Synthesis, Spectroscopic Characterization, Thermal Analysis and Biological Studies of Hydrazine Schiff Base and its Co(II), Cu(II), Th(IV) and Zr(IV) Metals Complexes

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Abstract

The new bidentate Schiff base ligand (E)-N-(4-hydroxy-3-(1-(2-isonicotinoylhydrazono)ethyl)phenyl)acetamide (LH) and its Cu(II), Co(II), Th(IV) and Zr(IV) complexes have been synthesized by the conventional method. Compounds have been characterized by elemental analysis, IR, FAB-Mass, molar conductivities, magnetic measurements, electronic spectra, ESR and thermal analysis. Analytical data suggested 1:2 (metal: ligand) mole ratio for all the complexes. The low molar conductance values of the metal complexes in DMSO reveal their non-electrolytic nature. From the observed data of magnetic moment and electronic spectra, the six coordinated structures for all the complexes, have been proposed. The thermodynamic analysis shows that the complexes lose hydrated and/or coordinated water molecules in the first step; followed by decomposition of ligand moiety in the further steps leading to formation of stable oxide. The antibacterial screening results also indicate that the metal complexes are good antibacterial agents as compared to the Schiff base.

Keywords: Isonicotinoyl hydrazine, Schiff base, Electronic Spectra, ESR, Thermal analyses, Antibacterial activity.

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INTRODUCTION

In the Schiff base family, hydrazones constitute an important class as they contain strong donor sites, stability and flexibility [1, 2]. Azomethine linkage in hydrazones plays a crucial role towards the biological activities such as antimicrobial, anti-convulsant, anticancer, antioxidant, antilgycation, antidepressant, anthelmintic and analgesic activities [3, 4]. It is evident that, the biological activity of the hydrazine is deviated by its coordination with metal ions via azomethine Nitrogen and other donor atoms [5]. Isoniazide is potent antitubercular agent [6], 4-acetamidophenol (paracetamol) is an analgesic and antipyretic drug [7] and derivatives of 4-acetamidophenol possess promising antibacterial, antifungal and antitubercular activity [8]. One of its derivatives, 3-acetyl-4-hydroxyphenyl acetamide is found to be functional starting material for the synthesis of a wide variety of hydrazine ligands. However, no work has been reported on the synthesis of transition metal complexes of hydrazine, an asymmetrical Schiff base, derived from isonicotinoyl hydrazide and 3-acetyl-4-hydroxyphenyl acetamide. Promoted by these facts, in this paper, the synthesis and characterization of complexes of Cu (II), Co (II), Th(IV) and Zr(IV) with newly synthesized hydrazine have been carried out. The thermal analysis and antibacterial activities of newly synthesized compounds have also been reported.
**Experimental Section**

**Materials**

The acetate salts of Co (II) and Cu (II), the nitrate salt of Th(IV) and oxychloride salt of Zr(IV) were used in the synthesis of the complexes. All the chemicals and reagents used in this work were of analytical grade (Aldrich), used without further purification. The solvents were of analytical grade and purified by standard methods.

**Analytical and Physical measurements**

The elemental analyses (C, H and N) were performed at Sophisticated Analytical Instrument Facility, Chandigarh. The IR spectra of the compounds were recorded in KBr pellets in the 4000-400 cm⁻¹ on a Perkin-Elmer spectrophotometer (L1280032). The electronic spectra (DMF) of the ligand and complexes were recorded on a Shimadzu (UV-1800 Series) UV/Vis spectrophotometer in the region 200-800 nm. Room temperature molar conductance of the complexes (DMF) were determined in DMSO using solution of about 10⁻² M on the Equip-Tronic conductivity meter. ¹H NMR spectrum of the ligand was recorded in DMSO-d₆ solution on a Bruker 300-FT-NMR spectrophotometer. ESR spectra (RT and LNT) were recorded on a JES - FA200 ESR Spectrometer at IIT, Mumbai. The magnetic susceptibility values of the complexes were recorded at room temperature by the Gouy method. Thermal analysis results of the complexes were obtained at a rate of 10°C per minute on a Rijaku-Thermo plus EVO2 thermodilatometer.

**Synthesis of the Schiff base (LH)**

N-(3-acetyl-4-hydroxyphenyl)acetamide was prepared by the method reported earlier [8]. The mixture of isonicotinoyl hydrazide (0.01mole, 1.37g) with N-(3-acetyl-4-hydroxyphenyl)acetamide (0.01mol, 1.93g) (1:1 ratio) in absolute ethanol was heated under reflux for 2 h as shown in scheme 1. The reaction mixture then allowed for cooling to room temperature for half an hour. A yellow precipitate of (E)-N-(4-hydroxy-3-(1-(2-isonicotinoylhydrazono)ethyl)phenyl)-acetamide (LH) was formed, which was filtered, washed with cold distilled water, and dried under vacuum (Yield 72%).

**Synthesis of metal complexes**

All the complexes were prepared by mixing equimolar quantities (0.002 mol) of LH, in ethanol, and ethanolic solution of the acetate salt of Cu(II) or Co(II); the nitrate salt of Th(IV). The Zr(VI) complex was prepared by earlier reported method [9]. The above mixtures were refluxed separately for about 4-6 h. The solid products obtained on cooling were filtered off, washed thoroughly with ethanol and finally with petroleum ether and dried under vacuum over CaCl₂. (Yield 52-65%).

**Test Organisms and Determination of Zone of Inhibition**

In the disc diffusion test sterile Whatman filter paper disc were impregnated with 20µl of different samples. The test organism’s cultures of *Escherichia coli* (ATCC 14948), *Staphylococcus aureus* (ATCC 33591), *Staphylococcus epidermis* (MTCC 3086), *Klebsiella pneumonia* (MTCC 4030) were obtained from the microbial bank of the HiMedia laboratories Pvt. Ltd. Mumbai, Maharashtra, India. The bacterial isolates were standardized by colony suspension and matching the strain’s suspension with 0.5 McFarland standard to give a final concentration of 1.5 x 10⁸cfu/mL. The culture of each of the respective organism was spread on the surface of sterile Mueller Hinton Agar plates. The impregnated discs with respective samples were then placed on the inoculated surface of the agar plates. The agar plates were incubated at 37°C for 24h. Antibacterial activity of each sample against the test species was measured by growth free “zone of inhibition” near the respective spots [10]. The assay was performed in triplicate.

**Results and Discussion**

Scheme 1 shows the condensation of isonicotinoyl hydrazide with N-(3-acetyl-4-hydroxyphenyl)acetamide (1:1) in ethanol yields the Schiff base ligand (LH). All the complexes derived from LH are colored and non-hygrosopic solids and are stable in air. They are insoluble in water, but soluble in coordinating solvents like DMF and DMSO. The molar conductance values of the complexes in DMF...
(10⁻³M) are very low (3.7-11.5 Ω⁻¹ cm²mol⁻¹) indicating their non-electrolytic nature. The analytical and physical data of the ligand and its complexes are given in Table 1. The analytical data of all the complexes suggested 1:2 (metal: ligand) stoichiometry. The FAB mass spectra of the ligand and the complexes were recorded. All the spectra exhibited parent peaks due to molecular ions (M+). The proposed molecular formulae of these complexes were confirmed by comparing their molecular formula weights with the m/z values. The molecular ion peaks obtained were as follows: m/z 312 (ligand), 717 (Co (II) complex), 770 (Cu(II) complex), 982 (Th(IV) complex) and 723 (Zr(IV)complex). These data are in good agreement with the proposed molecular formula for these complexes. In addition to the molecular ion peaks, the spectra exhibited different peaks assignable to various fragments arising from the thermal cleavage of the complexes.

| Compound       | Color      | Molar cond.  | Yield (%) | % Found (calcd.) | % Found (calcd.) | % Found (calcd.) | % Found (calcd.) | Formula Weight |
|----------------|------------|--------------|-----------|-----------------|-----------------|-----------------|-----------------|----------------|
| LH             | Light Yellow | -            | 72        | 61.48           | 17.96           | 5.21            | 312             |
| [CoL₂(H₂O)₂]   | Dark Brown  | 11.50        | 63        | 53.51           | 15.60           | 4.75            | 8.18            | 718            |
| [CuL₂(H₂O)₂]·3H₂O | Green      | 3.71         | 65        | 49.50           | 14.43           | 3.16            | 8.16            | 777            |
| [ThL₂(NO₃)₂]   | Off White   | 7.20         | 54        | 39.29           | 14.30           | 3.05            | 23.68           | 978            |
| [Zr(OH)₂L₂]   | Cream       | 4.80         | 52        | 51.31           | 14.87           | 4.35            | 12.15           | 747            |

³H NMR spectrum of the compounds

The ¹H NMR spectrum of ligand shows signals at 9.73 ppm corresponding to proton of phenolic OH. The signals observed at 9.51 ppm and 3.36 ppm may be due to the NH, and (6H) methyl protons respectively. The aromatic protons showed signals in the range 6.93-7.87 ppm as shown in figure 1.

**IR spectra**

To study the binding modes of ligand toward metal ion, IR spectral data of the ligand was compared with those of respective metal complexes (Table 2). The IR spectrum of the free ligand shows a band at 2981 cm⁻¹ due to intramolecular hydrogen bonded hydroxyl group. Absence of this band in the spectra of all the metal complexes evidences subsequent deprotonation of the phenolic group and coordination of phenolic Oxygen to the metal ion [11]. The band at 1274 cm⁻¹ due to v(C-O phenolic) band shifted to upward frequency by 26-37 cm⁻¹, confirms the coordination of ligand through phenolic Oxygen [12-14]. The v(C=N) band of the ligand at 1622 cm⁻¹ is found to be shifted to lower energies by 10-30 cm⁻¹ in the spectra of all the complexes, indicating the coordination via the azomethine Nitrogen[15]. This coordination is further supported by the shift of v (N-N) vibration observed at 964 cm⁻¹ in the ligand shifted to a higher frequency by...
44-57 cm⁻¹ in the complexes [16]. In the IR spectra of Cu (II) and Co (II) complexes, a considerable band observed at 3433 and 3438 cm⁻¹ may be attributed to the vibration of water molecules coordinated to the metal ions [17]. The ν(N-H) and ν(C=O) bands of the ligand at 3169 and 1656 cm⁻¹ respectively, remain almost unaffected after complexation in all the complexes, suggest that ligand exist in keto form in free state as well as in all the complexes [18, 19]. In the spectrum of Th(IV) complex, two additional medium intensity bands are observed around 1050 and 1390 cm⁻¹ that are assigned to ν₁ and ν₃ vibrations of nitrate groups coordinated with the metal ion. The coordinated ligand moieties and two nitrate groups imparting coordination number six for Th(IV) complex. The spectra of Zr(IV) complex show new band at 1105 cm⁻¹ due to ν(Zr(OH)₃) vibration [20]. The far IR spectra of the complexes shows new bands in the region 476-455 cm⁻¹ and 516-503 cm⁻¹, corresponding to ν(M-N) and ν(M-O) vibrations respectively [21]. From the above IR spectral data of all the complexes, it is evident that the ligand in the present work behaves as monobasic bidentate ON donor, coordinating through azomethine Nitrogen and the deprotonated Oxygen atom.

Table-2: Infrared frequencies (cm⁻¹) of the ligand LH and its metal complexes

| Compound                  | H bonded-OH stretching | ν(N-H) | Coordinated water ν(OH) | ν(C=O) | ν(C=O) phenolic | ν(N-O) | ν(M-O) | ν(M-N) |
|---------------------------|------------------------|--------|-------------------------|--------|----------------|--------|--------|--------|
| LH                        | 2981                   | 3169   | -                       | 1622   | 1274           | 974    | -      | -      |
| [CoL₂(H₂O)₃]             | -                      | 3155   | 3438                    | 1592   | 1311           | 1018   | 516    | 476    |
| [CuL₂(H₂O)₃]·3H₂O         | -                      | 3142   | 3433                    | 1605   | 1301           | 1025   | 503    | 455    |
| [ThL₂(NO₃)₃]             | -                      | 3164   | -                       | 1603   | 1300           | 1028   | 509    | 482    |
| [Zr(OH)₂L₂]              | -                      | 3163   | -                       | 1612   | 1303           | 1031   | 516    | 455    |

Electronic absorption spectra and magnetic moments

The electronic absorption spectra data and magnetic moments of the metal complexes are listed in Table-3. The electronic spectrum of the Co(II) complex exhibits two bands at 460 and 625 nm assigned to ¹T₁g → ⁴A₂g(F) and ⁴T₁g(F)→¹T₂g(P) transitions respectively. These bands significantly suggest octahedral geometry for Co (II) complex [22]. The measured magnetic moment at 4.23 B.M. also supports the expected high spin octahedral geometry for Co (II) ion [23]. The electronic spectrum of the Cu (II) complex shows the first band at 580 nm assigned to the ²E_g→²T₂g transition which suggests a distorted octahedral arrangement around the metal ion [24]. The distortion may be due to the Jahn Teller effect since the transition indicates the further splitting of both ²E_g and ²T₂g due to deviation of symmetry from 0ₖ to D₄h symmetry. The ESR spectrum of Cu (II) complex (Figure 2) supports the absence of any metal-metal interaction with the neighboring molecules, also confirmed by magnetic moment 1.76 B.M. [25]. Th(IV) complex in DMF solution gave no significant bands in the 350–750 nm region. The absorption bands obtained below 330 nm correspond to the ligand π→π* transitions and are not much helpful in determining the geometry of Th(IV) complex [26]. The UV spectrum of the diamagnetic Th(IV) complex in DMSO showed absorption bands at 325 and 470 nm respectively [27, 28] may be due to π→π* transition of ligand and charge transfer transitions of ligand to metal respectively. The electronic spectrum of Zr(IV) chelate displays two absorption bands at 270 and 355 nm due to charge transfer transition [29, 30]. The magnetic susceptibility measurements reveal the both Th(IV) and Zr(IV) complexes are diamagnetic as expected.

Table-3: Electronic and magnetic data of LH and its complexes

| Compound                  | ν(nm) | d-d transition | μ₄µ(B.M.) |
|---------------------------|-------|----------------|-----------|
| LH                        | 357   | n→π           | -         |
|                           | 298   | π→π*          | -         |
| [CoL₂(H₂O)₃]             | 625   | ¹T₁g→³A₂g(F)  | 4.62      |
|                           | 480   | ⁴T₁g(F)→¹T₂g(P) |          |
| [CuL₂(H₂O)₃]·3H₂O         | 580   | ²E_g→²T₂g     | 1.65      |
| [ThL₂(NO₃)₃]             | 480   | LMCT          | Diamagnetic |
| [Zr(OH)₂L₂]              | 270, 355 | LMCT     | Diamagnetic |

ESR Spectra

X-Band ESR spectra of Copper (II) complex were recorded at 299 K (solid state) and at 77 K (DMF) (Figure 2 and 3). The spectral parameters are summarized in Table 4. It exhibits an axially symmetric g-tensor parameters with g₉ = 2.27 > g₁ = 2.06 > 2.0023. The g values reflect tetragonally distorted octahedral geometry for Cu (II) center with the presence of d₉2, 2 ground state[31-32]. The tetragonally distorted octahedral geometry of complex is supported from an index of tetragonal distortion, empirical factor f ≈ g₉/g₁ cm⁻¹ was found to be 155 cm⁻¹ [33]. For a covalent complex, g₉ < 2.3, and for the ionic environment, normally g₉=2.3 or more. For present Cu complex, g₉ >
2.3 (i.e. 2.27 in solid-state) indicating covalent nature of M-L bond in this complex. In axial symmetry the g-values are related to the G-factor by the expression, \( G = g_\parallel - 2.002 / g_\perp - 2.002 = 4 \) which measures the exchange interaction between Copper centers in the solid complex [34]. According to Hathaway, if the value of \( G \) is greater than 4, the exchange interaction between Copper (II) centers in the solid state is negligible [35]. The calculated \( G = 4.37 \) supports the absence of exchange coupling between Copper (II) centers in the solid state.

### Table 4: ESR data of Cu (II) Complex

| Complex           | \( g_\parallel \) | \( g_\perp \) | \( |g| \) | Hyperfine contents x \( 10^{-4} \) cm\(^{-1} \) |
|-------------------|-------------------|----------------|--------|---------------------------------------------|
| Cu RT (Powder)    | 2.273             | 2.064          | 2.13   | 166.5                                      |
| Cu LNT (DMF)      | 2.575             | 2.025          | 2.20   | 19.0                                        |

**Fig-2: ESR spectrum of Cu (II) complex (RT)**

**Fig-3: ESR spectrum of Cu (II) complex (LNT)**

**Thermal analysis**

Thermal decomposition of metal complexes is an important study as it provides useful information about the thermal stability of complexes as well as the coordination ability of water whether it is inside the coordination sphere or outside. The half decomposition temperature, Entropy Change (\( \Delta S \)), Free Energy Change (\( \Delta F \)) and Frequency Factor (\( Z \)) of compounds were calculated by employing Freemann Carroll and Sharp Wentworth method [36-38]. The thermal curves of ligand and complexes were obtained with heating rate 10\(^{\circ}\) C min\(^{-1}\) are provided in Figure 4, while the kinetic parameters are assigned in Table 5. The ligand shows two-step decomposition pattern with the lowest half decomposition temperature. The Th(IV) and Zr(IV) complexes indicate a two-stage decomposition pattern whereas Co(II) and Cu(II) complex shows a three-stage decomposition pattern. The Cu (II) complex shows the elimination of three lattice water molecules up to 120\(^{\circ}\)C indicates the presence of non-coordinated water molecules in the complexes. On the other hand, Co(II) and Cu(II) complexes exhibit loss of two water molecule between 150-220\(^{\circ}\)C which indicates the presence of coordinated water molecules in the complexes. [\% wt. loss, obs./calcd.] Cu (II): 6.66/6.95 for lattice water while Co (II): 5.37/5.01 and Cu(II): 4.97/4.63; for coordinated water. In the TG curve of Th(IV) and Zr(IV) complexes, there is no
weight loss up to 220°C and this rules out the presence of any water molecule. Further weight loss was been observed above 250°C, which may be due to the thermal degradation of the free part of the ligand moiety along with some other side chain present in the complexes. A gradual weight loss observed above 440°C, due to the degradation of the actual coordination part of the ligand and TG curves attain a horizontal level above 580°C suggesting the formation respective stable metal oxides. From the half decomposition temperature, the relative thermal stability of the compounds is found to be Co (II)>Th(IV)>Cu(II)>Zr(IV) > LH.

![Fig-4: Thermal graph of LH and metal complexes.](image)

**Table-5: Thermal analysis data of metal complexes**

| Compound          | Half Decomposition Temp (°C) | Ea(kj/mole) | ΔS (J/mol/K) | ΔF (kJ/mol) | Z (S⁻¹) | S* (kJ) | n   |
|-------------------|------------------------------|-------------|---------------|-------------|---------|---------|-----|
| LH                | 290                          | 14.30       | 14.81         | -305.64     | 92.62   | 156.2   | 0.93|
| [CoL₂(H₂O)₂]      | 470                          | 13.46       | 13.65         | -340.61     | 103.22  | 126.75  | 0.96|
| [CuL₂(H₂O)₂].3H₂O | 430                          | 14.83       | 14.37         | -324.48     | 98.33   | 143.86  | 0.93|
| [ThL₂(NO₃)₂]      | 460                          | 24.24       | 22.74         | -282.11     | 85.50   | 168.34  | 0.95|
| [Zr(OH)₂L₂]       | 355                          | 23.20       | 21.66         | -315.02     | 95.47   | 187.32  | 0.91|

**Antibacterial Activity**

The antibacterial activity results presented in Table 6, show that the newly synthesized compounds possess moderate to good biological activity. These new derivatives obtained by condensation of the isonicotinoyl hydrazide and 3-acetyl-4-hydroxyphenyl acetamide were screened for their antibacterial activity against *E. coli*, *K. pneumonia* *S. aureus* and *S. epidermis* by disc diffusion method. The Co (II), Cu (II) and Th(IV) complexes exhibit good bactericidal activity against all the microbes. In general, the results reveal that, the biological activity of the ligand was found to be enhanced on complexation with metal ions. According to the chelation theory, the polarity of central metal atom descends because of the complexation, which results in ascending lipophilic nature of the central atom and enhanced permeation of the complexes through the lipid layer of the cell membrane [39, 40]. Due to complexation, metal complexes show enhanced antibacterial activity as compared to the LH against the same microorganism under identical experimental conditions.

**Table-6: Antibacterial activity of the ligand LH and its metal complexes**

| No. | Compound          | E. coli (ATCC 14948) | S. aureus (ATCC 33591) | S. epidermis (MTCC 3086) | K. pneumonia (MTCC 4030) |
|-----|-------------------|-----------------------|------------------------|--------------------------|--------------------------|
| 1   | LH                | 10                    | 11                     | 09                       | 10                       |
| 2   | [CoL₂(H₂O)₂]      | 19                    | 16                     | 21                       | 20                       |
| 3   | [CuL₂(H₂O)₂].3H₂O | 16                    | 14                     | 18                       | 16                       |
| 4   | [ThL₂(NO₃)₂]      | 15                    | 14                     | 13                       | 15                       |
| 5   | [Zr(OH)₂L₂]       | R                     | R                      | R                        | 12                       |

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CONCLUSION

The Schiff base, (E)-N-(4-hydroxy-3-(1-(2-isonicotinoylhydrazono)ethyl)phenyl)acetamide coordinates to the Co(II), Cu(II), Th(IV) and Zr(IV) metal ions (1:2 mole ratio) as a monobasic bidentate ligand using the azomethine Nitrogen and phenolic Oxygen donor atoms. Based on the analytical, conductance, thermal, spectral and magnetic moment’s data, the assignment of octahedral geometry has been corroborated for Co (II) and Cu (II) complexes. The calculated spin Hamiltonian parameters from the ESR spectra of complex confirmed the distorted octahedral geometry for the mononuclear Cu (II) complex. Absence of lattice and coordinated water molecules was confirmed from the thermograms of both Th(IV) and Zr(IV) complexes. The activation energy calculated by the Freemann-Caroll and Sharp-Wentworth methods are in good agreement with each other. Based on chelation theory, the enhanced biological activity of the complexes over the ligand was observed. The probable structures of complexes are shown below, Figure 5.

Conflict of Interest

The authors declare that they have no conflict of interest.

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