Investigation on Antimicrobial Activity of Nickel(II) and Zinc(II) Complexes with Schiff Base Derived from Aminoacid Valine With Citral: Synthesis, Spectroscopic Analysis

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Abstract — Ni(II) and Zn(II) metal complexes with Schiff base derived from Citral and Valine are synthesised and characterized on the basis of spectroscopic techniques (FT-IR, and UV-Visible) and magnetic susceptibility studies. The IR spectral data indicated that the Schiff base coordinated to central Ni(II) and Zn(II) ions in a bridged-tridentate and bidentate fashion respectively. Magnetic moment and spectral studies suggest distorted octahedral around the Ni(II) ion and tetrahedral geometry around Zn(II) ion. The preliminary antimicrobial activity has been evaluated against two Gram-negative bacteria; namely, Pseudomonas aeruginosa and Escherichia coli, one gram-positive bacteria Staphylococcus aureus, and antifungal activity are tested against Aspergillus sps and Candida albicans using disc diffusion method. The result revealed that Ni(II) complex exhibited potent activity when compared to Zn(II) complex and Schiff base.

Keywords — Schiff base, Citral, valine, metal complexes, antimicrobial activity.

I. INTRODUCTION

Development of novel pharmacologically active Schiff bases and their metal complexes attract the attention of medicinal chemist nowadays. Schiff base and its metal complexes are multifaceted compounds, exhibit a broad range of biological activities, for instance, antibacterial, antifungal, antimalarial, anti-inflammatory, antiviral, etc. [1],[2],[3]. Deep-rooted of transition metal ions to active biological Schiff bases afford new compounds which exhibit a considerable change in intrinsic chemical structure and biological activities, promoted a noteworthy interest in the study of their coordination behaviour [4]. The growing of the area of bioinorganic chemistry has been becoming greater interest in Schiff base transition metal complexes derived from aminoacids since a lot of these complexes exhibit substantial antimicrobial activity [5].

The newly synthesized compounds are screened for their antimicrobial activity.

II. MATERIALS AND METHODOLOGY

Materials

All the chemicals used in the preparation of Schiff base and their M(II) complexes were of analytical grade. Citral and Valine were purchased from Spectrochem, and M(II) nitrates were purchased from Merck, used as received without further purification. Ethanol, DMSO, Diethyl ether were used solvents, was of reagent grade.

Physical Measurements

Fourier transform infrared (FTIR) spectra of the new compounds were recorded in the spectral range 4000-500 cm⁻¹ on Perkin Elmer-spectrum one FT-IR Spectrometer. Electronic spectra were recorded using a Perkin Elmer Lambda-950 UV-VIS spectrometer using DMSO as a solvent in the range of 200-800 nm. Magnetic susceptibility measurements of complexes were carried out using Gouy balance at room temperature using Hg[Co(NCS)] as an internal reference.
Synthesis of Schiff base ligand
The ligand was synthesized by adding hot ethanolic solution of citral (10 ml, 0.5 mmol) to aqueous solution of valine (10 ml, 0.5 mmol) and refluxed for 2 hours at 60°C during which the color of the mixture turned to yellow-orange. The reaction mixture was further refluxed for 2 hours. The mixture was kept aside without shaking for overnight to afford the brownish red precipitate. The product obtained was repeatedly washed well with hot water and diethyl ether and dried in air.

Preparation of Metal(II) complexes
The M(II) complexes with above synthesized Schiff base ligand were prepared using an in-situ method by adding an aqueous of metal(II) nitrate (Ni²⁺ and Zn²⁺ 0.5 mmol, 10 ml) to the hot ethanolic solution of Schiff base and obtained mixture was continuously refluxed for 3 hours. On cooling the light green Ni(II) complex (1a) and dirty white Zn(II) complex (1b) was obtained, which was filtered off and washed well with ethanol, diethyl ether and dried in air.

Antimicrobial activity
The synthesized Schiff base ligand and its 1a and 1b complexes were screened for their antibacterial activity against Staphylococcus aureus (gram positive), Escherichia coli and Pseudomonas aeruginosa (gram negative) using streptomycin as standard drug and antifungal activity against Aspergillus sps and Candida albicans using fluconazole as standard drug using the agar diffusion method. The solvent DMSO is used for dissolving the samples to be tested. The bacterial strains were cultured in Mueller Hinton agar medium and made to spread over the sterilized Petri dish using a cotton swab. Further, the medium was allowed for solidification. The paper discs which impregnated with samples were allowed to dry at room temperature and DMSO impregnated disc was used as negative control. The prepared discs were incubated at 37°C for 24 hours under aseptic conditions. Anti-fungal activity was investigated using a modified Kirby Bauer disc diffusion method. The fungal species are spread on to the potato-dextrose agar plate. Precise discs of 6 mm were developed in medium, well sterilized and then impregnated the discs with the samples to be tested. Standard antibiotic and DMSO were acted as positive and negative control respectively. Plates were incubated at 37°C at room temperature for 3-4 days. Zones of inhibition (mm) formed by the synthesized compounds were measured at the end of the incubation period.

III. RESULTS AND DISCUSSION

INFRARED SPECTRAL STUDIES
The comparison of the IR spectra of Schiff base ligand and the complexes can render structural evidence for the mode of coordination of the ligand to the metal center, and their assignments are tabulated in Table1. The IR spectra of Schiff base ligand and its M(II) complexes are shown in Figure 1. In the FT-IR spectrum of Schiff base, the characteristic stretching frequency of the azomethine group, \( \nu(-C=N) \) has occurred at 1608 cm\(^{-1}\) and the \( \nu_{as}(COO^-) \) and \( \nu_{s}(COO^-) \) have appeared, respectively at 1587 and 1384 cm\(^{-1}\) [6]. The azomethine band \( \nu(-C=N) \) in Schiff base ligand on complexation, undergoes a considerable shift to higher frequencies values in 1a and 1b complexes (1628 and 1632 cm\(^{-1}\)) which indicates that the azomethine nitrogen is coordinated to the metal centers. The asymmetric carboxylate \( \nu_{as}(COO^-) \) is shifted to lower frequency region 1565 cm\(^{-1}\) and the symmetric carboxylate \( \nu_{s}(COO^-) \) is shifted to higher frequency region 1423 cm\(^{-1}\) [\( \Delta\nu=142 \text{ cm}^{-1} \)] in 1a, whereas 1b \( \nu_{as}(COO^-) \) shifted to higher 1581 cm\(^{-1}\) and \( \nu_{s}(COO^-) \) shifted to lower 1364 cm\(^{-1}\) [\( \Delta\nu=217 \text{ cm}^{-1} \)], indicating the linkage between the metal centers and carboxylato oxygen atom. The asymmetric \( \nu_{as}(COO^-) \) and symmetric \( \nu_{s}(COO^-) \) stretching frequencies of the carboxylate group in the 1a complex shows the separation value \( \Delta \nu=142 \text{ cm}^{-1} \) less than 200 cm\(^{-1}\), indicates the bridging coordination (Ni-O-C-O-Ni) between adjacent Ni(II) center and the other one shows greater than 200 cm\(^{-1}\) \( \Delta \nu \) value, indicates monodentate binding in 1b complex [7]. Furthermore, the presence of coordinated water molecules as evidenced by the broad band’s appeared at 3389–3415 cm\(^{-1}\) in complexes may be attributed to O–H stretching vibration. The IR spectra of the complexes show the bands appeared at 1456-1448 cm\(^{-1}\), 1322–1318 cm\(^{-1}\) and 960-957 cm\(^{-1}\), which can be ascribed to monodentate coordination of NO\(_3\) group. The appearance of new non-ligand bands at region 543-516 cm\(^{-1}\) and 449-417 cm\(^{-1}\) correspond to \( \nu(M-O) \) and \( \nu(M-N) \) vibrations, respectively [8]. The IR spectra confirm that the Schiff base ligand is acting as bridging ligand via carboxylate moiety thus indicates that Ni(II) complex is in dimeric/polymeric form. In 1b complex carboxylato oxygen atoms is acting as monodentate nature hence the complex is assigned to monomeric form. Furthermore, suggested that Ni(II) centers incorporated to Schiff base ligand through azomethine nitrogen, \( \mu^2 \) carboxylato oxygen atoms whereas in Zn(II) complex ligand coordinated to central metal ion via azomethine nitrogen and carboxylato oxygen atom [9]. Water molecules would complete the other positions in the coordination sphere.

| Compounds | \( \nu(C=N) \) | COO⁻ | O-NO₂ | \( \nu(H_2O) \) | N→M | O→M |
|-----------|---------------|------|-------|-----------------|------|------|
| \( \nu_{as} \) | \( \nu_{s} \) | \( \nu (\Delta) \) | \( \nu_{as} \) | \( \nu_{s} \) |

Table 1: IR spectral assignments (cm\(^{-1}\)) of Ni(II) and Zn(II) complexes with SB
Magnetic moment and electronic spectral studies

The information regarding the geometry of the complexes is obtained from their electronic spectral data and magnetic moments. The electronic absorption regions, assignments, and magnetic moment data are given in Table 2. The electronic spectra of Schiff base ligand and its M(II) complexes are shown in Figure 2 and 3.

The observed magnetic moment value of the 1a complex at 300 K is 1.7 B.M, which is lower than the expected spin-only value of 2.8 B.M for the octahedral Ni(II) complexes. The very low magnetic moment value indicates the strong antiferromagnetic interaction between two Ni ions. Further, the presence of Ni-O-C-O-Ni fragment in the complex is supported by IR spectra. The electronic spectrum of 1a displays the band at 301 nm is assignable to n-π* transition associated with azomethine coordination to the central metal ion. The band at 659 nm may be assignable to 3A2g(F) → 3T1g(F) d-d transition. The bands displayed at 733 and 751 nm assignable to 3A2g→Eg spin-forbidden transitions. Based on the above observations, distorted octahedral geometry has been predicted for the complex [10].

The electronic spectra of 1b complex showed two bands around 294, and 449 nm is attributed to the n-π* and charge transfer transitions respectively. Generally, Zn(II) complexes are in d10 configuration, diamagnetic and do not show any d-d transitions. Taking into account of the appearance of charge transfer transition around 449 nm in the electronic spectrum of 1b, and based on the configuration of the Zn(II) center, a tetrahedral geometry has been proposed for the complex [11].

Table 2. Electronic spectral (nm) and magnetic moment (B.M) assignments of Ni(II) and Zn(II) complexes with SB

| Compounds | Colour | Electronic absorption bands and their assignments (nm) | Magnetic moment B.M at room temp |
|-----------|--------|--------------------------------------------------------|----------------------------------|
| SB        | Brownish red | n-π*, LMCT                                                | -                                |
| 1a        | Light green   | 313, -                                                  | 1.7                              |
| 1b        | Dirty white   | 294, 449                                                | -eramic                          |
Antimicrobial Activity

The antibacterial screening of the Schiff base and its complexes (10 mg/ml) are carried out against two Gram-negative bacteria, namely, *Pseudomonas aeroginosa* and *Escherichia coli*, one gram-positive bacteria *Staphylococcus aurous*, and antifungal activity is tested against *Aspergillus sps* and *Candida albicans* using disc diffusion method using Streptomycin (standard for bacterial strains) and fluconazole (standard for fungal strains) as positive control. The noteworthy 1b complex is not screened for *Pseudomonas aeroginosa* (gram-negative), and the growth inhibitory action of ligand and its metal complexes are reported in Table 3. Zone of inhibition recorded by the Schiff base and its metal complexes are shown in Figure 4 and represented as graph in Figure 5. The metal complexes are found to be manifest more activity than the free ligand. The 1a complex displays good inhibition activity against *Staphylococcus aurous* and *Candida albicans*, moderate activity against *Escherichia coli* and *Pseudomonas aeroginosa*. But 1b complex revealed only moderate activity against *Escherichia coli* and *Aspergillus sps*. The bioactivity of the ligand and its complexes are found to be in the following order: Ni(II) > Zn(II) > SB. Generally, the biological activity of M(II) complexes is influenced by many factors, especially the geometric structure of the complexes. Based on spectral assignments, the structures of the complexes are proposed as bridged geometrical arrangement (1a) and monomeric geometrical arrangement (1b). Hence bridged geometric structure arrangement of 1a complex might be the reason for the enhanced antimicrobial activity, and the low activity of 1b complex might be owing to low lipophilicity behavior i.e., the 1b complex is not well enough to penetrate through the outer membrane layer over the cells of the screened microorganisms [12],[13],[14],[15],[16].

Table 3: Effect of Schiff base and its Metal(II) complexes on the growth of pathogens (mm)

| Culture                  | SB | 1a | 1b |
|--------------------------|----|----|----|
| *Escherichia coli* (G-)  | +  | ++ | ++ |
| *Staphylococcus aureus* (G-) | +  | ++ | +  |
| *Pseudomonas aeroginosa* (G+) | +  | +++| x  |
| *Candida albicans*       | +  | +++| +  |
| *Aspergillus sps*        | +  | + | ++ |

- 15 and above =++, 14-10= ++, >10 =+, x= not analysed
• SB = schiff base ligand, 1a = Ni(II) complex, 1b = Zn(II) complex

**IV. CONCLUSION**

Ni(II) and Zn(II) complexes of the Schiff base ligand derived from citral and valine were synthesized and characterized via FT-IR, UV-Vis and magnetic susceptibility studies. The FT-IR spectra demonstrate that the Schiff base ligand coordinated in bridged-tridentate (azomethine nitrogen, μ²-carboxylato oxygen atoms) and bidentate (azomethine nitrogen, carboxylato oxygen atoms) fashion around Ni(II) and Zn(II) centers respectively. The structure has been proposed as distorted octahedral and tetrahedral for Ni(II) and Zn(II) complexes based on electronic spectra. Magnetic moment studies disclosed that Ni(II) complex is bridged between the Ni(II) center with anti-ferromagnetic interaction and Zn(II) complex are diamagnetic in nature. The antimicrobial activity of the ligand and its complexes indicates that the Ni(II) complex possesses potent antimicrobial activity than Zn(II) complex and parent ligand. The bridged structural arrangement of Ni(II) complex has been proposed as the reason for the enhanced antimicrobial activity.

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