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ORIGINAL ARTICLE

Synthesis, characterization and biological studies on some metal complexes with Schiff base ligand containing pyrazolone moiety

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Abstract 1:2 Complexes of Co(II), Ni(II), Cu(II) and Zn(II) with the Schiff base ligand Indal-4-AAP, derived from indole-3-carboxaldehyde and 4-aminoantipyrine were synthesized and characterized by elemental analyses, mass, IR, electronic spectra, magnetic moment, molar conductance and cyclic voltammetry. The complexes were found to have the general formulae $[ML_2Cl_2]$ (M = Co(II), Ni(II), Cu(II) and Zn(II)). The IR results demonstrate that the co-ordination sites are the azomethine nitrogen and carbonyl oxygen atoms of the Schiff base ligand. The electronic spectral and magnetic measurement data indicate that the complexes exhibit octahedral geometry around the metal center. The *in vitro* biological screening effects of the synthesized compounds were tested against various microbial species and the results show that the metal complexes are more biologically active than the ligand. The DNA cleavage activity of the ligand and its complexes was assayed on pUC18 DNA using gel electrophoresis. The result shows that Ni(II), Cu(II), and Zn(II) complexes have completely cleaved the DNA.

1. Introduction

The Schiff base ligands with nitrogen and oxygen donor atoms act as good chelating agents for the transition and non-transition metal ions (Singh et al., 2012; Wang et al., 2009; Mohanan et al., 2009). The interests in metal Schiff base complexes, particularly those of transition metal ions, are due to their potential applications in pharmaceutical and industrial fields (Paryzek et al., 2005; Kumar et al., 2009; Cozzi, 2004). The heterocyclic Schiff base ligands and their metal complexes have been the subject of extensive investigation because of their wide use in biological field (Dasilva et al., 2011; Chohan et al., 2010; Rosu et al., 2010; Raman et al., 2009). Transition metal complexes have been extensively studied for their nuclease-like activity using the redox properties of the metal and dioxygen to produce reactive oxygen species to promote DNA cleavage, yielding direct strand scission or base modification (Clever and Shionoya, 2010; Yang et al., 2010). Metal

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complexes of nitrogen–oxygen chelating agents derived from 4-aminoantipyrine Schiff bases have pronounced applications in biological, clinical, analytical and pharmacological areas (Raja et al., 2012; El-Sonbati et al., 2012; Rosu et al., 2011; Mohamed et al., 2009). The present study deals with the synthesis, characterization and biological studies of the Schiff base (Indal-4-AAP) derived from indole-3-carboxaldehyde and 4-aminoantipyrine and its Co(II), Ni(II), Cu(II) and Zn(II) complexes.

2. Materials and methods

4-Aminoantipyrine and indole-3-carboxaldehyde were obtained from Sigma. Metal(II) chlorides were purchased from Merck. All other chemicals used were of AnalaR grade. Solvents were purified and distilled before use. The metal content in the complexes was determined by EDTA titration (Vogel, 1978). Elemental analysis was obtained using a Perkin-Elmer elemental analyzer. Conductivity measurements were made on freshly prepared 10^{-3} M solutions in DMSO at room temperature with a coronation digital conductivity meter. The IR spectra were recorded in KBr pellet on a JASCO FT/IR-410 spectrometer in the range 4000–400 cm^{-1}. Electronic spectra were recorded on a Perkin Elmer Lambda-25 UV/VIS spectrometer. The room temperature magnetic measurements were carried out using Guoy balance and the diamagnetic corrections were made using Pascal's constant (Kettle, 1969). Cyclic voltammetric measurements were carried out in a Bio-Analytical system (BAS) model CV-50W electrochemical analyzer. The three electrode cell comprised of a reference Ag/AgCl, auxiliary platinum and working glassy electrodes. Tetrabutylammonium perchlorate was used as supporting electrolyte.

2.1. Synthesis of Schiff base ligand (Indal-4-AAP)

An 1:1 equimolar methanolic solution of 4-aminoantipyrine (0.4064 g, 2 mmol) and indole-3-carboxaldehyde (0.2092 g, 2 mmol) was mixed and gently heated for 2 h after the addition of pinch of p-toluenesulphonicacid with constant stirring. The characteristic pale yellow precipitate obtained by Schiff base condensation was filtered out and kept for crystallization, dissolving in DMSO. Fine yellow crystals were obtained upon slow evaporation at room temperature. It was washed with alcohol, ether and dried in vacuum desiccator over anhydrous calcium chloride. The purity of the Schiff base was checked by TLC. (Yield: 87%).

2.2. Synthesis of metal Schiff base complexes

To the pale yellowish solution of Indal-4-AAP in 20 ml of THF (1.6555 g, 5 mmol) taken in a RB flask, a solution of metal(II) chloride in 20 ml of aqueous MeOH (5 mmol) was added dropwise with constant stirring. The reaction mixture was heated under reflux for 2 h and the volume was reduced to half of the initial volume under reduced pressure. The resultant precipitate was filtered, washed several times with cold EtOH, ether and then dried in vacuo over anhydrous $CaCl_2$ (Yield: 60–70%).

2.3. In vitro antimicrobial activity

Antibacterial and antifungal activities of the ligand and its complexes were tested *in vitro* against the bacterial species *Escherichia coli*, *Bacillus subtilis*, *Pseudomonas aeruginosa* and *Staphylococcus aureus*; fungal species, *Aspergillus niger*, *Aspergillus flavus*, and *Candida albicans* by the disk diffusion method (Bauer et al., 1966). Amikacin was used as the standard antibacterial agent, whereas Nystatin was used as the standard antifungal agent. The test organisms were grown on nutrient agar medium in petri plates. The compounds were prepared in DMF and soaked in filter paper disk of 5 mm diameter and 1 mm thickness. The disks were placed on the previously seeded plates and incubated at 37 °C and the diameter of inhibition zone around each disk was measured after 24 h for bacterial and 72 h for fungal species.

2.4. DNA cleavage analysis

The compounds were added separately to the pUC18 DNA sample. The sample mixtures were incubated at 37 °C for 2 h. The electrophoresis of the samples was done by weighing 300 mg of agarose and dissolving it in 25 ml of TAE buffer (4.84 g Tris base, pH 8.0, 0.5 M EDTA/1 L) by boiling. When the gel attained ~55 °C, it was poured into the gel cassette fitted with comb and allowed the gel to solidify. The comb was removed carefully and the gel was placed in the electrophoresis chamber flooded with TAE buffer. DNA sample (mixed with bromophenol blue dye at 1:1 ratio) was loaded carefully into

Table 1 Analytical and physical data of the Schiff ligand and its complexes.

Compound	Empirical formula	Color	Elemental analysis found (calcd)%				Λc (Ohm^{-1} cm^2 mol^{-1})	λ_{max} (nm)	μ_{eff} (B.M)
			C	H	N	M			
L	$C_{20}H_{18}N_4O$	Pale yellow	72.56 (72.71)	5.73 (5.49)	16.85 (16.96)	–	–	220, 270, 364	–
$[CoL_2Cl_2]$	$C_{40}H_{36}Cl_2N_8O_2Co$	Green	60.84 (60.77)	4.68 (4.59)	14.03 (14.17)	7.61 (7.45)	6.0	679, 613	5.13
$[NiL_2Cl_2]$	$C_{40}H_{36}Cl_2N_8O_2Ni$	Yellow	60.58 (60.79)	4.38 (4.59)	14.32 (14.18)	7.24 (7.43)	12.8	~1100, 779, 380	2.98
$[CuL_2Cl_2]$	$C_{40}H_{36}Cl_2N_8O_2Cu$	Brown	60.54 (60.41)	4.67 (4.56)	14.33 (14.09)	8.06 (7.99)	15.0	850, 380	1.92
$[ZnL_2Cl_2]$	$C_{40}H_{36}Cl_2N_8O_2Zn$	Yellow	60.65 (60.27)	4.41 (4.55)	13.95 (14.06)	8.37 (8.20)	14.0	220, 250, 326	Dia