JETIR.ORG ISSN: 2349-5162 | ESTD Year : 2014 | Monthly Issue
JOURNAL OF EMERGING TECHNOLOGIES AND INNOVATIVE RESEARCH (JETIR)
An International Scholarly Open Access, Peer-reviewed, Refereed Journal

A Study Towards Synthesis, Structural Characterization and Antimicrobial Assay of Novel Ketone Hydrazide Complexes of Cu (II)

Atul Sahebrao Patil[1], S.S. Dipke[2], M. S. Thakare[3], J.R. Gujarathi[4]

[1, 3] S.S.M.M. Arts, Commerce, Science College, Pachora, Dist. Jalgaon, (M.S.) India

[2, 4] Department of Chemistry, Pratap College (Autonomous), Amalner, Dist.-Jalgaon (M.S.) India

Abstract

Hydrazide ligands were synthesized by the reaction of acetohydrazide with 3- methyl -2-hydroxy acetophenone, 5-methyl-2-hydroxy acetophenone and 4- methyl 2-hydroxy acetophenone. The complexes of Cu (II) complexes were synthesized by copper chloride with hydrazide ligand in mole ratio 1:2. The ligands and complexes were characterized by Elemental Analysis, ESI-MS, Infrared (FT-IR) spectroscopy, EPR spectra, Reflectance spectra, Nuclear Magnetic Resonance (^{1}HNMR and ^{13}CNMR), magnetic susceptibility measurement and conductivity measurement. The metal complexes and corresponding ligands were tested against bacterial parasites. It was found that the complexes synthesized showed biological activity than corresponding hydrazide ligands.

Keywords: Ligand, Metal salt, biologically active metal complexes, MIC.

I. Introduction

Condensation of semicarbazide with carbonyl compounds (ketones, aldehydes) yields hydrazine carboxamide molecules [1]. Semicarbazone ligands function as neutral or charged ligands and contain donor atoms like nitrogen and oxygen. [2-6]. By reacting with metal ions, these ligands tend to form metal complexes. [7-10]. With these ligands, a range of metal complexes are formed, which advances bioinorganic chemistry and coordination chemistry. [11]. Semicarbazone compounds are essential in agriculture [12], pharmaceuticals [13], synthetic chemistry [14], and other fields. They are also utilized as catalysts in many biological systems [15], as well as in the preparation of dyes and polymers. [16]. The activity of semicarbazone complexes depend on type and charge of metal ions [17]. In this work, Cr (III), Mn (II), Fe (II), and Zn (II) metal complexes with (2E) -2-(4-methoxy benzylidene) hydrazine carboxamide are synthesized and characterized using different spectroscopic techniques such as H^{1}NMR, IR, ESI-MS. The prepared ligands and their metal complexes are screened toward many biological functions such as antifungal [18-20], antitumor [21], antiviral [22], antimalarial and antiparasital activities [5, 23-26]. In this article the synthesis, spectral characterization and biological studies of four coordinate complexes of Cu (II) with hydrazide ligands have been reported.

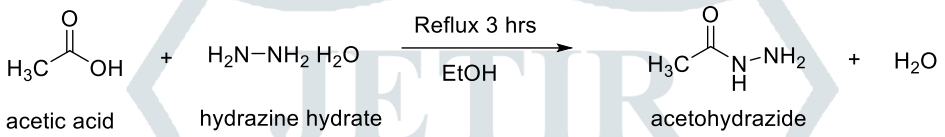
II. Materials and Methods

All the Chemicals of A.R. grade. Magnetic susceptibility measurement was carried out by Faraday method at room temperature. IR spectra were recorded in solid state in the range 4000-200 cm^{-1} range. Thermo gravimetric analysis was carried out in the temperature range 30-800 ℃. Metal was estimated by standardized (0.01 M approx.) E.D.T.A using muroxide indicator and pH-10 ammonia buffer solution.

III. Experimental

a. General procedure for the synthesis of acetohydrazide:

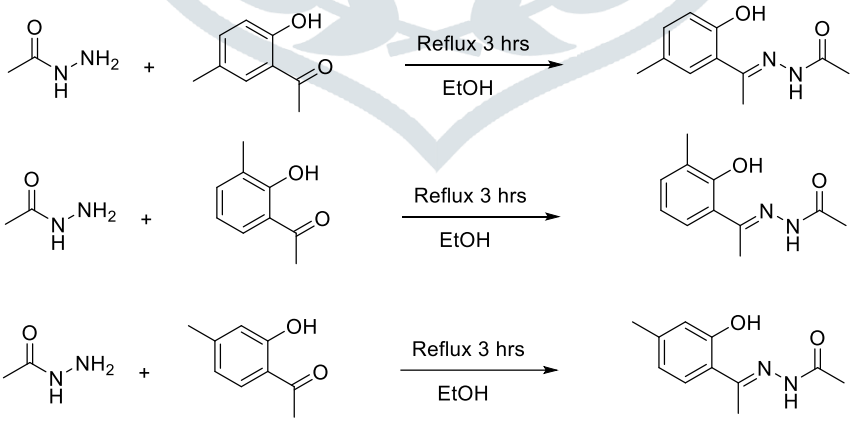
20 ml ethanolic solution of glacial acetic acid (0.01 mole) was added to 20 ml ethanolic solution of hydrazine hydrate (0.01 mole) in the mole ratio 1:1. The reaction mixture was refluxed for three hours. On cooling pale yellow product was filtered and washed with hot water then cold ethanol and finally with diethyl ether. The compound was then purified in ethanol and dried in vacuum.



Scheme 1: General synthesis of acetohydrazide from hydrazine hydrate and acetic acid

b. General procedure for the synthesis of acetohydrazide Ligands:

20 ml ethanolic solution of acetohydrazide (0.01 mole) was added to 20 ml ethanolic solution 5- methyl-2-hydroxy acetophenone/3-methyl-2-hydroxy acetophenone/4-methyl-2-hydroxy acetophenone (0.01 mole) in the mole ratio 1:1. The reaction mixture was refluxed for three hours. On cooling pale yellow product was filtered and washed with hot water then cold ethanol and finally with diethyl ether. The compound was then purified in ethanol and dried in vacuum.



Scheme 2: General procedure for the synthesis of acetohydrazide Ligands

c. Synthesis of Complex

The complexes of the type $Cu.L_2$ was synthesized by adding slowly ethanolic solution of $CuCl_2.4H_2O$ (0.01mole) to the hot ethanolic solution of 5-methyl-2-hydroxy acetophenone/3-methyl-2-hydroxy acetophenone/4-methyl-2-hydroxy acetophenone acetohydrazide (0.01 mole) in the ratio 1:2 and stirred the

reaction mixture for half an hour at 30 ℃. The brown product obtained was filtered and washed with hot water to remove excess metal salt, cold ethanol and diethyl ether and dried in vacuum.

Table-1: Physical Properties of the Complexes

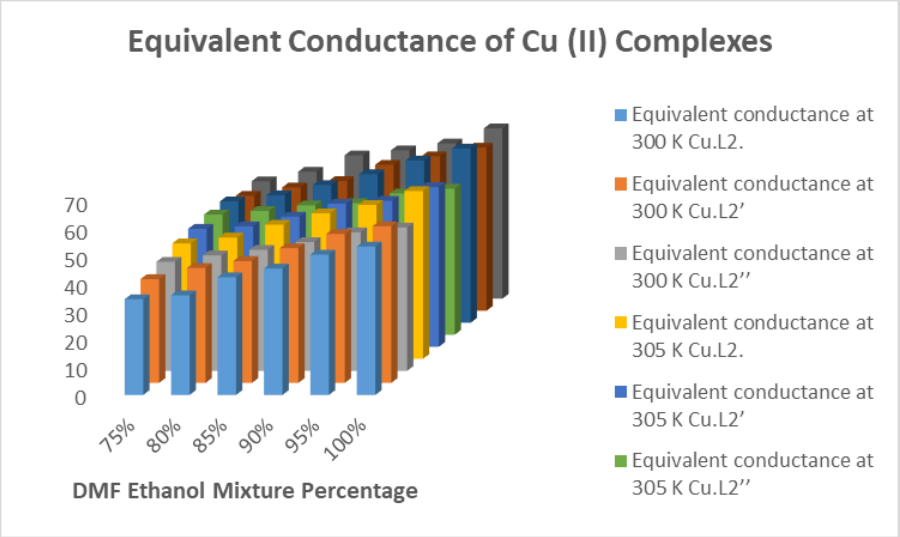
Compounds	*Color*	*Empirical Formula*	*Magnetic Moment (B.M.)*
L	*Yellow*	$C_{11}H_{14}O_2N_2$	-
L'	*Yellow*	$C_{11}H_{14}O_2N_2$	-
L''	*Yellow*	$C_{11}H_{14}O_2N_2$	-
Cu.L₂.	*Brown*	$C_{22}H_{28}O_4N_4Cu$	*1.87*
Cu.L₂'	*Brown*	$C_{22}H_{28}O_4N_4Cu$	*1.85*
Cu.L₂''	*Brown*	$C_{22}H_{28}O_4N_4Cu$	*1.83*

Conductivity Measurement

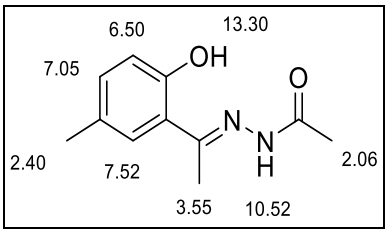
The conductivity measurement was carried out in DMF solvent and equivalent conductance was calculated. 0.001M solution of complexes were prepared in different percentages of DMF-ethanol mixture and the parameter of solution under study was calculated at temperature 300 K, 305 K and 310 K.

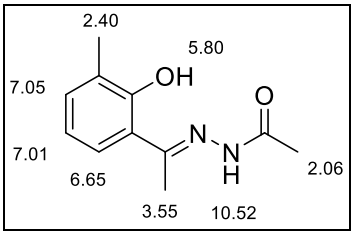
Table-2: Equivalent Conductance of the Complexes at Different Temperatures

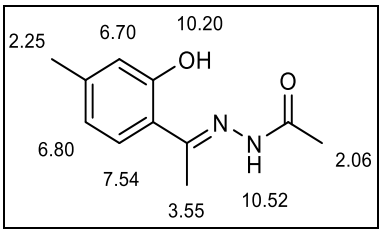
DMF-Ethanol Mixture	*Equivalent conductance at 300 K*			*Equivalent conductance at 305 K*			*Equivalent conductance at 310 K*		
	Cu.L₂.	*Cu.L₂'*	*Cu.L₂''*	*Cu.L₂.*	*Cu.L₂'*	*Cu.L₂''*	*Cu.L₂.*	*Cu.L₂'*	*Cu.L₂''*
75%	*34.4*	*37.3*	*39.2*	*41.5*	*42.4*	*43.2*	*43.6*	*41.3*	*42.2*
80%	*35.8*	*41.3*	*41.5*	*43.6*	*43.3*	*44.5*	*45.8*	*44.3*	*45.6*
85%	*42.3*	*43.8*	*43.5*	*48.2*	*46.8*	*46.5*	*49.5*	*46.6*	*51.5*
90%	*45.4*	*48.4*	*46.3*	*52.3*	*51.4*	*47.3*	*53.4*	*52.4*	*53.3*
95%	*50.4*	*53.5*	*49.8*	*55.3*	*52.5*	*50.8*	*58.3*	*55.5*	*55.8*
100%	*53.3*	*56.3*	*51.5*	*60.3*	*57.4*	*52.5*	*62.6*	*58.6*	*61.2*



^{1}H-NMR Study of L, L' and L"







^{1}H-NMR (L):

^{1}H-NMR signals at 13.30 and 2.06 ppm and 3.55 ppm are assigned to – OH and O=C-CH3 and–N=C-CH3 protons respectively. Signal at 10.52 ppm corresponds to-NH. Aromatic protons show multiplets at 7.05,7.52, 6.50 ppm.

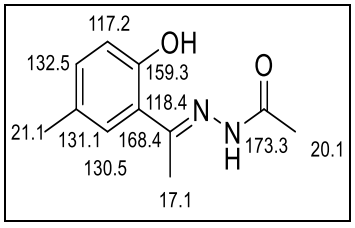
^{1}H-NMR(L'):

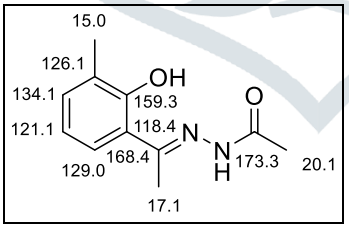
^{1}H-NMR signals at 5.80 and 2.06 ppm and 3.55 ppm are assigned to – OH and O=C-$CH_3$and –N=C-CH_3 protons respectively. Signal at 10.52 ppm corresponds to -NH. Aromatic protons show multiplets at 7.01, 7.05 and 6.65 ppm.

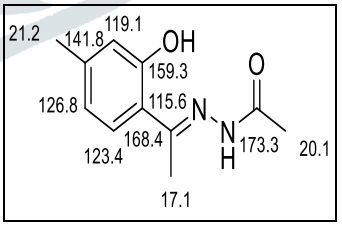
^{1}H-NMR(L''):

^{1}H-NMR signals at 10.20 and 2.06 ppm and 3.55 ppm are assigned to –OH and O=C-CH_3 and–N=C-CH_3 protons respectively. Signal at 10.52 ppm corresponds to -NH. Aromatic protons show multiplets at 7.54, 6.70 ppm.

^{13}C-NMR data of (L), (L') and (L'') in δ ppm







ESI-MS m/z, ion M^+ (Calcd.) found

$C_{11}H_{14}O_2N_2$ (206.23) 206.91, $C_{11}H_{14}O_2N_2$ (206.23) 206.53, $C_{11}H_{14}O_2N_2$ (206.23) 206.61, $C_{22}H_28O_4N_4Cu$ (476.00) 476.80, $C_{22}H_28O_4N_4Cu$ (476.00) 476.75, $C_{22}H_28O_4N_4Cu$ (476.00) 476.92

Table-3: Analytical Data

Compounds	*Metal Analysis*	*Elemental analysis*			
	M%	*C%*	*H%*	*N%*	*O%*
L	-	*64.84*	*6.06*	*13.75*	*15.70*
		(64.06)	*(6.84)*	*(13.58)*	*(15.52)*
L'	-	*64.72*	*6.12*	*13.09*	*15.72*
		(64.06)	*(6.84)*	*(13.58)*	*(15.52)*
L''	-	*64.92*	*6.04*	*13.11*	*15.79*
		(64.06)	*(6.84)*	*(13.58)*	*(15.52)*
Cu.L₂.	*3.61*	*55.37*	*5.84*	*11.35*	*13.73*
	13.35)	*(55.51)*	*(5.93)*	*(11.77)*	*(13.45)*
Cu.L₂'	*3.52*	*55.36*	*5.96*	*11.18*	*13.273*
	13.35)	*(55.51)*	*(5.93)*	*(11.77)*	*(13.45)*
Cu.L₂''	*3.52*	*55.36*	*5.96*	*11.18*	*13.273*
	13.35)	*(55.51)*	*(5.93)*	*(11.77)*	*(13.45)*

Table-4: IR Spectroscopic Data (cm^{-1})

Assignments	*L*	*L'*	*L''*	*Cu.L₂.*	*Cu.L₂'*	*Cu.L₂''*
ν(-OH)	*3260*	*3264*	*3292*	*3215*	*3264*	*'295*
ν(C=N)	*1670*	*1672*	*1685*	*1555*	*1562*	*575*
ν(N–N)	*1057*	*1075*	*1085*	*1182*	*1175*	*182*
ν(N-H)	*3250*	*3261*	*3265*	*3254*	*3257*	*'265*
ν(C–O)	*1290*	*1285*	*1295*	*1215*	*1217*	*218*
ν(Cu-N)	-	-	-	*454*	*458*	*'65*
ν(Cu-O)	-	-	-	*535*	*544*	*'47*

Table-5: Electronic spectral assignments (cm^{-1})

Assignments	*L*	*L'*	*L''*	*Cu.L₂'*	*Cu.L₂'*	*Cu.L₂''*
'-d				*18795*	*18503*	*18500*
'→M				*25775*	*25700*	*25650*
'→π*	*8750*	*8790*	*8760*	*30850*	*30623*	*30754*
'→π*	*9860*	*9840*	*9650*	*42530*	*42700*	*42600*

IV. TGA Analysis Data

1) Cu.L_2.: First step, 123°C, Mass loss14.0% second step, 353°C, Mass loss, 52.8% Third Step 650°C, Mass loss, 74.0% Residue 781°C, % of CuO, 16.03 (16.71).

2) Cu.L_2'**:** First step, 121°C, Mass loss 10.0% second step, 356°C, Mass loss, 48.0% Third Step 652°C, Mass loss, 76.0% Residue, 780 °C, % of CuO, 16.17 (16.71).

3) Cu.L_2''**:** First step, 122°C, Mass loss 9.2% second step, 362°C, Mass loss, 50.0% Third Step 660°C, Mass loss, 75.0% Residue 780°C, % of CuO, 16.10 (16.71).

V. Biological Activity (Agar Plate Diffusion Method)

Table-6: Minimum Inhibitory concentration L, L', L'' Cu (II) complexes and standard

Compound	*Staphylococcus aureu*		*Bacilus subtilis*		*Escherichia Coli*		*Peudomonasaeruginosa*	
Gram positive					*Gram negative*			
	'µg/ml	*'.5µg/ml*	*'µg/ml*	*'.5µg/ml*	*'µg/ml*	*'.5µg/ml*	*'µg/ml*	*'.5µg/ml*
	'.67	*'.38*	*'.70*	*'.42*	*'.70*	*'.42*	*'.68*	*'.42*
,'	*'.62*	*'.32*	*'.62*	*'.34*	*'.61*	*'.33*	*'.64*	*'.31*
,''	*'.60*	*'.30*	*'.61*	*'.30*	*'.60*	*'.32*	*'.62*	*'.31*
Cu-L_2	*'.52*	*'.28*	*'.54*	*'.27*	*'.55*	*'.28*	*'.55*	*'.22*
Cu-L_2'	*'.53*	*'.23*	*'.47*	*'.24*	*'.52*	*'.22*	*'.50*	*'.23*
Cu-L_2''	*'.21*	*'.22*	*'.46*	*'.17*	*'.48*	*'.21*	*'.48*	*'.17*
Cu.4H_2O	*'.17*	*'.15*	*'.40*	*'.12*	*'.42*	*'.13*	*'.42*	*'.11*
*'tandard**	*'.14*	*'.11*	*'.13*	*'.9*	*'.13*	*'.9*	*'.14*	*'.8*

***Ampicillin**

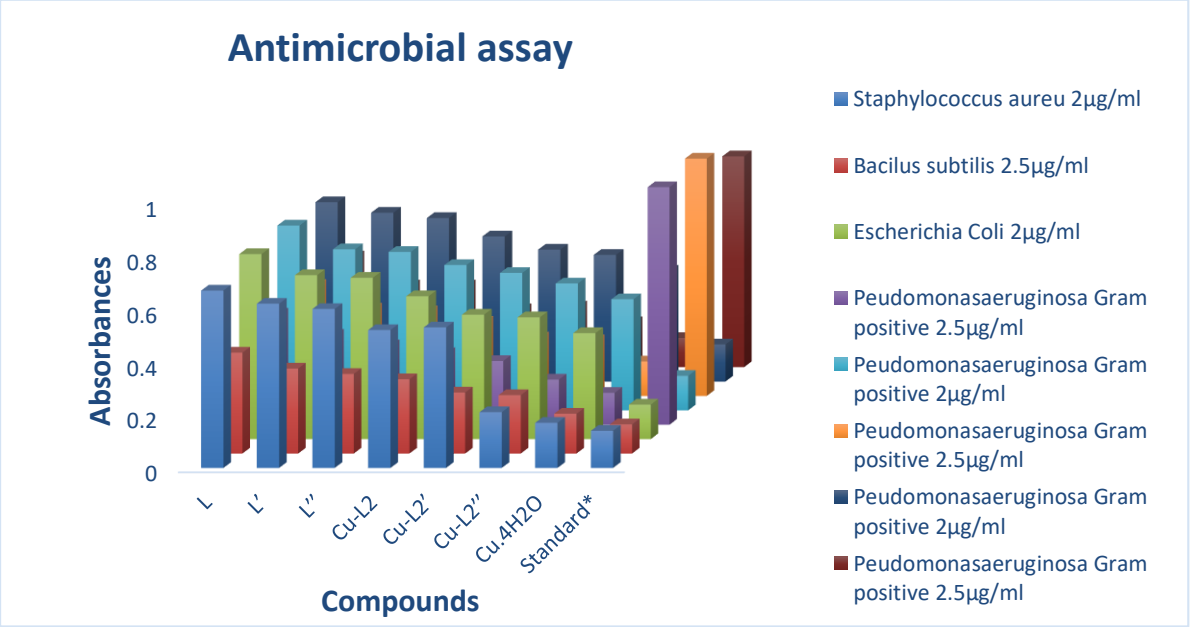


Fig-1: Antimicrobial assay of semicarbazone ligands and Cu (II) semicarbazone complexes

VI. Results and Discussion:

The complexes are insoluble in water, methanol and ethanol and soluble in DMF. Mass spectral data confirmed the structure of ligands and complexes as indicated by molecular ion peak (M^{+1}) corresponding to their molecular weights.

The magnetic susceptibility measurement was carried out at room temperature by Faraday method. Cu (II) ion has the electronic configuration $3d^1$ with one unpaired electron. It has been pointed out that the stereochemistry is expected to have little effect on magnetic moment of Cu (II) ion, which should be somewhat above the spin-only value of 1.72 B.M. Recently, a large number of Cu (II) complexes having sub-normal magnetic moments at room temperature have been reported. The magnetic moments in the present study are in the range 1.83-1.87 B.M.

The equivalent conductance of electrolyte solution depends on concentration and temperature. It is found that equivalent conductance of an electrolyte increases with increase in dilution. In dilute solution conductance is more. All complexes showed increasing value of conductance with increase in the dilution at 300 K, 305 K, and 310 K. The conductivity of an electrolyte depends upon the temperature. The conductivity of an electrolyte increases with increase in temperature. This may be due to at higher temperature the mobility of ions increases and hence more conductivity has been observed.

The frequency due to >C=N is shifted to the lower side. This indicates participation of azomethine nitrogen [27] A band at 454-465 cm^{-1} confirms the coordination of azomethine nitrogen [28-30]. There is increase in N-N frequency due to the increase in double bond character off-setting the loss of electron density via donation to the metal. This confirms the coordination of L through azomethine nitrogen atom. The band due to N-H in in the complexes is not affected. The band due to Cu-O in complexes is in the range 535-547 cm^{-1} confirms coordination through oxygen.

L, L', L'' showed bands due to n $\rightarrow$ π^* and $\pi \rightarrow \pi^*$ observed in the range 28,000- 29,000 cm^{-1} and 39,000-40,000 cm^{-1}. These bands shifted to higher side on complexation. The L-M charge transfer bands are observed in the range 30,000-31,000 cm^{-1} and 42,000 – 43,000 cm^{-1}. The d-d bands are observed in the range 17,000-18,000cm^{-1}. This shows square planer geometry [31-36].

Hydrated layer was removed in between 120 ^oC – 122 ^oC. No coordinated water molecules were found. The decomposition proceeded in three steps. The compounds are stable up to about 350 ^oC. The organic molecule was lost up to 650 ^oC. The mass lost corresponding to this step is about 65-70%. The decomposition was complete and metal oxide was formed at a temperature about 780-785 °C. The metal complexes are more stable than organic molecule.

The antibacterial assay was carried out by the agar plate diffusion method. Activity was measured by measuring the absorbance at 517 nm. The minimum inhibitory concentration was determined by liquid dilution method [37, 38]. The solutions with 2 µg/ml, 2.5µg/ml and 3 µg/ml concentrations were prepared in the solvent DMF. The solutions of standard drug ampicillin and metal salt were also prepared in the same concentration. Inoculums of the overnight culture were prepared. 0.2 ml of the inoculums was added to the test tubes containing the solutions of the compounds of different

concentrations. Sterile water to each of the test tubes was added and these were incubated for 24 hours and observed for turbidity. The same procedure was carried out for standard [39]. All ligands showed less activity than corresponding complexes. This might be due to coordination with metal which reduces the polarity of the central metal ion because of the partial sharing of its positive charge with donor groups and possible π- electron delocalization within the whole chelating ring. So, the lipophilic nature of the central metal ion increases, which favors the permeation of the solution of complexes through the lipid layer of the cell membrane [40]. The absorbance is more at 2 µg/ml and less at 2.5 µg/ml and no absorbance observed at 3 µg/ml. The inhibition is more at 2.5 µg/ml. The chelation theory explains the reason behind the better activity of these complexes. The polarity of the metal ion is minimized to an advanced level, due to the ligand and positive charge of the metal ion with donor groups.

VII. Conclusion

The synthesized ligands are bidentate -O, -N donors. The spectral and magnetic measurements revealed square planar shape for complexes. The compounds displayed para-magnetic properties. The complexes were found to be thermally stable. TGA demonstrates the development of metal oxides following three stages of breakdown at 780-785 °C. The complexes inhibited the development of bacteria. The absorbance is greater at 2 µg/ml than at 2.5 µg/ml. This demonstrated that increasing the concentration of complexes increases activity. Metal salts shows more inhibition effect than the synthesized ligands.

References

[1] Glukhacheva, Vera S., et al.; *ACS omega* 6.12 **(2021)**: 8637-8645.

[2] Muleta, Fekadu, T. Alansi, and R. Eswaramoorthy.; *J Nat Sci Res* 9 (2019): 33-46.

[3] Seleem, H. S., et al.; *Journal of Coordination Chemistry* 58.6 (2005): 479-493.

[4] Shaabani, B., et al.; *Inorganica Chimica Acta* 394 (2013): 563-568.

[5] Dhabale, Raj Hasmukh, et al.; *Journal of Pharmaceutical Negative Results* (2022): 2416-2424.

[6] Afrasiabi, Zahra, et al.; *Journal of Inorganic Biochemistry* 99.7 (2005): 1526-1531.

[7] Padhye, Subhash, and George B. Kauffman; *Coordination Chemistry Reviews* 63 (1985): 127-160.

[8] Siji, V. L., et al.; *Spectrochimica Acta Part A: Molecular and Biomolecular Spectroscopy* 76.1 (2010): 22-28.

[9] Enyedy, Éva A., et al.; *Polyhedron* 67 (2014): 242-252.

[10] Sarker, Dipta, et al.; *Asian Journal of Chemical Sciences* 6.4 (2019): 1-8.

[11] Dahikar, P. M. *Synthesis of Physico-Chemical Properties of Metal Oximes, Hydrazones and Semicarbazones*, 2022.

[12] More, M. S., et al.; *Materials Today Chemistry* 14 (2019): 100195.

[13] Singh, Har Lal, J. B. Singh, and Sunita Bhanuka; *Research on Chemical Intermediates* 42 (2016): 997-1015.

[14] Mohan, Chandra, et al.; *Adv. J. Chem. Sect. B* 2 (2020): 187-196.

[15] Muleta, Fekadu, T. Alansi, and R. Eswaramoorthy.; *J Nat Sci Res* 9 (2019): 33-46.

[16] Farhadi, Saeed, et al.; *Journal of Molecular Structure* 1130 (2017): 592-602.

[17] Venkatachalam, Taracad K., et al.; *Journal of inorganic biochemistry* 162 (2016): 295-308.

[18] Bajaj, Kritika, Robert M. Buchanan, and Craig A. Grapperhaus.; *Journal of Inorganic Biochemistry* 225 (2021): 111620.

[19] Sapna, Kumari, Navin Kumar Sharma, and Seema Kohli.; *Oriental journal of chemistry* 28.2 (2012): 969.

[20] Paiva, Rojane de Oliveira, et al.; *Ciência e Agrotecnologia* 38 (2014): 531-537.

[21] Enyedy, Éva A., et al.; *Polyhedron* 67 (2014): 242-252.

[22] Fabián, Lucas, et al.; *Mol. Med. Chem* 12 (2007): 70-72.

[23] Likius, Daniel S.*;* Diss. 2009.

[24] Scalese, Gonzalo, et al.; *Journal of Inorganic Biochemistry* 147 (2015): 116-125.

[25] de Oliveira, Renata B., et al.; *European journal of medicinal chemistry* 43.9 (2008): 1983-1988.

[26] V Silva, Barbara, and Bianca NM Silva.; *Medicinal Chemistry* 13.2 (2017): 110-126.

[27] Abdullah, Sallal AH.; *Journal of Wasit for Science and Medicine* 10.2 (2017): 157-170.

[28] Sumrra, Sajjad Hussain, et al.; *Bioinorganic chemistry and applications* 2014 (2014).

[29] Dhanaraj, Chellaian Justin, et al.; *Journal of Coordination Chemistry* 66.8 (2013): 1416-1450.

[30] Hegde, Vindhya, et al.; *Journal of Molecular Structure* 1266 (2022): 133512.

[31] Reena, T. A., E. B. Seena, and MR Prathapachandra Kurup.; *Polyhedron* 27.17 (2008): 3461-3466.

[32] Reena, T. A., and MR Prathapachandra Kurup; *Spectrochimica Acta Part A: Mol. and Biomol. Spec.* 76.3-4 (2010): 322-327.

[33] Santiago, Pedro HO, et al.; *Structural Chemistry* 31 (2020): 171-180.

[34] Gatto, Claudia C., Francielle C. Lima, and Patrícia M. Miguel.; *Journal of Chemical Sciences* 132 (2020): 1-14.

[35] Adly, Omima MI, Ali Taha, and Shery A. Fahmy.; *Journal of Molecular Structure* 1186 (2019): 362-376.

[36] Layana, S. R., et al.; *Journal of Molecular Structure* 1157 (2018): 579-586.

[37] Kizilcikli, İrfan, et al.; *Folia microbiologica* 52 (2007): 15-25.

[38] Souza, Marina Azevêdo, et al.; *Memórias do Instituto Oswaldo Cruz* 108 (2013): 342-351.

[39] Shukla, S., et al.; *Medicinal Chemistry Research* 22 (2013): 1604-1617.

[40] Agh-Atabay, Naz M., Basaran Dulger, and Fahrettin Gucin.; *European journal of medicinal chemistry* 40.11 (2005): 1096-1102.