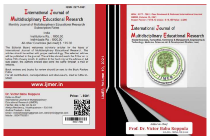

Cover Page

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SYNTHESIS, CHARACTERIZATION AND ANTIMICROBIAL ACTIVITIES OF MOLYBDENUM(VI) SCHIFF'S BASE COMPLEX DERIVED FROM SALICYLALDEHYDE AND L-ALANINE

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ABSTRACT

Synthesis, characterization and antimicrobial activities of Molybdenum (VI) metal complex with 2-(2-hydroxybenzylideneamino) propanoic acid (HBAPA)-Schiff's Base were carried out in this study. The synthesized Schiff bases and its complex were subjected to physiochemical tools; in terms of molar conductivity, FTIR, UV spectroscopy, and elemental analysis. The CHN elemental analysis results showed the formation of the Schiff bases and the complex in 1:2 ratio. The infrared spectral data of the mixed Schiff base complexes exhibited chelating behavior between the metal ion and the Schiff base through the active groups presented in the HBAPA such as nitrogen atom of the azomethine and oxygen atom of the hydroxyl group. The antimicrobial studies revealed that the synthesized ligands and its metal complex recorded strong potency against the pathogens being investigated, suggesting that it could serve as good antimicrobial agents against the selected pathogens.

KEYWORDS: Alanine Schiff base, Antimicrobial activity, Molybdenum complexes, Schiff base, Coordination Chemistry.

INTRODUCTION

Schiff base metal complexes have been studied extensively for years due to the synthetic flexibilities of these Schiff base ligands and their selectivity as well as sensitivity towards the transition metal ions [1]. Coordination complexes with mixed ligands are of considerable importance in this regard especially in the field of metalloenzymes, and are known to possess various biological activities [2]. The Schiff base compounds obtained from aromatic amines and aldehydes have wide variety of applications in inorganic, analytical and organic chemistry and are a field of coordination chemistry [3,4]. Schiff bases derived from the condensation of an amino and a carbonyl compound, form an important class of ligands that have the propensity to bind almost all metal ions via azomethine nitrogen [5,6]. Schiff base compounds and their complexes play an important application in the area of food and dyes industry, agriculture, polymer, biological sciences as antibacterial and antifungal [7,8]. The medicinal application of metal complexes has been a subject of great interest recently [9]. Apart from the huge success of platinum-based drugs, some other metal compounds such as titanium and ruthenium complexes have shown some potential for chemotherapy. Copper complexes have indeed demonstrated a wide range of pharmacological activity such as antibacterial, antifungal, antiviral, anticancer and anti-inflammatory activity [10-12]. It was found that copper complexes often demonstrate enhanced biological activity than the parent ligand alone [13].

Molybdenum (Mo) possesses diverse valances (+II to +VI), and is involved in forming cofactors in more than 60 enzymes in biology. Molybdenum complexes of Schiff bases have been investigated because they play an important role not only in the development in coordination chemistry, but also in catalysis, enzymatic reaction, magnetism, molecular architectures. Redox switching of the element in these enzymes catalyzes a series of metabolic reactions in both prokaryotes and eukaryotes [14]. More than 60 metalloenzymes and proteins have been identified containing Mo including nitrogenase and nitrate reductase, which tie the element to the nitrogen cycle [15-17]. Oxo and peroxo complexes of Molybdenum (VI) with different ligands have been reported and it is shown that the ligands coordinate to the metal ion in a symmetrical bidentate fashion through heterocyclic nitrogen and carbonyl oxygen or thiocarbonyl sulfur [18,19].

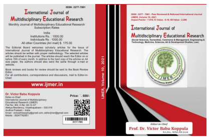
EXPERIMENTAL

Materials and Methods

All chemicals, reagents and solvents used in the synthesis of the complex were of analytical grade, while L-alanine, salicylaldehyde, amonium molybdate were obtained from Merck Specialties Private Limited and were used without further purification. MoO_3 was obtained by heating ammonium molybdate. Carbon, hydrogen and Nitrogen analysis were carried out by micro analytical methods. The analysis of metal Molybdenum was carried out by reported method [20]. The molar conductivity of the complexes was measured at room temperature in DMF solvent using digital conductivity meter CMD-650. The infrared spectra over the region 4000-400 cm^{-1} were carried out applying KBr disc technique using IFS-25 DPUS/IR spectrometer. The electronic spectra were measured in DMF solvent by using a Perkin-Elmer lambda-4β spectrophotometer.

Synthesis of HBAPA Schiff's Base Ligand

The Schiff base 2-(2-hydroxybenzylideneamino) propanoic acid (HBAPA) was synthesized as follows: NaOH (0.01 mol; 0.4gm) was dissolved in 30 cm^3 of methanol and amino acid (L-alanine) (0.01 mol; 0.89gm) was added to it. The content was stirred



magnetically at room temperature to obtain a homogenous mixture to which 1.05 cm^3 of 2-hydroxybenzaldehyde was added in small portions with constant stirring. The resulting mixture was evaporated to 1/3rd of its original volume to which 1-2 cm^3 of acetic acid was added immediately. After 2 hours, light yellow crystals of 2-(2-hydroxybenzylideneamino) propanoic acid were formed. The product was filtered, washed, dried and recrystallized from hot methanol (yield ≈ 91%).

Preparation of Metal Complex

MoO$_3$ 1.44g (1 mmol) was added in 20mLof ethanol and to this a solution of Schiff base ligand HBAPA (2 mmol 3.86g in 25mL of ethanol) was added in the presence of 1 mmol of NaOH. The resulting mixture was refluxed for one hour while stirring. The solid mass (Mo-HBAPA complex) so obtained was filtered off, washed several times with ethanol and was finally dried under vacuum. The structure of the Metal-Ligand complex is proposed as under.

Antimicrobial Activities

The Schiff base ligand and the complexes were screened for biological activity against four different fungi and bacteria species respectively. Four bacterial stains; Staphylococcus aureus, Escherichia coli, Pseudomonas aeruginosa, and Bacillus subtilis were incubated for 24 h at 36 ^{0}C, and fungal stains; Aspergillus niger, Candida albicans, and Rhizoctonia bataticola were incubated for 48 h at 36 ^{0}C following the reported procedure [21]. The stock solution (0.001 mol) was prepared by dissolving the compounds in DMSO, and the solutions were serially diluted to find the minimum inhibitory concentration (MIC) values (μgmL^{-1}). The test chemicals of different dilutions were added to sterile blank antimicrobial susceptibility disks. The bacteria were subcultured in agar medium and the disks were kept onto the same. Antibacterial activity of the ligand and metal complexes were determined by measuring the zones of growth inhibition surrounding the disks. The standard was also screened under similar conditions for comparison. The solvent DMF alone was added to a separate disk and used as control, and it showed no activity against microbial strains. Standard antibacterial Streptomycin and antifungal drug nystatin were used for comparison under similar conditions. Antimicrobial activity studies were performed in triplicate, and the average was taken as the final reading.

RESULTS AND DISCUSSION

The Schiff base ligand (HBAPA) was prepared by reacting equimolar amounts of 2-hydroxybenzaldehyde with amino acid (L-alanine) in methanol medium. The structures of the ligand and the complexes were established from their IR, UV-Vis's spectra, elemental analyses and magnetic susceptibility measurements. The complex is intensely coloured stable solids, and the low molar conductance values of the complexes reveal their nonelectrolytic nature. The melting point is sharp indicating the purity of the prepared Schiff base. The complex is soluble in common organic solvents like DMF, DMSO, acetonitrile and partially soluble in ethanol. The results of the elemental analysis (Table 1) of the Schiff base are in good agreement with those calculated for the suggested formula and agree with a 1: 2 metals to ligand stoichiometry for the complex. The synthesis and structure of the Schiff base ligand and its complex under study is shown as under.

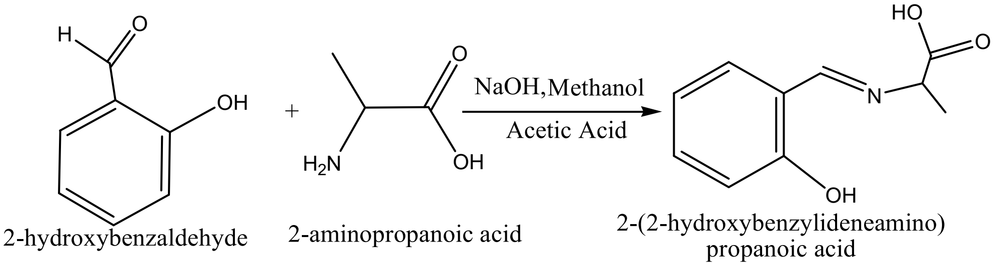


Fig-1: Synthesis and structure of the Schiff base ligand

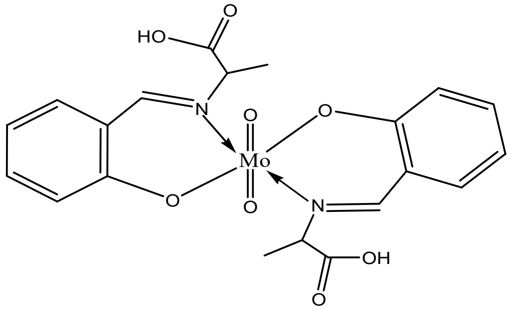


Fig-2: Proposed structure of Molybdenum (VI) – HBAPA complex

Table 1: Analytical and Physical data of ligand and complex

Compound	Color	Mol. Formula	Formula wt. (g mol^{-1})	Elemental Analysis Found (Cal)				λ_M Ohm^{-1} cm^2 mol^{-1}
				C	H	N	Mo	
HBAPA	Light Yellow	$C_{10}H_{11}O_3N$	193.20	62.19 (62.17)	5.78 (5.74)	7.26 (7.25)	----	----
Mo-HBAPA complex	Yellow	$MoO_2(C_{10}H_{10}O_3N)_2$	512.32	46.95 (46.89)	3.95 (3.93)	5.53 (5.47)	18.76 (18.73)	35

Conductance measurement

The molar conductivity measurement carried in 10-3 M DMF solution for the Mo-HBAPA complex was found to be 35 Ohm^{-1} cm^2 mol^{-1} which is much less than the value of 70-160 Ohm^{-1} cm^2 mol^{-1} obtained for 1:1 electrolyte in this solvent. Thus, it can be concluded that the complex in study is un dissociated which indicates the non-electrolytic nature of this complex.

Infrared Spectra

The structurally significant IR bands for free ligand and metal-ligand complex are reported in Table 2. The band at 1692 cm^{-1} observed in the IR spectra of free ligand can be attributed to ν(C=O) stretching vibration, whereas another band at 1625 cm^{-1} can be assigned to ν(C=N). The bands at 3422 and 3178 cm^{-1}in the free ligand is attributed to the free OH stretching of the carboxylic acid moiety and phenolic moiety [22]. In the complexes, the band due to phenolic OH vibrations disappeared, indicating deprotonation of the OH group and subsequent coordination of the oxygen to the metal ion. The band at 1625 cm^{-1} due to the ν(C=N) stretching vibrations of the ligand underwent a shift to lower frequency (1588 cm^{-1}) after complexation indicating the coordination of nitrogen to metal ion [23]. This suggestion is supported by the appearance of new bands at 526 cm^{-1} and 455 cm^{-1} which was taken as an indication of coordination between the metal ion and the oxygen and nitrogen, respectively [24].

Table 2: IR (cm^{-1}) and UV (nm) spectral data

Compound	ν(OH)	ν(C=O)	ν(C=N)	ν(Mo-N)	ν(Mo-O)	λ_{max}
HBAPA	3422, 3178	1692	1625	---	----	252, 281,360
Mo-HBAPA complex	3418	1685	1588	455	525	235, 321, 519

Electronic spectra

The electronic spectra of compounds were recorded using DMSO as solvent between 200-700nm at room temperature. Three bands observed in the region of 235-281 nm correspond to π-π* transition of phenyl rings. A broad band at 321-360nm may be due to n-π* transition of -C=N chromophore. It is well known that Schiff bases exhibit two peaks for π-π* transition which are very sharp at lower wavelength region, while n-π* band occurring between higher wavelength region is a broad band [21,22]. The absorption band of the Schiff base complex is slightly shifted to shorter wavelength (blue shift) when compared to those of free ligand indicating the coordination of metal with the ligand. In the electronic spectra of complex, a band at 243nm may be attributed to the presence of -C=N group and presence of an intense band at 519 nm in the complex can be assigned to a charge transfer (CT) transition.

Antimicrobial Study

The antimicrobial activity results (Table 3) reveal that the complex shows fairly good activity against all the tested bacterial strains, as compared to ligand or free metal ions. The higher activity of the metal complexes may be owing to the effect of metal ions on the normal cell membrane [25]. The antimicrobial activities are found to increase with increase in concentration of experimental solutions. Metal chelates bear polar and nonpolar properties together; this makes them suitable for permeation to the cells and tissues. In addition, chelation may enhance or suppress the biochemical potential of bioactive organic species. Further, lipophilicity, which controls the rate of entry of molecules into the cell, is modified by coordination, so the metal complex can become more active than the free ligand. Therefore, the metal complexes show greater antimicrobial activities than the uncoordinated ligand and free metal ion which in fact is in agreement with the literature [26]. These metal –ligand complex have an advantage in that the respective bioactivities of the uncoordinated ligands and metal ions are combined which could make them more potent antimicrobial agents.

Table 3: The in vitro antimicrobial activity of ligand, Mo (VI) complexes, and free-metal cations evaluated by minimum (MIC inhibitory concentration, µg/mL).

Compound	**Antibacterial activity** **Metal complexes (free-metal cations)**				**Antifungal activity** **Metal complexes (free-metal cations)**		
	S. aureus	**E. coli**	**P. aeruginosa**	**B. subtilis**	**A. niger**	**C. albicans**	**R. bataicola**
HBAPA	195	110	335	400	315	215	295
Mo-HBAPA complex	25(215)	15 (150)	20 (475)	15 (495)	10 (505)	10 (490)	30 (580)
Standard	5	5	10	5	10	10	5

CONCLUSION

In the present studies the synthesis and spectroscopic characterization of complex with a novel amino acid bidendate schiff base ligand derived from L-alanine and 2-hydroxybenzaldehyde (salicylaldehde) is reported. IR, UV-vis spectra, and magnetic measurements of the ligand and its metal complex confirmed the suggested coordination of the ligand through phenolic oxygen of -OH group, and nitrogen of the azomethine group as bidentate. The newly synthesized metal – ligand complex possesses better antibacterial activity. The process of chelation dominantly affects the biological activity of the complex that are potent against pathogens. Based on these facts, it could be proposed that this novel complex can be better accommodated for antimicrobial applications being more potent antimicrobial agent.

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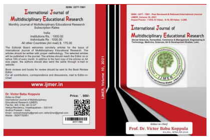

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