table 2. Infrared and electronic spectral data

Compounds	Free -OH	$\nu(C-H)$ (cm ⁻¹)	$\nu(N-O)$ (cm ⁻¹)	$\nu(M-N)$ (cm ⁻¹)	$\nu(M-O)$ (cm ⁻¹)	λ_{max}
C ₃₀ H ₂₀ N ₂ O ₂	3380	1610	--	--	--	--
[Cu ₂ (C ₅₂ H ₃₄ N ₄ O ₄)]	--	1608	--	458	515	593
[Ni ₂ (C ₅₂ H ₃₄ N ₄ O ₄)]	--	1602	--	474	518	564, 642
[VO ₂ (C ₄₀ H ₂₆ N ₄ O ₄)]	--	1605	942	478	534	520, 580, 620

Reducing power assay:

BHA is used as a standard reference. In this assay, the pres-

ence of reducers (i.e., antioxidants) causes the reaction of the Fe^{3+} /ferricyanide complex to the ferrous form the Perl's Prussian blue after the addition of trichloroacetic acid and ferric chloride, that can be monitored at 700 nm. The reducing power of test complexes solutions in DMSO increased with increase in concentration and showed absorbances nearer to those of the standard. The copper complex showed pronounced reducing power than the other metal complexes and ligand (Figure 4).

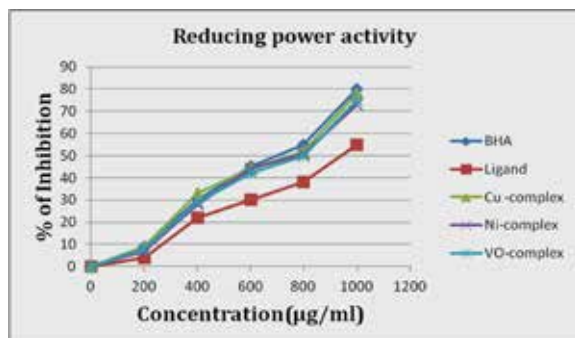


Figure 4. Reducing power assay of various concentration of metal complexes.

Electrophoretic analysis:

The DNA cleavage activities of the Schiff base ligand and its metal complexes at a 50 μM concentration were studied using 40 μM pUC18 in H_2O_2 (50 μM) in 50 mM Tris-HCl buffer (pH 7.2) at 37°C for 2 h and upon irradiation with UV light of 280 nm. The reaction is modulated by metallo complexes bound hydroxyl radical generated from the co-reactant H_2O_2 (Babu et al., 2007). In the control experiment using DNA alone (lane 1) and DNA+ H_2O_2 (lane 2), did not show any apparent cleavage of DNA. The Cu(II) complex (lane 3) cleave DNA more efficiently in the presence of an oxidant than other complexes (lane 4 & 5).

CONCLUSION

The synthesized Schiff bases act as tetradentate ligands through the coordination of four azomethine nitrogen atoms to the metal ion. The bonding of ligand to metal ion was confirmed by the analytical, IR, electronic, magnetic, EPR and ^1H NMR. In biological results it confirms that, all the Schiff bases are biologically active and their metal(II) complexes have shown more promising activities than the Schiff bases. From the observation, it was found that Schiff base metal (II) complexes cleave DNA more efficiently.

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