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Research Article

Synthesis, characterization, antimicrobial activity and transition metal complexes of 3-bromo-N'-(1-(5-chloro-2-hydroxyphenyl)ethylidene) benzohydrazide ligand.

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ABSTRACT
A series of Mn(II), Co(II), Ni(II), Cu(II) and Zn(II) transition metal complexes of 3-bromo-N'-(1-(5-chloro-2-hydroxyphenyl)ethylidene)-benzohydrazide (H_2L) were synthesized and characterized by IR, elemental analysis, UV-visible and thermal analysis. Spectral data suggests that the ligand acts as dibasic, tridentate coordinated through oxygen of phenolic OH, nitrogen of azomethine group and enolic oxygen of hydrazide. Antimicrobial activity of the metal complexes was found to be excellent against fungi than the parent ligand as compared to standard drug and moderate activity against bacterial stains.

KEYWORDS
Ligand, Metal complex, Antimicrobial

1. INTRODUCTION

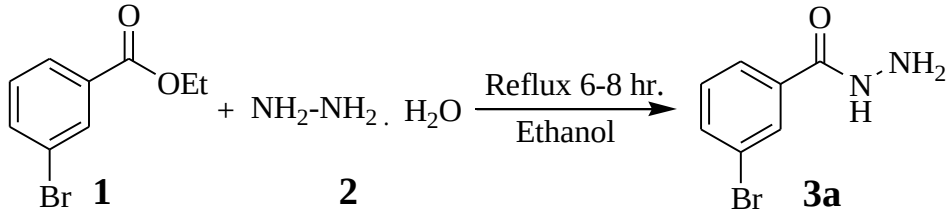
Hydrazones constitute an important class of compounds with a wide range of pharmacological properties; receiving more importance due to significant applications in medicinal field. These compounds have numerous biological activities after coordination with metals. Hydrazides form stable complexes with different metals which can be used in chelation therapy. Aroylhydrazone metal complexes have a broad rang applications in biological processes such as in the treatment of tuberculosis, tumor, leprosy and mental disorder [1-2]. The chemistry of organotin (IV) complexes of aroylhydrazone has been extensively studied due to their thermal stability, structural diversity and the compounds possess good antitumor [3-6], antimicrobial [7-9], antioxidant [10] and anti-inflammatory activities [11].

In the present article, we report synthesis of aroylhydrazone by the condensation of 3-bromobenzhydrazide with 5-chloro-2-hydroxyacetophenone which were characterized by spectroscopic data and evaluated for antimicrobial activity.

2. MATERIALS AND METHODS

2.1. Synthesis of 3-Bromobenzhydrazide (3a)

To a solution of ethyl-3-bromobenzoate (1) (2 mmol) in ethanol (10 ml) was added hydrazine hydrate (80%) (2) (3 mmol) and the mixture was refluxed for 6-8 hr. After completion of reaction, the reaction mixture was cooled and filtered off. The obtained white product (3a) was recrystallized from ethanol & confirmed by melting point and ^{1}H NMR (Scheme 1).

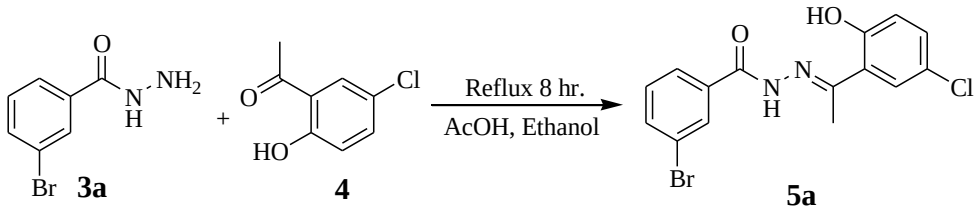


Scheme 1. Synthesis of 3-bromobenzhydrazide

^{1}H NMR (200 MHz, DMSO-d_6) δ ppm 4.54 (br s, 2 H, NH_2), 7.37 - 7.47 (dd, J = 8.5, 8 Hz, 1 H), 7.67 - 7.86 (m, 2 H), 7.98 (dd, J=1.83, 1.71 Hz, 1 H), 9.89 (br s., 1 H, NH).

2.2. Synthesis of 3-bromo-N'-(1-(5-chloro-2-hydroxyphenyl)ethylidene) benzohydrazide (H_2L) (5a)

The ligand was synthesized by condensation of equimolar mixture of 5-chloro-2-hydroxyacetophenone (4) (2 mmol) with 3-bromobenzhydrazide (3a) (2 mmol) in ethanol (10 ml). The resulting reaction mixture was then refluxed for 8 hr. On cooling, the reaction mixture was poured onto crushed ice, stirred and filtered on Buchner funnel and finally crystallized from ethanol as a white solid (5a); Yield : 85%, M. P.= 240°C (Scheme 2).



Scheme 2. Synthesis of Ligand (H_2L).

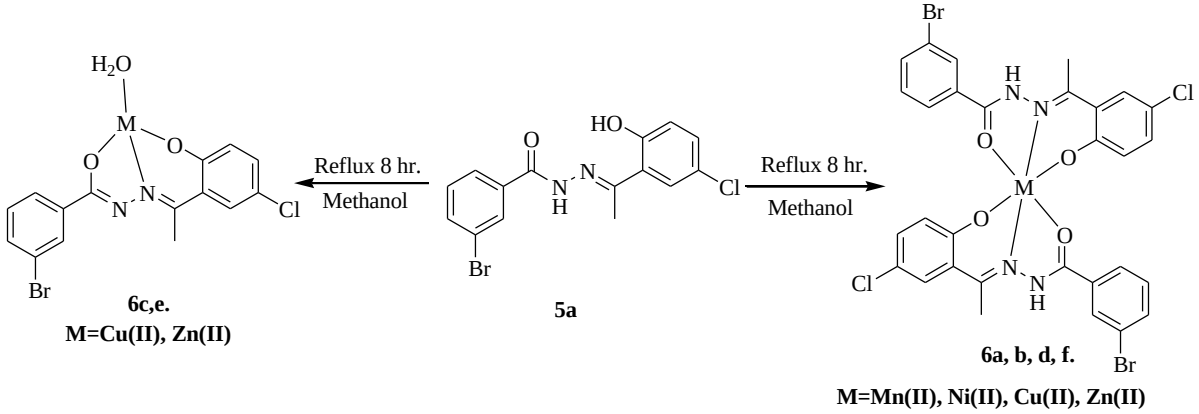
2.3. Spectral data of ligand (H_2L)

IR (KBr) cm^{-1} : 3206 (-OH, -NH), 1647 (-C=N), ^{1}H NMR (200 MHz, DMSO-d_6) δ ppm 2.51 (s, 3 H), 6.95 (d, *J* = 8.59 Hz, 1 H), 7.29 - 7.39 (m, 1 H), 7.45 - 7.58 (m, 1 H), 7.63 - 7.68 (m, 1 H), 7.79 - 7.87 (m, 1 H), 7.92 (d, *J* = 8.08 Hz, 1 H), 8.06 - 8.20 (m, 1 H), 11.53 (s, 1 H), 13.36 (s, 1 H); ^{13}C NMR (200 MHz, DMSO-d_6): δ ppm 14.37, 119.16, 120.82, 121.65, 122.20, 127.42, 127.81, 130.70, 130.73, 130.94, 134.82, 34.94, 157.31, 157.46, 163.15; LCMS: m/z (%) : 367.0 (M+H).

2.4 General method for the synthesis of metal complexes (6a-f)

To a hot methanolic solution of ligand (5a) (H_2L) different transition metal chloride/acetate in methanol were added and the contents were refluxed for 8 hr to prepare complexes with 1:1 and 1:2 metal to ligand stoichiometry, respectively. The precipitates of metal complexes thus formed were filtered off and washed with methanol (Scheme 3).

Analytical and physical data of the synthesized compounds is given in Table 1.



Scheme 3. Synthesis of metal complexes (6a-f).

Table 1. Analytical and physical data of the synthesized compounds.

Comp.	Compounds	Mol. Formulae (F.W.)	M.P.°C	Color	Elemental analysis Obs. (Cal.)%			
					% C (cal.)	**% H (cal.)**	**% N (cal.)**	**% M (cal.)**
5a	Ligand (H_2L)	$C_{15}H_{12}BrClN_2O_2$ (367.62)	240°C	White	49.00 (49.01)	3.20 (3.29)	7.55 (7.62)	-
6a	$[Mn(HL)_2]$	$C_{30}H_{22}Br_2Cl_2MnN_4O$	>250°C	Orange	45.81 (45.72)	2.86 (2.81)	7.05 (7.11)	6.91 (6.97)

		(788.17)						
6b	[Ni $(HL)_2$]	$C_{30}H_{22}Br_2Cl_2N_4NiO_4$ (791.92)	>250°C	Orange	45.84 (45.50)	2.87 (2.80)	7.26 (7.07)	7.35 (7.41)
6c	[Cu(L)(H_2O)]	$C_{15}H_{12}BrClCuN_2O_3$ (447.17)	>250°C	Green	40.25 (40.29)	2.75 (2.70)	6.32 (6.26)	14.11 (14.21)
6d	[$Cu(HL)_2$]	$C_{30}H_{22}Br_2Cl_2CuN_4O_4$ (796.78)	>250°C	Green	45.15 (45.22)	2.77 (2.78)	7.06 (7.03)	7.80 (7.98)
6e	[Zn(L)(H_2O)]	$C_{15}H_{12}BrClN_2O_3Zn$ (449.01)	>250°C	yellow	40.41 (40.12)	2.82 (2.69)	6.15 (6.24)	14.43 (14.56)
6f	[Zn $(HL)_2$]	$C_{30}H_{22}Br_2Cl_2N_4O_4Zn$ (798.62)	>250°C	yello-wish	45.05 (45.12)	2.83 (2.78)	7.10 (7.02)	8.12 (8.19)

3. RESULTS & DISCUSSION

3.1. Infrared Spectra

A comparative study of IR spectra of the ligand and metal complexes shows that the band appearing at 1604-1647 cm^{-1} for ν(C=O) in ligands and the ν(N-H) peak at 3206 cm^{-1} were absent in the spectra of [Cu(L)(H_2O)] and [Zn(L)(H_2O)] complexes. This is due to the ketoenol tautomerism of ligands and their successive coordination with enolic oxygen [12]. The presence of bands at 1327 cm^{-1} in complexes is attributed to ν(C-O) due to coordination of enolic oxygen after deprotonation [13].

The IR spectrum of [$Mn(L)_2$] complex showed ν(N-H) and ν(C=O) bands indicating that the ligands remain in their keto form. In IR spectra of complex the azomethine ν(C=N) band of hydrazone at 1647 cm^{-1} shifts to lower wave number suggesting the coordination of azomethine nitrogen to metal ion [14].

3.2. Thermogravimetric analysis

Thermogravimetric analysis of metal complexes gives an idea about the presence of lattice, coordinated water or any solvent molecule and confirms their composition and thermal stability. Thermal analysis of complex was carried out under nitrogen atmosphere in the temperature range between 25-800 ^oC with a heating rate of 10 $^oC\ min^{-1}$. TG curve of [Zn (L)(H_2O)] complex decomposed in two stages. The first stage of decomposition in the temperature range between 160-250 ^oC corresponds to the removal of coordinated water molecule; whereas the second stage of decomposition temperature range between 300-380^oC, corresponds to removal of organic moiety or ligand and finally form metal oxide.

The TGA curve of [$Mn(HL)_2$] complex decomposed in only one stage in the temperature range between 450-550 ^oC, corresponding to complete removal of organic moiety and form metal oxide which clearly provides an evidence for the absence of lattice or coordinated water molecule (Fig. 1) .

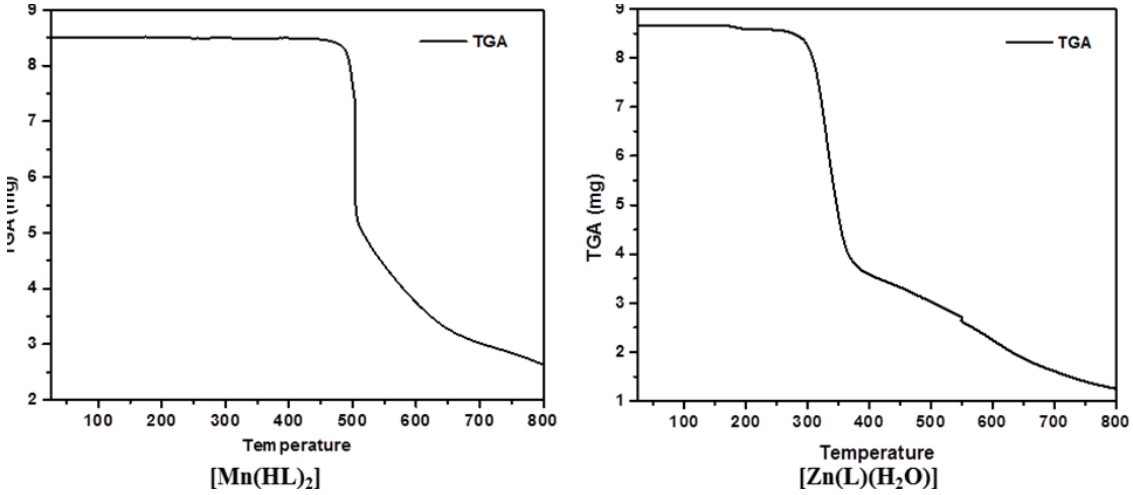


Fig. 1. TGA curves of the metal complexes.

3.3. Electronic spectra

UV-Visible spectra of metal complexes were recorded in DMSO solvent at room temperature. Electronic spectra of Mn(II), Ni(III), Cu(II), and Zn(II) metal complexes displayed three bands in the range 250-290 nm, 300-350 nm and 400-410 nm which were assigned for $\pi \longrightarrow \pi^*$ and charge transfer spectra which were observed after complexation [15] indicating the coordination of azomethine nitrogen to metal ion and the third peak was observed due to d-d transition (Fig. 2).

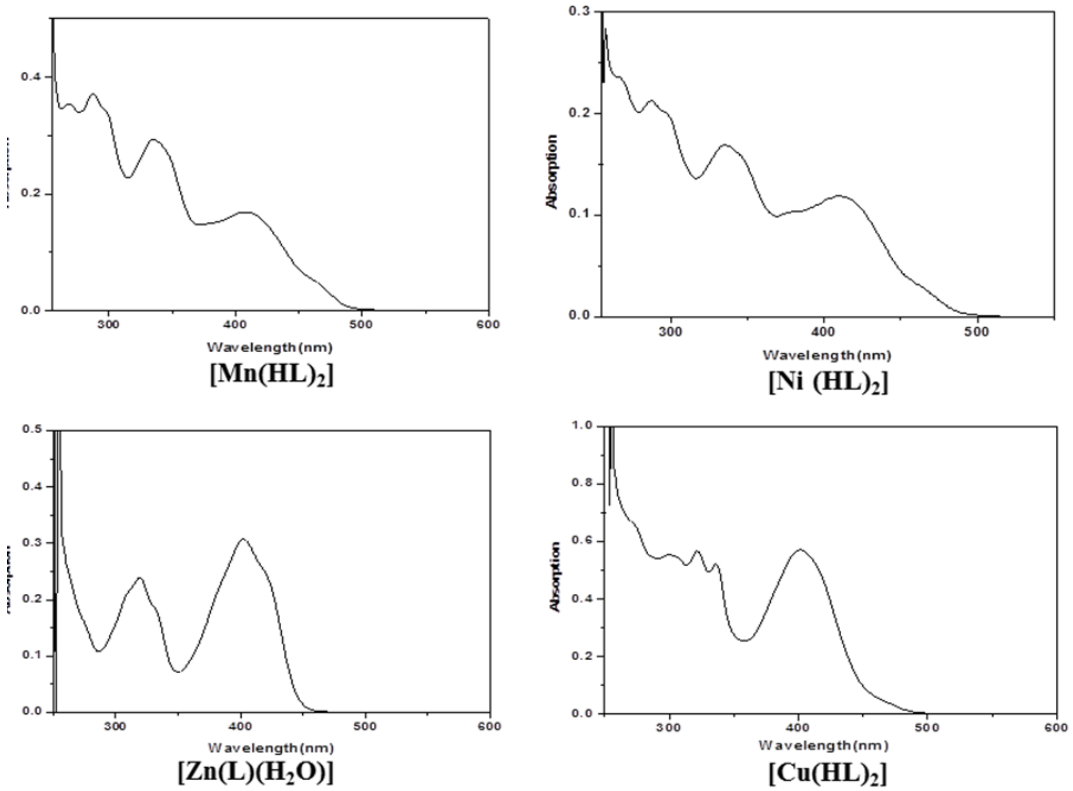


Fig. 2. UV spectra of transition metal complexes.

3.4. Antimicrobial activity

The synthesized ligand and complexes were screened for antibacterial and antifungal activity. The screenings were done on petri plates containing solidified 20 ml Muller Hinton Agar and Potato Dextrose Agar medium for bacterial and fungal sensitivity, respectively. These plates were incubated at 37 ^{o}C for 24 and 48 hr for antibacterial and antifungal activity respectively. The activities were measured in terms of zone of inhibition in mm.

The antibacterial and antifungal activities were carried out on four bacteria viz Staphylococcus aureus, Streptococcus Pyogenes, Escherichia coli, salmonella Typhi at 500 ppm and two fungi i.e. Candida albicans, Trichophyton rubrum at 500 ppm in DMSO as solvent and using Ofloxacin and Fluconozole as positive control reference drug in antibacterial and antifungal activity assay respectively. The metal complexes display more inhibitory effects than the free ligand against the same organism under identical conditions. Increasing activity of metal complexes can be explained on the basis of Tweedy chelation theory [16].

Mn(II), Ni(II) and Zn(II) complexes exhibited enhanced inhibitory activity against candida Albicans and Mn(II), Ni(II) and Cu(II) showed more inhibitory activity against T. Rubrum fungal species (Table 2).

Table 2. Antimicrobial screening of synthesized compounds.
SA = S. Aureus, SP = S. Pyogenes, EC = E. Coli, ST = S. Typhi, CA = C. Albicans, TR = T. Rubrum

Compounds		**Antibacterial Activity (Zone of Inhibition in mm)**				**Antifungal Activity (Zone of Inhibition in mm)**	
		SA	**SP**	**EC**	**ST**	**CA**	**TR**
5a(VII)	Ligand (H_2L)	19	16	12	16	11	11
6a(V)	[$Mn(HL)_2$]	19	18	12	17	**18**	**20**
6b(VI)	[Ni $(HL)_2$]	19	16	14	16	**17**	**21**
6c(II)	[$Cu(L)(H_2O)$]	10	18	10	15	12	**18**
6d(IV)	[$Cu(HL)_2$]	11	15	11	12	16	11
6e(I)	[$Zn(L)(H_2O)$]	9	12	10	11	11	12
6f(III)	[Zn $(HL)_2$]	11	15	10	11	**19**	11
Ofloxacin		**39**	**32**	**42**	**32**	**-**	**-**
Fluconozole		**-**	**-**	**-**	**-**	**13**	**15**

4. CONCLUSION

In summary different transition metal complexes were synthesized from 3-bromo-N'-(1-(5-chloro-2-hydroxyphenyl)ethylidene)benzohydrazide ligand and characterized by various spectral techniques. Spectroscopic data suggested that the [$Zn(L)(H_2O)$] and [$Cu(L)(H_2O)$] complexes adopted a tetrahedral and square planer geometry respectively, whereas the remaining complexes were octahedral in shape. The synthesized compounds were screened for antibacterial and antifungal activities against different species of bacteria and fungi. The Mn(II), Ni(II), Cu(II) and

Zn(II) complexes exhibited excellent activity against fungal species than standard drug Fluconazole.

5. ACKNOWLEDGEMENTS

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6. REFERENCES

1. El-Bahnasawy R. M., El-Meleigy S. E., and El-Tawansi A. (1994) *Trans. Met. Chem.* 19, 270.
2. Maurya R. C., Verma R., and Singh T. (2010) *Synth. React. Inorg. Met. Org. Chem.* 33, 309.
3. Koch B., Baul T. S. B., and Chatterjee A. (2008) *J. Appl. Toxicol.* 28, 430.
4. Rehman W., Badshah A., Khan S., and Tuyet L. T. A. (2009) Eur. *J. Med. Chem.* 44, 3981.
5. Hong M., Yin H., Zhang X., Li C., Yue C., and Cheng S. (2013) *J. Organomet. Chem.*, 23, 724.
6. Gielen M., and Tiekink E. R. T. (Eds.) (2005) Metallotheraupeutic drug and metal-based diagnostic agents: The use of metals in medicine, *Wiley*, UK 421.
7. Sirajuddin M., Ali S., Haider A., Shah N. A., Shah A., and Khan M. R. (2012) *Polyhedron*, 19, 40.
8. Yenisehirli G., Oztas M. A., Sahin, M. Celebier, N. Ancin, and S. G. Oztas (2010) *Heteroatom Chem.* 21, 373.
9. Oztas N., Yenisehirli G., Ancin N., Oztas S., Ozcan Y., and Ide S. (2009) *Spectrochim. Acta, Part A* 72, 929.
10. Gonzalez A., Gomez E., Cortes-Lozada A., Hernandez S., Ramirez-Apan T., and Nieto-Camacho A. (2009) *Chem. Pharm. Bull.* 5, 57.
11. Nath M., Saini P. K., and Kumar A. (2009) *Appl. Organometal. Chem.* 23, 434.
12. Wang H. Y., Shi Y. H., and Lu H. Y. (2012) *J. Coord. Chem.,* 65, 2811.
13. Abdallah S. M. (2012) *Arab. J. Chem.* 5, 251.
14. Thaker B. T., Surati K. R., Patel P., and Parmar S. D. (2006) *J. Iran. Chem. Soc.* 3, 371.
15. Kamat V., Kokare D., Naik K., Kotian A., Naveen S., Dixit S. R., Lokanath N. K., Joshi S. D., and Revankar V. K. (2017) *Polyhedron* 127, 225.
16. Gowda K. R. S., Naik H. S. B., Kumar B. V., Sudhamani C. N., Sudeep H. V., Naik T. R. R., and Krishnamurthy G. (2013) *Spectrochimica Acta Part A: Molecular and Biomolecular Spectroscopy* 105, 229.