

Synthesis, Characterization and *in vitro* Anti-fungal Screening of Manganese(II) and Copper(II) Complexes of Hexaaza [N₆] Macrocyclic Ligand

U. Kumar^{*,1} and S. Chandra²

¹Department of Chemistry, J. V. College, Baraut, C. C. S. University, Meerut, India

²Department of Chemistry, Zakir Husain College, University of Delhi, India
e-mail: umendra_khokhar@rediffmail.com, schandra_00@yahoo.com

Abstract

New manganese(II) and copper(II) complexes of 12-membered macrocyclic Schiff base ligand containing thiosemicarbazone moiety have been prepared of general composition [MLX₂] where M = Mn(II) or Cu(II), L = 3,4,9,10-tetra-2-furanyl-1,2,5,6,8,11-hexaazacyclododeca-7,12-dithione-2,4,8,10-tetraene, X = Cl, NO₃⁻ and NCS. The complexes have been characterized by elemental analysis, molar conductance, magnetic susceptibility measurements and spectral (IR, electronic, EPR and mass) analyses. The IR spectra of complexes suggested that ligand is coordinated to the metal ion through imine nitrogen atoms. On the basis of spectral studies, an octahedral and tetragonal geometry has been assigned for Mn(II) and Cu(II) complexes, respectively. EPR spectra of polycrystalline Mn(II) complexes gave an isotropic signal with g value centered around free electron g value. EPR spectra of Mn(II) complexes in DMSO showed hyperfine splitting containing six lines, whereas EPR spectra of polycrystalline Cu(II) complexes showed anisotropic signal. Conductivity measurements support the non electrolytic nature of the complexes. Magnetic moment data suggest that reported complexes are paramagnetic and of high spin type. All the examined complexes have also been tested *in vitro* against a number of pathogenic fungi. Results indicated that the complexes exhibited good antifungal activities.

Keywords: Macrocyclic, octahedral, antifungal, tetragonal, anisotropic.

Introduction

Metal complexes with macrocyclic ligands have gained great research interest in recent years¹. The importance of macrocyclic complexes in coordination chemistry is mainly due to various applications in biological processes such as photosynthesis and dioxygen transport². Schiff base macrocyclic ligands derived from thiosemicarbazones are

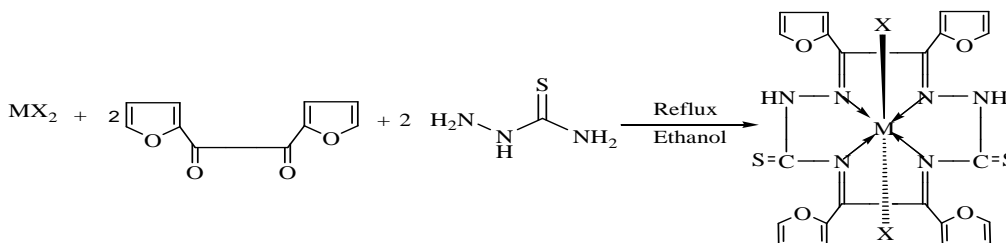
* Corresponding author

of significant interest not only for their wide biological properties as antibacterial, anticancer, antiviral, and antifungal agents^{3,4} but also for their capacity for chemical recognition of anions and metals of biochemical and environmental importance⁵⁻⁷. Macrocyclic complexes have been attracted attention of Chemist because of their resemblance with many natural systems like porphyrins and cobalamines⁸. The activity of such compounds is strongly dependent upon the nature of the heteroatomic ring and position of attachment to the ring as well as the form of the thiosemicarbazone moiety⁹⁻¹¹. In the light of above facts, the present study deals with the synthesis, characterization and antifungal evaluation of manganese(II) copper(II) complexes.

Experimental Methods

All the chemicals (from Sigma–Aldrich Company) used in this research work were of AR grade and used as received without further purification.

A template reaction was carried out to synthesize the complexes. An EtOH solution (20 ml) of the respective divalent metal salt (10 mmol) and a hot EtOH solution (20 ml) of thiosemicarbazide (20 mmol) were mixed. Then, an EtOH solution (20 ml) of furil (20 mmol) in the presence of a few drops of concentrated hydrochloric acid was added to the resultant solution. The solution was refluxed for about 5-7 hours. The colored complexes precipitated out on cooling the reaction solution overnight. The complexes were filtered, washed with ethanol and dried over P₄O₁₀. The purity of complexes was checked by thin layer chromatography (TLC). The general reaction for the formation of complexes is given in scheme 1.



Scheme 1: $M = Mn(II), Cu(II)$ and $X = Cl, NO_3^-, NCS^-$.

The C, H and N were analyzed on Carlo-Erba 1106 elemental analyzer. The nitrogen content of the complexes was determined using Kjeldahl method. Molar conductance was measured on the ELICO (CM82T) conductivity bridge. Magnetic susceptibilities were measured at room temperature on Gouy balance using CuSO₄·5H₂O as calibrant. Electronic spectra were recorded in DMSO on Shimadzu UV mini–1240 spectrophotometer. IR spectra (KBr) were recorded on FTIR spectrum BX–II spectrophotometer. EPR spectra of Mn(II) and Cu(II) complexes were recorded on E₄-EPR spectrometer using the DPPH as the g marker. EIMS mass spectra were recorded on Jeol, JMS–DX–303 mass spectrometer.

Results and Discussion

The general composition for the complexes was found MLX_2 (where $M = Mn(II)$, $Cu(II)$ and $X = Cl^-, NO_3^-, NCS^-$). The physical properties and elemental analysis of the complexes are given in Table 1. The complexes were insoluble in common organic solvents but were soluble in DMSO and DMF.

The low value of molar conductance ($12-18 \text{ ohm}^{-1} \text{ cm}^2 \text{ mol}^{-1}$), which was carried out in DMF at the concentration of 10^{-3} M , indicates (Table 1) the non-electrolytic nature of complexes¹². The low value of the molar conductance suggested that the anions are inside the coordination sphere and bonded to the metal ion. Therefore, these complexes may be formulated as $[MLX_2]$. It has been also reported that the low value of molar conductance is due to large size of anionic coordination sphere¹³.

Table 1: Physical properties and analytical data of Mn(II) and Cu(II) complexes.

Complexes	Color	M. P. (°C)	Molar conductance ($\Omega^{-1} \text{ cm}^2 \text{ mol}^{-1}$)	Yield (%)	Elemental analysis found (calculated)			
					M	C	H	N
$[MnLCl_2]$ $MnC_{22}H_{12}N_6O_4S_2Cl_2$	Pale yellow	248	12	62	9.02 (8.92)	42.82 (42.85)	2.19 (2.27)	13.64 (13.63)
$[MnL(NO_3)_2]$ $MnC_{22}H_{12}N_6O_{10}S_2$	Light yellow	260	15	65	8.92 (8.22)	39.15 (39.46)	2.19 (2.09)	16.76 (16.74)
$[MnL(NCS)_2]$ $MnC_{22}H_{12}N_6O_4S_4$	Off white	256	18	68	8.52 (8.30)	43.25 (43.57)	2.19 (2.11)	16.72 (16.94)
$[CuLCl_2]$ $CuC_{22}H_{12}N_6O_4S_2Cl_2$	Light blue	252	15	64	9.98 (10.09)	42.75 (42.30)	2.15 (2.24)	13.64 (13.46)
$[CuL(NO_3)_2]$ $CuC_{22}H_{12}N_6O_{10}S_2$	Light green	245	14	60	8.99 (9.30)	39.05 (38.99)	2.15 (2.06)	16.78 (16.54)
$[CuL(NCS)_2]$ $CuC_{22}H_{12}N_6O_4S_4$	Green	255	12	64	8.96 (9.41)	43.45 (43.04)	2.17 (2.09)	16.95 (16.74)

Magnetic moment measurements for the complexes were made at room temperature. The manganese(II) complexes show magnetic moment in the range 5.91-5.95 BM (Table 2), which is close to the spin only value (5.92 BM) a value in accordance with a high spin configuration showing the presence of octahedral¹⁴ environment around the manganese(II) ion in the complexes. On the other hand, the copper(II) complexes showed the magnetic moment in the range of 1.96-1.98 BM, corresponding to one electron. It is slightly higher than those expected for a d^9 system. This may be attributed to the incomplete quenching of the orbital contribution to the magnetic moment or to spin orbit coupling¹⁵.

The relevant IR spectral bands of complexes are listed in (Table 3). The IR spectra of the complexes showed the absence of absorption at 3400 cm^{-1} , indicating the absence of free amino group. A medium intensity band at $1580-1620 \text{ cm}^{-1}$ characteristic to the imine $\nu(C=N)$ ¹⁶ stretching frequency was appeared at lower frequencies, suggesting that coordination takes place through the azomethine nitrogen atoms. The appearance of a band at $410-450 \text{ cm}^{-1}$ $\nu(M-N)$ also indicated that metal is bonded with imine nitrogen. The band assigned to thioamide at 825 cm^{-1} $\nu(C=S)$ ¹⁷ was appeared in the spectrum of free thiosemicarbazide remained almost at the same position in the complexes, indicating that

thioamide sulphur is not involved in coordination. Thus, it may be concluded that ligands act in tetradentate fashion and binds to metal ions through imine nitrogen atoms.

Table 2: Electronic, EPR spectral & magnetic moment data of Mn(II) & Cu(II) complexes.

Complexes	ν_1 (cm^{-1})	ν_2 (cm^{-1})	ν_3 (cm^{-1})	ν_4 (cm^{-1})	μ_{eff} (B.M.)	ξ_{\parallel}	ξ_{\perp}	G
[Mn LCl ₂]	19950	23204	29883	31650	5.91	-	-	-
[Mn L(NO ₃) ₂]	19680	23980	28680	31530	5.95	-	-	-
[Mn L(NCS) ₂]	19760	24915	28860	31740	5.93	-	-	-
[Cu LCl ₂]	14650	25560	-	-	1.96	2.15	2.07	2.14
[Cu L(NO ₃) ₂]	15384	-	-	-	1.98	2.27	2.14	1.92

Furthermore, the IR spectral bands at 1450–1400, 1320–1290 and 1070–1020 cm^{-1} , in the spectra of nitrate complexes suggested that both nitrate groups are coordinated to the central metal ion in unidentate fashion¹⁸. Thiocyanate anion may coordinate in different ways. It can show linkage isomerism. The complexes under study showed a single sharp band at 2050–2080 cm^{-1} indicating both thiocyanate groups were N-bonded¹⁹.

Table 3: IR spectral data (cm^{-1}) of Mn(II) and Cu(II) complexes.

Complexes	$\nu(\text{NH})$	$\nu(\text{C}=\text{N})$	$\nu(\text{C}=\text{S})$	$\nu(\text{MN})$
[Mn L Cl ₂]	3216 b	1565 s	827 m	420 m
[Mn L(NO ₃) ₂]	3220 b	1550 s	820 m	425 m
[Mn L(NCS) ₂]	3220 b	1545 s	825 m	410 m
[Cu LCl ₂]	3220 b	1562 s	827 m	445 m
[Cu L(NO ₃) ₂]	3218 b	1560 s	822 m	430 m
[Cu L(NCS) ₂]	3220 b	1558 s	820 m	450 m

The electronic spectra of reported complexes were recorded in DMSO. The Mn(II) complexes show weak electronic spectral bands in the range 19680–19950, 23204–24915, 28680–29883 and 31650–31740 cm^{-1} (Table 2) and these bands are assigned to ${}^6\text{A}_{1g} \rightarrow {}^4\text{T}_{1g}({}^4\text{G})$, ${}^6\text{A}_{1g} \rightarrow {}^4\text{E}_g({}^4\text{G})$, ${}^6\text{A}_{1g} \rightarrow {}^4\text{E}_g({}^4\text{D})$ and ${}^6\text{A}_{1g} \rightarrow {}^4\text{T}_{1g}({}^4\text{P})$ transitions, respectively. The positions of bands indicated that Mn(II) complexes have an overall octahedral geometry²⁰. The electronic spectra of Cu(II) complexes (Fig. 1) display one broad absorption band (Table 2) in the range 14650–15384 cm^{-1} and in some complexes a well defined shoulder at 25450 - 25560 cm^{-1} , these spectral bands may be assigned to ${}^2\text{B}_{1g} \rightarrow {}^2\text{A}_{1g} (d_{x^2-y^2} \rightarrow d_{z^2} \nu_1)$ and ${}^2\text{B}_{1g} \rightarrow {}^2\text{B}_{2g} (d_{x^2-y^2} \rightarrow d_{zy} \nu_2)$ transitions. These spectral bands indicated a tetragonal environment around Cu(II) ion in the complexes²¹.

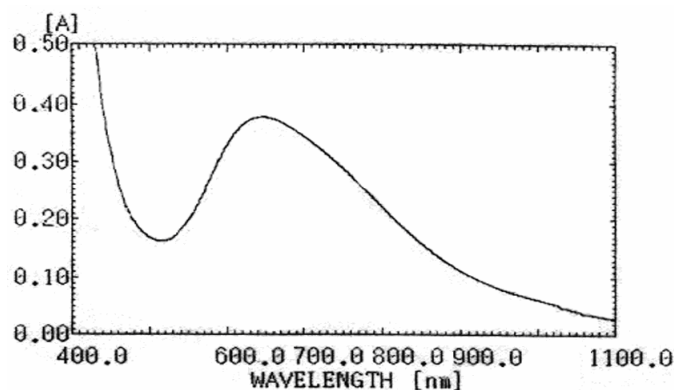


Figure 1: Electronic spectrum of $[Cu L(NO_3)_2]$.

EPR spectra of Cu(II) complexes were recorded at room temperature in the polycrystalline state, on X band at frequency of 9.1 GHz under the magnetic field strength of 3000G. The present Cu(II) complexes exhibited well resolved anisotropic signals in the parallel and perpendicular regions. The observed data showed that $g_{\parallel} = 2.15 - 2.26$ and $g_{\perp} = 2.07 - 2.14$. The g_{\parallel} and g_{\perp} values are closer to 2 and $g_{\parallel} > g_{\perp}$ is suggested major distortion from O_h symmetry in the Cu(II) complexes²². Kivelson and Neiman have shown that g_{\parallel} is a moderately sensitive function for indicating covalency. Relatively speaking $g_{\parallel} > 2.3$ is characteristic of anionic environment and $g_{\parallel} < 2.3$ of a covalent environment in M-L bonding²³. The observed g_{\parallel} values are less than 2.3 in agreement with the covalent character of the M-L bond. The trend $g_{\parallel} > g_{\perp} > 2.0023$ observed for the complexes indicates that unpaired electron is localized in $d_{x^2-y^2}$ orbital of the Cu(II) ion. Thus a tetragonal geometry is proposed for the aforesaid complexes. $G = (g_{\parallel} - 2)/(g_{\perp} - 2)$, which measure the exchange interaction between the metal centers in a polycrystalline solid has been calculated. According to Hathaway²⁴, if $G > 4$ the exchange interaction is negligible and if $G < 4$ indicates considerable exchange interaction in the solid complexes. The reported complexes showed G value are < 4 indicating the exchange interaction in complexes. EPR spectra of Mn(II) complexes were recorded as polycrystalline sample and in DMSO solution. EPR spectrum of a polycrystalline sample gave one broad isotropic signal centered on the approximate free electron g value (2.0023). In DMSO solution, the complexes give EPR spectra containing six lines (Fig. 2) arising due to hyperfine interaction²⁵ between the unpaired electrons with the Mn nucleus ($I = 5/2$).

The antifungal activities of reported macrocyclic complexes were tested against various fungi viz. *A. niger*, *A. alternata*, *F. oxysporum* and *F. odum* under laboratory conditions by food poison technique²⁶ at 50–100 ppm concentrations. The experimental data (Table 4) suggested that complexes provided satisfactory antifungal properties. The percentage inhibition is calculated by using the formula²⁷, $\% I = 100(C-T)/C$, where C and T are the diameter (mm) of the fungus colony in the control and treatment, respectively.

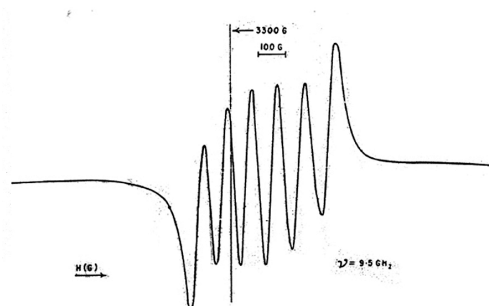


Figure 2: The X band EPR spectrum of $[MnLCl_2]$.

Table 4: Antifungal screening data of Mn(II) and Cu(II) complexes.

Complexes	Fungal inhibition % (conc. in ppm)							
	<i>A. niger</i>		<i>A. alternata</i>		<i>F. oxysporum</i>		<i>F. odum</i>	
	50	100	50	100	50	100	50	100
$[MnLCl_2]$	45	55	45	58	47	60	42	48
$[MnL(NO_3)_2]$	47	55	46	56	49	53	48	58
$[MnL(NCS)_2]$	42	50	44	58	47	51	46	55
$[CuLCl_2]$	48	58	49	55	48	58	45	57
$[CuL(NO_3)_2]$	45	60	45	60	45	55	47	62
$[CuL(NCS)_2]$	48	55	47	60	46	58	49	60

Conclusions

The synthesis and spectral characterization of manganese(II) and copper(II) complexes of 12-membered hexaaza macrocyclic ligand have been reported. All the complexes are non electrolyte in nature. IR spectra show that coordination between ligand and metal ions takes place through azomethine nitrogen atoms. Spectral studies suggest six coordinated structure for the complexes. The EPR spectra of copper(II) complexes indicated that unpaired electron is localized in $d_{x^2-y^2}$ orbital. *In vitro* antifungal activities of the reported complexes have also been screened. Results indicated that the complexes possess good antifungal properties.

Acknowledgements

We greatly acknowledge the principal of Zakir Husain College (University of Delhi) for providing research facilities to carry out this research work and Indian Institute of

Technology, Bombay for recording EPR spectra as well as University Grant Commission for financial support.

References

1. A. Bayri and M. Karakaplan, *Pra. J. Phy. Ind. Aca. Sci.*, 2007, **69(2)**, 301.
2. M. Shakir, P. Chingsubam, H. T. N. Chishti; Y. Azim and N. Begum, *Ind. J. Chem.*, 2004, **43A**, 556.
3. S. Chandra and Sangeetika, *Ind. J. Chem.*, 2002, **41A**, 1629.
4. L. D. S. Yadav and S. Singh, *Ind. J. Chem.*, 2001, **40B**, 440.
5. E. Labisbal, A. Sausa, A. Casticeiras, A. V. Gracia, J. Romero and D. X. West, *Polyhedron.*, 2000, **19**, 1255.
6. M. K. Srivastava, B. Mishra and M. Nizamuddin, *Ind. J. Chem.*, 2001, **40B**, 342.
7. D. K. Dermertzi, N. Kourkoumetis, M. A. Dermertzi, J. R. Miller, C. S. Frampton, J. K. Swearingen and D.X. West, *Eur. J. Inorg. Chem.*, 2000, 727.
8. S. Chandra and S. Sharma, *Trans. Met. Chem.*, 2007, **32**, 150.
9. S. Chandra, S. Raizada, M. Tyagi and A. Gautam, *Bioinorg. Chem. App.*, 2007, Article ID51483.
10. R. V. Singh, N. Fahmi and M. K. Biyala, *J. Ira. Chem. Soc.*, 2005, **2(1)**, 40.
11. B. Dietrich, P. Viout and J. M. Lehn, "Macrocyclic Chemistry" (*VCH, Weinheim*) 1993.
12. S. Chandra and U. Kumar, *Spec. Chim. Acta*, 2004, **A60**, 2825.
13. R. Rojavel, M. Senthil and C. Anitha, *E. J. Chem.*, 2008, **5(3)**, 620.
14. S. Chandra and S. D. Sharma, *Trans. Met. Chem.*, 2002, **27**, 732.
15. R. N. Prasad, M. Agarwal and R. George, *J. Ind. Chem. Soc.*, 2003, **80**, 79
16. C. Lodeiro, R. Baritida, E. Bertolo, A. Macias and R. Rodriguz, *Trans. Met. Chem.*, 2003, **28**, 388.
17. S. Chandra and U. Kumar, *Synth. React. Met – Org. Chem.*, 2004, **34 (8)**, 1417.
18. S. Chandra and U. Kumar, *Spec. Chim. Acta.*, 2005, **A61**, 219.
19. V. B. Rana, D. P. Singh, P. Sing hand M. P. Teotia, *Trans. Met. Chem.*, 1981, **6**, 36.
20. S. Chandra, G. Singh, V. P. Tyagi and S. Raizada, *Synth. React. Inorg. Met-Org. Chem.*, 2001, **31(10)**, 1759.
21. S. Chandra and A. Kumar, *Spec. Chim. Acta*, 2007, **A66(4-5)**, 1347.
22. S. N. Choi, E. R. Menzel and J. R. Wasson, *J. Inorg. Nucl. Chem.*, 1977, **39**, 417.
23. D. N. Kumar, B. K. Singh, B. S. Garg and P. K. Singh, *Spec. Chim. Acta*, 2003, **A59**, 1487.
24. B. J. Hathaway, G. N. Bardley and R. D. Gillard, Eds, "Essays in Chemistry" Academic press, New York, USA, 1971.
25. D. M. Hong, H. H. Wei, L. L. Gan, G. H. Lee and Y. Wang, *Polyhedron.*, 1996, **15**, 2335.
26. R. K. Saini and A. Kumar, *J. Phytol. Res.*, 1997, **10 (1-2)**, 141.
27. N. Fahmi and R. V. Singh, *Trans. Met. Chem.*, 1994, **19**, 1.