Est. 1984

ORIENTAL JOURNAL OF CHEMISTRY
An International Open Access, Peer Reviewed Research Journal

www.orientjchem.org

ISSN: 0970-020 X
CODEN: OJCHEG
2020, Vol. 36, No.(3):
Pg. 572-576

Characterization, Biological Activity and DNA Studies of Atomexetine and Ortho hydroxy benzaldehyde Imine Metal Complexes

G. S. SANJANEYA VASAVI[1] and J. SREERAMULU[2]

[1]Department of Chemistry, RGM College of Engineering & Technology, Nandyal, Andhra Pradesh, India.
[2]Department of Chemistry, S.K University, Anantapuramu, Andhra Pradesh, India.
Corresponding author E-mail: vasavi.sunny@gmail.com

http://dx.doi.org/10.13005/ojc/360331

(Received: May 26, 2020; Accepted: June 22, 2020)

ABSTRACT

The rapid increasing applications and anti-bacterial and anti hyperactive properties of different drug the author have synthesized Imine complexes of Atomexetine with O-hydroxy benzaldehyde. These were depicted with various techniques via Elemental Analysis, UV, FT-IR, NMR, ESR, VSM, Conductivity and TG-DTA. These ligands and metal complexes were also screened for biological activity and DNA Studies.

Keywords: Atomexetine, Copper chloride, Ruthenium chloride and Biological activity.

INTRODUCTION

Imines are the condensed products of Carbonyl compounds and Amines[1]. These are also known as Schiff Bases. The Scientist Hugo Schiff was introduced in 1864[2]. Imines show a unique property in the participation of covalent bond with transition metal ions, since the easy formation of ligands act as intermediates for the formation of complexes with transition metal ions. Imine complexes perform biological activities like anti inflammatory, anti fungal, anti bacterial, anti viral, anti diabetic, anti cancer and in pharmaceuticals etc[3-9]. Biological activity of the Ligands were recorded by the presence of >C=N moiety of the Schiff bases. These are also having uncountable appliances in technical fields like automobiles, electro plating, printing technology, textile and detergents[10-11].

The author has reported characterization, biological activity and DNA studies of the ligands and their metal complexes. The synthesis of Imine metal complexes has been carried out by conventional method and characterization with various techniques like FT-IR, H^1-NMR, ESR, UV-Vis and Conductometry. Thermal stability of the complexes was identified by TG-DTA with various temperatures. Biological activity of Imines and their Cu and Ru complexes was performed in *In vitro* conditions and DNA binding mode with UV-Vis Spectroscopic technique.

MATERIALS AND METHODS

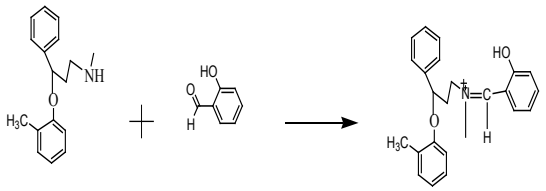
Atomexetine (AT), O-hydroxy benzaldehyde (OHB), methanol, DMF, chlorides of Copper and ruthenium.

Instrumentation

IR Spectral data with KBr Pellets, H^1-NMR Spectral data with BRUKER 400MHZ SUPERCON Spectrometer, ESR Spectral data with Bruker ESP 300E spectrometer, UV-Vis Spectral data with Schimadzu UV-1800 model Spectrometer, XRD on Panalytical X'pert3 difractometer, conductivity measurements with digital conductivity meter DCM-900, VSM with EG and G-155 magnetometer were recorded.

Synthesis of OHB-AT Ligand

The equal concentration of AT and OHB was dissolved separately, this mixture was heated for 2 h by adding few drops of concentrated HCL, pink colored solution was obtained and this was cooled to room temperature. Then pink color precipitate was obtained. These crystals were washed with methanol and dried in micro wave. The percentage yield of ligand was 80.



Scheme 1. Synthesis of OHB-AT Ligand

Synthesis of OHBAT-Cu(II) & Ru(III) metal complexes

The complexes were prepared by mixing 1:2 ratio of an aqueous solution of metal ions with the methanolic solution of Imine separately and stirred with magnetic stirrer for proper mixing of contents. Then the contents in the flask were reflexed for six hours and kept in ice bath for cooling, bluish green color sharp needle like crystals were obtained. These were washed and recrystallized with methanol. The yield of copper and ruthenium complexes was 75% and 78%.

RESULTS AND DISCUSSIONS

The main purpose of the present work is to study the characterization of metal complexes with various techniques, Biological activity in *In vitro* conditions with different micro-organisms and DNA studies on UV-Vis Spectrophotometer.

IR spectral data

The nature of Imine metal complexes were identified by obtaining strong band at 1627 cm^{-1} indicated the development of Imine group, which on complexing with the metals viz. Cu (II) and Ru (III) the bands appeared at 1605 cm^{-1} and 1622 cm^{-1} indicated the coordination between Imine group of nitrogen with electron deficient metal ions because of decreased electron density on Nitrogen atom[12,13]. The another strong bands at 420 cm^{-1} and 429 cm^{-1} for copper and ruthenium expressed coordination between metal and ligand[14,15]. IR data of the ligand and complexes were represented in the Table 1.

Table 1: IR Spectral data of the ligand and its complexes

Compound	ν OH Water	ν OH Phenolic	ν C=N	ν M-O	ν M-N
OHBAT	-	3363	1627	-	-
OHBAT-Cu	3304	-	1605	620	420
OHBAT-Ru	3413	-	1622	649	429

NMR spectral data

A singlet at 5.6 ppm revealed aromatic–OH protons of OHB, this was absent in complex given the coordination between oxygen moiety of OHB and metal ions of Cu (II) and Ru (III). A singl *et at.,* 6.26 ppm specified the presence of Imine group of ligand[16], this was shifted to 7.6 ppm and 7.26 ppm by the coordination of ligand with metal ions. Another singlet at 4.1 ppm and 4.65 ppm appeared only by the coordination of water molecules with metal ions. NMR data of the ligand and complexes were represented in the Table 2.

Table 2: NMR spectral data of OHBAT and its metal complexes

S.No	Compound	H-C=N	Ar-H	OH-Phenilic	OH-H_2O	-CH_3
1	OHBAT	6.26	6.7-7.3	5.6	-	3.4
2	OHBAT-Cu	7.2	7.4-7.9	-	4.1	3.7
3	OHBAT-Ru	7.26	7.3-7.7	-	4.65	3.3

ESR spectral data

The value of G is >4 shows mononuclear nature of complex. This value can be calculated as, $G = [g^{\parallel} - 2.0023/g^{\perp} - 2.0023]$.

α^2 value of Copper and Ruthenium complexes(0.4518 and 0.4794) specified the covalent nature of complexes. The values of $g^{\parallel}$

> g_{ave}> $g^{\perp}$ values were greater than 2.0023 said that unpaired electrons of $d_{x^2-y^2}$ and d_{z^2} orbital is delocalized for Cu and Ru ions respectively[17]. ESR spectral data of the complexes were represented Table in 3.

Table 3: ESR Spectral data of OHBAT-Cu and OHBAT-Ru

Parameters	OHBAT-Cu	OHBAT-Ru
$g^{\parallel}$	2.5864	2.6885
$g^{\perp}$	2.2038	2.3698
g_{ave}	2.3313	2.4968
G	4.327	4.5138
$A^{\parallel}$*	0.00869	0.00981
$A^{\perp}$*	0.0097	0.0168
A_{ave}	0.0099	0.0126
$K^{\parallel}$	0.0762	0.0865
$K^{\perp}$	0.0848	0.0896
P*	0.0336	0.0418
α^2	0.2798	0.4198

UV-Vis spectral data

The transition of ligand was 277 nm, which on complexation with Cu (II) and Ru (III) metal complexes change in transitions at 289 nm and 306 nm signified the charge transfer transition from L→M[18]. UV-Vis Spectral data was represented in the Table 4.

Table 4: UV-Vis Spectral of OHBAT and ITS Cu (II) and Ru (III) Metal complexes

S.No	compound	λ_{max}
1	OHBAT	277
2	OHBAT-Cu	289
3	OHBAT-Ru	306

XRD of OHBAT-Cu and OHBAT-Ru metal complexes

The diffracto grams, calculated miller indices (h k l) values, '2Θ'and'd' values were represented in the Table 5 suggested a good agreement between'2Θ' and'd' values. 2Θ values recommended poor crystallinity of the complexes[19].

The miller indices values are calculated as,

$N\lambda = 2d \sin \Theta$

One of the value of

$2\Theta = 5.2805$

$\Theta = 2.64025$

$\text{Sin}\Theta = 0.046064$

h k l = 1 1 1

XRD values of the complexes were represented in the Tables 5–6.

Table 5: XRD studies of OHBAT-Cu metal complex

S.No	d exp	d Cal.	2Θ exp	2Θ Cal.	h k l
1	0.0354	0.0349	5.2805	5.2801	1 1 1
2	0.03917	0.03912	5.8303	5.8299	1 1 1
3	0.04428	0.04422	6.5921	6.5915	1 1 1
4	0.04925	0.04919	7.3326	7.3321	2 1 1
5	0.05915	0.05910	8.8085	8.8081	2 2 1
6	0.0623	0.0619	9.2791	9.2785	2 2 1
7	0.0965	0.0959	14.3999	14.3994	5 4 4
8	0.1039	0.1033	15.5905	15.5901	5 5 2
9	0.1088	0.1081	16.2419	16.2414	5 5 3
10	0.1255	0.1250	18.7663	18.7659	6 6 3
11	0.1311	0.1308	19.6003	19.6000	6 6 4
12	0.1466	0.1459	21.9204	21.9199	6 6 6
13	0.1800	0.1796	27.0421	27.0415	9 8 4
14	0.1891	0.1886	28.4342	28.4339	9 9 4
15	0.1948	0.1944	29.2495	29.2489	9 9 5
16	0.2165	0.2161	32.6565	32.6559	10 10 6
17	0.2308	0.2301	34.8814	34.8809	11 10 7
18	0.2582	0.2579	39.1821	39.1816	12 11 8
19	0.2882	0.2876	42.9935	42.9931	12 11 10
20	0.2929	0.2924	44.7026	44.7021	12 12 12
21	0.2982	0.2976	45.5550	45.5546	13 13 10
22	0.3252	0.3249	49.9612	49.9606	14 14 12
23	0.3742	0.3737	58.1390	58.1384	16 16 14
24	0.4059	0.4055	63.5485	63.5481	17 17 16
25	0.4693	0.4688	75.0662	75.0658	20 19 19
26	0.5132	0.5129	83.560	83.555	21 21 20

Table 6: XRD studies of OHBAT-Ru metal complex

S.No	d exp	d Cal.	2Θ exp	2Θ Cal.	h k l
1	0.0407	0.0401	6.0709	6.0701	1 1 1
2	0.0490	0.0485	7.2553	7.2549	1 1 1
3	0.0563	0.0558	8.3951	8.3945	2 1 1
4	0.0634	0.0631	9.4552	9.4546	2 2 1
5	0.0855	0.0851	12.7476	12.7470	4 4 2
6	0.0934	0.0929	13.9398	13.9392	5 4 1
7	0.1246	0.1241	18.6317	18.6312	6 5 4
8	0.1306	0.1299	19.5272	19.5266	6 6 4
9	0.1328	0.1321	19.9280	19.9274	7 6 1

Analysis of TG-DTA

By observing modifications at different temperature ranges one can easily explain thermal stability of the complexes. The temp ranges between 110^{0}C-222.10^{0}C and 215^{0}C-280^{0}C specified the loss of two water molecules at the first level[20], the second level at 261.03^{0}C and 450^{0}C specified the formation of stable intermediate peaks as the results of decomposition at the temperature range of 818^{0}C and 600^{0}C. At high temp metallic oxides formation takes by the exothermic process. Thermal data of Cu (II) and Ru (III) metal complexes were represented in the Table 7.

Table 7: Thermal Data of OHBAT-Cu & OHBAT-Ru Metal Complexes

Complex	Molecular weight (grams)	Temperature range in ^{0}C	Probable assignment	Mass loss (%)	Total mass loss (%)
OHBAT-Cu	894.68	110 -222.10	Loss of two H_2O molecules	4.5	
			Loss of two ligand molecules		
		261.03-818.34	Formation of CuO	25.53	70.22
		Above 818.34		40.35	
OHBAT-Ru	932.41	215-280	Loss of two H_2O molecules	5.35	
			Loss of two ligand molecules		
		450-600	Formation of CuO	27.35	88.33
		Above 600		55.63	

Conductometry

Molar Conductivity value of the complexes at 58 and 60 $Ohm^{-1}cm^2mol^{-1}$ for Cu(II) and Ru(III) specified non electrolytic in nature[21]. Molar conductance values of the complexes were represented in the Table 8.

Table 8: conductivity values of OHBAT-Cu (II) and OHBAT-Ru(III) metal complexes

S.No	Complex	Conductance $Ohm^{-1}cm^2mol^{-1}$
1	OHBAT-Cu	58
2	OHBAT-Ru	60

VSM analysis

The magnetic momentum values of OHBAT-Cu and OHBAT-Ru complexes at 4.28 and 5.56 BM specified octahedral geometry[22,23] of the complexes due to the presence of lone pair of electrons in d-orbital of the metal ions. The magnetic susceptibility values of OHBAT-Cu and OHBAT-Ru complexes were represented in the Table 9.

Table 9: Magnetic momentum values of OHBAT-Cu and OHBAT-Ru complexes

S.No	Complex	Magnetic momentum (BM)
1	OHBAT-Cu	4.28
2	OHBAT-Ru	5.56

Biological studies

Biological studies of the ligands and complexes were performed in *In vitro* conditions; represented biological activity of Imines was less than their corresponding metal complexes because of the reduced electron density of metal ions by the transfer of charge, according to Chelating theory[24]. The biological activity values of Imines and their metal complexes were represented in the Table 10.

Table 10: Biological studies of the metal complexes of Copper & Ruthenium metal ions

Compound	*E. coli*	*Klebsiella*	*Bacillus*
OHBAT	9	11	14
OHBAT-Cu	10	13	15
OHBAT-Ru	11	14	16

DNA binding mode of the complexes

DNA binding activity of the complexes was performed with di sodium salt of calf DNA. The spectrum was performed in the absence and presence of CT-DNA. In the presence of CT-DNA the complexes conveyed hypochromic shift because of the presence of chromophores of the ligand. The quantitative comparisons of binding parameters from the following equation

$$[DNA]/(\varepsilon_a - \varepsilon_f) = [DNA]/(\varepsilon_b - \varepsilon_f) + 1\ K_b\ (\varepsilon_b - \varepsilon_f)$$

The binding constants of the complexes were represented in the Table 11.

Table 11: DNA activity of OHBAT-Cu and OHBAT-Ru metal complexes

S.No	Complex	λ_{max} nm Free	Bound	$\Delta\lambda$ nm	H%	$K_b(M^{-1})$
3	OHBAT-Cu	305	311	6	6.35	3.94×10^6
4	OHBAT-Ru	313	317	6	6.29	3.28×10^6

CONCLUSION

In the present article author has reported characterization, biological activity and DNA studies of the metal complexes of Cu (II) and Ru (III) metal ions. The characterization reports suggested, the complex was mono nuclear with molecular formula of $[M\ (L)_2]$. The stoichiometry of the complex was 1:2 ratios and proposed geometry of the complexes was octahedral. The complexes were exhibit more biological activity than their corresponding ligands.

ACNOWLEDGEMENT

1) I would like to express my deepest appreciation to my Professor J. Sreeramulu garu department of chemistry, SK University, Anantapuramu for his continuous support in my research area.

2) I would like thanks to RGM college of Engineering and technology for encouraging in the area of research.

Conflicts of interest

The author has no conflicts regarding publication of this paper.

REFERENCES

1. Sreenatha Sharma, T.; Sreeramulu, J.; Siddaiah, M.; *Global trends pharm Sci*., **2017**, *8*, 4528-4536.
2. Schiff, *Ann. Chem*., **1864**, *131*, 118-119.
3. Sreevidhya, N.; Arulanantham Xavier, Dr.; *IJREAT*., **2017**, *4*, 1-10.
4. Xie, M.; yang, X.D.; Liu, W.; Yan, S.; Meng, Z.; *J. Inorg. Biochem*., **2010**, *104*, 851–857.
5. Montalban, A.G.; Alonso, J.; White, A.J.P.; Williams, D.J.; *Tetrahedron Lett.,* **2010**, *51*, 5543–5545.
6. Feng Jiao,Ti.; Juan Zhou1, JingXin Zhou1, LiHua Gao1, YuanYuan Xing1, and XuHui Li1, *Iranian Polymer Journal.,* **2011**, *20*(2).
7. Bharti, S.K.; Patel, S.K.; Nath, G., Tilak, R., Singh, S.K; *Transition Metal Chemistry*., **2010**.
8. Kumar, S.; Dhar, D.N.; Saxena, P.N.; Applications of metal complexes of Schiff bases—a review, *Journal of Scientific and Industrial Research*., **2009**, *68*(3), 181–187.
9. Nazirkar, Bhushan.; Mandewale, Mustapha.; Yamgar, Ramesh.; *Journal of taibah university for science*., **2019**, *13*(1), 440–449.
10. Sreenatha Sharma, T.; Vasavi, G.S.S.; Sreeramulu, J.; *Acta Ciencia Indica*., **2017**, *XLIIIC*(3), 407-410.
11. Olar, R.; Badea, M.; Marinescu, D., Carmen Chifiriuc, M.; Bleotu, C.; Nicoleta Grecu, M.; Iorgulescu, E.E., Lazar, V.; *Eur. J. Med. Chem*., **2010**, *45*, 3027.
12. Ravanasiddappa, M.; Sureshg, T.; Syed, K.; Radhavendray, S. C.; Basavaraja, C.; S. D. Angadi, S.D.; *E J. chem*., **2008**, *5*(2), 395.
13. Sumathi, R.B.; Halli, M.B.; *Bioinorg. Chem. Appl*., **2014**, *1.*
14. Franz, AM.; Roland, CF.; Mark, S.; Andres, RA.; Diana, HT.; Salah, SM.; Metal(II) complexes of compartmental poly nuclear Schiff bases containing phenolate and alkoxy groups. *Crystals*., **2016**, *6*(9), 1–17.
15. Kumar, V.A.; Sarala, Y.; Siddikha, A.; Vanitha, S.; Babu, S.; Reddy, AV.; Synthesis, characterization antimicrobial and antioxidant activities of 2,4-dihydroxybenzaldehyde-4-phenyl-3- thiosemicarbazone (DHBPTSC) and its Pd(II), Ni(II)dppm mixed ligand and Cu(II) complex having heterocyclic bases. *J Appl Pharm Sci.,* **2018**, *8*(04), 07, 1–8.
16. Mishra, A.P.; Mishra, R.K.; Srivastava, S.P.; *J.Serb.Chem.Soc*., **2009**, *74*, 523-535.
17. Ranga Reddy, G.N.; Kondaiah, S.; Nagaraja Setty, K.; Mallikarjuna Rao, R.; Sreeramulu, J.; *Orient. J. Chem*., **2012**, *28*, 1673-1683.
18. Suraj B. Ade.; Deshpande, M.N.; Kolhatkar, D.G.; *Int.J. ChemTech Res*., **2012**, *4*(2), 578-583.
19. Sujamol, M.S.; Athriya, C.J.; Sindhu, Y.; Mohanan, K.; *Speectrochim.Acta.,* **2010**, *75*A; 106.
20. Basim Hatim Al-Zaidi.; Mohammed Mujbel Hasson.;, *Ahmad Hussein Ismail Journal of Applied Pharmaceutical Science.,* **2019**, *9* (04), 045-057.
21. Shigehisa, A.; Tatsuya, N.; Novel thiosalamo ligand as a remarkably stable N2S2 salen-type chelate and synthesis of a nickel(II) complex. *Inorg Chem*., **2005**, *44*(5), 1205–07.
22. Bushra Begum, A.; Asha, M.S.; Shaukath Ara Khanum.; *Chem Sci Rev Lett*, **2014**, *3*(11), 673-684.
23. Tas, E.; Kilic, A.; Konak, N.; Yilmaz, I.; *Polyhedron*., **2008**, *27*, 1024.
24. Bimal Kumar.; Rai, B.K.; Nisha Ambastha.; *Orient. J. Chem*., **2011**, *27*, 1173-1178.