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Studies on DNA Cleavage and Antimicrobial Screening of Transition Metal Complexes of 4-Aminoantipyrine Derivatives of N_2O_2 Type

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A new series of transition metal complexes of Cu(II), Ni(II), Zn(II) and VO(IV), were synthesized from the Schiff base (L) derived from 4-aminoantipyrine, 3-hydroxy-4-nitrobenzaldehyde and acetylacetone. The structural features were arrived from their elemental analyses, magnetic susceptibility, molar conductance, Mass, IR, UV-Vis., ^{1}H NMR and ESR spectral studies. The data show that the complexes have composition of [ML]X type. The UV-Vis., magnetic susceptibility and ESR spectral data of the complexes suggest a square-planar geometry around the central metal ion except for VO(IV) complex which has square-pyramidal geometry. The redox behavior of copper and vanadyl complexes were studied by cyclic voltammetry. The antimicrobial screening tests were also recorded and gave good results in the presence of metal ion in the ligand system. The nuclease activity of the above metal complexes shows that the copper and nickel complexes cleave DNA through redox chemistry, whereas other complexes are not effective.

Keywords: Square-planar geometry, Calf Thymus DNA, Nuclease activity, Antimicrobial activity

INTRODUCTION

Compounds containing an azomethine group are known as imines (Schiff bases). The chelating abilities and analytical and biological applications of these compounds have attracted remarkable attention [1-3]. These compounds are readily hydrolyzed under acidic conditions leading to active aldehydes which can act as alkylating agents [4]. Besides, several azomethines have been reported to possess remarkable antibacterial [5-9], antifungal [10-12], anticancer [13-16] and diuretic activities [17]. Antibiotics such as Streptomycin, Aspergillic acid, Usnic acid and Tetracycline are known to have chelating properties. Presumably, some antibiotics are delicately balanced so as to be able to compete successfully with the metal-binding agents of bacteria while not disturbing the metal processing by the host. There is evidence that at least some bacteria have developed resistance to antibiotics through the development of altered enzyme systems that can compete successfully with antibiotics. The action of the antibiotic need not be a simple competitive one. The chelating properties of antibiotics may be used in metal transport across membranes or used to attach the antibiotic to a specific site from which it can interfere with the growth of bacteria [18]. Pyrazolone and its derivatives are a group of antibiotics that have been extensively used in treating several bacterial diseases [19-21]. They have antibacterial activity against gram-negative and gram-positive strains. Transition metal complexes of these antibiotics with enhanced potentiality against bacterial strains have been reported elsewhere [22].

Moreover, mimicking the activities of nuclease is currently

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*Corresponding author. E-mail: drn_raman@yahoo.co.in an attractive research area in molecular biology since artificial nucleases have potential applications as novel restriction enzymes and anticancer therapeutic agents [23]. Among the different therapeutic strategies to eradicate cancer cells through DNA damage, the view of using small water soluble transition metal complexes, capable of oxidative or hydrolytic DNA cleavage as anticancer drugs is a challenging issue in bioinorganic chemistry [24,25]. Many transition metal complexes with vanadium [26], iron [27], copper [28,29], cobalt [30], lanthanides [31,32] and also actinides [33] have been reported as efficient DNA cleavage agents with or without sequence specificity, moreover the ligand or the metal in these complexes can be varied in an easily controlled manner to facilitate the individual applications [34].

In continuation of our series of investigations, we attempted to widen the scope of derivatization by providing more flexibility through Schiff base formation with 4-aminoantipyrine containing keto group, >C=N and complexation with metal ions. The Schiff base structure affords a greater choice and flexibility, and complexation with a metal ion adds to the stability and versatility of the compounds. The novel investigated compounds and their metal complexes were also evaluated for their antimicrobial activity against several bacterial strains and nuclease activity against calf thymus (CT) DNA.

EXPERIMENTAL

All reagents, 4-aminoantipyrine, 3-hydroxy-4-nitrobenzaldehyde and acetylacetone and various metal chlorides and vanadyl sulphate were Merck products, CT DNA from GENEI and used as supplied. For the voltammetric experiments, tetrabutylammonium perchlorate (TBAP) used as supporting electrolyte, was purchased from Sigma. Anhydrous grade ethanol, DMF and DMSO were purified according to standard procedures. Microanalytical data of the compounds were recorded at the Sophisticated Analytical Instrument Facility, Central Drug Research Institute (SAIF, CDRI), Lucknow. The mass spectra of the ligand and its complexes were recorded at the Sophisticated Analytical Instrument Facility (SAIF), Indian Institute of Technology, Mumbai. ^{1}H NMR spectra (300 MHz) of the samples were recorded in $CDCl_3$ and DMSO-d_6 by employing TMS as internal standard at Madurai Kamaraj University, Madurai. The IR spectra of the samples were recorded on a Perkin-Elmer 783 spectrophotometer in 4000-400 cm^{-1} range using KBr pellet. The UV-Vis. spectra were recorded on a Shimadzu UV-1601 spectrophotometer using DMF as solvent. The X-band ESR spectra of the copper and vanadyl complexes were recorded at 300 and 77 K on a Varian ESR spectrophotometer using diphenylpicrylhydrazyl (DPPH) as internal standard at RSIC, IIT, Chennai. Magnetic susceptibility measurements of the complexes were carried out by Gouy balance using copper sulphate as the calibrant. Electrochemical studies were carried out using EG&G Princeton Applied Research Potentiostat/ Galvanostat Model 273A, controlled by M270 software. CV measurements were performed using a glassy carbon working electrode, platinum wire auxiliary electrode and an Ag/AgCl reference electrode. All solutions were purged with N_2 for 30 min prior to each set of experiments. The molar conductance of the complexes was measured using a Systronic conductivity bridge at room temperature in DMSO solution. Solutions of CT DNA (calf thymus DNA) in 50 mM NaCl/50 mM tris-HCl (pH = 7.2) gave a ratio of UV absorbance at 260 and 280 nm, A_{260}/A_{280} of *ca.* 1.8-1.9, indicating that the DNA was sufficiently free of protein contamination [35]. The DNA concentration was determined by the UV absorbance at 260 nm after 1:100 dilutions. The molar absorption coefficient was taken as 6600 M^{-1} cm^{-1}. Stock solutions were kept at 4 °C and used within 4 days. Doubly distilled H_2O was used to prepare the buffer. The antimicrobial activities of the ligand and its complexes were carried out by well diffusion method.

Synthesis of Knoevenagel Condensate β-Diketone (I)

Condensation of acetylacetone with 3-hydroxy-4-nitrobenzaldehyde was performed by heating equimolar amounts (10 mmol) under reflux in 50 ml ethanol, in the presence of 5 drops of piperidine as a catalyst for not less than 10 h. The solution was then cooled and the condensed solid product of Knoevenagel condensate (I) β-diketone was isolated by filtration, washed and recrystallised from ethanol.

Synthesis of Schiff Base

An ethanolic solution (50 ml) of 3(3$'$-hydroxy-4$'$-nitrobenzalidene)-2,4-pentanedione (I) (5 mmol) and 4-aminoantipyrine (10 mmol) was boiled under reflux for *ca.* 3 h. The resultant solution was cooled to room temperature. The yellow solid of 3(3'-hydroxy-4'-nitrobenzalidene)-2,4-di (imino-4''-antipyrinyl)pentane was formed which was filtered and recrystallised in ethanol (Fig. 1).

Synthesis of Metal Complexes

A solution of metal chloride in ethanol (2 mmol) was refluxed with an ethanolic solution of the Schiff base (2 mmol) for *ca.* 5 h. Then the solution was reduced to one-third in a water bath. The solid complex precipitated was filtered and washed thoroughly with ethanol and dried *in vacuo*. The oxovanadium(IV) complex was synthesized from the sulphate salt by the same procedure but in the presence of 5 ml of 5% aqueous sodium acetate solution.

Antimicrobial Activity

The *in vitro* biological screening effects of the investigated compounds were tested against the bacteria *Salmonella typhi, Pseudomonas aeruginosa, Escherichia coli* and *Bacillus subtilis* by the well diffusion method [36] using agar nutrient as the medium. The antifungal activities of the compounds were evaluated by the well diffusion method against the fungi *viz*., *Aspergillus niger, Aspergillus flavus* and *Rhizoctonia bataicola* cultured on potato dextrose agar as medium. The stock solution (10^{-2} M) was prepared by dissolving the compounds in DMSO and the solutions were serially diluted in order to find the MIC values. In a typical procedure [37], a well was made on the agar medium inoculated with microorganisms. The well was filled with the test solution using a micropipette and the plate was incubated 24 h for bacteria and 72 h for fungi at 35 °C. During this period, the test solution diffused and the growth of the inoculated microorganisms was affected. The inhibition zone was developed, at which the concentration was noted.

Gel Electrophoresis

The DNA cleavage experiment was conducted using CT DNA by gel electrophoresis with the corresponding metal complex in the presence of H_2O_2 as an oxidant. Incubation of reaction mixture was performed before electrophoresis experiment at 35 °C for 2 h as follows. The samples CT DNA 30 μM, 50 μM each complex, 50 μM H_2O_2 in 50 mM tris-HCl buffer (pH = 7.2) were electrophoresed for 2 h at 50 V on 1% agarose gel using tris-aceticacid-EDTA buffer, pH = 8.3. After electrophoresis, the gel was stained using 1 μg cm^{-3} ethidiumbromide (EB) and photographed under UV light using Nikon camera.

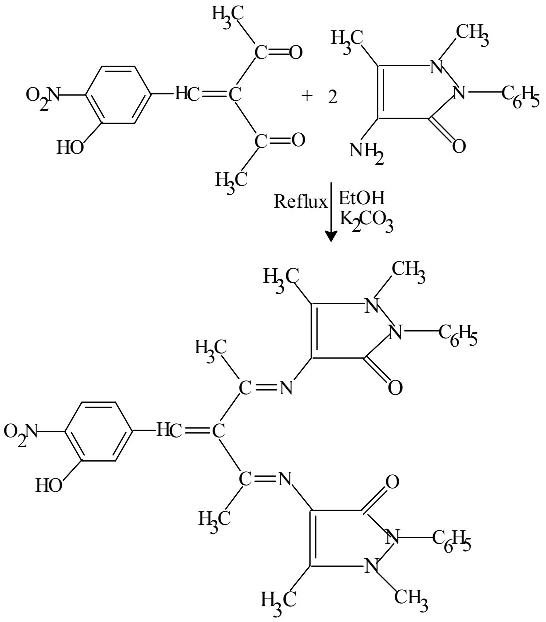

Fig. 1. Formation of Schiff Base Ligand (L).

RESULTS AND DISCUSSION

The analytical data for the ligand and complexes together with some physical properties are summarized in Table 1. The analytical data of the complexes correspond well with the general formula [ML]X, where M = Cu(II), Ni(II), Zn(II) and VO(IV); L = Ligand; X = $2Cl^-$ and SO_4^{2-}. The magnetic susceptibilities of the complexes at room temperature are consistent with square-planar geometry around the central metal ion, except for the VO(IV) complex which shows a square-pyramidal one. The molar conductance data of the Cu(II), Ni(II) and Zn(II) chelates show that the complexes are 1:2 electrolytes while the $[VOL]SO_4$ complex is 1:1 electrolyte.

Mass Spectra

Electron spray ionization (ESI) mass spectra of the ligand

Table 1. Physical Characterization, Analytical, Molar Conductance and Magnetic Susceptibility Data of the Complexes

Compound	Color	Yield (%)	(%) Found (Calcd.) M	C	H	N	Molar conductance Λ_m (ohm^{-1} cm^2 mol^{-1})	μ_{eff} (BM)
L	Yellow	65	-	65.2 (65.9)	5.1 (5.3)	15.2 (15.8)	-	-
[CuL]Cl$_2$	Dark brown	50	8.1 (8.4)	53.9 (54.1)	4.4 (4.4)	12.8 (13.0)	79	1.74
[NiL]Cl$_2$	Pale green	42	7.7 (7.8)	54.3 (54.5)	4.4 (4.4)	12.9 (13.0)	65	-
[ZnL]Cl$_2$	Pale yellow	32	8.4 (8.6)	53.9 (54.0)	4.4 (4.4)	12.8 (12.9)	74	-
[VOL]SO$_4$	Green	58	6.6 (6.7)	52.8 (53.9)	4.4 (4.3)	12.3 (12.9)	49	1.72

(L) and its copper complex [CuL]Cl$_2$, were recorded at room temperature and were used to compare their stoichiometry composition. The Schiff base shows a molecular ion peak at m/z 619 which is also supported by the "Nitrogen Rule", since the compound possesses add number of nitrogen atoms. The molecular ion peak for the copper complex, observed at m/z 754 confirms the stoichiometry of metal chelates as [CuL]Cl$_2$ type. It is also supported by the mass spectra of the other complexes and the microanalytical data of the complexes.

Infrared Spectra

The IR spectra provide valuable information regarding the nature of the functional group attached to the metal atom. The IR spectra exhibit a strong band at *ca*. 1615 cm^{-1} which is characteristic of the azomethine group (>C=N-) in the free Schiff base. In IR spectra of complexes, this band shifts to lower frequency of *ca*. 1595-1580 cm^{-1} which indicates that the azomethine nitrogen is one of the coordinating atoms in the Schiff base [38-40]. The band observed at 1660 cm^{-1} is characteristic of the keto group in a pyrazolone ring [41,42]. In the complexes, this band is shifted to lower frequency 1640-1630 cm^{-1}, indicating the coordination of carbonyl oxygen to the metal ion which is further supported by the formation of new bands in the regions 460-510 cm^{-1} and 410-460 cm^{-1} which are due to ν_{M-N} and ν_{M-O} bands respectively [43,44]. The ligand shows a broad band for the -OH group at *ca*. 3300-3500 cm^{-1}.

The appearance of this peak in all the spectra of the complexes indicates that the chelation does not take place *via* the -OH group. These observations are in accordance with the structure of metal complexes with the ligand in which the central metal ion acquires a coordination number of four. In the vanadyl complex, a new band appears at 943 cm^{-1} which is attributed to V=O frequency [45].

^{1}H NMR Spectra

The ^{1}H NMR spectra of the ligand (L) and its zinc complex were recorded in DMSO-d$_6$. The ^{1}H NMR spectrum of the ligand shows the following signals: Phenyl multiplets at 7.2-7.4 δ range, $=C-CH_3$ at 2.4 δ, $-N-CH_3$ at 3.0 δ, $N=C-CH_3$ at 2.8 δ and the peak at 10.4 ppm is attributable to the phenolic -OH group present in the 3-hydroxy-4-nitrobenzaldehyde moiety. The presence of the phenolic -OH proton noted for the zinc complex confirms the -OH proton free from complexation. The azomethine proton signal in the spectrum of the zinc complex is shifted downfield compared to the free ligand, suggesting deshielding of the azomethine group due to the coordination with metal ion. There is no appreciable change in other signals of this complex.

Electronic Absorption Spectra

The electronic absorption spectra of the Schiff base, Cu(II), Zn(II), Ni(II) and VO(IV) complexes were recorded at 300 K. The absorption region is assigned and the proposed geometry of the complexes is given in Table 2. Based on these data, a square-planar geometry is assigned to the complexes except for VO(IV) complex which has square-pyramidal geometry (Fig. 2). These values are comparable with that of the other reported complexes [46-50].

Electron Spin Resonance Spectra (ESR)

The ESR spectrum of the copper complex was recorded in DMSO at 300 and 77 K. The frozen solution spectrum shows a

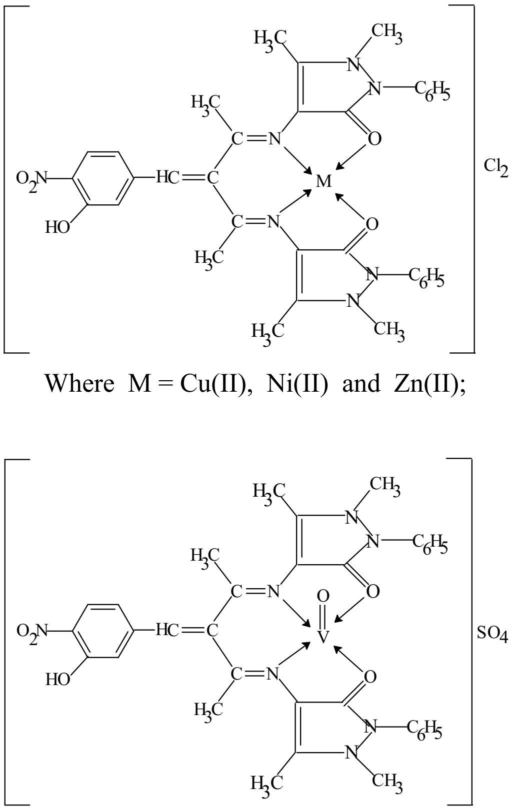

Fig. 2. The proposed structures of the Schiff base complexes.

Table 2. Electronic Absorption Spectral Data of the Compounds

Compound	Solvent	Absorption (cm^{-1})	Band assignment	Geometry
L	EtOH	26737	INCT	-
		38759	INCT	
$[CuL]Cl_2$	DMF	26100	INCT	
		37735	INCT	Square-planar
		18248	$^2B_{1g} \rightarrow {}^2A_{1g}$	
$[NiL]Cl_2$	DMF	28011	INCT	
		36900	INCT	
		14705	$^1A_{1g} \rightarrow {}^1A_{2g}$	Square-planar
		23752	$^1A_{1g} \rightarrow {}^1B_{1g}$	
$[VOL]SO_4$	DMF	27700	INCT	
		38910	INCT	
		13793	$^2B_2 \rightarrow {}^2E$	Square-pyramidal
		21834	$^2B_2 \rightarrow {}^2B_1$	
$[ZnL]Cl_2$	DMF	27624	INCT	-

INCT = Intra ligand charge transfer.

Table 3. ESR Spectral Data of Copper and Vanadium Complexes in DMSO at 300 and 77 K

Complex	A_{II}	$A_{\perp}$	A_{iso}	g_{II}	$g_{\perp}$	g_{iso}
$[CuL]Cl_2$	145	49	75	2.30	2.06	2.12
$[VOL]SO_4$	170	64	104	1.78	1.94	1.98

well-resolved four line spectrum and no features characteristic for a dinuclear complex. This is also supported by the magnetic moment of copper complex (1.77 B.M.) which confirms the mononuclear nature of the complex. The spin Hamiltonian parameters, calculated for the copper complex from the spectra, are given in Table 3. The "g" tensor values of this copper(II) complex can be used to derive the ground state. In square-planar complexes, the unpaired electron lies in the $d_{x^2-y^2}$ orbital giving $g_{II} > g_{\perp} > 2$ while the unpaired electron lies in the d_{z^2} orbital giving $g_{\perp} > g_{II} > 2$. From the observed values, it is clear that $g_{II} > g_{\perp} > 2$ which suggests that the complex is square-planar and is supported by the unpaired electron which lies predominantly in the $d_{x^2-y^2}$ orbital [51-54], as is evident from the value of the exchange interaction term G, estimated from the expression:

$$G = \frac{g_{II} - 2.0036}{g_{\perp} - 2.0036}$$

The observed value for the exchange interaction parameter for the copper complex (G = 5.2) suggests that the local tetragonal axes are aligned parallel or slightly misaligned and the unpaired electron is present in the $d_{x^2-y^2}$ orbital. This finding also indicates that the exchange coupling effects are not operative in the present complex [55].

The ESR spectra of the vanadyl complex, recorded in DMSO solution at 300 and 77 K, show a typical eight line and sixteen line pattern respectively (Fig. 3). The isotropic ESR parameters $g_{iso} = 1.97$ and $A_{iso} = 101$ can be calculated from the position spacing of the resonance lines from the room temperature solution spectrum of the complex. The spectrum is like a typical eight line pattern which shows that a single vanadium is present in the molecule *i.e.*, it is a monomer. In the frozen solid state, the spectrum shows two types of resonance components, one set due to the parallel features and the other set due to the perpendicular features, which indicate axially symmetric anisotropy with well-resolved sixteen line hyperfine splitting, characteristic of an interaction between the electron and vanadium nuclear spin. From the anisotropic spectrum, the anisotropic parameters were calculated. The observed order ($A_{II} = 170 > A_{\perp} = 64$; $g_{\perp} = 1.94 > g_{II} = 1.78$) indicates that the unpaired electron is present in the d_{xy} orbital with square-pyramidal geometry around the VO(IV) chelates [56-58].

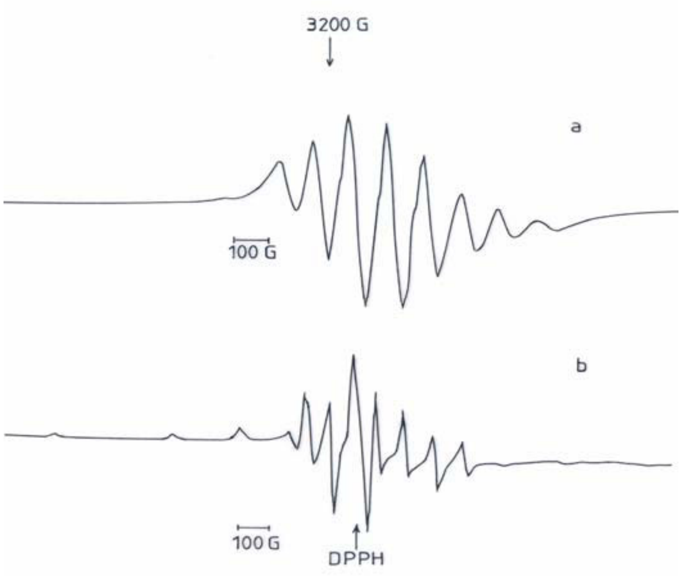

Fig. 3. ESR spectrum of the $[VOL]SO_4$ complex in DMSO at (a) 300 K and (b) 77 K.

Cyclic Voltammetric Studies

The cyclic voltammogram of the $[CuL]Cl_2$ complex in DMF (0.8 to -0.8 V potential range) shows a well-defined redox process (Fig. 4b) corresponding to the formation of the copper(II)/copper(III) couple at $Ep_a = 0.21$ V and the

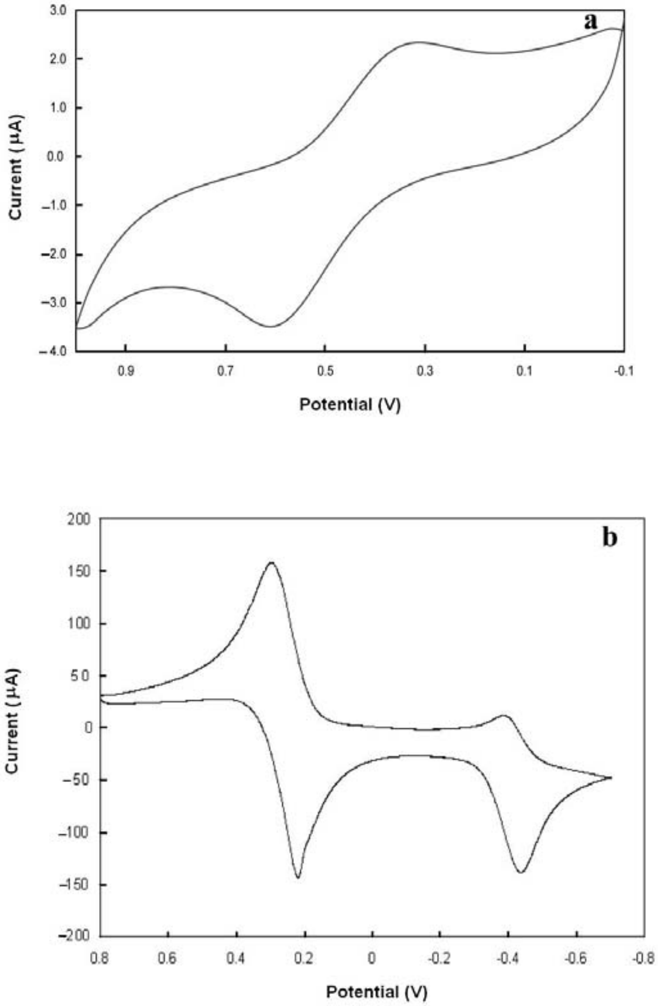

Fig. 4. Cyclic voltammogram of the $[NiL]Cl_2$ (a) and $[CuL]Cl_2$ complex (b) in DMF at 300 K (0.1 M TMAP). Scan rate 50 mVs^{-1}.

associated cathodic peak at $Ep_c = 0.29$ V. This couple is found to be reversible with $\Delta Ep = 0.08$ V and the ratio, anodic to cathodic peak currents ($Ip_c/Ip_a \approx 1$) is corresponding to simple one electron process. The complex also shows another quasi-reversible peak in the negative region characteristics for copper(II) → copper(I) couple at $Ep_c = -0.39$ V, with the associated anodic peak at $Ep_a = -0.44$ V for copper(I) → copper(II) oxidation. The cyclic voltammogram for the vanadyl complex was recorded in DMSO solution and the data in Table 4 show two well-defined one-electron transfer redox peaks, corresponding to the formation of the VO(IV)/VO(V) and VO(IV)/VO(III) couples [59,60]. The peak current functions of both waves in complex are different which indicate the involvement of two different electroactive species in solution [61,62] corresponding to VO(V) and VO(III). The cyclic voltammograms of the nickel (Fig. 4a) and zinc complexes recorded in DMF solution show a well-defined redox process corresponding to the formation of the Ni(II)/Ni (0) and Zn(II)/Zn(0) couple at $Ep_C = 0.34$ V ($Epa = 0.61$ V, $\Delta Ep = 0.27$ V) and $Ep_C = -0.28$ V ($Epa = -0.07$ V, $\Delta Ep = -0.21$), respectively.

Antimicrobial Activity

For *in vitro* antimicrobial activity, the investigated compounds were tested against the bacteria *Salmonella typhi, Pseudomonas aeruginosa, Escherichia coli* and *Bacillus subtilis* and fungi *Aspergillus niger, Aspergillus flavus* and *Rhizoctonia bataicola*. The minimum inhibitory concentration (MIC) values of the compounds against the growth of microorganisms are summarized in Tables 5 and 6. From Table 5, it is observed that the copper and vanadyl complexes are more active in *Pseudomonas aeruginosa* and *Salmonella typhi* respectively compared to other bacterial organisms. Nickel and zinc complexes are moderatively active in all bacterial organisms. Moreover, all the complexes are moderatively active in the above four bacterial organisms compared with standard Streptomycin. From Table 6, it is found that the copper complex is more active in *Aspergillus* flavus than the other complexes. Both the nickel and zinc complexes are more active in *Aspergillus niger* organism compared with other complexes. In *Rhizoctonia bataicola* fungus organism copper complex is less active than the other complexes. However, all the complexes are more active in the above three fungal organisms than the standard Nystatin. A comparative study of the ligand and their complexes (MIC values) indicates that the metal complexes exhibit higher antimicrobial activity than the free ligand. Such increased activity of the complexes can be explained with respect to Overtone's concept and Tweedy's chelation theory. According to Overtone's concept of cell permeability, the lipid membrane that surrounds the cell favors the passage of only the lipid soluble materials whose liposolubility is an important factor, which controls the antimicrobial activity. On chelation, the

Table 4. Cyclic Voltammetric Data of Copper and Vanadium Complexes in DMSO Containing 0.1 M (TBAP) at Scan Rate of 50 mV s^{-1}

Complex	Couple	Ep_c (V)	Ep_a (V)	Ip_c (μA)	Ip_a (μA)
$[CuL]Cl_2$	Cu(II)/Cu(III)	0.29	0.21	14.87	-16.09
	Cu(II)/Cu(I)	-0.39	-0.44	3.96	-10.37
$[VOL]SO_4$	VO(IV)/VO(V)	0.43	0.52	22.28	-26.55
	VO(IV)/VO(III)	-0.98	-0.34	14.75	-10.44
$[NiL]Cl_2$	Ni(II)/Ni(0)	0.34	0.61	1.12	-2.51
$[ZnL]Cl_2$	Zn(II)/Zn(0)	-0.28	-0.07	0.66	-0.58

Table 5. Antibacterial Activity of the Schiff Base Ligand and its Metal Complexes (Minimum Inhibitory Concentration × 10^{-2} M)

Compound	*S. typhi*	*P. aeruginosa*	*E. coli*	*B. subtilis*
L	7.2	8.1	8.3	7.5
$[CuL]Cl_2$	5.9	3.8	7.2	5.6
$[VOL]SO_4$	3.1	5.5	5.8	4.9
$[NiL]Cl_2$	4.9	4.8	4.7	4.8
$[ZnL]Cl_2$	6.2	5.8	4.2	4.9
Streptomycin	2.1	1.8	2.3	2.0

Table 6. Antifungal Activity of the Schiff Base ligand and its Metal Complexes (Minimum Inhibitory Concentration × 10^{-2} M)

Compound	*A. niger*	*A. flavus*	*R. bataicola*
L	8.9	6.6	9.8
$[CuL]Cl_2$	5.6	4.1	7.3
$[VOL]SO_4^{2-}$	8.1	6.3	6.5
$[NiL]Cl_2$	4.8	7.5	6.9
$[ZnL]Cl_2$	4.9	5.2	6.5
Nystatin	10	8	14

polarity of the metal ion is reduced to a great extent due to the overlap of the ligand orbital and partial sharing of the positive charge of the metal ion with donor groups. Further, it increases the delocalization of π-electrons over the whole chelate ring and enhances the lipophilicity of the complexes. This increased lipophilicity enhances the penetration of the complexes into lipid membranes and blocking of the metal binding sites in the enzymes of microorganisms. These complexes also disturb the respiration process of the cell and thus block the synthesis of proteins, which restricts further growth of the organism [44]. Further more, 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 interference with the normal cell process.

DNA Cleavage Studies

The cleavage efficiency of the complexes compared with that of the control is due to their efficient DNA-binding ability. The metal complexes were able to convert super coiled DNA into open circular DNA. The general oxidative mechanisms proposed account for DNA cleavage by hydroxyl radicals *via.* abstraction of a hydrogen atom from sugar units and predict the release of specific residues arising from transformed sugars, depending on the position from which the hydrogen atom is removed [63]. The cleavage is inhibited by the free radical scavengers implying that hydroxyl radical or peroxy derivatives mediate the cleavage reaction. The reaction is modulated by a metallocomplexes bound hydroxyl radical or a peroxo species generated from the co-reactant H_2O_2.

In the present study, the CT-DNA gel electrophoresis experiment was conducted at 35 °C using our synthesized complexes in the presence of H_2O_2 as an oxidant. It was found that, at very low concentrations, few complexes exhibit nuclease activity in the presence of H_2O_2. Control experiment using DNA alone does not show any significant cleavage of CT-DNA even on longer exposure time. Hence, we conclude that the copper complex cleaves DNA as compared with control DNA, while other complexes do not cleave DNA in the presence of H_2O_2. Probably this may be due to the formation of redox couple of the metal ions and its behavior. The redox property of the metal complexes mediates oxidation of nucleic acids. In oxidative DNA cleavage mechanism, metal ions in the complexes react with H_2O_2 to generate the hydroxyl radical which attacks at the C4' position of the sugar moiety and finally cleaves the DNA. Copper complex reacts with H_2O_2 to produce hydroxyl radical, hydroxyl ion and Cu(III) form. The formation of hydroxyl radical by the copper complex is further compared with other complexes with H_2O_2. Hence, copper complex can promote redox mediated cleavage of DNA reaction on sugar ring. The Cu(III) ion formation is supported by electrochemical study. Further, the presence of a smear in the gel diagram indicates the presence of radical cleavage [64].

CONCLUSIONS

In this paper, coordination chemistry of a Schiff base ligand, obtained from the reaction of 4-aminoantipyrine, 3-hydroxy-4-nitrobenzaldehyde and acetylacetone, is described. Cu(II), Ni(II), Zn(II) and VO(IV), complexes were synthesized using the above Schiff base ligand and characterized by spectral and analytical data. Based on these data, a square planar geometry has been assigned to the complexes except for VO(IV) complex which has square-pyramidal geometry. The metal complexes have higher antimicrobial activity than the ligand. The interaction of these complexes with CT-DNA was investigated by gel electrophoresis. It is concluded that copper complexes cleave DNA in the presence of H_2O_2, whereas the control DNA and other complexes are not effective.

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