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Effect of chelation on therapeutic potential of drugs: Synthesis, structure, antimicrobial and insecticidal activity of 3d-metal complexes involving Schiff-bases

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ABSTRACT

VO(II), Fe(II), Co(II), Cu(II) and Zn(II) metal complexes of Schiff bases derived from 2-thiophenecarboxaldehyde with 2,6-dichloro-4-nitroaniline (TDNA) and 4-anisidine (TCA) are reported and characterized based on elemental, FT-IR, UV-visible, molar conductance, FAB-mass, ESR, magnetic susceptibility, thermal and XRD analysis. IR spectra show that TDNA and TCA are coordinated to the metal ions in a bidentate manner with S and N donor sites of azomethine -N and thiophene-S. FAB-mass spectra of $[VO(TCA)_2].SO_4.4H_2O$ *have been investigated. FAB-mass and thermal data show degradation pattern of the complexes. The thermal behavior of metal complexes shows that the hydrated complexes loses water molecules of hydration in the first step; followed by decomposition of ligand molecules in the subsequent step. The metal complexes exhibited good microbial screening results against a number of medically important bacterial strains namely Escherichia coli, Staphylococcus aureus, Proteus mirabilis and fungi as Aspergillus niger and Candida albicans. The antimicrobial activity was evaluated using well diffusion technique. The solvent used, was DMSO. Schiff bases and their metal complexes were also evaluated for their insecticidal activity on cockroaches (Periplanata americana) as the test insect. Schiff bases and their metal complexes have been found active as an insecticide. Thus, the aim of this study is to observe the impact of chelation on the therapeutic value of the bioactive organic compounds. The antimicrobial and insecticidal screening results also indicate that the metal complexes are better antimicrobial and insecticidal agents as compared to the Schiff bases.*

Keywords: Schiff bases; Transition metal complexes; Spectral characterization; Antimicrobial activity; Insecticidal activity.

INTRODUCTION

The formation of variety of metal complexes with such ligands, indicate the spectacular progress in coordination and bioinorganic chemistry. Schiff base complexes of transition metals containing ligand with N, S donors are known to exhibit interesting biological activity. Still, development of new Schiff bases long term administration for chelation of metal deposits [1]. A large number of

Schiff bases and their complexes have been studied for their interesting and important properties e.g. their ability to reversibly bind oxygen, transfer of an amino group and complexing ability towards some toxic metals [2]. The high affinity for the chelation of the Schiff bases towards the transition metal ions is utilized in preparing their solid complexes. The real impetus towards developing their coordination chemistry is their physico-chemical properties and significant biological activities [3-4].

Metal complexes of Schiff bases play a central role in the development of coordination chemistry. Schiff bases provide potential sites for chemical and biological activity of compounds [5-6]. From the survey of existing literature, it appears that 2- thiophenecarboxaldehyde and their complexes have a variety of applications in biological, clinical and analytical fields. Keeping the above facts in the mind and in continuation of our research work on transition metal (II) complexes with Schiff bases, we report the synthesis and characterization of VO(II), Fe(II), Co(II), Cu(II) and Zn(II) metal complexes of Schiff bases derived from the condensation of thiophene-2-carboxaldehyde with 2,6-dichloro-4-nitroaniline and 4-anisidine as ligands. Antimicrobial and insecticidal activity of Schiff bases and their metal complexes have also been explored. Thus the aim of this study is to observe the impact of chelation on the therapeutic value of the organic compounds / drugs as biocidal or static agent by creating impact on morphological or physiological cycles [7-10].

EXPERIMENTAL SECTION

Materials and Reagents: Thiophene-2-carboxaldehyde, 2,6-dichloro-4-nitroaniline, p-anisidine, VO(II), Fe(II), Co(II), Cu(II) and Zn(II) chloride/sulphate, were obtained from Aldrich, Loba and Fluka. All the other chemicals and solvents were of A.R. grade.

Characterization of the complexes (Instrumentation): Elemental analysis of the ligands and complexes were performed micro-analytically on Elementar Vario EL III Carbo Erba 1108 model, micro-analyzer. The molar conductance of the complexes were determined by preparing (10^{-3} M) solution of the complexes in methanol at room temperature and measured on Elico-CM82 conductivity Bridge. Room temperature magnetic susceptibility measurement were carried out on a Faraday balance using $Hg[Co(SCN)_4]$ as calibrant. The electronic spectra of the complexes were recorded in DMSO solution on Perkin Lambda-2B spectrophotometer in the range 1000-200 nm. IR spectra of ligands and complexes were recorded on Perkin Elmer RX-I spectrophotometer as KBr pellets. FAB-mass were recorded on JEOL SX_{102}/DA-6000 mass spectrometer/ data system using argon/xenon (accelerating voltage 10 KV). Thermal studies of the complex were carried out on Perkin Elmer between room temperature to 800^0C. X-band EPR spectra were recorded at room temperature on Varian E-112 spectrophotometer (TCNA g=2.0027 as standard). X-ray diffraction, operated at 1.54056 Å as the radiation source using the CuKα line between 5° to 100° (2θ) at 25 °C.

Synthesis of Schiff bases and their VO(II), Fe(II), Co(II), Cu(II) and Zn(II) complexes: Two Schiff bases (TDNA and TCA) have been synthesized by condensing the methanolic solution of thiophene-2-carboxaldehyde (0.05 mole) to the methanolic solution of 2,6-dichloro-4-nitroaniline (TDNA) (0.05 mole) / 4-anisidine (TCA) (0.05 mole) in equimolar ratio on a water bath at 100^0C for about 6-7 hours. The mixture was allowed to stand overnight. After that the colored solid product was filtered off, recrystallized thrice with ethanol and finally washed with petroleum ether. The final product was dried under reduce pressure over anhydrous $CaCl_2$. The purity of the synthesized compound was monitored by TLC using silica gel G. (Yield- 69-73.5%)

VO(II), Fe(II), Co(II), Cu(II) and Zn(II) complexes of Schiff bases have been prepared by mixing the methanolic solution of $M^{II}\ Cl_2$ / $M^{II}\ SO_4$. nH_2O (0.01 mole) to the methanolic solution of Schiff bases (TDNA and TCA) (0.02 mole) in 1:2 molar ratio. The reaction mixture was then refluxed on a water bath for about 8-10 hours. A colored product appeared on standing and cooling the above solution. The complexes were filtered off, washed with alcohol and ether, recrystallized thrice and dried under reduced pressure over anhydrous $CaCl_2$ in a desiccator. The progress of the reaction and purity of the products was monitored by TLC using silica gel G. (Yield- 57.5-78 %)

2-thiophenecarboxylidine-2,6-dichloro-4 -nitroaniline (TDNA)

2-thiophenecarboxylidine-p-anisidine (TCA)

Figure-1. Structure of Schiff base ligands

Biological Activity

The Schiff bases and their VO(II), Fe(II), Co(II), Cu(II) and Zn(II) metal complexes were screened *in-vitro* antibacterial activity against Gram positive bacteria *Staphylococcus aureus* and Gram negative bacteria *Escherichia coli* and *Proteus mirabilis* species by well diffusion method using agar as nutrient medium [10-11]. Synthesized ligands and metal complexes have also been screened *in-vitro* antifungal activity against the following fungi like *Aspergillus niger* and *Candida albicans* by well diffusion method using potato dextrose agar as nutrient medium. A 0.5 ml spore suspension (10^{-6}-10^{-7} spore / ml) of each of the investigated organisms was added to a sterile nutrient medium just before solidification, then poured into sterile Petri dishes and left to solidify. Using a sterile cork borer (6 mm in diameter) four holes (wells) were made in each dish, and then 0.1 ml of the tested compounds dissolved in DMSO (100μg/ml) was poured into these wells. Finally, the dishes were incubated at 37^0C for 24 hours for bacterial and 28˚C for 3-4 days for fungus. Then clear inhibition zones were detected around each hole in millimeter. DMSO (0.1 ml) alone was used as a control under the same condition for each organism, and subtracting it from the diameter of inhibition zone of test compounds in each case [12-13].

Insecticidal Activity

Schiff bases and their metal complexes were evaluated for their insecticidal activity on cockroaches (*Periplanata americana*) as the test insect. The method of Joshi et al [14] was used to determine the insecticidal activity against adult cockroaches (*Periplanata americana*). Solutions of the synthesized Schiff bases and their metal complexes were prepared in water at 100 and 50 ppm. Solution of synthesized compounds was injected into the abdominal region of the cockroach with the help of microsyringe. The *time of death was noted as the KD value* (knock down value). At the time of death, the antennal becomes motionless, the appendages shrunk and folded towards the ventral side and cockroach lay dorsally. For each sample, four replication were performed and average KD values were noted [15-16].

Table-1: Analytical data, molar conductance of Schiff base ligands and their metal complexes.

S.No.	Compounds / Molecular Formulae	M.P. (˚C)	Elemental Analysis % Found/(Cal.)				Yield%	S^{-1}
	Molecular Wt./Colour		C	H	N	Metal		
1.	$C_{11}H_6N_2O_2Cl_2S$ (TDNA) 301 (Light Yellow)	135	43.07 (43.85)	2.07 (1.99)	9.68 (9.30)	-	69.0	-
2.	$[VO(TDNA)_2].SO_4.3H_2O$ 819 (Dark Yellow)	150	32.01 (32.23)	1.59 (1.47)	6.43 (6.84)	8.2 (8.4)	64.9	98.5
3.	$[Fe(TDNA)_2.(H_2O)_2].SO_4$ 790 (Light green)	>300	33.02 (33.42)	1.26 (1.52)	7.42 (7.09)	7.5 (7.1)	73.8	106.5
4.	$[Co(TDNA)_2].Cl_2.4H_2O$ 804 (Green fluorescent)	150	33.03 (32.84)	1.77 (1.59)	7.23 (6.97)	7.6 (7.3)	57.5	107.3
5.	$[Cu(TDNA)_2].Cl_2.H_2O$ 754 (light green)	>250	35.29 (35.01)	1.78 (1.59)	7.33 (7.43)	8.1 (8.4)	68.2	120.5
6.	$[Zn(TDNA)_2].Cl_2.2H_2O$ 774 (Green)	167	34.67 (34.14)	1.37 (1.55)	7.46 (7.24)	8.9 (8.5)	62.0	130.6
7.	$C_{12}H_{11}NOS$ (TCA) 217 (Dark grey)	38-40	66.30 (66.36)	5.08 (5.07)	6.38 (6.45)	-	75.5	-
8.	$[VO(TCA)_2].SO_4.4H_2O$ 669 (Black)	>300	46.82 (46.04)	3.62 (3.28)	4.86 (4.18)	9.9 (10.0)	58.0	101.0
9.	$[Fe(TCA)_2.(H_2O)_2].SO_4.H_2O$ 640 (Dark Brown)	115	45.02 (44.50)	3.30 (3.44)	4.88 (4.37)	8.5 (8.7)	69.0	95.5
10.	$[Co(TCA)_2].Cl_2$ 564 (Dark green)	120	51.09 (51.07)	3.98 (3.90)	4.50 (4.97)	10.2 (10.5)	70.0	129.0
11.	$[Cu(TCA)_2].Cl_2$ 568.5 (Black)	110-115	51.69 (50.65)	3.80 (3.87)	4.76 (4.93)	10.5 (11.3)	72.5	103.9
12.	$[Zn(TCA)_2].Cl_2$ 570 (steel grey)	190	50.56 (50.50)	3.90 (3.86)	4.70 (4.90)	10.9 (11.4)	78.0	118.5

(TDNA)-2-thiophenecarboxylidine-2,6-dinitro-4-nitroaniline, (TCA)-2-thiophenecarboxylidine-p-anisidine; Conductance = S^{-1}

RESULTS AND DISCUSSION

The analytical and physical data of complexes are presented in table-1. All the chelates are colored and non-hygroscopic solids. They are soluble in alcohols and DMSO. The analytical and spectroscopic data showed that all complexes are binuclear having 1:2 metal, ligand stoichiometry. The molar conductance in methanol (10^{-3} M), indicates that all the complexes are electrolytic in nature. As expected, the Zn(II) complexes are diamagnetic while other complexes are paramagnetic by magnetic measurements [17-18].

Infrared Spectra

A careful comparison of spectra of ligands with its complexes results the following information, regarding coordination of various groups. IR frequency of ligands and their metal complexes are given in table-2.

Complexes of VO(II), Fe(II), Co(II), Cu(II) and Zn(II) with 2-thiophenecarboxylidine-2,6-dichloro-4-nitroaniline (TDNA): A band at about 1620 cm^{-1} due to $\upsilon_{(C=N)}$ (azomethine) group in ligand, shift down by 18-30 cm^{-1} in complexes. This suggests coordination through azomethine nitrogen, due to donation of electron from nitrogen. Thiophene ring $\upsilon_{(C\text{-}S\text{-}C)}$ shows absorption band at 851 cm^{-1} in the ligand spectrum. This band shows lower shift 20-25 cm^{-1} in the complexes, suggesting participation of thiophene $\upsilon_{(C\text{-}S\text{-}C)}$ sulfur in complexation [21-22]. The appearance of broad band around 3365±20 cm^{-1} in the spectra of all complexes may be due to υ_{stre} of water. A medium intensity band at 798 cm^{-1}, suggests the presence of coordinated water in Fe(II) complex. A weak band is also observed at 551 cm^{-1} due to $\upsilon_{(M\text{-}O)}$ mode, suggesting the coordination of water molecule in Fe(II) complex. The new bands in all complexes at 480±4 cm^{-1} and 406±4 cm^{-1} have been assigned to $\upsilon_{(M\text{-}N)}$ and $\upsilon_{(M\text{-}S)}$ modes respectively. In VO(II) complex, a new band appears at 994 cm^{-1}, which is assigned to $\upsilon_{(V=O)}$ vibration [19-22].

Table-2: IR frequencies of Schiff bases and its metal-complexes.

Compounds	IR frequencies of Schiff bases and metal-complexes. (cm^{-1})						
	υ(C=N)	υ(C-S-C)	υ(H_2O)	υ(M-N)	υ(M-S)	υ(V=O)	υ(R-O-CH_3) (Sym & Asym)
(TDNA)	1620	851	-	-	-	-	-
$[VO(TDNA)_2].SO_4.3H_2O$	1602	826	3358	484	402	994	-
$[Fe(TDNA)_2.(H_2O)_2].SO_4$	1594	825	3384 798	482	402	-	-
$[Co(TDNA)_2].Cl_2.4H_2O$	1597	830	3346	482	408	-	-
$[Cu(TDNA)_2].Cl_2.H_2O$	1590	823	3355	476	402	-	-
$[Zn(TDNA)_2].Cl_2.2H_2O$	1601	825	3367	482	410	-	-
(TCA)	1614	852	-	-	-	-	2833 1456
$[VO(TCA)_2].SO_4.4H_2O$	1606	835	3498	490	410	1004	2839 1456
$[Fe(TCA)_2.(H_2O)_2].SO_4.H_2O$	1589	836	3452 815	506	418	-	2835 1456
$[Co(TCA)_2].Cl_2$	1604	827	-	504	410	-	2833 1456
$[Cu(TCA)_2].Cl_2$	1606	835	-	506	406	-	2839 1456
$[Zn(TCA)_2].Cl_2$	1600	823	-	495	415	-	2833 1454

Complexes of VO(II), Fe(II), Co(II), Cu(II) and Zn(II) with 2-thiophenecarboxylidine-4-anisidine (TCA): IR spectrum of the (TCA) ligand shows a strong band at 1614 cm^{-1} due to $\upsilon_{(C=N)}$ azomethine group. This shifted down in complexes by 1590-1606 cm^{-1}, suggesting participation of azomethine nitrogen in chelation. A strong ligand band was observed at 852 cm^{-1}, assignable to thiophene $\upsilon_{(C\text{-}S\text{-}C)}$. On coordination of metal ion with sulphur of thiophene, the band position of $\upsilon_{(C\text{-}S\text{-}C)}$ group has shifted to lower side by 16-30 cm^{-1}, in complexes [23-24]. The appearance of broad band at around 3452 and 3498 cm^{-1} in the spectra of Fe(II) and VO(II) complexes respectively, have been assigned to associated water molecules. A weak intensity band at 815 cm^{-1}, suggests coordinated water molecule present in Fe(II) complex, which was further supported by $\upsilon_{(M\text{-}O)}$ at 521 cm^{-1} in Fe(II) complex. In all complexes new bands at 498±8 cm^{-1} and 412±6 cm^{-1} have been assigned to $\upsilon_{(M\text{-}N)}$ and $\upsilon_{(M\text{-}S)}$ respectively. A strong band at 1118 cm^{-1} and 1134 cm^{-1} corresponding to SO_4 appears in VO(II) and Fe(II) complexes. In VO(II) complex, a new band appears at 1004 cm^{-1}, which is assigned to $\upsilon_{(V=O)}$ vibration [19-25].

It is tentatively proposed that TDNA and TCA Schiff base ligands coordinate through the nitrogen of azomethine group and sulfur of the thiophene ring, forming a stable bidentate chelating ring.

Electronic absorption spectra and magnetic studies

Complexes of VO(II), Fe(II), Co(II), Cu(II) and Zn(II) with 2-thiophenecarboxylidine-2,6-dichloro-4-nitroaniline (TDNA): The information referring to the geometry of these complexes is obtained from electronic spectra and from values of the magnetic moment.

The VO(II) complex exhibits two bands at 12345 cm^{-1} and 20408 cm^{-1}, which have tentatively been assigned to $^2B_2$-^2E (ν_1) and $^2B_2$-$^2B_1$ (ν_2) transitions respectively. The suggested geometry for this complex may be square pyramidal based on coordination number five. The value of the magnetic moment for this complex is 1.71 B.M., confirm the square pyramid geometry for VO(II)-TDNA complex. In Fe(II) complex, the absorption band at 17857 cm^{-1} may be attributed to the transition ^5T_2g-^5Eg. The magnetic moment of Fe(II) complex (5.14 B.M.) corresponds to octahedral symmetry [26-27].

The electronic spectra of Co(II) complex shows two bands of appreciable intensity at 16393 cm^{-1} and 20833 cm^{-1}. These transitions have tentatively been assigned to $^4A_2$-$^4T_1$ (F) (ν_2) and $^4A_2$-$^4T_1$ (P) (ν_3) respectively. The magnetic moment value of Co(II)-complex is 4.34 B.M., which favors tetrahedral geometry. The electronic spectrum of Cu(II) complex shows two bands at 14084 cm^{-1} and 19607 cm^{-1}, corresponding to transitions ^2B_1g-^2B_2g (ν_1) and ^2B_1g-^2Eg (ν_2) respectively. The magnetic moment value for Cu(II) complex is 1.89 B.M., therefore square planar geometry has been suggested for this Cu(II)-TDNA complex [28].

Complexes of VO(II), Fe(II), Co(II), Cu(II) and Zn(II) with 2-thiophenecarboxylidine-4-anisidine (TCA): The VO(II)-TCA complex exhibits two bands at 17857 cm^{-1} and 20833 cm^{-1}, which have been assigned to $^2B_2$-$^2B_1$(ν_2) and $^2B_2$-$^2A_1$ (ν_3) transitions respectively. The value of the magnetic moment for this complex is 1.76 B.M. These data suggest the square pyramidal geometry for VO(II) complex. The Fe(II) complex exhibit one band at 19417 cm^{-1}, which may be attributed to the transition ^5T_2g-^5Eg for octahedral complexes. The magnetic moment of this complex is 5.30 B.M. [20-24].

The electronic spectrum of Co(II)-TCA complex shows two bands of appreciable intensity at 13248 cm^{-1} and 20408 cm^{-1}, these transitions have tentatively been assigned to $^4A_2$-$^4T_1$ (F) (ν_2) and $^4A_2$-$^4T_1$ (P) (ν_3) respectively. The magnetic moment of Co(II) complex is 4.30 B.M.; thus the tetrahedral geometry has been suggested for this complex. The electronic spectra of Cu(II)-TCA complex have two characteristic bands at 15151 cm^{-1} and 17543 cm^{-1}, assignable to ^2B_1g-^2B_2g (ν_1) and ^2B_1g-^2Eg (ν_2) transitions respectively. The magnetic moment is 1.82 B.M. for this complex, these finding suggest that the ligand’s environment around Cu(II) ion to be square planar.

Zn(II)-TDNA and Zn(II)-TCA complexes did not show d-d transition due to diamagnetic properties of Zn(II) complexes, therefore we proposed tetrahedral geometry for Zn(II) complexes [26-28].

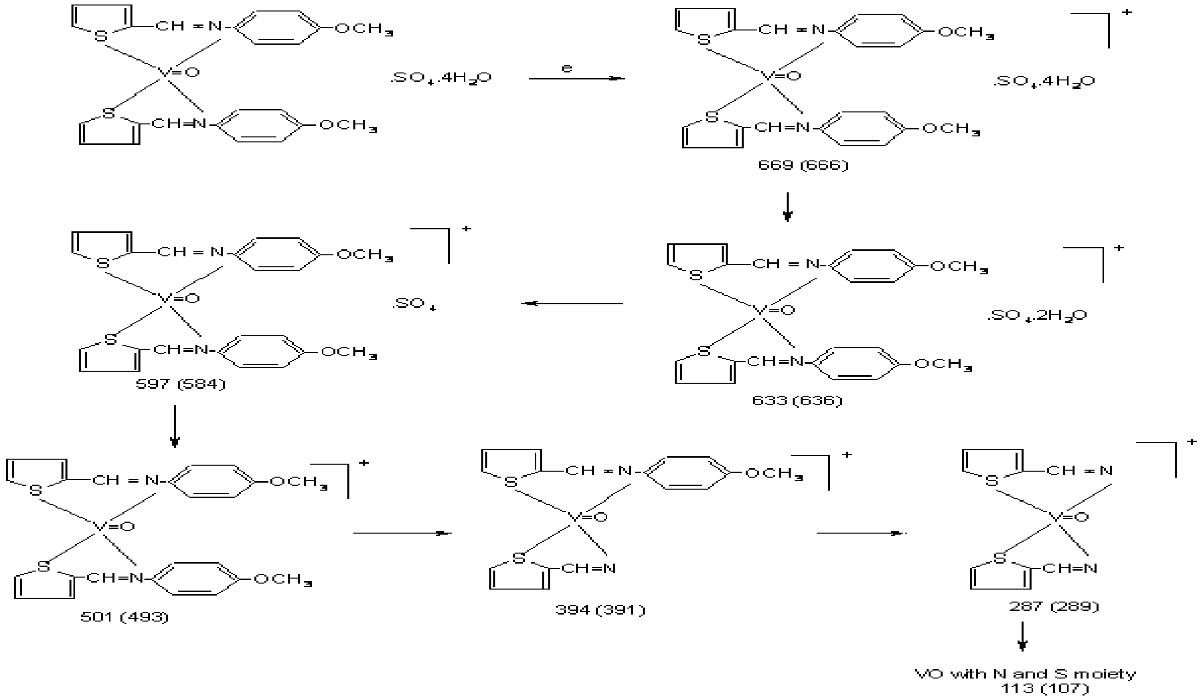
ESR spectra

The ESR spectra of metal complexes provide information on the basis of hyperfine and superhyperfine structures. ESR spectra of the VO(II)-TDNA and Cu(II)-TCA complexes have been recorded on X -band and their $g_\|$, $g_\perp$, g_{av}, Δg and G values have been calculated. The value of ESR parameters of VO(II)-TDNA complex, $g_\|$, $g_\perp$, g_{av} and Δg are 1.94, 1.99, 1.97 and 0.05 respectively. The X-band EPR spectrum of VO(II)-TDNA complex shows a single line at $g \approx 1.94$ which is attributed to a single s=1/2 species; this provides information about the extent of the delocalization of unpaired electron [25,28]. The $g_\| < g_\perp$ value reflect the covalent nature of the metal-ligand bond.

The value of ESR parameters of Cu(II)-TCA complex, $g_\|$, $g_\perp$, g_{av}, Δg and G are 2.104, 2.062, 2.072, 0.042 and 1.7 respectively. The covalent nature of the metal-ligand bond in the complex is further supported by the G value which is <4.0. The value $g_\| > g_\perp$ is well consistent with a primarily dx^2-y^2 ground state having elongated tetragonal or square planar structure. The G value of 1.7 indicates considerable exchange interaction in the complex. According to Hathway, if the value of G is greater than four (G>4), the exchange interaction is negligible; whereas when the value of G is less than 4 (G<4) a considerable exchange interaction is indicated in the complex. The parameter g_{av} was obtained by equation $[g_{av}=(1/3\ g_{\parallel}+g_{\perp})]$. The $g_{\parallel}$ value (<2.3) indicates covalent character of the metal-ligand bond [29].

FAB mass spectra

The FAB-mass spectrum of $[VO(TCA)_2].SO_4.4H_2O$ complex has been recorded. The FAB-mass spectrum of the complex $[VO(TCA)_2].SO_4.4H_2O$ exhibited the molecular ion (M^+) peak at m/z 666 suggesting the monomeric nature of the complex. Other important peaks observed at m/z 636, 584, 493, 391, 289 and 107 correspond to the fragmented species **(Scheme-1)** after the successive removal of different groups. The m/z value 666 correspond to composition of $[VO(TCA)_2]$ $.SO_4.4H_2O$ and 107 to VO with some chelated-N and -S ligand [24-25].

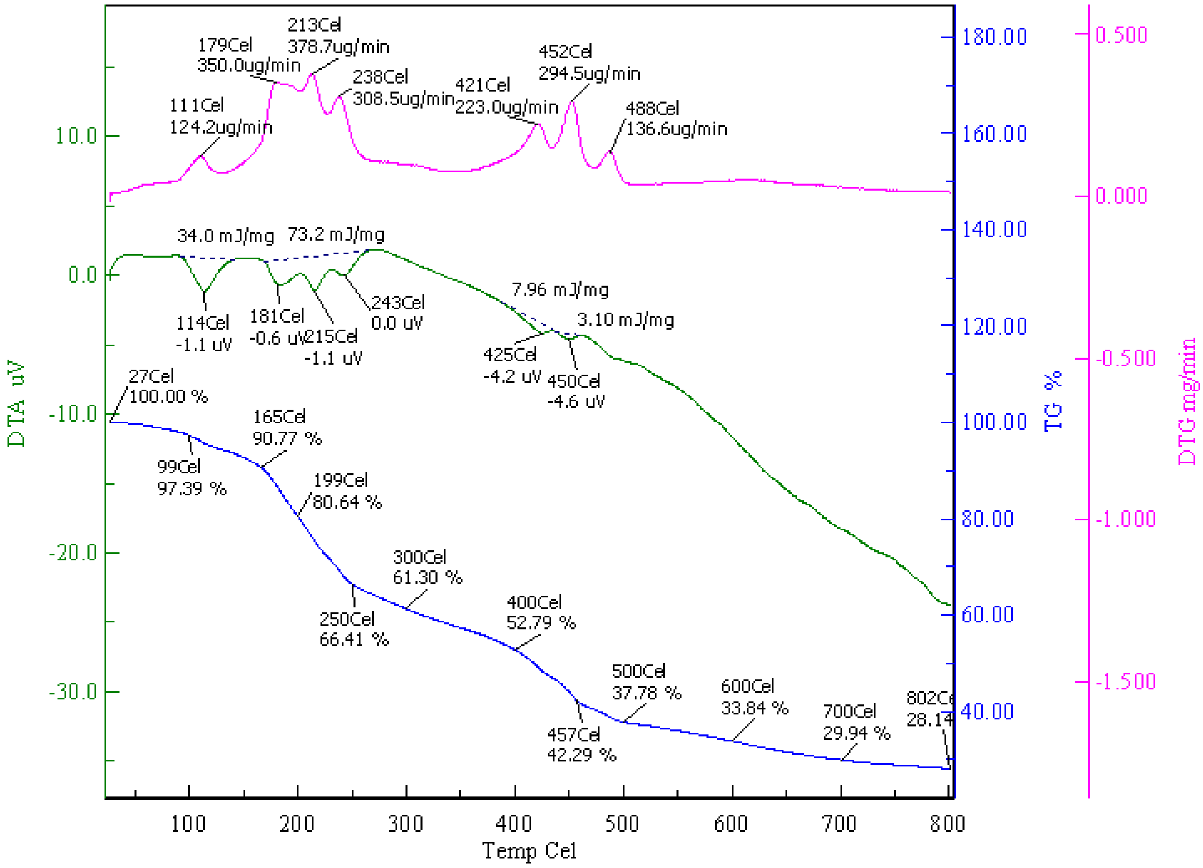


Scheme-1

Thermal Studies

TG, DTA and DTG thermal studies of $[Fe(TCA)_2.(H_2O)_2].SO_4.H_2O$ complex have been recorded in nitrogen atmosphere. Thermogram of this complex is given in figure. A careful analysis of thermogram of TG, indicates that Fe(II) complex is stable upto 60^0C. Elimination of one lattice water molecule has been observed on raising the temperature upto 100^0C. After 100^0C weight loss has been observed upto 170^0C, correspond to two coordinated water molecules.

After that three main steps have been found; Step-1 above 170^0C temperature, a gradual weight loss has been found upto 250^0C, correspond to the release of sulphate moiety and methoxy groups from the metal chelate (Remaining wt.% obs./cal. 66.87/66.41). The DTA and DTG curve of this complex show peaks at 181^0C, 215^0C, 243^0C (endothermic) and 179^0C, 213^0C, 238^0C respectively. An endothermic peak at 114^0C in the DTA curve of Fe(II) complex is also observed which may be due to the change in composition of the complex.



Step-2, after 250^{0}C a slow weight loss continues upto 450^{0}C, indicates the loss of ligand parts (Remaining wt.% obs./cal. 43.13/43.00). The DTA curve depicts endothermic peaks at 425^{0}C and 450^{0}C respectively, whereas the corresponding DTG curve show peaks at 421^{0}C and 452^{0}C respectively. The decomposition of remaining ligand moiety occur between 450-750^{0}C (Remaining wt.% obs./cal. 28.14/24.84). In this step, DTA and DTG curve of this complex show peak at 460^{0}C (endothermic) and 488^{0}C respectively. After 750^{0}C a horizontal curve has been obtained upto 800^{0}C. This suggests the formation of an ultimate metal oxide in nitrogen atmosphere.

DTA curve of this complex appears in negative peaks depending on the nature of heat change, indicates that endothermic heat change occur during the decomposition of metal complex [30-31].

X-ray diffraction study

[Fe(TCA)$_2$.(H$_2$O)$_2$].SO$_4$.H$_2$O complex was subjected to X-ray powder diffraction analysis. The crystal system, lattice parameters, cell volume and density have been determined in present studies for selected complex compound. X-ray crystal system has been worked out by trial and error method for finding the best fit between observed and calculated Sin$^2\theta$ value. Sin$^2\theta$ and hkl values for different lattice planes have been calculated. The calculated and experimental value of density of complex show good agreement and are within the experimental error limits. The X-ray powder diffractogram of Fe(II) complex was recorded using CuKα as source in the rang 5^0-100^0 (2θ). Data reveals that the complex has crystallized in cubic system. Crystal data for [Fe(TCA)$_2$.(H$_2$O)$_2$].SO$_4$.H$_2$O complex are as: a =37.99 Å, $D_{(obs)}$ = 1.708 g/cm^3, $D_{(cal)}$ = 1.709 g/cm^3. The calculated values of cell volume and particle size are 54828.691 $Å^3$ and 10.62 nm, respectively. The number of molecules (n) per unit cell have also been calculated using equation D=nM/N.V.; the value of n is 8 molecules per unit cell [32].

Biological screening

The biocidal activities of the Schiff bases and VO(II), Fe(II), Co(II), Cu(II) and Zn(II) complexes were tested *in-vitro* against microorganism by well diffusion method using DMSO solvent. The aim of this investigation was to study the changes in the activity with the variation in the structures of the molecule and thereby to draw some inferences whether the structure of the compound may have some correlation with antimicrobial activity [33-36].

Antibacterial activity: The Schiff bases and their complexes have been screened *in-vitro* against the Gram positive bacteria *S.aureus* and Gram negative bacteria *E.coli* and *P.mirabilis* species by well diffusion method using agar as nutrient medium. Here streptomycin has been used as a standard. Observations of the activity are given in table-3. The Cu(II) complexes of both Schiff base exhibit higher antibacterial activity against *E.coli* and *S.aureus*. On the other hand for *P.mirabilis,* the biological activity of VO-(TCA) complex shows higher activity.

Antifungal activity: The Schiff bases and their complexes have been screened *in-vitro* against the following fungi like *A.niger* and *C.albicans* by well diffusion method using potato dextrose agar as nutrient medium. Here Griseofulvin has been used as a standard. Observations of the activity are given in table-3. The Schiff base (TDNA), complex Cu-(TDNA) and VO-(TCA) exhibit higher antifungal activity against *A.niger* and nearly the same as antifungal drug (Griseofulvin). On the other hand for *C.albicans,* the antifungal activity of Cu-(TCA) complex shows higher activity.

Table-3: Antimicrobial activity of Schiff bases and their metal complexes

Compounds	**Antibacterial**									**Antifungal**					
	E. coli			***S. aureus***			***P. mirabilis***			***A. niger***			***C. albicans***		
	$25^{\blacklozenge}$	**$50^{\blacklozenge}$**	**$100^{\blacklozenge}$**	**$25^{\blacklozenge}$**	**$50^{\blacklozenge}$**	**$100^{\blacklozenge}$**	**$25^{\blacklozenge}$**	**$50^{\blacklozenge}$**	**$100^{\blacklozenge}$**	**$25^{\blacklozenge}$**	**$50^{\blacklozenge}$**	**$100^{\blacklozenge}$**	**$25^{\blacklozenge}$**	**$50^{\blacklozenge}$**	**$100^{\blacklozenge}$**
(TDNA)	-	12	15	-	-	12	9	9	10	21	25	29	-	-	12
VO (TDNA)	18	20	23	15	18	24	14	16	19	18	20	24	17	20	26
Fe (TDNA)	15	18	20	12	14	19	12	15	19	20	24	29	12	14	20
Co (TDNA)	18	20	25	14	17	20	11	13	16	12	16	22	10	12	13
Cu (TDNA)	24	27	30	10	12	14	15	17	22	20	25	30	19	21	25
Zn (TDNA)	12	15	19	10	12	15	10	13	14	15	18	20	11	14	17
(TCA)	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
VO (TCA)	16	19	26	13	19	25	16	19	23	22	25	32	16	19	22
Fe (TCA)	16	20	25	15	19	21	15	18	20	16	20	24	13	16	19
Co (TCA)	19	22	26	13	16	20	12	15	19	11	14	16	11	13	15
Cu (TCA)	19	21	25	19	23	27	13	16	20	15	18	20	22	25	32
Zn (TCA)	14	17	20	10	12	13	12	14	17	-	11	15	12	15	19
Streptomycine	22	23	28	18	22	25	15	18	22	-	-	-	-	-	-
Griseofulvin	-	-	-	-	-	-	-	-	-	20	24	29	20	24	30
DMSO	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-

The observations in table-3 show that the majority of the complexes are more active than their respective Schiff base ligands. The chelation either enhances or reduces the antimicrobial activity, sometimes it remains neutral. Thus, metal chelation may increase or decrease / suppress the therapeutic value of organic compounds (drug). It may keep the property intact by further stabilizing the drug and /or reducing the biodegradability / metabolic decay of the organic ligands through chelation. The aim of this investigation was to observe the changes the activity of parent organic compound (Schiff bases) on chelation with metals. The greater antimicrobial activities of these transition metal complexes are due to their ability to form chelates with essential metal ions bonding through nitrogen and sulfur donor atom. It was observed that there existed some relationship between the lability of M-O, M-N, M-S and M-X and the biological activities viz. the activity increased with increasing lability of the metal complexes. The chelation also reduces the polarity of the central metal atom, mainly because of partial sharing of its electron density with ligand.

Insecticidal activity

Complexes with life essential metal ions have emerged as organic ligands / drug stabilizing agents in biochemical / insecticidal industries. Schiff bases and their complexes were evaluated for their insecticidal activity on cockroaches (*Periplanata americana*) as the test insect. The method of Joshi et al [14] was used to determine the insecticidal activity against adult cockroaches (*Periplanata americana*) [16,36]. Compounds were dissolved in water at a 100 and 50 ppm. Results of compounds are given in table-4. Schiff base (TDNA), VO(II) and Co(II) complexes have been found to be most potent for its insecticidal activity.

Table-4: Insecticidal activity of Schiff bases and their Cu(II) and VO(II) complexes.

Compounds	**Mean K.D time (minutes) / ppm concentration**	
	50*	**100***
(TDNA)	50	20
VO (TCA)	40	18
Fe (TCA)	70	30
Co (TCA)	51	24
Cu (TCA)	65	25
Zn (TCA)	75	40
(TCA)	75	35
VO (TCA)	40	22
Fe (TCA)	57	25
Co (TCA)	45	20
Cu (TCA)	85	60
Zn (TCA)	78	35
Cypermethrin	55	25

**concentration in ppm*

These observations show the majority of the complexes are more active than their respective Schiff bases (ligands). In some cases, Schiff base are more active than their metal complexes. The activity increases with increasing concentration. The time of death was noted and the average time of death was recorded as K.D. values (knock down value). These studies demonstrate that the concentration reached levels that are sufficient to inhibit and kill the insects.

CONCLUSION

The coordination complexes of VO(II), Fe(II), Co(II), Cu(II) and Zn(II) with bidentate ligands were synthesized and characterized. Ligand coordinates with life essential metal ions through N and S donor atoms. The complexes exhibits the geometry based coordination number 4, 5 and 6. A comparative study of antimicrobial and insecticidal activity of the ligand and their metal complexes indicate that the chelation may be helpful in tailoring the structure and monitoring the activities; thus chelation tends to make the ligand act as a more powerful and potent antimicrobial and insecticidal agent. The higher activity of the metal complexes may be owing to the effect of metal ions on the normal cell membrane. Such increased activity of the metal chelates can be explained on the basis of chelation theory; tailoring and tuning of hydrophilicity and lipophilicity of a drug by coordinating a metal ion may probably lead to bring down the solubility and permeability barriers to get into the cell, this in turn may enhance the bioavailability of chemotherapeutics on one hand and potentiality at another. Thus, the aim of this study is to observe the impact of chelation on the therapeutic value of the organic compounds / drugs as biocidal or static agent by creating impact on morphological or physiological cycles.

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