

Synthesis of New VO(II), Co(II), Ni(II) and Cu(II) Complexes with Isatin-3-Chloro-4-Floroaniline and 2-Pyridinecarboxylidene-4-Aminoantipyrine and their Antimicrobial Studies

Anand P. Mishra*, Rudra Mishra, Rajendra Jain and Santosh Gupta

Bio-coordination Laboratories, Department of Chemistry, Dr. H.S. Gour Central University, Sagar, Madhya Pradesh 470003, India

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The complexes of tailor made ligands with life essential metal ions may be an emerging area to answer the problems of multi drug resistance. The coordination complexes of VO(II), Co(II), Ni(II) and Cu(II) with the Schiff bases derived from isatin with 3-chloro-4-floroaniline and 2-pyridinecarboxaldehyde with 4-aminoantipyrine have been synthesized by conventional as well as microwave methods. These compounds have been characterized by elemental analysis, molar conductance, electronic spectra, FT-IR, FAB mass and magnetic susceptibility measurements. FAB mass data show degradation of complexes. Both the ligands behave as bidentate and tridentate coordinating through O and N donor. The complexes exhibit coordination number 4, 5 or 6. The Schiff base and metal complexes show a good activity against the bacteria; *Staphylococcus aureus*, *Escherichia coli* and *Streptococcus fecalis* and fungi *Aspergillus niger*, *Trichoderma polysporum*, *Candida albicans* and *Aspergillus flavus*. The antimicrobial results also indicate that the metal complexes are better antimicrobial agents as compared to the Schiff bases. The minimum inhibitory concentrations of the metal complexes were found in the range 10~40 µg/mL.

KEYWORDS : Isatin, MIC, Spectral studies, 2-Pyridinecarboxylidene, 4-Aminoantipyrine

Introduction

Antimicrobial resistance of pathogenic microorganisms has presently emerged both in the community and hospital leading to increased deaths, illness, hospitalization and treatment costs and duration. The increasing incidence of bacterial drug resistance imposes an improvement of the existing antimicrobial drugs and the development of new ones. Isatin possesses some biological properties. Isatin (1H-indol-2,3-dione) is a synthetically versatile substrate, that can be used for synthesis of a larger variety of heterocyclic compounds, such as indoles and quinolines. It also acts as raw material for drug synthesis. Presence of isatin has also been reported in mammalian tissues. The coordination chemistry of transition metal ions and isatin derivatives may be an interesting subject for further studies. Schiff bases derived from isatin showed anticonvulsant, tuberculostatic, antibacterial and antifungal activities. Schiff base of 4-aminoantipyrine and its complexes have variety of applications in biological, clinical, analytical and pharmacological areas. Antimicrobial and DNA cleavage studies of copper metal complexes containing Schiff base

derived from 4-amino antipyrine copper complexes in the presence of ascorbate or hydroquinone have been reported [1-8].

Microwave-assisted synthesis is a branch of green chemistry. Microwave-assisted synthesis has gained much attention in recent years. The applications of microwave irradiation are used for carrying out chemical transformations, which are pollution free, eco-friendly, low cost and offer high yields together with simplicity in processing and handling. The salient features of microwave approach are shorter reaction times, simple reaction conditions and enhancements in yields [9-14].

In this paper, we have described the synthesis, physicochemical characterization and biological significances of VO(II), Co(II), Ni(II) and Cu(II) complexes with ligands derived from isatin-3-chloro-4-floroaniline (ICFA), 2-pyridinecarboxylidene-4-aminoantipyrine (PCAP) (Fig. 1). The reaction was carried out by both conventional and microwave methods. These ligands coordinate with the metal ions in a tridentate manner. The metal complexes formed with these two new ligands may be used as precursors for the synthesis of new compounds. Some of

*Corresponding author <E-mail : jainrajchem@gmail.com, apm19@rediffmail.com>

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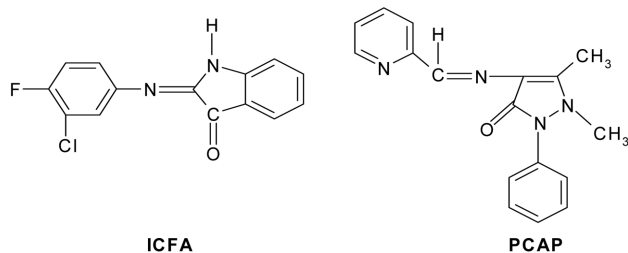


Fig. 1. Structure of Schiff base ligands.

which they may exhibit interesting physical and chemical properties and potentially useful biological activities.

Materials and Methods

Materials. All the used chemicals and solvents were of Anal R grade. All the reagents used for the preparation of the Schiff bases were obtained from Sigma Aldrich (St. Louis, MO, USA). Metal salts were purchased from Loba Chemie (Mumbai, India).

Physical measurements. Elemental analyses were performed on an Elemental Vario EL III Carlo Erba 1108 analyzer (Lucknow, India). FAB-mass spectra were recorded on a JEOL SX 102/DA 6000 Mass Spectrometer (Tokyo, Japan) using argon/xenon (6 kV, 10 mA) as the FAB gas. The accelerating voltage was 10 kV and the spectra were recorded at room temperature. Electronic spectra in (MeOH) were recorded on Perkin-Elmer Lambda-2B-Spectrophotometer (Shelton, CT, USA). Molar conductance (10^{-3} M) was measured by Elico-conductivity bridge at room temperature. Magnetic susceptibility measurements were carried out on a Gouy balance at room temperature using $\text{Hg}[\text{Co}(\text{SCN})_4]$ as the calibrant. FT-IR spectra were recorded in KBr pellet on a Perkin Elmer RX1 spectrophotometer in wave number region 4,000~400/cm. Microwave assisted synthesis were carried out in open glass vessel on a modified microwave oven model 2001 ETB (Bajaj Electricals Limited, Mumbai, India) with rotating tray and a power source 230 V, microwave energy output 800 W and microwave frequency 2,450 MHz. A thermocouple device was used to monitor the temperature inside the vessel of the microwave. The microwave reactions were performed using on/off cycling to control the temperature.

Antimicrobial activity. The *in vitro* biological activity of the investigated Schiff base and its metal complexes was tested against the bacteria *Escherichia coli*, *Staphylococcus aureus*, and *Streptococcus fecalis* by disc diffusion method using nutrient agar as medium and streptomycin as control. The antifungal activities of the compounds were also tested by the *in vitro* well diffusion method against the

fungi *Aspergillus niger*, *Trichoderma polysporum*, *Candida albicans*, and *Aspergillus flavus*, on potato dextrose agar as the medium and nystatin and miconazole as control. Each of the compounds was dissolved in dimethyl sulfoxide and solutions of the concentrations were prepared separately. In a typical procedure, a well was made on agar medium inoculated with microorganism. The well was filled with the test solution using a micropipette and the plate was incubated 24 hr for bacteria at 37°C and 72 hr for fungi at 30°C. During this period, the test solution diffused and the growth of the inoculated microorganism was affected. The inhibition zone was developed, at which the concentration was noted. All biological experiments were performed in triplicates. The minimum inhibitory concentration (MIC) of the complexes was determined by the serial dilution technique.

Conventional method for the synthesis of Schiff bases (ligand). Two Schiff bases (ICFA, PCAP) (Fig. 1) have been synthesized by adding the methanolic solution of isatin/2-pyridine carboxaldehyde (0.05/0.04 mol) with methanolic solution of 3-chloro-4-fluoro aniline/4-aminoantipyrene (0.05/0.04 mol) in equimolar ratio. The reaction mixture was then refluxed on a water bath for about 4~5 hr. The condensation product was filtered, thoroughly washed with ethanol and petroleum ether, re-crystallized and dried *in vacuo*. The purity of the synthesized compounds was monitored by thin layer chromatography (TLC) using silica gel (yield: isatin = 85%, 2-pyridine carboxaldehyde = 80%).

Microwave method for the synthesis of Schiff bases. The equimolar (1 : 1) ratio of isatin/2-pyridinecarboxaldehyde (0.05/0.04 mol) with 3-chloro-4-fluoroaniline/4-aminoantipyrene (0.05/0.04 mol) were mixed thoroughly in a grinder. The reaction mixture was then irradiated by the microwave oven by taking 3~4 mL of dry ethanol as a solvent. The reaction was completed in a short time (4~5 min) with higher yields. The resulting product was then recrystallized with ethanol, finally dried under reduced pressure over anhydrous CaCl_2 in a desiccator. The progress of the reaction, purity of the product was monitored by TLC using silica gel G (yield: 90~92%).

Conventional method for the preparation of metal complexes. All the complexes (Figs. 2 and 3) have been prepared by mixing the methanolic solution of $\text{MCl}_2/\text{SO}_4 \cdot n\text{H}_2\text{O}$ (0.003/0.006 mol) with the Schiff base (ICFA/PCAP) (0.007/0.006 mol) in 1 : 2 and 1 : 1 molar ratio. The resulting mixture was refluxed on water bath for 6~9 hr. A coloured product appeared on standing and cooling the above solution. The complexes were filtered, washed with petroleum ether and dried under reduced pressure over anhydrous CaCl_2 in a desiccator. It was further dried in an

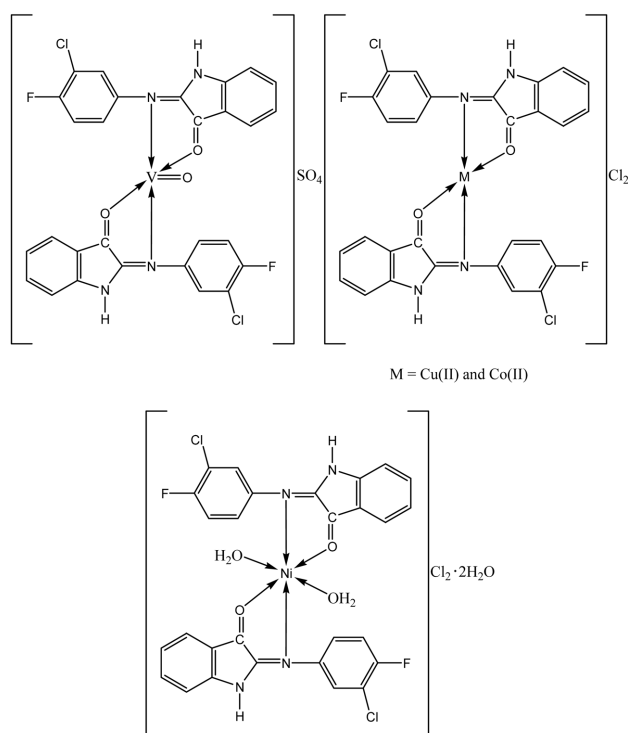


Fig. 2. Proposed structure of Schiff base metal complexes of ICFA ligand.

electric oven at 60~70°C.

Microwave method for the synthesis of metal complexes. The ligand and the metal salts were mixed in 1 : 2 (metal : ligand) ratio in a grinder. The reaction mixture was then irradiated by the microwave oven by taking 3~4 mL of dry ethanol as a solvent. The reaction was completed in a short time (6~9 min) with higher yields. The resulting product was then recrystallized with ethanol and ether and finally dried under reduced pressure

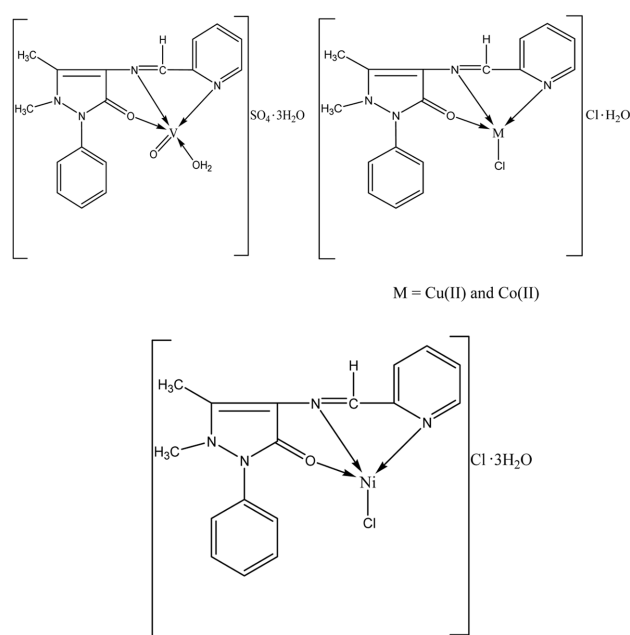


Fig. 3. Proposed structure of Schiff base metal complexes of PCAP ligand.

over anhydrous CaCl_2 in a desiccator. The progress of the reaction and purity of the product was monitored by TLC using silica gel G (yield: 79~84%).

Results and Discussion

As a result of microwave assisted synthesis, it was observed that the reaction was completed in a short time with higher yields compared to the conventional method. In the microwave method homogeneity of reaction mixture was increased by the rotating of reaction platform tray. The confirming of the results was also checked by the repeating of the synthesis process.

Table 1. The comparative results of conventional and microwave methods, analytical and physical data of the compounds

Compound	Colour	Reaction period		Yield (%)		Elemental analysis, found (calcd.) (%)				m_{eff} B.M.	Λ_m^a
		CM (hr)	MM (min)	CM	MM	C	H	N	Metal		
$\text{C}_{14}\text{H}_8\text{N}_2\text{OCIF}$	Orange	4.5	4.2	85	90	61.1 (61.15)	2.8 (2.91)	10.1 (10.19)	-	-	-
$[\text{VO}(\text{C}_{14}\text{H}_8\text{N}_2\text{OCIF})_2]\text{SO}_4$	Golden yellow	7.2	8.9	68	82	47.1 (47.19)	2.2 (2.24)	4.8 (7.86)	9.3 (9.40)	1.72	92.2
$[\text{Co}(\text{C}_{14}\text{H}_8\text{N}_2\text{OCIF})_2]\text{Cl}_2$	Tobacco green	8.2	7.9	69	81	49.4 (49.46)	2.3 (2.35)	8.2 (8.24)	8.6 (8.67)	4.38	125
$[\text{Ni}(\text{C}_{14}\text{H}_8\text{N}_2\text{OCIF})_2(\text{H}_2\text{O})_2]\text{Cl}_2 \cdot 2\text{H}_2\text{O}$	Light green	6.9	8.2	68	79	44.7 (44.74)	3.1 (3.19)	7.4 (7.45)	7.7 (7.81)	3.38	124
$[\text{Cu}(\text{C}_{14}\text{H}_8\text{N}_2\text{OCIF})_2]\text{Cl}_2$	Light green	6.3	6.5	76	80	49.0 (49.10)	2.3 (2.33)	8.1 (8.18)	9.0 (9.27)	1.87	115
$(\text{C}_{17}\text{H}_{16}\text{N}_4\text{O})$	Dark red	4.1	4.5	80	92	69.7 (69.77)	5.4 (5.47)	19.1 (19.15)	-	-	-
$[\text{VO}(\text{C}_{17}\text{H}_{16}\text{N}_4\text{O})(\text{H}_2\text{O})]\text{SO}_4 \cdot 3\text{H}_2\text{O}$	Dark brown	8.1	8.0	75	82	38.6 (38.68)	4.5 (4.55)	10.5 (10.62)	12.6 (12.70)	1.71	85.3
$[\text{Co}(\text{C}_{17}\text{H}_{16}\text{N}_4\text{O})\text{Cl}]\text{Cl} \cdot \text{H}_2\text{O}$	Dark green	7.3	8.1	68	81	46.3 (46.34)	4.0 (4.08)	12.6 (12.72)	13.2 (13.38)	4.39	67.5
$[\text{Ni}(\text{C}_{17}\text{H}_{16}\text{N}_4\text{O})\text{Cl}]\text{Cl} \cdot 3\text{H}_2\text{O}$	Blackish brown	7.8	7.0	67	80	42.8 (42.85)	4.6 (4.62)	11.7 (11.76)	12.2 (12.33)	Dia.	60.2
$[\text{Cu}(\text{C}_{17}\text{H}_{16}\text{N}_4\text{O})\text{Cl}]\text{Cl} \cdot \text{H}_2\text{O}$	Dark brown	7.0	6.2	78	84	44.0 (44.06)	3.8 (3.88)	12.0 (12.09)	13.6 (13.71)	1.86	65.5

CM, conventional method; MM, microwave method.

$\Lambda_m^a = (\Omega^{-1} \text{ cm}^2 \text{ mol}^{-1})$.

All the metal complexes are coloured, solid and stable towards air and moisture at room temperature. They decompose on heating at high temperature and more or less soluble in common organic solvents. The comparative results of microwave and conventional methods, with analytical and physical data of the compounds are given in the Table 1. All the metal chelates have 1 : 2 and 1 : 1 (metal : ligand) stoichiometry. The molar conductance values of the complexes in methanol (10^{-3} M) suggest the electrolytic nature.

FAB mass spectra. The FAB-mass spectra suggested that all the complexes have a monomeric nature. These complexes show molecular ion peaks in good agreement with the empirical formula suggested by elemental analyses.

The FAB mass spectrum of $[\text{Ni}(\text{B})\text{Cl}]\text{Cl}\cdot 3\text{H}_2\text{O}$ complex has been studied as one of the representative case. The peaks of appreciable intensity have been observed at m/z value 472, 417, 385, 351, 293 and 107 suggesting the fragmentation pattern. The m/z value 472 corresponds to nearest composition $[\text{Ni}(\text{B})\text{Cl}]\text{Cl}\cdot 3\text{H}_2\text{O}$; 417 to $[\text{Ni}(\text{B})\text{Cl}]\text{Cl}$, 385 to $[\text{Ni}(\text{B})\text{Cl}]$, 349 to $[\text{Ni}(\text{B})]$ 293 to ligand alone and 107 to Ni with chelated ligand moiety [15, 16].

IR spectra. The data of the IR spectra of Schiff base ligand and its metal complexes are listed in Table 2. The IR spectra of the complexes were compared with those of the free ligand in order to determine the involvement of coordination sites in chelation. Characteristic peaks in the spectra of the ligand and complexes were considered and compared.

IR spectrum of the ICFA ligand shows a medium band at 3,149/cm due to $\nu(\text{N-H})$. A strong absorption band at 1,726/cm ($\text{C}=\text{O}$) present in the free Schiff base ligand has shifted to lower side by 20~35/cm in all four complexes, this indicates the involvement of $\text{C}=\text{O}$ group in coordination. A band at about 1,610/cm due to $\nu(\text{C}=\text{N})$ (azomethine group) shift down by 5~10/cm in the complexes suggesting involvement of azomethine nitrogen in coordination. The appearance of broad band around 3,390/cm in the spectra of complexes may be due to lattice water. A band of

medium intensity at 838/cm (rocking) in Ni(II) complex suggest the presence of coordinated water. Some new bands at $520 \pm 5/\text{cm}$ and $486 \pm 10/\text{cm}$ have been assigned to $\nu(\text{M-O})$ and $\nu(\text{M-N})$ modes, respectively. A characteristic non-ligand sharp band in the spectra of VO(II) complex at 955/cm has been assigned to $\nu(\text{V}=\text{O})$. The IR spectra of the PCAP ligand shows a strong band at 1,595/cm due to $\nu(\text{C}=\text{N})$ (azomethine group). This has shifted down by 10~20/cm in the complexes suggesting coordination through azomethine nitrogen. A strong absorption band at 1,644/cm due to $\nu(\text{C}=\text{O})$ present in the free Schiff base ligand has shifted to lower wave number by 20~30/cm in complexes. This indicates the involvement of $\text{C}=\text{O}$ group in coordination. The stretching frequency due to N-N in the free ligand was observed at 1,034/cm. This band was slightly affected in metal complexes, indicating non-involvement of this linkage in coordination with the central metal ions. Pyridine ring shows absorption band at 1,421 and 1,047/cm in the ligand spectrum. These bands shows positive shift 10~15/cm in the complexes suggesting participation of pyridine nitrogen in complexation. A broad band at 3,370~3,360/cm in the spectra of complexes suggests the presence of water molecules. A band of medium intensity at 830/cm suggests the presence of coordinated water in VO(II) complex. The new bands at $530 \pm 5/\text{cm}$ and $485 \pm 5/\text{cm}$ have been assigned to $\nu(\text{M-O})$ and $\nu(\text{M-N})$ modes, respectively. A characteristic non-ligand sharp band in the spectra of VO(II) complex at 950/cm has been assigned to $\nu(\text{V}=\text{O})$ [17-19].

Electronic spectra. The nature of the ligand field around the metal ion has been deduced from the electronic spectra.

The electronic spectrum of the $[\text{VO}(\text{A})_2]\text{SO}_4$ (i) complex was recorded in methanol. It exhibits bands at 13,698/cm, 19,607/cm and 24,390/cm, which are assignable to transitions ${}^2\text{B}_2\text{-}{}^2\text{E}$ (ν_1), ${}^2\text{B}_2\text{-}{}^2\text{B}_1$ (ν_2), and ${}^2\text{B}_2\text{-}{}^2\text{A}_1$ (ν_3), respectively. The geometry of these five coordinated mononuclear complex can be described in terms of a trigonal bipyramid distorted towards a tetragonal pyramid. The value of the magnetic moment for this complex is 1.72 B.M. It indicates presence of one unpaired electron in VO(II) complex. The electronic

Table 2. IR spectral data (1/cm) of Schiff bases and their metal complexes

Compound	$\nu(\text{N-H})$	$\nu(\text{C}=\text{O})$	$\nu(\text{C}=\text{N})$	$\nu\text{C}=\text{C}$	H_2O	$\nu(\text{M-N})$	$\nu(\text{M-O})$	$\nu(\text{V}=\text{O})$
ICFA	3,149	1,726	1,610	1,460	–	–	–	–
$[\text{VO}(\text{A})_2]\text{SO}_4$	3,150	1,690	1,602	1,463	–	480	525	955
$[\text{Co}(\text{A})_2]\text{Cl}_2$	3,150	1,700	1,600	1,461	–	485	522	–
$[\text{Ni}(\text{A})_2(\text{H}_2\text{O})_2]\text{Cl}_2\cdot 2\text{H}_2\text{O}$	3,152	1,679	1,608	1,464	3,390 (838)	486	520	–
$[\text{Cu}(\text{A})_2]\text{Cl}_2$	3,155	1,695	1,605	1,464	–	495	515	–
PCAP	–	1,644	1,595	1,491	–	–	–	–
$[\text{VO}(\text{B})(\text{H}_2\text{O})]\text{SO}_4\cdot 3\text{H}_2\text{O}$	–	1,614	1,585	1,489	3,365 (830)	490	525	950
$[\text{Co}(\text{B})\text{Cl}]\text{Cl}\cdot \text{H}_2\text{O}$	–	1,615	1,581	1,488	3,360	485	530	–
$[\text{Ni}(\text{B})\text{Cl}]\text{Cl}\cdot 3\text{H}_2\text{O}$	–	1,620	1,578	1,485	3,368	487	535	–
$[\text{Cu}(\text{B})\text{Cl}]\text{Cl}\cdot \text{H}_2\text{O}$	–	1,624	1,585	1,489	3,370	480	530	–

absorption spectra of the $[\text{Co}(\text{A})_2]\text{Cl}_2$ (ii) complex was recorded in methanol show the bands at 12,987/cm and 21,739/cm. These transitions have tentatively been assigned to ${}^4\text{A}_2\text{-}{}^4\text{T}_1$ (F) (ν_2) and ${}^4\text{A}_2\text{-}{}^4\text{T}_1$ (P) (ν_3) respectively. The value of magnetic moment of this complex is 4.38 B.M. Thus, the tetrahedral geometry has been suggested with one unpaired electron for Co(II) complex. The electronic spectrum of the $[\text{Ni}(\text{A})_2(\text{H}_2\text{O})_2]\text{Cl}_2\cdot 2\text{H}_2\text{O}$ (iii) complex (in methanol) was recorded shows two distinct bands at 18,518/cm and 2,4390/cm. These transitions have tentatively been assigned to ${}^3\text{A}_2\text{g}$ (F)- ${}^3\text{T}_1\text{g}$ (F) and ${}^3\text{A}_2\text{g}$ (F)- ${}^3\text{T}_1\text{g}$ (P). The values of various ligand field parameters 10Dq, B, β , ν_1/ν_2 , λ and LFSE are as 10,287/cm, 803/cm, 0.74, 1.8, (-)499/cm, 147 kJ/mol which are characteristic for hexacoordinated Ni(II) complex. The value of the magnetic moment for this complex is 3.38 B.M, hence high-spin octahedral geometry for this Ni (II) complex has been proposed. The electronic spectrum of the methanolic solution of $[\text{Cu}(\text{A})_2]\text{Cl}_2$ (iv) complex was recorded; it exhibits bands at 13,157/cm and 19,230/cm which have been assigned to ${}^2\text{B}_2\text{g-}{}^2\text{B}_2\text{g}$ and ${}^2\text{B}_1\text{g-}{}^2\text{Eg}$ transitions. The magnetic moment of this complex is 1.87 B.M. Therefore, square planar stereochemistry has been suggested.

The electronic spectrum of the $[\text{VO}(\text{B})(\text{H}_2\text{O})]\text{SO}_4\cdot 3\text{H}_2\text{O}$ (v) complex (in methanol) exhibit bands at 13,888/cm, 20,000/cm and 22,727/cm which are assignable to transitions ${}^2\text{B}_2\text{-}{}^2\text{E}$ (ν_1), ${}^2\text{B}_2\text{-}{}^2\text{B}_1$ (ν_2) and ${}^2\text{B}_2\text{-}{}^2\text{A}_1$ (ν_3) respectively. The geometry of this five coordinated mononuclear complex can be described in terms of a trigonal bipyramid distorted towards a tetragonal pyramid. The value of the magnetic moment for this complex is 1.71 B.M. It indicates presence of one unpaired electron. The electronic absorption spectra of the $[\text{Co}(\text{B})\text{Cl}]\text{Cl}\cdot\text{H}_2\text{O}$ (vi) complex (in methanol) show the bands at 13,157/cm and 19,607/cm. These transitions have tentatively been assigned to ${}^4\text{A}_2\text{-}{}^4\text{T}_1$ (F) (ν_2) and ${}^4\text{A}_2\text{-}{}^4\text{T}_1$ (P) (ν_3) respectively. The value of magnetic moment of this complex is 4.39 B.M. Thus, the tetrahedral geometry

with one unpaired electron has been suggested for Co(II) complex. The electronic spectrum of $[\text{Ni}(\text{B})\text{Cl}]\text{Cl}\cdot 3\text{H}_2\text{O}$ (vii) complex (in methanol) show two bands at 1,2658/cm and 21,739/cm which are assignable to ${}^1\text{A}_1\text{g-}{}^1\text{Eg}$ (ν_1) and ${}^1\text{A}_1\text{g-}{}^1\text{B}_2\text{g}$ (ν_2), transitions respectively. This complex is diamagnetic in nature. Therefore, a square-planar geometry has been suggested. The electronic spectrum of the $[\text{Cu}(\text{B})(\text{H}_2\text{O})]\text{Cl}_2\cdot\text{H}_2\text{O}$ (viii) complex gives exhibit bands at 13,513/cm and 19,607/cm assignable to ${}^2\text{B}_1\text{g-}{}^2\text{B}_2\text{g}$ and ${}^2\text{B}_1\text{g-}{}^2\text{Eg}$ transitions. The magnetic moment of this complex is 1.86 B.M. Therefore, square planar stereochemistry has been suggested [20-22].

Antimicrobial activity. The *in vitro* anti-microbial activity of the investigated compounds were, tested against the microorganisms *E. coli*, *S. aureus*, *S. fecalis*, *A. niger*, *T. polysporum*, *C. albicans*, and *A. flavus* by the serial dilution method. The MIC values of the compounds against the growth of micro-organisms using Streptomycin and Nystatin as standard are summarized in Table 3. MIC values and zone of inhibition (in mm) of synthesized compounds against fungi using Miconazole as standard are given in Table 4.

All of the tested compounds showed good biological activity against microorganism. On comparing the biological activity of the Schiff base and its metal complexes with the standard bactericide and fungicide, it is show that the metal complexes have moderate activity as compared to the standard but all the complexes are more active than their respective ligands. The higher inhibition zone of metal complexes than those of the ligands can be explained on the basis of Overtone's concept and Chelation theory. On chelation, the polarity of the metal ion will be reduced to greater 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 δ -electrons over the whole chelating ring and enhances

Table 3. Minimum inhibitory concentration of the synthesized compounds against bacteria and fungi ($\mu\text{g/mL}$)

Compound	<i>Escherichia coli</i>	<i>Staphylococcus aureus</i>	<i>Streptococcus fecalis</i>	<i>Aspergillus niger</i>	<i>Candida albicans</i>	<i>Trichoderma polysporum</i>	<i>Aspergillus flavus</i>
ICFA	45	55	65	50	64	70	55
$[\text{VO}(\text{A})_2]\text{SO}_4$	22	24	38	15	18	22	16
$[\text{Co}(\text{A})_2]\text{Cl}_2$	40	34	28	19	16	24	14
$[\text{Ni}(\text{A})_2(\text{H}_2\text{O})_2]\text{Cl}_2\cdot 2\text{H}_2\text{O}$	15	24	20	22	28	24	32
$[\text{Cu}(\text{A})_2]\text{Cl}_2$	10	15	19	16	12	14	19
PCAP	70	75	60	70	80	69	60
$[\text{VO}(\text{B})(\text{H}_2\text{O})]\text{SO}_4\cdot 3\text{H}_2\text{O}$	20	18	21	24	32	19	25
$[\text{Co}(\text{B})\text{Cl}]\text{Cl}\cdot\text{H}_2\text{O}$	16	20	15	17	21	18	24
$[\text{Ni}(\text{B})\text{Cl}]\text{Cl}\cdot 3\text{H}_2\text{O}$	24	30	35	35	31	22	40
$[\text{Cu}(\text{B})\text{Cl}]\text{Cl}\cdot\text{H}_2\text{O}$	18	12	17	87	11	16	12
Streptomycin ^a	10	12	14	–	–	–	–
Nystatin ^a	–	–	–	12	13	11	8

Standard; ICFA, isatin-3-chloro-4-floroaniline; PCAP, 2-pyridinecarboxylidene-4-aminoantipyrene.

Table 4. Antifungal activity of the synthesized compounds

Compound	MIC value in $\mu\text{g/mL}$ (zone of inhibition in mm)			
	<i>Aspergillus niger</i>	<i>Candida albicans</i>	<i>Trichoderma polysporum</i>	<i>Aspergillus flavus</i>
ICFA	65 (10)	58 (14)	62 (12)	72 (9)
$[\text{VO}(\text{A})_2]\text{SO}_4$	18 (26)	25 (22)	24 (24)	20 (25)
$[\text{Co}(\text{A})_2]\text{Cl}_2$	16 (28)	15 (30)	18 (25)	14 (32)
$[\text{Ni}(\text{A})_2(\text{H}_2\text{O})_2]\text{Cl}_2 \cdot 2\text{H}_2\text{O}$	30 (18)	38 (15)	32 (17)	30 (19)
$[\text{Cu}(\text{A})_2]\text{Cl}_2$	22 (24)	16 (30)	23 (20)	24 (21)
PCAP	50 (14)	49 (15)	52 (12)	42 (16)
$[\text{VO}(\text{B})(\text{H}_2\text{O})]\text{SO}_4 \cdot 3\text{H}_2\text{O}$	14 (30)	15 (30)	18 (28)	16 (27)
$[\text{Co}(\text{B})\text{Cl}]\text{Cl} \cdot \text{H}_2\text{O}$	12 (30)	16 (26)	15 (23)	17 (26)
$[\text{Ni}(\text{B})\text{Cl}]\text{Cl} \cdot 3\text{H}_2\text{O}$	22 (18)	24 (20)	20 (18)	26 (19)
$[\text{Cu}(\text{B})\text{Cl}]\text{Cl} \cdot \text{H}_2\text{O}$	30 (18)	32 (21)	19 (25)	24 (25)
Miconazole ^a	10 (32)	8 (35)	10 (34)	12 (28)

MIC, minimum inhibitory concentration; ICFA, isatin-3-chloro-4-floroaniline; PCAP, 2-pyridinecarboxylidene-4-aminoantipyrine.

^aStandard.

the penetration of the complexes into lipid membranes and blocking of the metal binding sites in the enzymes of microorganisms. There are other factor which also increases the activity are solubility, conductivity and bond length between the metal and ligand [23-27].

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