



Synthesis, characterization and Antifungal activity of transition metal (II) complexes of Schiff base derived from *p*-aminoacetanilide and salicylaldehyde

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Abstract

Tridentate Schiff base (L) has been synthesized by condensation of salicylaldehyde and *p*-aminoacetanilide in ethanol and treating with copper, nickel, cobalt and zinc chlorides form metal complexes. The synthesized compounds are characterized by analytical and spectral methods. The results indicate that the complexes are having ML₂ the composition. Moreover, geometry of the complexes is confirmed from electronic absorption and magnetic susceptibility data. The data show that all the complexes are distorted octahedral geometry around the central metal ion. The synthesized complexes were also exposed to various fungi to establish their bioactivities which show significant results. All the synthesized compounds are active against fungi but metal complexes are more active than ligand. Minimum Inhibitory Concentrations (MIC) values of synthesized compound range 25-55 $\mu\text{g/ml}$ against fungal species.

Keywords: Anti-fungal activity, Schiff base, Transition metal complexes

Introduction

Due to the increasing number of multi-drug-resistant microbial pathogens and the inclusion of emerging infectious diseases such as severe acute respiratory syndrome and avian influenza, the treatment of microbial infections still remains a challenging job with the available antimicrobials and remains a worldwide problem for clinical management. Development of newer molecules with less expense and minimum toxicity for the management of infections due to multi-drug-

resistant (MDR) microbial pathogens should represent the vital sphere of antimicrobial research today (Shaoo *et al.*, 2017). A literature survey revealed that Schiff base metal complexes are popular for versatile uses such as antiseptics, drug synthesis (Raman, *et al.*, 2007), bioinorganic chemistry, (Raman, *et al.*, 2009) electrochemistry (Gubendran, *et al.*, 2007) dioxygen uptake and catalysis (Tadavi *et al.*, 2017). The present work is the continuation of our previously reported work to obtain some novel Schiff base prepared from salicylaldehyde and p-aminoacetanilide complexes with different transitional metals with an intention to produce target molecules possessing good DNA binding and cleavage properties with CT DNA. Based on the above facts, we intend to report the antifungal activities our synthesized compounds were tested against fungi such as *Aspergillus niger*, *Aspergillus flavus*, *Rhizopus stolonifer*, *Candida albicans*, *Rhizoctonia bataicola* and *Trichoderma harizanum*. All the metal complexes showed stronger antifungal activities than the free ligand.

Materials and Methods

Apparatus and Reagents

All of the chemical were obtained from Merck in analytical grade. Elemental analysis, ¹H NMR and mass spectra (JEOL SX 102/DA-6000 mass spectrometer/data system using argon/xenon (6 kV, 10 mA) as the FAB gas) of synthesized compounds were recorded at RSIC, Lucknow. Systronic Conductivity Bridge is used to find molar conductance of metal complexes. Guoy balance is used to find magnetic moment of the complexes using copper sulphate as the calibrant. Electronic absorption spectra of our synthesized compounds were recorded using UV-1601 spectrophotometer. Perkin-Elmer 783 spectrophotometer in 4000-200 cm⁻¹ range is used to record the IR spectra of synthesized compounds.

In vitro antifungal activity

Well diffusion method is used to find antifungal activity of synthesized compounds and nystatin was used as control. Synthesized compounds were tested against microorganism such as *Trichoderma harizanum*, *Rhizoctonia bataicola*, *Candida albicans*, *Aspergillus niger*, *Aspergillus flavus* and *Rhizopus stolonifer* cultured on potato dextrose agar as medium. In petri plates using nutrient agar medium test organism were grown. The synthesized compounds were

dissolved in DMSO (200 $\mu\text{mol/ml}$). All the plates were incubated at 300K for 72h. The antifungal activity of synthesized by compounds were measured by MIC values (by visual observation no fungal growth in agar medium using low concentration of synthesized compounds by serial dilution method) (Reiner, 1982).

Synthesis of Schiff base

The NO_2 type Schiff base and its metal complexes were prepared by the reported method (Raman *et al.*, 2007).

Results and Discussion

The analytical data for the Schiff base and its complexes together with some physical properties are summarized in Table 1. The analytical data of the complexes correspond well with the general formula ML_2 where $\text{M} = \text{Cu(II)}$, Ni(II) , Co(II) and Zn(II) & $\text{HL} = \text{C}_{15}\text{H}_{14}\text{N}_2\text{O}_2$. The magnetic susceptibilities of the complexes at room temperature are consistent with octahedral geometry around the central metal ion, The molar conductance values of the complexes in DMF lie in the range 1.9 to 3.6 $\text{mho cm}^2 \text{mol}^{-1}$ which is quite lower than that expected for an electrolyte and reveal their non-electrolytic nature.

Table 1: Physical Characterisation, analytical, molar conductance and magnetic susceptibility data of the ligand and the complexes.

Compound / Complex	Colour	Melt/pt. ($^{\circ}\text{C}$)	Found (Calcd.)				Molar Conductance \wedge_m ($\text{ohm}^{-1} \text{cm}^2 \text{mol}^{-1}$)	μ_{eff} (BM)
			M	C	H	N		
$\text{C}_{15}\text{H}_{14}\text{N}_2\text{O}_2$	Yellow	162	----	69.75 (70.86)	5.43 (5.57)	11.59 (11.02)	-----	----
CuL_2	Black	283	11.89 (11.20)	63.31 (63.49)	4.67 (4.58)	8.89 (9.87)	3.2	1.95
CoL_2	Light brown	295	8.87 (10.44)	64.25 (63.95)	4.27 (4.61)	7.59 (9.94)	2.6	3.05
NiL_2	Pale green	265	10.72 (10.46)	63.82 (63.97)	4.73 (4.62)	10.25 (9.95)	3.6	4.10
ZnL_2	White	270	11.81 (11.48)	62.92 (63.22)	4.50 (4.56)	10.35 (9.83)	1.9	----

Mass spectra

The FAB mass spectra of the ligand (HL) and its copper complex [CuL₂] were recorded and they are used to compare their stoichiometry composition. The Schiff base shows a molecular ion peak at m/z 254. The molecular ion peak for the copper complex, observed at m/z 575 confirms the stoichiometry of metal chelates as ML₂ type. This composition is also supported by the mass spectra of other complexes. It is in good agreement with the microanalytical data.

¹H NMR spectrum

The ¹H-NMR spectra of the Schiff base and its zinc complex were recorded in CDCl₃ at room temperature. The ligand shows the following signals: phenyl multiplet at 7-7.5 δ, -CO-CH₃ at 2.1 δ, =C=NH- at 7.9 δ, -OH at 12.5 δ, and PhNH at 8.5 δ. The absence of peak at 12.5 δ in the zinc complex suggests that the phenolic proton is lost upon coordination. There is no appreciable change in all other signals in this complex. Thus, ¹H-NMR study reinforces the conclusions drawn from the IR spectra.

IR spectra

In order to study the binding mode of the Schiff base to the metal ion of the complexes, the IR spectrum of the free ligand was compared with the spectra of the complexes. The IR spectrum exhibits a strong band at *ca.*1615-1620 cm⁻¹ 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 cm⁻¹ which indicates that the azomethine nitrogen is one of the coordinating atoms in the Schiff base (R.Ramesh *et al.*,2002). Another strong band, observed at 1270-1280 cm⁻¹, is assigned to phenolic (C-O) stretching. On complexation, this band is shifted to higher frequency 1319 cm⁻¹ indicating the metal coordination through the phenolic oxygen (G.Venkatachalam *et al.*,2005). This has been further supported by the disappearance of the band at *ca.*3100-3300 cm⁻¹ in the free ligand, due to ν(OH), upon complexation with metal ion indicating the deprotonation of phenolic proton. The band observed in the region, 3340-3470 cm⁻¹ reveals the presence of ν(NH) of amide group. The strong band observed in the free ligand at 1675 cm⁻¹ is assigned to ν(C=O)

amide carbonyl group. In the complexes, this band is shifted to lower wave number 1654 cm^{-1} , indicating the coordination of carbonyl oxygen to the metal ion (S.N.Pal *et al.*, 2002).

Electronic absorption spectra

The electronic absorption spectra of the Schiff base and its Cu(II), Ni(II), and Co(II) complexes were recorded at 300 K. The absorption region, assigned and the proposed geometry of the complexes are given in Table 2. These values are comparable with that of the other reported complexes (Lewis *et al.*, 1967, Casella *et al.*, 1981 and Lever, 1968) and consistent with distorted octahedral geometry.

The magnetic moment of the complexes at room temperature is consistent with an octahedral geometry around the central metal ion. Thermal analysis of the complexes at 170°C indicates that there is no water molecules present in the complexes, which is further confirmed by their characteristic IR spectra. Based on the above spectral data, the following structure has been proposed for the complexes (Fig.1).

Table 2: Electronic absorption spectral data of the compounds

S.No	Compound	Solvent	Absorption (cm^{-1})	Band Assignment	Geometry
1	HL	EtOH	45600 3333	INCT INCT	----
2	CuL ₂	DMF	13,812 23,255	${}^2\text{B}_{1g} \rightarrow {}^2\text{A}_{2g}$ ${}^2\text{B}_{1g} \rightarrow {}^2\text{E}_g$	distorted octahedral
3	NiL ₂	DMF	13,888, 15,220 25,380	${}^3\text{A}_{2g}(\text{F}) \rightarrow {}^3\text{T}_{2g}(\text{F})$, ${}^3\text{A}_{2g}(\text{F}) \rightarrow {}^3\text{T}_{1g}(\text{F})$ ${}^3\text{A}_{2g}(\text{F}) \rightarrow {}^3\text{T}_{1g}(\text{P})$	distorted octahedral
4	CoL ₂	DMF	14,858, 16,978	${}^4\text{T}_{1g}(\text{F}) \rightarrow {}^4\text{T}_{1g}(\text{P})$ ${}^4\text{T}_{1g}(\text{F}) \rightarrow {}^4\text{A}_{2g}(\text{F})$	distorted octahedral

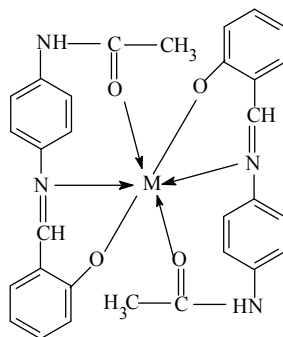
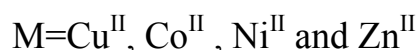


Fig. 1. Structure of the metal complexes



Antifungal activity

Antifungal activity of ligand and its Cu^{II} , Co^{II} , Ni^{II} and Zn^{II} complexes were tested *in vitro* against *Trichoderma harizanum*, *Rhizoctonia bataicola*, *Candida albicans*, *Aspergillus niger*, *Aspergillus flavus* and *Rhizopus stolonifer* by well diffusion method. MIC value of synthesized compounds summarized in Table 3. Antifungal activity of synthesized compounds indicates that all compounds were active against fungal species but copper complex have more active than other compounds which can be explained on the basis of Overtone's concept (Anjaneyula *et al.*, 1986) and Tweedy's Chelation theory (Dharmaraj *et al.*, 2001). Furthermore, ligand contains azomethine functional group which is also form hydrogen bond with active centre cell.

Table 3: Minimum inhibitory concentration of the synthesized compounds against growth of six fungi ($\mu\text{g/ml}$)

S.No	Compound	<i>A. niger</i>	<i>A. flavus</i>	<i>R. stolonifer</i>	<i>C. albicans</i>	<i>R. bataicola</i>	<i>T. harizanum</i>
1	HL	85	50	65	65	55	80
2	CuL_2	30	25	25	20	25	30
3	NiL_2	45	35	50	55	50	40
4	CoL_2	50	55	45	35	35	45
5	ZnL_2	50	55	25	30	35	35
6	Nystatin	10	8	16	12	14	13

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