

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

Prashant R. Mandlik^{1*}, Pratik K. Deshmukh²

¹Assistant Professor, ²Research Student, Department of Chemistry, Shri Shivaji Science College, Amravati 444603, Maharashtra, India

DOI: [10.36348/sjmpps.2020.v06i12.002](https://doi.org/10.36348/sjmpps.2020.v06i12.002)

| Received: 28.11.2020 | Accepted: 06.12.2020 | Published: 13.12.2020

*Corresponding author: Prashant R. Mandlik

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.

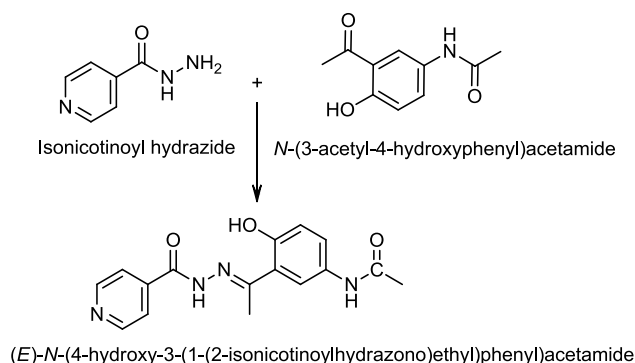
Keywords: Isonicotinoyl hydrazone, Schiff base, Electronic Spectra, ESR, Thermal analyses, Antibacterial activity.

Copyright © 2020 The Author(s): This is an open-access article distributed under the terms of the Creative Commons Attribution 4.0 International License (CC BY-NC 4.0) which permits unrestricted use, distribution, and reproduction in any medium for non-commercial use provided the original author and source are credited.

INTRODUCTION

In the Schiff base family, hydrazones constitute an important class as they contain strong donor sites, stability and flexidentacity [1, 2]. Azomethine linkage in hydrazones plays a crucial role towards the biological activities such as antimicrobial, anti-convulsant, antitubercular, anticancer, antioxidant, antiglycation, antidepressant, anthelmintic and analgesic activities [3, 4]. It is evident that, the biological activity of the hydrazone 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 hydrazone ligands. However, no work has been reported on the synthesis of transition metal complexes of hydrazone, 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 hydrazone have been carried out. The thermal analysis and antibacterial activities of newly synthesized compounds have also been reported.



Scheme 1: Synthesis of the Schiff base ligand.

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^{-3} M on the Equip-Tronic conductivity meter. ^1H NMR spectrum of the ligand was recorded in DMSO- d_6 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 10^0C 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 (0.01 mole, 1.37g) with N-(3-acetyl-4-hydroxyphenyl)acetamide (0.01 mol, 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 CaCl_2 . (Yield 52-65%).

Test Organisms and Determination of Zone of Inhibition

In the disc diffusion test sterile Whatman filter paper disc were impregnated with 20 μl 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 $1.5 \times 10^8 \text{cfu/mL}$. 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 37^0C 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-hygroscopic 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^{-3}M) are very low ($3.7\text{-}11.5 \Omega^{-1} \text{cm}^2 \text{mol}^{-1}$) 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.

Table-1: The analytical and physical data of the compounds

Compound	Color	Molar cond. ($\Omega^{-1} \text{cm}^2 \text{mol}^{-1}$)	Yield (%)	%Found (calcd.)				Formula Weight
				C %	N %	H %	M %	
LH	Light Yellow	-	72	61.48 (61.53)	17.96 (17.94)	5.21 (5.16)	-	312
$[\text{CoL}_2(\text{H}_2\text{O})_2]$	Dark Brown	11.50	63	53.51 (53.56)	15.60 (15.62)	4.75 (4.78)	8.18 (8.21)	718
$[\text{CuL}_2(\text{H}_2\text{O})_2] \cdot 3\text{H}_2\text{O}$	Green	3.71	65	49.50 (49.51)	14.43 (14.44)	5.16 (5.19)	8.16 (8.19)	777
$[\text{ThL}_2(\text{NO}_3)_2]$	Off White	7.20	54	39.29 (39.27)	14.30 (14.31)	3.05 (3.09)	23.68 (23.71)	978
$[\text{Zr}(\text{OH})_2\text{L}_2]$	Cream	4.80	52	51.31 (51.39)	14.87 (14.98)	4.35 (4.31)	12.15 (12.20)	747

^1H NMR spectrum of ligand

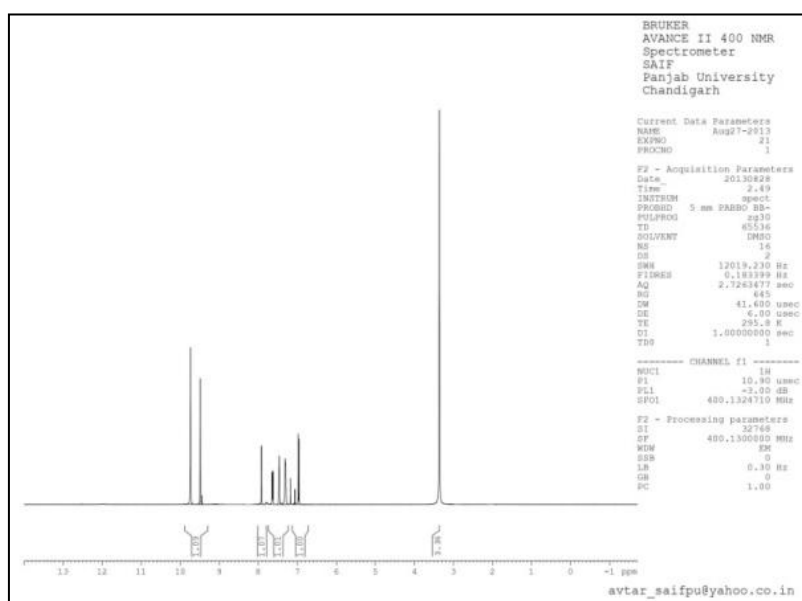


Fig-1: ^1H NMR spectrum of LH Ligand.

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 2981cm^{-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 1274cm^{-1} due to $\nu(\text{C-O}$ phenolic) band shifted to upward frequency by $26\text{-}37 \text{cm}^{-1}$, confirms the coordination of ligand through phenolic Oxygen [12-14]. The $\nu(\text{C=N})$ band of the ligand at 1622cm^{-1} is found to be shifted to lower energies by $10\text{-}30 \text{cm}^{-1}$ in the spectra of all the complexes, indicating the coordination via the azomethine Nitrogen[15]. This coordination is further supported by the shift of $\nu(\text{N-N})$ vibration observed at 964cm^{-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 3438cm^{-1} may be attributed to the vibration of water molecules coordinated to the metal ions. [17]. The $\nu(\text{N-H})$ and $\nu(\text{C=O})$ bands of the ligand at 3169 and 1656cm^{-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 1390cm^{-1} that are assigned to ν_1 and ν_3 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 1105cm^{-1} due to $\nu(\text{Zr}(\text{OH})_2)$ vibration [20]. The far IR spectra of the complexes shows new bands in the region $476\text{-}455\text{cm}^{-1}$ and $516\text{-}503\text{cm}^{-1}$, corresponding to $\nu(\text{M-N})$ and $\nu(\text{M-O})$ 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	$\nu(\text{N-H})$	Coordinated water $\nu(\text{OH})$	$\nu(\text{C=N})$	$\nu(\text{C-O})$ phenolic	$\nu(\text{N-N})$	$\nu(\text{M-O})$	$\nu(\text{M-N})$
LH	2981	3169	-	1622	1274	974	-	-
$[\text{CoL}_2(\text{H}_2\text{O})_2]$	-	3155	3438	1592	1311	1018	516	476
$[\text{CuL}_2(\text{H}_2\text{O})_2].3\text{H}_2\text{O}$	-	3142	3433	1605	1301	1025	503	455
$[\text{ThL}_2(\text{NO}_3)_2]$	-	3164	-	1603	1300	1028	509	482
$[\text{Zr}(\text{OH})_2\text{L}_2]$	-	3163	-	1612	1303	1031	516	455

Electronic absorption spectra and magnetic moments

The electronic absorption spectral 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 ${}^4\text{T}_{1g} \rightarrow {}^4\text{A}_{2g}(\text{F})$ and ${}^4\text{T}_{1g}(\text{F}) \rightarrow {}^4\text{T}_{1g}(\text{P})$ 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 ${}^2\text{E}_g \rightarrow {}^2\text{T}_{2g}$ 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 ${}^2\text{E}_g$ and ${}^2\text{T}_{2g}$ due to deviation of symmetry from O_h to

D_{4h} 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 $\pi \rightarrow \pi^*$ 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 $\pi \rightarrow \pi^*$ 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	$\nu(\text{nm})$	d-d transition	$\mu_{\text{eff}}(\text{B.M.})$
LH	357 298	$n \rightarrow \pi^*$ $\pi \rightarrow \pi^*$	-
$[\text{CoL}_2(\text{H}_2\text{O})_2]$	625 480	${}^4\text{T}_{1g} \rightarrow {}^4\text{A}_{2g}(\text{F})$ ${}^4\text{T}_{1g}(\text{F}) \rightarrow {}^4\text{T}_{1g}(\text{P})$	4.62
$[\text{CuL}_2(\text{H}_2\text{O})_2].3\text{H}_2\text{O}$	580	${}^2\text{E}_g \rightarrow {}^2\text{T}_{2g}$	1.65
$[\text{ThL}_2(\text{NO}_3)_2]$	480	LMCT	Diamagnetic
$[\text{Zr}(\text{OH})_2\text{L}_2]$	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 $g_{\parallel} = 2.27 > g_{\perp} = 2.06 > 2.0023$. The g values reflect tetragonally distorted octahedral

geometry for Cu (II) center with the presence of $d_{x^2-y^2}$ ground state[31-32]. The tetragonally distorted octahedral geometry of complex is supported from an index of tetragonal distortion, empirical factor $f = g_{\parallel}/A_{\parallel}$ cm^{-1} was found to be 155cm^{-1} [33]. For a covalent complex, $g_{\parallel} < 2.3$, and for the ionic environment, normally $g_{\parallel} = 2.3$ or more. For present Cu complex, $g_{\parallel} >$

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 $\times 10^{-4} \text{cm}^{-1}$		
				A_{\parallel}	A_{\perp}	$ A $
Cu RT (Powder)	2.273	2.064	2.13	166.5	19.0	68.50
Cu LNT (DMF)	2.575	2.025	2.20			

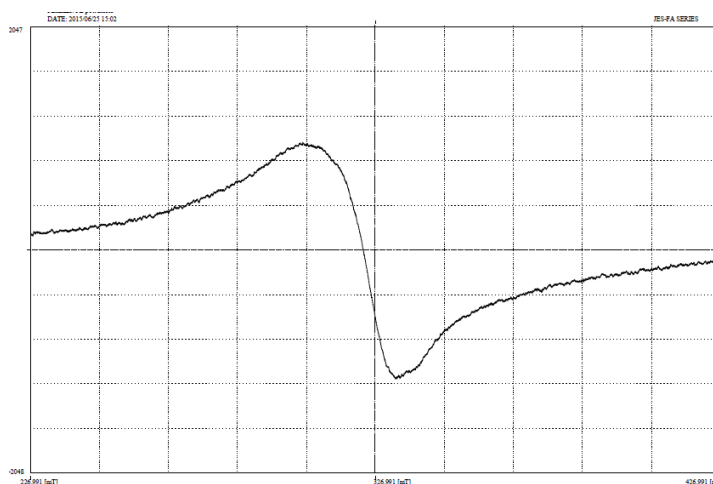


Fig-2: ESR spectrum of Cu (II) complex (RT)

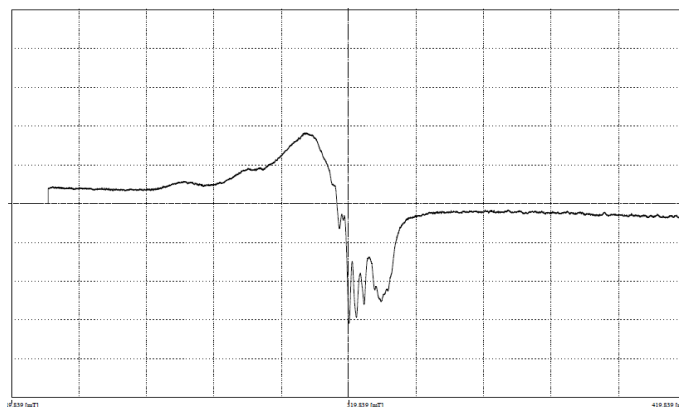


Fig-3: ESR spectrum of Cu (II) complex (LNT)

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 (ΔS), Free Energy Change (ΔF) and Frequency Factor (Z) of compounds were calculated by employing Freeman Carroll and Sharp Wentworth method [36-38]. The thermal curves of ligand and complexes were obtained with heating rate $10^{\circ} \text{C min}^{-1}$ 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°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 $150-220^{\circ} \text{C}$ 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 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.

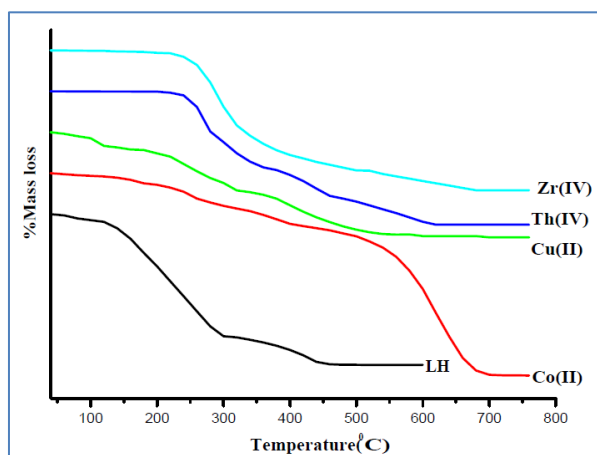


Fig-4: Thermal graph of LH and metal complexes.

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
		FC	SW					
LH	290	14.30	14.81	-305.64	92.62	156.2	-24.38	0.93
[CoL ₂ (H ₂ O) ₂]	470	13.46	13.65	-340.61	103.22	126.75	-25.49	0.96
[CuL ₂ (H ₂ O) ₂].3H ₂ O	430	14.83	14.37	-324.48	98.33	143.86	-24.86	0.93
[ThL ₂ (NO ₃) ₂]	460	24.24	22.74	-282.11	85.50	168.34	-24.77	0.95
[Zr(OH) ₂ L ₂]	355	23.20	21.66	-315.02	95.47	187.32	-24.40	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	<i>E. coli</i> (ATCC 14948)	<i>S. aureus</i> (ATCC 33591)	<i>S. epidermis</i> (MTCC 3086)	<i>K. pneumoniae</i> (MTCC 4030)
1	LH	10	11	09	10
2	[CoL ₂ (H ₂ O) ₂]	19	16	21	20
3	[CuL ₂ (H ₂ O) ₂].3H ₂ O	16	14	18	16
4	[ThL ₂ (NO ₃) ₂]	15	14	13	15
5	[Zr(OH) ₂ L ₂]	R	R	R	12

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.

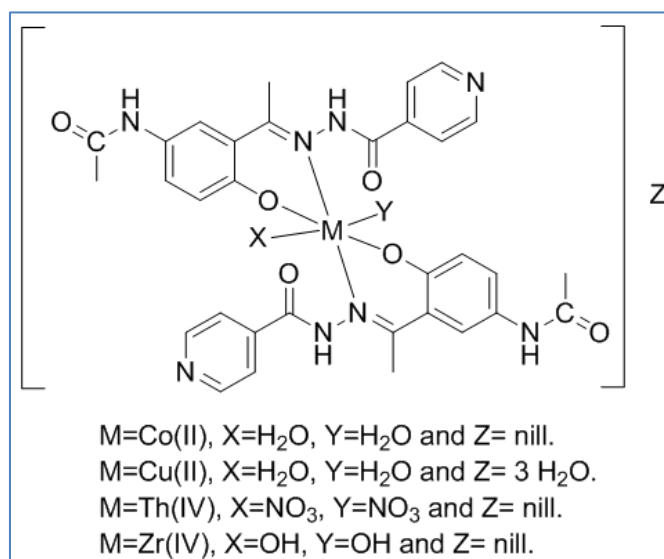


Fig-5: The probable structure for Co (II), Cu(II), Th(IV) and Zr(IV) metal complexes.

Conflict of Interest

The authors declare that they have no conflict of interest.

ACKNOWLEDGMENT

P. R. Mandlik thanks the University Grants Commission, New Delhi, India for financial support in the form of Major research project [MRP. F. No. 41-315/2012(SR)] and P. K. Deshmukh for the award of project fellowship under the above project. Thanks are also due to authorities of Shri Shivaji Science College, Amravati, India for providing necessary research facilities.

REFERENCES

- Kajal, A., Bala, S., Sharma, N., Kamboj, S., & Saini, V. (2014). Therapeutic potential of hydrazones as anti-inflammatory agents. *International Journal of Medicinal Chemistry*, (761030), 1–11.
- Avaji, P. G., Vinod Kumar, C. H., Patil, S. A., Shivananda, K. N., & Nagaraju, C. (2009). Synthesis, spectral characterization, in-vitro microbiological evaluation and cytotoxic activities of novel macrocyclicbis hydrazone. *European Journal of Medicinal Chemistry*, 44(9), 3552–3559.
- Bingol, M., & Turan, N. (2020). Schiff base and metal(II) complexes containing thiophene-3-carboxylate: Synthesis, characterization and antioxidant activities. *Journal of Molecular Structure*, 127542.
- Malik, S., Ghosh, S., & Mitu, L. (2011). Complexes of some 3d-metals with a Schiff base derived from 5-acetamido-1,3,4-thiadiazole-2-sulphonamide and their biological activity. *Journal of the Serbian Chemical Society*, 76(10), 1387–1394.
- Bhaskar, R. S., Ladole, C. A., Salunkhe, N. G., Barabde J. M., & Aswar, A. S. (2020). Synthesis, characterization and antimicrobial studies of novel ONO donor hydrazone Schiff base complexes with some divalent metal (II) ions. *Arabian Journal of Chemistry*, 12(8), 6559-6567.
- Mohammad, A. (2012). A review on potent antitubercular agent isoniazide and its analogues. *International Journal of Pharmaceutical Chemistry*, 2(4), 110-120.
- Alia, O. M., Amer, H. H., Nayel, M., & Abdel-Rahman, A. A. (2016). Synthesis and antimicrobial activity of new synthesized paracetamol derivatives and their acyclic nucleoside analogues. *International Journal of Scientific and Research Publications*, 6(4),408-418.

8. Ahmad, A., Husain, A., Khan, S. A., Mujeeb, M., & Bhandari, A. (2014). Synthesis, antimicrobial and antitubercular, activities of some novel pyrazoline derivatives. *Journal of Saudi Chemical Society*, 20(5), 577-584.
9. Mandlik, P. R., & Aswar, A. S. (2003). Schiff base metal complexes of Chromium(III), Manganese(III), Iron(III), Ovovanadium(IV), Zirconium(IV) and Dioxouranium (VI). *Polish J. Chem*, 77, 129-135.
10. Balouri, M., Sadiki, M., & Ibsouda, S. K. (2016). Methods for in vitro evaluating antimicrobial activity. *Journal of Pharmaceutical Analysis*, 6: 71-79.
11. Gawande, P. U., Mandlik P. R., & Aswar, A. S. (2015). Synthesis and Characterization of Cr(III), Mn(III), Fe(III), VO(IV), Zr(IV) and UO (VI) complexes of Schiff base derived from isonicotinoyl hydrazone. *Indian J. Pharm. Sci.*, 77(4), 376-381.
12. Mishra, A. P., & Soni, M. (2008). Synthesis, structural, and biological studies of some Schiff bases and their metal complexes. *Metal-Based Drugs*, 875410, 1-7.
13. Knittel, E. T., Abou-Hussein, A. A., & Linert, W. (2017). Syntheses, characterization and biological activity of novel mono and binuclear transition metal complexes with a hydrazone Schiff base derived from a coumarin derivative and oxalyldihydrazone. *Monatsh. Chem.*, 149(2), 431-443.
14. Chandrakala, M. (2018). Reactions of Fe(III), Co(II) and Cu(II) ions with 2-Salicylidene-4-aminophenyl benzimidazole. *Asian Journal of Chemistry*, 31(1), 73-78.
15. Suryawanshi, N. J., Pethe, G. B., Yaul, A. R., & Aswar, A. S. (2014). Synthesis, characterization and biological studies of some transition metal chelates derived from hydrazone Schiff base ligand. *Jordan Journal of Chemistry*, 9(3), 199-216.
16. Badwaik, V. B., & Aswar, A. S. (2009). Carbohydrazone polychelates: Synthesis, physicochemical characterization, solid state conductance and biological studies. *Russian Journal of Inorganic Chemistry*, 54(10), 1611-1618.
17. Rakha, T. H., El-Gammal, O. A., Metwally, H. M., & Abu El-Reash, G. M. (2014). Synthesis, characterization, DFT and biological studies of (Z)-N'-(2-oxoindolin-3-ylidene)picolinohydrazone and its Co(II), Ni(II) and Cu(II) complexes. *Journal of Molecular Structure*, 1062, 96-109.
18. Lal, R. A., Pal, M. L., Chakraborty, J., & Kumar, A. (2000). Alkali metal and ammonium oxoperomolybdenum(IV) complexes derived from salicylaldehyde isonicotinoyl hydrazone. *Indian journal of chemistry*, 39(A), 1194-1197.
19. Singh, V. P., Singh, S., Singh, D. P., Tiwari, K., & Mishra, M. (2014). Synthesis, spectroscopic (electronic, IR, NMR and ESR) and theoretical studies of transition metal complexes with some unsymmetrical Schiff bases. *Journal of Molecular Structure*, 1058, 71-78.
20. Kumar, D., Chadda, S., Sharma, J., & Surain, P. (2013). Syntheses, Spectral characterization, and antimicrobial studies on the coordination compounds of metal ions with Schiff base containing both aliphatic and aromatic hydrazide moieties. *Bioinorganic Chemistry and Applications*, 1-10.
21. Mane, P. S., Salunke, S. M., & More, B. S. (2011). Synthesis and structural studies of transition metal complexes with bidentate Schiff base derived from 3-Acetyl-6-methyl-(2H)-pyran-2,4(3H)-dione. *E-Journal of Chemistry*, 8(S1), S245-S252.
22. Abu-Khadra, A. S., Farag, R. S., & Abdel-Hady, A. (2018). Synthesis, characterization and antimicrobial activity of Schiff base (E)-N-(4-(2-Hydroxybenzylideneamino) Phenylsulfonyl) acetamide metal complexes. *American Journal of Analytical Chemistry*, 7(3), 233-245.
23. Sharma, A., & Shah, M. (2013). Synthesis and characterization of some transition metal complexes derived from bidentate Schiff base ligand. *IOSR Journal of Applied Chemistry*, 3(5), 62-66.
24. Mishra, A., Sharma, N., & Jain, R. (2013). Microwave synthesis, spectral, thermal and antimicrobial studies of some Ni (II) and Cu(II) Schiff base complexes. *Open Journal of Synthesis, Theory and Applications*, 2(5), 56-62.
25. Reddy, V., Patil, N., Reddy, T., & Angadi, S. D. (2008). Synthesis, characterization and biological activities of Cu(II), Co(II), Ni(II), Mn(II) and Fe(III) complexes with Schiff base derived from 3-(4-Chloro- phenoxy)methyl)-4-amino-5-mercapto-1,2,4-triazole. *E-Journal of Chemistry*, 5(3), 529-538.
26. Reddy, K. R., & Mahendra, K. N. (2008). Synthesis, characterization and the antimicrobial and anthelmintic activities of some metal complexes with a new Schiff base 3-[(Z)-5-Amino-1,3,3-Trimethyl-Cyclohexylmethylimino]-1,3-Dihydroindol-2-One. *Russian Journal of Inorganic Chemistry*, 53(6), 906-912.
27. Prakash, B. S., Raj, I. S., & Raj, A. G. (2017). Synthesis, characterization of Zirconium and Thorium Schiff base complex and its spectral and biological nature. *IOSR Journal of Engineering*, 7(11), 26-36.
28. Yaul, A. R., Dhande, V. V., Pethe, G. B., & Aswar, A. S. (2014). Synthesis, characterization, biological and electrical conductivity studies of some Schiff base metal complexes. *Bull. Chem. Soc. Ethiop*, 28(2), 255-264.

29. El-ajaily, M. M., Abdullah, H. A., Al-janga Ahmed, Saad, E. E., & Maihub, A. A. (2015). Zr(IV), La(III), and Ce(IV) chelates with 2-[(4-[(Z)-1-(2-Hydroxyphenyl)ethylidene]aminobutyl)-ethanimidoyl]phenol: Synthesis, spectroscopic characterization, and antimicrobial studies. *Advances in Chemistry*, 1-15.
30. Mohapatra, R. K., & Dash, D. C. (2010). Synthesis and Characterization of UO₂ (VI), Th(IV), ZrO(IV) and VO(IV) complexes with Schiff-base octaazamacrocyclic ligands. *Journal of the Korean Chemical Society*, 54(4), 395-400.
31. Reddy, P. S., Ananthalakshmi, P. V., & Jayatyagaraju, V. (2011). Synthesis and structural studies of first row transition metal complexes with tetradentate ONNO donor Schiff base derived from 5-Acetyl 2, 4-dihydroxyacetophenone and Ethylenediamine. *E-Journal of Chemistry*, 8(1),415-420.
32. Orojloo, M., Nourian, F., Arabahmadi, R., & Amani, S. (2015). Ni (II), Cu(II), and Zn(II) complexes derived from a new Schiff base 2-((Z)-(3-methylpyridin-2-yleimino)methyl)phenol and synthesis of nano sized metal oxide particles from these compounds. *Química Nova*, 38(9), 1187-119.
33. Ghumbre, S. K., Kohire, R. B., Ujgare, S. R., Renge, A. S., Lonkar S. M., & Khade, B. C. (2020). Electron spin resonance studies of Cu (II) complex of novel Schiff base. *Journal of Emerging Technologies and Innovative Research*, 7(3), 153-154.
34. Kavitha, N., & Lakshmi, P. V. (2017). Synthesis, characterization and thermogravimetric analysis of Co (II), Ni(II), Cu(II) and Zn(II) complexes supported by ONNO tetradentate Schiff base ligand derived from hydrazinobenzoxazine. *Journal of Saudi Chemical Society*, 21, S457–S466.
35. Benial, A. M., Ramakrishnan, V., & Murugesan, R. (2000). Single crystal EPR of Cu(C₅H₅NO)₆(BF₄)₂: An example of admixed ground state. *Spectrochimica Acta Part A*, 56, 2775–2781.
36. Jain, R., Mishra, A., Mishra, D., & Gupta, S. (2012). Microwave synthesis, spectral, thermal and electrical properties of Some Metal Complexes Involving 5- bromosalicylal-dehyde. *E-Journal of Chemistry*, 9(4), 1721-1727.
37. Butoliya, S., Gurnule, W., & Zade, A. (2010). Study of non-isothermal decomposition and kinetic analysis of 2, 4-dihydroxybenzoic acid- melamine-formaldehyde copolymer. *E-Journal of Chemistry*, 7(3), 1101-1107.
38. Nandekar, K., Dontulwar, J., & Gurnule, W. (2012). Thermoanalytical studies and kinetics of newly synthesized copolymer derived from p-hydroxybenzoic acid and semicarbazide. *Rasayan J. Chem*, 5(3), 261-268.
39. More, G., Raut, D., Aruna, K., & Bootwala, S. (2017). Synthesis, spectroscopic characterization and antimicrobial activity evaluation of new tridentate Schiff bases and their Co (II) complexes. *Journal of Saudi Chemical Society*, 21(8), 954–964.
40. Abu-Dief, A. M., & Mohamed, I. M. A. (2015). A review on versatile applications of transition metal complexes incorporating Schiff bases. *Beni-Suef University Journal of Basic and Applied Sciences*, 4(2), 119–133.