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Antimicrobial Screening of Novel Schiff Base Ni (II) Complex Derived From Glutaraldehyde and L-Histidine

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Abstract:
Transition metal complex of Ni (II) with Schiff base derived from Glutaraldehyde and L-Histidine have been synthesized. Both the ligand and the complex were characterized by magnetic susceptibility, conductance measurement, solubility, elemental analyses, UV-Visible, IR, 1H-NMR spectral studies, powder XRD and TGA. The complex was formed in moderate yield and has sharp melting point. The purity and composition of the Schiff base and the metal (II) complex were established by elemental analysis which metal: ligand ratio of 1:1.The IR spectra revealed that the complex coordinated through azomethine nitrogen and oxygen of the ligand. The magnetic and spectroscopic data indicate an octahedral geometry for the complex. The molar conductance measurement indicates that the complex is non-electrolytic in nature. The electronic absorption spectra of the complex shows intra ligand and charge transfer transitions. Room temperature magnetic susceptibility measurement reveals that the nature of the complex is paramagnetic. The powder XRD data shows that the complex is microcrystalline. Thermal study indicated the stability of the complex. The antimicrobial activities of ligand and its complex were screened by Disc Diffusion method. Metal complex showed better activity against the microbial species than the Schiff base ligand.

Keywords: *Schiff base, synthesis, characterization, spectral studies, antimicrobial activity*

1. Introduction

Compounds containing imine bases have not only found extensive application in organic synthesis, but several of these molecules display significant biological activity. Schiff bases and their coordination compounds have gained importance recently because of their application in biological, biochemical, analytical, anticancer, antibacterial and antifungal activities[1-6]. Studies of new kinds of chemotherapeutic Schiff bases are now attracted the attention of biochemists. They easily form stable complexes with most transition metal ions. Because of the relative easiness of preparation, synthetic flexibility, and the special property of C=N group, Schiff bases are generally excellent chelating agents. Metal complexes of Schiff bases and their applications have been widely investigated during the past years .A search through literature reveals that Schiff bases and their complexes have been studied for their corrosion inhibition properties [7]. Schiff bases are very good complexing agents. Versatility of Schiff base ligands and biological, analytical and industrial applications of their complexes make further investigations in this area highly desirable.

In continuation of the earlier work on Schiff base complexes in this paper, the synthesis, characterization and antibacterial studies of novel Schiff base ligand derived from Glutaraldehyde and L- histidine have been reported. The ligand has both oxygen and nitrogen donor sites. It coordinates with the metal ion in a tetradentate manner.

2. Materials and Methods

All the chemicals and solvents used in the present work were of analytical grade. The metal is used as its nitrate salt. The percentage compositions of the elements in the compound were determined using a Vario EL III elemental analyzer at Sophisticated Analytical Instruments facility, CUSAT, Kochi. The electronic spectra of the synthesized compounds were recorded using Shimadzu double beam visible spectrophotometer in the visible region. Conductance of the metal complex was determined in DMSO on SYSTRONICS digital conductivity meter. The room temperature magnetic susceptibility measurement of the complex reported in the present study was made by the Guoy's method using Copper sulphate as calibrant.IR spectra of the Schiff base and its complex in the range of 4000 to 400 cm^{-1} were recorded on a Perkin Elmer FT-IR spectrometer MODEL 1600 as KBR discs. The pellets were prepared by taking necessary precautions inorder to avoid moisture.^{1}H NMR spectra of the complex in DMSO-d_6 were recorded on by employing TMS as internal standard at NIIST Trivandrum. Powder XRD was recorded on a computer controlled X-ray diffractometer system JEOL JDX 8030.Thermal analysis (TG and DTA) was carried out in controlled nitrogen atmosphere on a Perkin-Elmer Diamond thermal analyzer

at NIIST, Trivandrum, by recording the change in weight of the complexes on increasing temperature upto 900^0C at the heating rate of 10^o c/min. Double distilled water was used throughout the experimental work. Antimicrobial studies of the compounds were studied by disc diffusion method.

2.1. Synthesis of Schiff Base

The Schiff base ligand was prepared by reacting Glutaraldehyde and L-histidine in 1:2 molar ratio by refluxing in distilled methanol. The mixture was refluxed for 1 hour. The reaction was examined by TLC with time to time till completion. The solvent was partially evaporated and the yellowish mass product was precipitated by cooling and filtered off, washed with distilled water, dried, recrystallised and finally preserved in a desiccator.

2.2. Synthesis of Schiff Base Complex

Metal (II) nitrate was dissolved in 200 cm^3 of methanol. The filtered solution was added dropwise into 20cm^3 methanol solution of the Schiff base ligand. The resulting mixture was refluxed and stirred for 8 hours. After refluxing, the volume of the solution was reduced to one third and the concentrate was cooled at 0ºC. The precipitated complex was filtered off, washed several times with cold ethanol and dried in vacuo over anhydrous $CaCl_2$.

3. Results and Discussion

Metal (II) salt reacts with Schiff base ligand in 1:1 molar alcoholic medium to afford brownish coloured complex. Ni(II) complex is normally stable at room temperature and hygroscopic in nature. The Schiff base ligand is soluble in common organic solvents like ethanol and methanol. The corresponding complex is soluble in DMSO. The Schiff base and its complex is subjected to elemental analysis. The analysis data along with some physical properties of the synthesized compounds are summarised in **Table 1**. The results obtained are in good agreement with those calculated for the suggested formulae. The Ni(II) complex is non-electrolytic in nature as the molar conductivity measurement in DMSO is 10.15 ohm^{-1} cm^2 mol^{-1}.

Ligand/Metal Chelate	**Empirical Formula**	**Colour**	**M:L ratio**	**Molar Cond. (Ohm^{-1} cm^2 mol^{-1})**	**Elemental analysis % Found (cal)**			
					C Found (Cal)	**\H Found (Cal)**	**N Found (Cal)**	**M Found (Cal)**
Glu-his ligand	$C_{17}H_{22}N_2O_4$	Yellow	-	-	57.32 (57.5)	4.13 (4.45)	15.84 (15.58)	-
[Ni(glu)(his)2H_2O]	$C_{17}H_{26}N_6O_6Ni$	Olive green	1:1	10.15	43.89 (44.06)	5.80 (5.63)	17.85 (17.70)	13.48 (13.40)

Table 1: Analytical data of Schiff base and its complex

3.1. UV/ Visible Spectra

The UV-Visible spectra are often very useful in the evaluation of results furnished by other methods of structural investigation [8]. The electronic spectral measurements were used for assigning the stereochemistry of metal ions in the complex based on the positions and number of d-d transition peaks [9]. The electronic absorption spectra of the Schiff base ligand and its complex was recorded in DMSO solution in the range of 200 to 800 nm region is given in Figure.1. It is usually recorded as a plot of absorbance (A) versus wavelength (cm^{-1}). The absorption spectrum of free ligand consist of an intense band centered at 255 nm which is assigned to π - π^* transition of the C=N chromophore. On complexation, this band was shifted to lower wavelength region at 225 nm suggesting the coordination of azomethine nitrogen with Ni(II) ion. The spectra also shows other transitions in the range of 340 and 350 nm which can be assigned to n - π^* transition. Another transition was found to be in the range of 360 and 370 nm which may be due to charge transfer transition. The spectra also show certain absorption bands at 595 and 615 nm which is in accordance with d-d transitions.

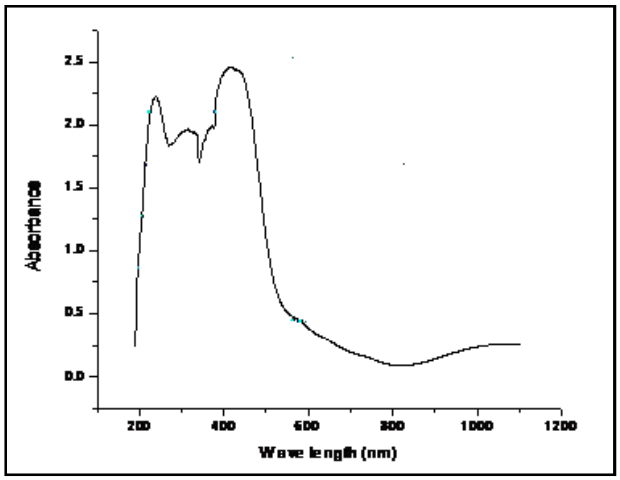

Figure 1: UV Spectrum of Ni (II) Complex

The effective magnetic moment value for the Ni (II) complex value offers possibility of an octahedral geometry around the metal ion.

3.2. Infra Red Spectra

The IR spectra of the synthesized compounds were studied to characterize their structures. The spectrum of the Schiff base ligand showed ν(C=N) azomethine band at 1655 cm^{-1}.On complexation ,this band was shifted to lower frequency region 1588 cm^{-1} [10] due to the coordination of azomethine to the Ni (II) ion. This fact can be explained by the withdrawing of electrons from nitrogen atom to the metal ion on coordination. New bands observed at 548 cm^{-1} and 483 cm^{-1} which are not seen in the spectrum of the free ligand can be attributed to the ν(M-O) and ν(M-N) vibrations respectively[11]. Appearance of a broad band in 3045 cm^{-1} region was assigned to the presence of lattice or coordinated water molecules in the metal complex. An additional band within the region of 820-850 cm^{-1} confirmed the water molecules are coordinated. The IR spectra of the complex is given in Figure 2.

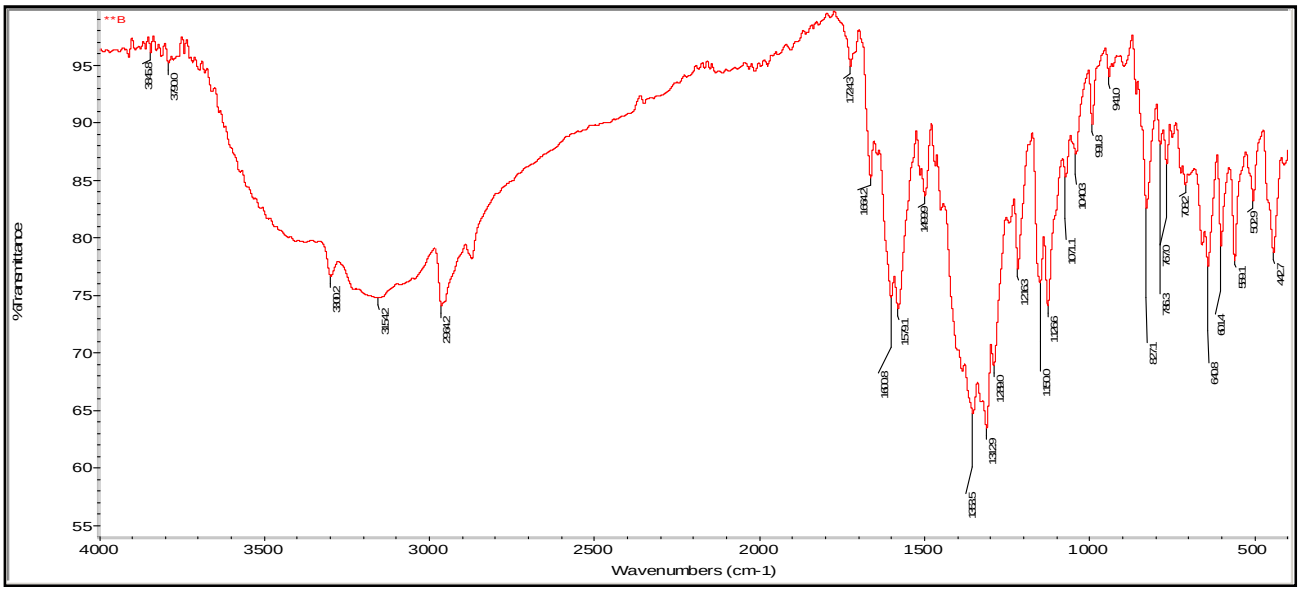

Figure 2: IR spectra of the Schiff base metal complex

3.3. 1H NMR Spectra

^{1}H NMR Spectrum of the ligand recorded in DMSO solution shows a multiplet at 2.7, 1.8 ppm due to the methyl protons [12]. The ^{1}H NMR Spectra of the Schiff base complex exhibit signals at 8.5 and 7.5 ppm attributed to CH=N- and –NH protons respectively. The azomethine proton signal in the spectrum of the corresponding complex is shifted downfield compared to the free ligand, suggesting the deshielding of the azomethine group due to the coordination with the metal ion [13]. There is no appreciable change in all other signals of the complex.

3.4. Powder XRD Study

X-ray diffraction pattern of Ni (II) complex shows sharp crystalline peaks. The crystallite size of the complex could be estimated from XRD pattern by the Scherre's formula,

$$D_{XRD} = 0.9\,\lambda \,/\, \beta \cos\theta$$

Where λ is the wavelength, β is the full width at half maxima and θ is the diffraction angle. The XRD shows that Ni(II) complex has the crystallite size of 45 nm and so it is microcrystalline in nature[14,15].

3.5. TGA study

The dynamic TGA with the percentage mass loss at different steps have been recorded. The complex lose its weight in the temperature range 150-260 ^{o}C corresponding to two coordinated water molecules with an endothermic peak in DTA curve.After the total loss of water molecules, the decomposition occurs at 670-750 ^{o} C that indicate the decomposition of the ligand. The observed residue corresponds to the respective metal oxide. Based on the spectral and analytical characterization studies the expected geometry for the Ni(II) complex is shown in Figure 3.

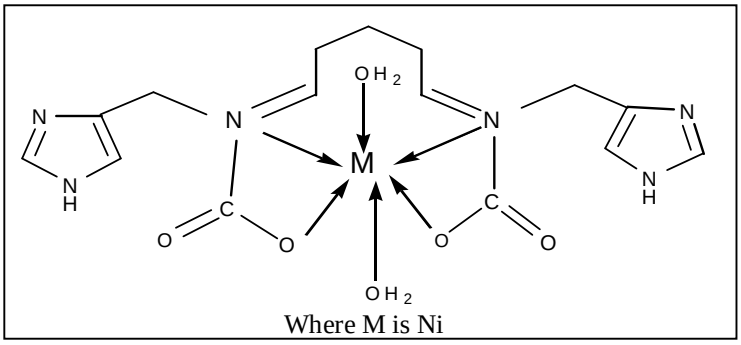

Figure 3: Structure of Ni(II) complex

3.6. Antimicrobial study

The main aim of the production and synthesis of any antimicrobial compound is to inhibit the causal microbe without any side effects on the patients [16]**.** Antimicrobial agents act selectively on vital microbial functions with minimal effects or without affecting host functions [17]. Different antimicrobial agents act in different ways**.** However, the mechanism of action of antimicrobial agents can be categorized based on the structure of the bacteria or the function that is affected by the agents**.** In addition, it is worthy to stress here on the basic idea of applying any chemotherapeutic agent which depends essentially on the specific control of only one biological function and not on, multiple ones. The *In vitro* antimicrobial activity of the Schiff base ligand and its Ni(II) metal complex were tested against the bacteria *Klebsiella sps, E.coli, Staphylococcus aureus* and fungi *Candida sps , Aspergillus niger* and *Aspergillus fumigates* by Disc diffusion method.

In this method, a standard 6.35 mm diameter sterilized filter paper disc impregnated with the compound (100 µg/ml in DMSO) was placed on an agar plate seeded with the test bacterial strains. The plates were incubated for 24 hours at 37^{o}C. The activity was determined by measuring the diameter of the inhibition zone (in mm) and chloramphenicol was used as a standard control. A comparative study of the ligand and its complex indicates that the metal chelate exhibited higher antimicrobial activity than the free ligand. The Schiff base ligand showed very low activity among all the microbial species. The metal complex showed higher antibacterial activity on the species *Klebsiella sps* and moderate activity on the species *Staphylococcus aureus.* The Ni(II) complex also showed better activity towards the fungi *Candida sps* and moderate activity on the fungal species *Aspergillus fumigates.* The increase in the antimicrobial activity of the metal chelate was found to be due to the effect of metal ion on the metal chelate which could be explained on the basis of Overtones concept and chelation theory.

Compound	**Microbial Species(Zone of inhibition)**					
	Kleb. sps	**E.coli**	**Staphy.aureus**	**Cand.sps**	**Asp.niger**	**Asp.fumig**
Control	24.0	22.0	25.0	20.0	20.0	30.0
Glu-his ligand	2.5	3.0	2.0	1.5	2.0	3.0
[Ni(glu)(his)2H_2O]	19.5	17.0	16.0	18.5	18.0	16.0

Table 2: Antimicrobial activity of the synthesized compounds

On chelation, the polarity of the metal ion gets reduced to the greater extent due to the overlap of the ligand orbital and partial sharing of positive charges of metal ion with donor groups. It was further noted that the delocalization of electrons over the whole chelate ring enhanced the lipophilicity of the complex. The increase of lipophilicity enhanced the penetration of the complex into the lipid membrane and blocking the metal site on enzymes of microorganism. The zones of inhibition of the ligand and its metal complex is presented in Table 2. The comparative zone of inhibition of the synthesized compounds are presented in the Figure 4.

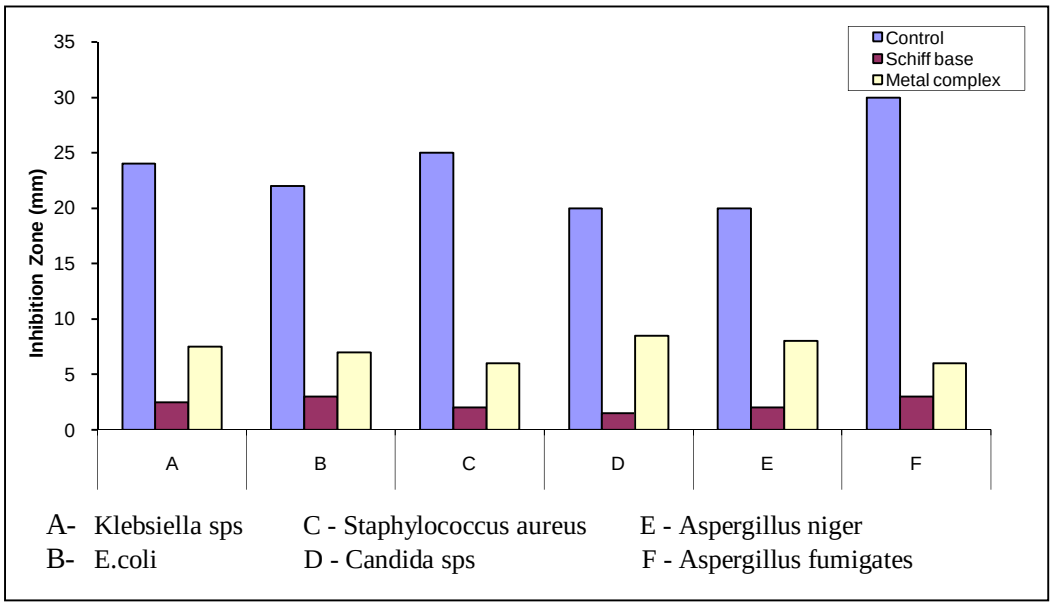

Figure 4: Inhibition zone of the synthesized compounds

4. Conclusion

The outcome of the above results confirms the stoichiometry of the complex to be 1:1 (M:L) as indicated by elemental analysis and conduct metric measurements. IR spectra suggests the presence of azomethine group and its linkage towards the metal ion. This has been further confirmed on the basis of NMR spectral studies. Powder XRD study suggest the microcrystalline nature of the complex. Electronic spectra and magnetic susceptibility measurement indicate the octahedral geometry for the Ni(II) complex and exhibit coordination number six.TGA study show the presence of water molecules in the complex. Antimicrobial study indicates the predominant activity of the complex than its corresponding ligand.

5. References

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