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Synthesis, Characterization and Antifungal Activity of Some Metal Complexes Derived From Quinoxaloylhydrazone

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Abstract New Complexes of Mn(II), Co(II), Ni(II), Cu(II), Zn(II), Cd(II), Hg(II) and Tin(II) with 3-methyl-2-(pyridine-2-yl-methylene-hydrazinocarbonyl)quinoxaline-4-oxide (LHP) and 2-(2-hydroxy benzylidene-hydrazinocarbonyl)-3-methylquinoxaline-4-oxide (LHS) were prepared. The new complexes were characterized by elemental analysis, conductivity, magnetic measurements, IR and UV-Vis spectroscopic measurements. The results indicate 1:1 [M:L] chelates with the general formula $[M(LHP)Cl_2].nH_2O$ where: M = Mn(II), n=4, Co(II), n=1/2, Cu(II), n=1, Hg(II), n=1, and 1:2 [M:L] in case of $[M(LHS)_2](OAc)_2.nH_2O$ when M = Zn(II), n= 3, Cd(II), n= 1, Hg(II), n= 1/2. The tin complex structure is suggested to be $[Sn(LHP)_2]Cl_2.2H_2O$, while copper produces $[Cu_2(LHS)_2SO_4].H_2O$ complexes. Also, the formula for mercuric complex found to be $[Hg(LHS)_2Cl_2].2H_2O$. The magnetic moment measurements and electronic spectra suggest octahedral geometry for the prepared complexes. The antifungal investigation reveals that the activity was enhanced by chelation. The Cu(II) complexes has the highest inhibition zone against *A. niger*. But, the antifungal activity was weaker than the standard drug used.

Keywords: *aroyl hydrazone, quinoxaline-4-oxide, schiff bases, metal complexes, antifungal activity*

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1. Introduction

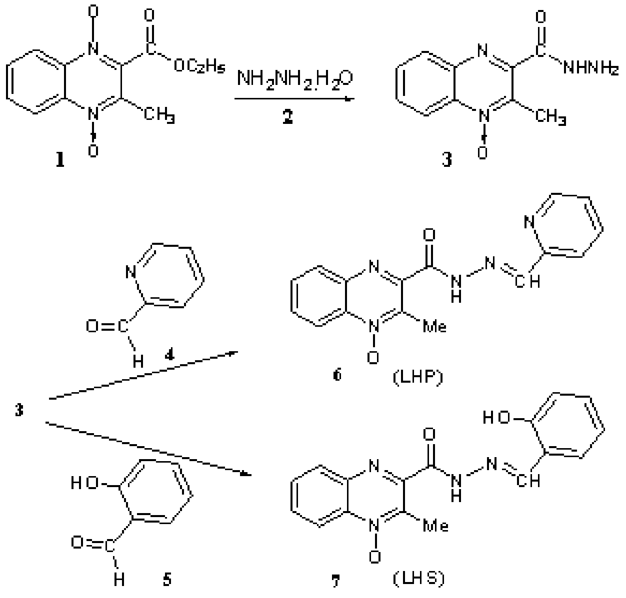
The development of bioinorganic chemistry field has increased the interest in Schiff base complexes, as they may serve as models for biologically important compounds and bioinorganic processes [1,2,3]. Biological activity of complexes derived from hydrazones has been widely studied and found to have numerous biological activities: antibacterial, antitumor, antimalarial and antituberculosis effects [4,5,6,7,8]. The acid hydrazides, $RCONHNH_2$ and their corresponding aroylhydrazones, RCONHN=CHR', have been widely investigated and have aroused interest due to their effective tridentate chelation with transition metal ions, and their ability to bind with the transition metal ions present in the living systems and possible biomimetic applications [9,10].

Metal complexes of substituted hydrazones have been reported to hold therapeutic activity and have pharmacological applications [11,12]. The complexes could bind and cleave the DNA strands via different mechanisms under different physiological conditions [13]. Aroyl hydrazone complexes of transition metals are used as models for elucidation the mechanism of enzyme inhibition [14].

Many reported research work shows that metal chelates are more biologically active than free ligands; this may be due to chelation which reduces the polarity of metal ions. This increases the hydrophobic character of the metal chelate and favors the penetration through liploid layers of microorganism membrane [15].

The Schiff bases having hydrazone moiety have proved to be strong chelating agents for transition metals and are attractive ligands from the structural point of view [16]. Aroyl hydrazones have donor properties in coordinating metals and prsent a combination of donor sites, such as protonaed/deprotonated amide oxygen and the imine nitrogen of hydrazone moiety. These ligands capable of undergoing keto-enol tautomerism [17]. Aroyl hydrazone ligands very often have additional donor site (usually N or O) which is provided by the aldehyde or ketone forming the Schiff base [16].

N-Aroylhydrazones as tridentate chelators derived from heterocyclic aldehydes and ketones and of methyl pyruvate forming selectively 2:1 (L:M) complexes and show considerable chelating ability towards metal ions [18,19] and can be used in analytical chemistry to recover and selectively determine transition metals as hydrazone complexes [19,20]. Also, The use of potentially tridentate ligands in the synthesis of organometallic compounds has received much more attention because tridentate metal complexes are expected to exhibit interesting catalytic properties, such as better stereoselective or chemoselective control of the reactions [21,22,23]. The present study deals with the synthesis and characterization of Schiff bases derived from quinoxaline-4-oxide hydrazide derivative **3**, i.e. 3-methyl-2-(pyridine-2-yl-methylene-hydrazinocarbonyl)quinoxaline-4-oxide (**6**, LHP) and 2-(2-hydroxybenzylidene-hydrazinocarbonyl)-3-methylquinoxaline-4-oxide (**7**, LHS) and their complexation with Mn(II), Co(II), Ni(II), Cu(II), Zn(II), Cd(II), Hg(II) and Sn(II). Synthesis of LHP and LHS ligands and their complexes are shown in Scheme 1, 2 and 3.



Scheme 1. Synthesis of LHP and LHS ligands

$MCl_2.mH_2O + 2\ LHP \longrightarrow [M(LHP)Cl_2].nH_2O$

8-11 6 17-20

$SnCl_2.2\,H_2O + LHP \longrightarrow [Sn(LHP)_2Cl_2].2H_2O$

12 6 21

	M	n	m
8, 17	Cu	1	2
9, 18	Hg	1	
10, 19	Mn	4	4
11, 20	Co	1/2	6

Scheme 2. Synthesis of LHP metal complexes

$M(OAc)_2.mH_2O + 2\ LHS \longrightarrow [M(LHS)_2](OAc)_2\ .nH_2O$

14-16 7 22-24

	M	n	m
14, 22	Zn	3	2
15, 23	Cd	1	2
16, 24	Hg	1/2	

$CuSO_4.5H_2O + 2\ LHS \longrightarrow [Cu_2(LHS)_2SO_4].H_2O$

13 7 25

$HgCl_2.H_2O + 2\ LHS \longrightarrow [Hg(LHS)_2]Cl_2.2H_2O$

9 7 26

Scheme 3. Synthesis of LHS metal complexes

2. Procedure and Expermintal Section

2.1. Material

All the starting chemicals and solvents were of analytical grade and used without further purification. The hydrated metal salts were obtained from Sigma-Aldrich and Luba.

2.2. Physical Measurenment

C, H, and N analysis for Ligands and complexes were determined using a Parkin-Elmer 2400 series (II) elemental analyzer. Metal analysis was performed on a Unicam 929 Atomic Absorption Spectrometer. Conductivity measurements were recorded on Conductivity Meter LF 538 at 25°C using 10-3 M solutions in dimethylsulfoxide (DMSO). Magnetic measurements were carried out in the solid state at room temperature on Johnson Matthy Magnetic Susceptibility susceptometer using $Hg[Co(SCN)_4]$ as calibrant. The IR spectra (KBr pellets) were recorded on Thermo Nicolet NEXUS 670 FT-IR spectrophotometer. Electronic absorption spectra were measured using a Unicam UV-Vis spectrometer for 10-3 M solution in DMSO. Melting Points were recorded on an Electrothermal 9001 apparatus. ^{1}H-NMR spectra and ^{13}C-NMR of the ligands were measured in d6-DMSO using TMS as internal standard on a Burker AV-300 spectrometer. Mass spectra of the ligands were recorded on shimadzo GC-MS-QP 1000 Ex at 70 ev mass spectrometer.

2.3. Synthesis of LHP and LHS

The ligands LHP **6** and LHS **7** were prepared according to the reported procedure [24,26]. A solution of 11.0 mmol pyridine-2-carboxyaldehyde (**4**) or 2-hydroxy benzlaldehyde (**5**) with 10.0 mmol (2.18 g) of 3-methyl-quinoxaline-2-carboxylic acid hydrazide 4-oxide (**3**) in 30 mL ethanol and 5 mL acetic acid was boiled under reflux for 20 min with stirring. The reaction mixture was concentrated by evaporation of the solvent. The solid was filtered and recrystallized from chloroform and petroleum ether (1:1) [24].

LHP (**6**): Yield 78%, colour : whitish, m.p. 194-196 °C, ($CHCl_3$ / Pet. Ether), elemental analysis calculated for $C_{16}H_{13}N_5O_2$ (307.31): C, 62.53, H, 4.26, N, 22.79, Found: C, 62.76, H, 4.34, N, 22.57, Mass, 307 (M+), IR (KBr disc, cm^{-1}) 3200 (NH), 1679 (C=O), 1570 (C=N), 1300 (amide), 927 (N-N), 1H NMR (DMSO-*d6*): δ 11.28 (s, 1H, NH), 8.52 (s, 1H, N=CH), 8.34 (m,1H, H5), 8.32 (m,1H, H6'), 8.07 (m, 1H, H8), 7.95 (m,1H, H3'), 7.82 (m,2H, H6+H7), 7.39 (m,1H, H4'), 6.91 (m,1H, H5'), 3.08 (s, 3H, CH3), 13C NMR (DMSO-d6 δ): 148.6 (C=N), 162.8 (C=O), 134.2 (C2), 138.5 (C3), 119.7 (C5), 132.8 (C6), 131.7 (C7), 119.7 (C8), 136.3 (C9), 137.6 (C10), 152.5 (C2'), 127.6 (C3'), 147.8 (C4'), 124.6 (C5'), 149.8 (C6'), 29.2 (C, CH_3).

LHS (**7**): Yield 72%, colour: yellow, m.p. 185-187 °C, ($CHCl_3$ / Pet. Ether), elemental analysis calculated for $C_{17}H_{14}N_4O_3$ (322.32), C, 63.35, H, 4.38, N, 17.38, Found: C, 63.56, H, 4.58, N, 17.18, Mass 322 (M+), IR (KBr disc, cm^{-1}): 3200 (NH), 1660 (C=O), 1570 (C=N), 1300 (amide), 959 (N-N), 1H NMR (DMSO-*d6* δ): 12.22 (s, 1H, OH), 11.42 (s, 1H, NH), 8.61 (s, 1H, N=CH), 7.52 (m,1H, H6’), 8.34 (m,1H, H5), 8.07 (m, 1H, H8), 7.91 (m,1H, H3’), 7.82 (m,2H, H6+H7), 7.25 (m,2H, H4’+ H5’), 3.08 (s, 3H, CH_3), ^{13}C NMR (DMSO-*d6* δ): 157.6 (C2), 148.3 (C=N), 162.9 (C=O), 138.4 (C3), 137.7 (C4a), 119.7 (C5), 132.8 (C6), 131.7 (C7), 119.6 (C8), 136.2 (C8a), 156.7 (C2’), 136.92 (C4), 132.73 (6’), 120.72 (1’), 119.84 (5’), 117.55 (3’), 29.1 (C, CH_3).

2.4. Synthesis of Metal Complexes

All complexes prepared were dried under vacuum at 25 °C and were prepared according to the following general procedures:

i) For preparation of $[M(LHP)Cl_2)].nH_2O$ (1:1 metal to ligand reaction ratio), M= Mn(II), n= 4, Co(II), n= 1/2, Cu(II), n=1, Hg(II), n= 1] **17-20**, the following procedure was followed:

To a stirred solution of 1.0 mmol (0.307 gm) of the ligand LHP **6** in 10 mL THF was added to a solution of the corresponding 1.0 mmol of metal (II) chloride 8-11 in 10 mL THF. The reaction mixture was stirred at room temperature (or heated at 50 °C in the case of Cu(II), and Mn(II)) for 1 h, then the reaction mixture was concentrated by the evaporation of THF. The solid was filtered and thoroughly washed with water and ethanol. {$[Cu(LHP)Cl_2].H_2O$ Yield = 74%, m.p. = 254 °C, colour = light green, $[Hg(LHP)Cl_2]$.H2O Yield = 82%, m.p. =267 °C, colour = Yellow, $[Mn(LHP)Cl]Cl.4H_2O$ Yield = 75%, m.p. =220 °C, colour = orange, $[Co(LHP)Cl_2]$. $0.5H_2O$ Yield = 73%, m.p. = 256 °C, colour = dark green}.

The $[Sn(LHP)_2]Cl_2.2H_2O$, **21** (1:2 metal to ligand reaction ratio), was prepared as in the above procedure using 2.0 mmol of the ligand LHP **6** with 1.0 mmol of tin(II) chloride and heating the mixture at 50 °C for half an hour. The precipitate obtained was washed with ethanol and then with distilled water. The complex obtained was 77% yield, yellow in colour and its m.p. = 313 °C. **ii)** For preparation of $[M(LHS)_2]$ $(OAc)_2.nH_2O$ (1: 2 metal to ligand reaction ratio), [M = Zn(II), n= 3, Cd(II), n= 1, Hg(II), n= 0.5, **22-24**, the following procedure was followed:

To a stirred solution of 2.0 mmol of the ligand LHS (**7**) in 10 mL water was added to a solution of the corresponding 1.0 mmole of hydrated metal acetate 14-16 in 10 mL water. The reaction mixture was stirred at room temperature for 1 h then the reaction mixture was concentrated. The solid obtained was filtered and thoroughly washed with water and acetone. {$[Zn(LHS)_2](OAC)_2.3H_2O$ Yield = 80%, m.p. =277-280°C, colour = brown, $[Hg(LHS)_2](OAC)_2.0.5H_2O$ Yield = 84%, m.p. =242 °C, colour = orange, $[Cd(LHS)_2](OAC)_2.H_2O$ Yield = 69%, m.p. = 280 °C, colour = orange}.

Under the same conditions, hydrated copper (II) sulfate (**13**) and Hg(II) chloride (**9**) form complexes of the structure $[Cu2(LHS)_2SO_4].H_2O$, **25**, and $[Hg(LHS)_2]Cl_2.2H_2O$, **26**, respectively. {$[Cu_2(LHS)_2SO_4].H_2O$ Yield = 80%, m.p. =225 °C, colour = yellow, $[Hg(LHS)_2]Cl_2.2H_2O$ Yield = 78%, m.p. =340 °C, colour = brown}.

2.5. Antifungal Activity Studies

The antifungal activity of the ligands and their complexes were tested by Well Diffusion Assay method [27,29]. The antifungal activities were tested for their in vitro growth inhibitory activity against the pathogenic fungal strains *Aspergillus niger* (*A. niger*) cultured on potato dextrose agar. The stock solution (10-2 mol. L-1) of the compounds was prepared by dissolving the compounds in DMSO as solvent. The concentration was diluted and the concentration used in this study was 200 ppm.

The solvent (DMSO) was used as a control in a similar manner to the prepared solutions of the tested compounds. Also, standard antifungal drug (Amphotricene B) was used for comparison.

Solutions of the ligands and its complexes in DMSO were plated onto the cultured agar medium and incubated for a period of 72 h at 30°C. After the incubation period, the plates were observed for zones of inhibition (in cm). Each sample was repeated three times, and statistical analysis were performed with SPSS 16.0 for windows. The limit of statistical analysis was set at $p < 0.05$. Data were presented as mean ± standard deviation (SD).

3. Result and Discussion

3.1. Preparation and Elemental Analysis

Quinoxalinoyl hydrazone ligands LHP **6**, and LHS **7**, were prepared by the condensation of pyridine-2-caroxyaldehyde (**4**) or 2-hydroxy benzlaldehyde (**5**) with 3-methyl-quinoxaline-2-carboxylic acid hydrazide 4-oxide (**3**) in ethanol and acetic acid. The latter hydrazide **3** was prepared by the hydrazinolysis of the 2-ethoxycarbonyl-3-methylquinoxaline 1,4-dioxide (**1**) in MeOH at 0-15 °C for 2 hours as reported [24] and shown in Scheme 1.

When solutions of the hydrazone derivative, LHP **6** was stirred with THF solution of the hydrated metal chloride salts **8-11** using 1:1 [M : L] molar ratio, colored air-stable mononuclear complexes of the formula $[M(LHP)Cl_2].nH_2O$ **17-20**, where [M= Cu(II), n= 1, Hg(II), n= 1, Mn(II), n=4, Co(II), n= 0.5] were formed. Under the same conditions using 1:2 [M: L], the $[Sn(LHP)_2]Cl_2.2H_2O$ **21** was formed in case of tin(II) chloride (12).

The $[M(LHS)_2](OAc)_2.nH_2O$ complexes, **22-24**, where: M = Zn(II), n= 4, Cd(II), n= 1, Hg(II), n= 1/2, were formed with 1:2 (metal: ligand) molar ratio in case of hydrazone derivative, LHS **7**. Under the same conditions, copper sulfate 13 and Hg(II) chloride **9** form complexes of the formula $[Cu_2(LHS)_2SO_4].H_2O$, **25**, and $[Hg(LHS)_2]Cl_2.2H_2O$, **26**, respectively. The elemental analysis and physical properties of the ligands are given in section (2.3.), while the elemental analysis for the prepared complexes is shown in Table 1.

3.1.1. Conductivity

The molar conductivities for the complexes 17-20 were measured in DMSO solutions and are shown in Table 1, indicate that most of the complexes are consistent with their non-electrolyte nature. This is in accordance with the fact that conductivity values for a nonelectrolytes are below 50 Ω-1 cm^2 mol-1 in DMSO solution. The presence of two chloride ions in the coordination sphere confirms that the ligands are neutral and supports the low conductance values of the complexes. This is in good agreement with those reported for similar complexes [6,30]. The complexes $[Sn(LHP)_2]Cl_2.2H_2O$, **21**, $[Zn(LHS)_2](OAc)_2.3H_2O$, **22**, and $[Hg(LHS)_2]Cl_2.2H_2O$, **26**, are found to be 1:1 electrolytes.

Table 1. The analytical and physical data for the complexes

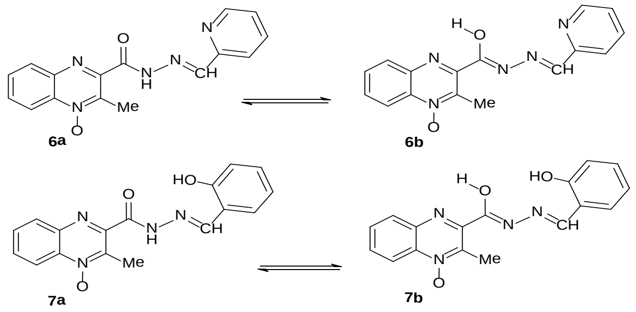
No.	Formula	Molar Mass	Calcd (Found) %				ΛM^a
			C	H	N	M	
17	$[Cu(LHP)Cl_2].H_2O$	459.77	41.79 (41.7)	2.85 (2.68)	15.23 (15.60)	13.81 (12.2)	9.6
18	$[Hg(LHP)Cl_2].H_2O$	596.28	32.22 (33.7)	2.53 (2.12)	11.74 (12.47)	—	3.6
19	$[Mn(LHP)Cl_2].4H_2O$	509.71	38.03 (35.2)	4.18 (2.25)	13.86 (12.72)	10.87 (10.9)	13.8
20	$[Co(LHP)Cl_2].½H_2O$	446.15	43.07 (43.6)	3.16 (3.09)	15.69 (15.05)	—	17.7
21	$[Sn(LHP)_2]Cl_2.2H_2O$	840.15	45.74 (45.0)	3.59 (3.00)	16.67 (15.86)	—	74.3
22	$[Zn(LHS)_2](OAc)_2.3H_2O$	880.07	39.42 (40.6)	4.35 (3.09)	12.73 (13.93)	7.42 (7.72)	68.5
23	$[Cd(LHS)_2](OAc)_2.H_2O$	891.13	45.82 (45.5)	3.84 (3.09)	12.57 (12.22)	12.61 (11.9)	—
24	$[Hg(LHS)_2](OAc)_2.½HO$	971.79	46.96 (46.2)	3.42 (2.64)	11.53 (12.16)	—	—
25	$[Cu2(LHS)_2SO_4].2H_2O$	517.94	39.42 (40.6)	3.50 (2.50)	10.81 (11.04)	12.26 (12.4)	—
26	$[Hg(LHS)_2]Cl_2.2H_2O$	1023.69	39.89 (40.0)	3.93 (2.54)	10.94 (11.02)	—	75.9

a: Ω^{-1} cm^2 mol^{-1}, (10^{-3} M) DMSO.

The molar conductance measurement agreed with the molecular formulae arrived from the analytical data. The conductivities of other prepared complexes were not measured because of their insolubility in common solvents.

3.1.2. Infrared Spectra

The infrared spectra of the ligands (LHP and LHS) exhibit bands characteristic of the stretching vibrations of N-H, N-N, C=N, C=O and OH (Table 2). The stretching vibrations of N-H at about 3200 cm^{-1}, whereas the C=O group gives rise to a strong band at about 1679 cm^{-1} for LHP and 1660 cm^{-1} for LHS. The hydrazonic chain is represented by two intense bands centered at about 1570 cm^{-1} and 1300 cm^{-1}, assigned to the amide systems. The N-N is represented by the band at 927 cm^{-1} for LHP and 959 cm^{-1} for LHS. It was expected the presence of two tautomeric structures of keto and enol forms for both ligands (LHP & LHS). The keto form was supported by the presence of the bands due to N-H and C=O in the IR spectrum. The presence of these bands suggests that these compounds predominantly exist in 'keto' form (Scheme 4) [18,31,33]. The significant bands observed in the IR spectra of the free ligands and their complexes are listed in Table 2. The main points are discussed below.



Scheme 4. Keto-enol toutomerization forms

i) Free ligands characteristic band of the carbonyl group υ(C=O) at 1679 cm^{-1} for LHP and 1660 cm^{-1} for LHS are shifted to higher bands (4-30 to 24-52 cm^{-1}) respectively (Table 2) indicating complexation with metal ions. This is in agreement with other reported research work [32,33].

Table 2. Important IR frequencies for the ligands and complxes (cm^{-1})

No.	Compound	ν (C=N)	ν (N-N)	ν (C=O)	ν (O-H)
6	LHP	1570 w	927 s	1679 vs	—
17	$[Cu(LHP)Cl_2].H_2O$	1560 w	953 s	1675 s	3420 br
18	$[Hg(LHP)Cl_2].H_2O$	1555 w	927 s	1666 m	3400 br
19	$[Mn(LHP)Cl_2].4H_2O$	1541 s	947 s	1653 vs	3425 br
20	$[Co(LHP)Cl_2].½H_2O$	1547 w	951 s	1673 w	3420 br
21	$[Sn(LHP)_2]Cl_2.2H2O$	1569 m	954 m	1649 vs	3430 br
7	LHS	1570 s	959 s	1660 s	3400 br
22	$[Zn(LHS)_2](OAc)_2.3H_2O$	1567 s	970 m	1613 s	3421 br
23	$[Cd(LHS)_2](OAc)_2.H_2O$	1560 m	966 w	1618 s	3421 br
24	$[Hg(LHS)_2](OAc)_2.½H_2O$	1560 m	974 s	1636 vs	3422 br
25	$[Cu_2(LHS)SO_4]. H_2O$	1567 s	969 m	1608 vs	3410 br
26	$[Hg(LHS)_2]Cl_2.6H_2O$	1565 s	964 s	1617 vs	3412 br

ii) In the Infrared spectra of the complexes there were bands in the range of 3160-3200 and 1595-1610 of the characteristic υ(N-H) and υ(C=O) stretching vibrations with a slight shift from the bands of the free ligands. This indicates the ligands are coordinated to the metal centers in the keto form [31].

iii) The bands at 1570 cm^{-1} and 927 cm^{-1} are assigned to azomethine group υ(C=N) and υ(N-N) of the free ligand respectively. The band of the azomethine group was reduced in intensity and shifted to lower frequency on complex formation by 10-30 cm^{-1} (Table 2), suggesting the participation of nitrogen atom of azomethine group in coordination in all metal complexes under investigation. Also, the shift of the band assigned to υ(N-N) to higher frequency can be taken as an additional evidence for participation of azomethine group in bonding. This is in agreement with what has been reported for such complexes before [8].

iv) The characteristic free ligand LHS broad band of hydroxyl group υ(O-H) at 3398 cm^{-1} has shifted to higher frequency by (10-22 cm^{-1}) in all of its complexes (Table 2). This indicates deprotonation with the involvement of the oxygen atom in bonding on complexation.

v) The bands at 1588, 1050, 777 and 480 cm^{-1} assigned to υ(C=N) py ring skeletal, and in-plan ring deformation mode and out-of-plan ring deformation mode of the free ligand respectively. These bands changes upon complexation and shifted slightly to higher frequencies indicating the participation of pyridyl nitrogen in coordination [34].

vi) The appearance of new weak broad bands in the region 425-530 and 550-570 cm^{-1} can be assigned to υ(M-N) and υ(M-O) respectively [6-36].

vii) The appearance of a medium, broad band in the range 3400-3430 cm^{-1}, due to υ(OH) indicate the presence of an H_2O molecules in the crystal of hydrated complexes [37,38]. These bands are absent in the free ligand LHP.

viii) The coordinated chloro atom in the complexes shows a far-IR absorption peak in the range 332-392 cm^{-1}, which may be attributed to υ(M-Cl) [6,30].

ix) The bridging SO_4^{-2} group in $[Cu_2(LHS)_2SO_4]$ **25** was characterized by the medium band at 683 and 1092-1125 cm^{-1} in the IR spectra [8,37].

x) The spectra of the complexes $[M(LHS)_2](OAc)_2.nH_2O$ (M = Zn (II), Hg(II) and Cd(II)) show a band in the range 1500 -1510 cm^{-1} which can be assigned to υ(C-O) asymmetric stretching of acetate group and a band at 1415-1420 cm^{-1} which can be assigned to υ(C-O) symmetric stretching vibration of acetate group [37]. These results predict that the acetate ions were coordinated outside the coordination sphere.

3.1.3. ^{1}H-NMR and ^{13}C-NMR Spectra Data of the Ligands

The 1H-NMR Spectral data of the ligands LHP and LHS in DMSO-*d6* shows a singlet signal at 11.28 ppm and 11.42 ppm at both ligands and were assigned for the NH proton.

The presence of the NH proton singlet indicates the presence of the ligands in the keto form. The singlet at 12.22 ppm in LHS ligand assigned for the hydroxyl proton (OH). The singlet at 8.52 and 8.61 in the spectrum of LHP and LHS respectively were assigned to azomethine proton (H-C=N) [39,40]. The presence of multiplet signals at the range 6.91-8.34 are assigned to the protons of pyridyl and phenyl rings. Also the singlet at 3.08 in both ligands spectra assigned to the proton of the CH_3 [35].

^{13}C-NMR Spectra shows Peaks at δ 148.6 and δ 162.8 in the spectra of LHP ligand and at δ 148.3 and δ 162.9 in the spectra of the ligand LHS were assigned for the groups (C=N) and (C=O) respectively [17]. The 13C-NMR spectra of LHP and LHS display signals in the range 117.55-156.7 ppm which have been assigned to the aromatic (phenyl and pyridyl) carbon atoms [28]. The peaks at 29.2 in the spectra of LHP and LHS respectively were assigned to the carbon atom of CH_3.

3.1.4. Magnetic Measurements

Magnetic moments susceptibility (μeff) for the complexes $[Mn(LHP)Cl_2].4H_2O$ 19 and $[Co(LHP)Cl_2].1/2H_2O$, **20**, were performed at room temperature and found to be 6.66 and 4.34 BM respectively.

The magnetic moment measurement for Mn(II) complex 19 under consideration has the value 6.66 BM which is higher than the spin-only magnetic moment of 5.9 BM, supporting the octahedral geometry around the metal ion [41]. Further the values indicate no antiferromagnetic interaction. The observed room temperature magnetic moment value of 4.34 BM for Co(II) complex 20 (higher than the spin-only value of 3.87 BM.) demonstrate paramagnetic behavior and consistent with their high-spin octahedral geometry around metal ion [8-42].

The Cu(II) complex ($[Cu(LHP)Cl_2].H_2O$), **17**, show magnetic moment 1.87BM which is slightly higher than the spin-only value (1.73BM) expected for one unpaired electron, which offers possibility of an octahedral geometry [42,43]. The magnetic moment value of 1.87 BM is consistent with d9 configuration and in the range suggested for monomeric copper complexes [40].

3.1.5. Electronic Absorption Spectrum

The electronic absorption spectral data for some complexes are summarized in Table 3. Insufficient solubility of other complexes has hindered their study.

A comparison of the electronic spectra of the free ligands with those of their corresponding metal complexes show some shifts that can be considered as evidence for the complex formation [44]. Upon complexation the Ligand-centered (LC) bands (n →π*, π →π*, σ →π*) undergo an intensity increase with a slight shift relative to the ligand. The spectra exhibit, in addition to LC bands, broad bands which are assigned to metal-ligand charge transfer (MLCT) transitions and d-d transitions, which are responsible for the characteristic colors of these complexes.

The electronic spectra (Table 3) show two bands at 40983 cm^{-1} and 31250 cm^{-1} for LHP ligand and two bands at 34246 cm^{-1} and 30487 for the ligand LHS due to the benzene and heterocyclic ring and to the π□ π* transition of the chromophore (-C=N-NH-CO-). These bands shifted in the electronic spectra of the complexes [7]. Complexes in general display weak absorption bands at around : 22522 cm^{-1}, 29069 cm^{-1}, 29411 cm^{-1}, 31746 cm-1, 37593 cm^{-1} in most complexes assigned to ligand-centered (LC), metal-ligand charge transfer (MLCT) and d-d transitions, which are characteristic for octahedral geometry [37,44,45].

The electronic spectra of the Cu(II) complex display a broad band at 25125 cm^{-1} were assigned to d-d transitions and the appearance of two bands at 27247 cm^{-1} and 29069 cm^{-1} assigned to charge transfer bands assuming an octahedral geometry environment around the metal ion [46]. This was supported by magnetic moment measurements.

Mn(II) complexes show three bands at 20833 cm^{-1}, 22522 cm^{-1}, 22935 cm^{-1} assigned to d-d transitions and another two bands at 29069 and 34246 cm^{-1} assigned to charge transfer. The band exhibited at 22935 cm^{-1} is assigned to 6A1g→ 4T1g (p) transition. This is the same range as reported for octahedral coordinated Mn(II) ion [46]. The high spin d5 configuration for Mn(II) gives high-spin magnetic moment of 6.66 BM is an additional evidence for the octahedral geometry around the metal ion.

The μeff value of 4.34 BM for Co(II) complex is indicative of a high-spin octahedral geometry for the ion. Two bands of medium intensity observed at 20491 cm^{-1} 29411 cm^{-1} for Co(II) complex were assigned 4T1g → 4T1g(P), 4T1g → 4A2g(F) transitions, respectively. Therefore these bands together with the magnetic moment are attributable to an octahedral environment around the Co(II) ion [41].

On the basis of the previous observations, it is tentatively suggested that all of the complexes show an octahedral geometries in which the ligands act as tridentate.

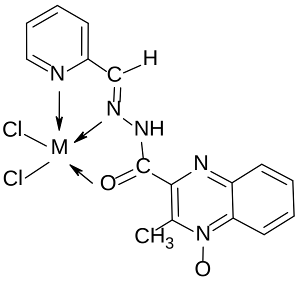
Table 3. Important UV-Visible spectra of Ligands LHP & LHS and their complexes

No.	Compound	Absorption Bands cm^{-1} (nm)	Assignments
6	LHP	40983 (244)	***LC***
		31250 (320)	LC
17	[Cu(LHP)Cl_2].H_2O	41666 (240)	LC
		37593 (266)	MLCT
		30581 (327)	LC
		29069 (344)	MLCT
		27247 (367)	MLCT
		25125 (398)br	d-d
18	[Hg(LHP)Cl_2].H_2O	37735 (265)	MLCT
		31746 (315)br	LC
		29411 (340)sh	LC / MLCT
19	[Mn(LHP)Cl_2].4H_2O	34246 (292)	MLCT
		32899 (304)	LC
		30864 (324)	LC
		29069 (344)	MLCT
		22935 (436)	d-d
		22522 (444)	d-d
		20833 (480)	d-d
20	[Co(LHP)Cl_2].½H_2O	40322 (248)	LC
		37593 (266)	MLCT
		29411 (340)	LC / MLCT
		21551 (464)	d-d
		20491 (488)	d-d
		20129 (496)	d-d
21	[Sn$(LHP)_2$]Cl_2.2H_2O	37593 (266)	MLCT
		32894 (304)br	LC
		29069 (344)sh	LC / MLCT
7	LHS	34246 (292)	LC
		30487 (328)	LC
26	[Hg$(LHS)_2$]Cl_2.6H_2O	37735 (265)	MLCT
		31746 (315)br	LC
		29411 (340)sh	LC

br: broad, sh: shoulder.

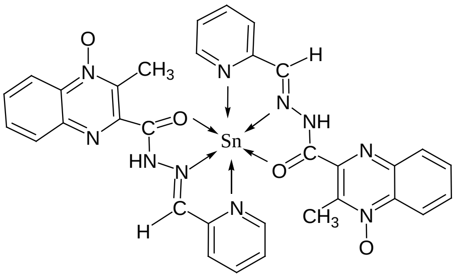
The weight loss shown by the complexes on heating in the 120–160 °C temperature range corresponds to the presence of half mole of water molecule in Co(II) **20** and Hg(II) **24** one mole of water molecule in Cu(II) 17, Hg(II) 18 and Cd(II) **23** complexes, two moles of water molecules in Hg(II) 26, three water molecules in Zn(II) complexes, four moles of water molecules in Mn(II) **19** and six moles of water molecules in Cu(II) **25**.

The following are the proposed tentative structures of the complexes.

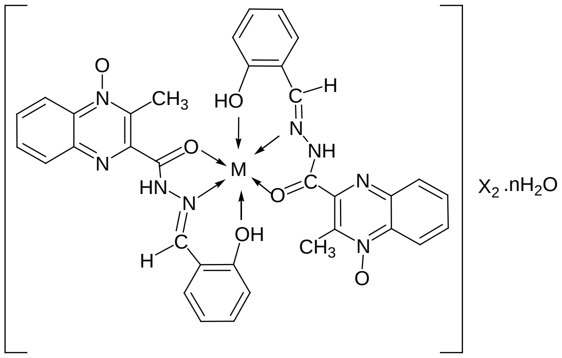


Structure I. [M(LHP)Cl_2].nH_2O, M= Mn(II), Co(II), Cu(II) or Hg(II)

In structure I the ligand LHP functions as a neutral tridentate in case of Mn(II), Co(II), Cu(II) and Hg(II) chloride complexes via the azomethine group, carbonyl group in the keto-form and the pyridine ring nitrogen. Similarly in case of Sn (structure II).

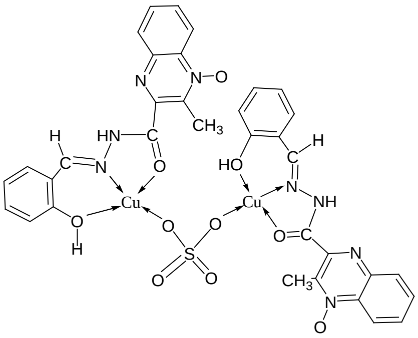


Structure II. [Sn$(LHP)_2$]Cl_2.2H_2O

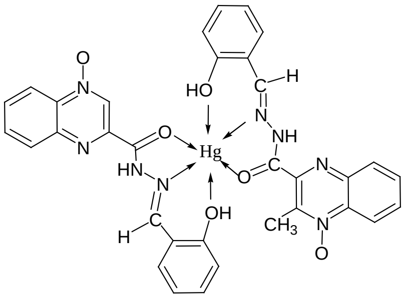


Structure III. M= Hg(II), Zn(II), Cd(II), Hg (II), X= AcO, Cl

In case of LHS it coordinates through azomethine group, carbonyl group in the keto-form and the OH group of the phenyl ring (structure III, IV, and V).



Structure IV. [$Cu_2(LHS)_2SO_4$]. H_2O



Structure V. [Hg$(LHS)_2$]Cl_2.2H_2O

3.1.6. Antifungal activity

The synthesized Schiff base ligands (LHP and LHS) and some of their soluble complexes were evaluated for their antifungal activities against fungal strains named *A. niger*. The ligands and their complexes showed variable antifungal activities (Table 4) against the fungal strains.

By careful study of the results obtained we can see that the ligands showed an inhibitory week effect against the tested organism with diameter of inhibition zones range of

0.90-1.10 cm. The activity of the ligand LHP was a little more effective than LHS. The ligands antifungal activity becomes more pronounced on coordination with the metal ions under the same experimental conditions. A synergistic effect involving the metal ion and the aroylhydrazone might be responsible for this enhancement. The metal complexes were found to be little more toxic than the parent ligands with inhibition zones range of of 1.3 – 1.5 cm for *A. niger*. The increase in antifungal activity of the metal chelate may be due to the effect of the metal ion on the normal cell process.

Table 4. Antifungal activity data for the ligands and their some metal complexes

No.	Compound	Zone of Inhibition (cm) [Conc (200 ppm)] ± SD
6	LHP	1.10 ± 0.01
17	$[Cu(LHP)Cl_2].H_2O$	1.50 ± 0.035
18	$[Hg(LHP)Cl_2].H_2O$	1.20 ± 0.02
19	$[Mn(LHP)Cl_2].4H_2O$	1.15 ± 0.025
20	$[Co(LHP)Cl_2].½H_2O$	1.40 ± 0.015
21	$[Sn(LHP)_2]Cl_2.2H_2O$	1.25 ± 0.01
7	LHS	0.90 ± 0.05
26	$[Hg(LHS)_2]Cl_2.6H_2O$	1.10 ± 0.045
	Amphotricene B	1.70 ± 0.015

Chelation considerably reduces the polarity of the metal ion because of partial sharing of its positive charge with the donor group and possible π-electron delocalization within the entire chelate ring system that is formed during coordination [47]. Such chelation could enhance the lipophilic character of the central metal atom and hence increase the hydrophobic character and liposolubilty of the complex favoring its permeation through the lipid layers of the cell membrane [28].

In addition to this, the mode of action of the compounds may involve the formation of a hydrogen bond through the azomethine nitrogen atom (>C=N) with the active centers of cell constituents, resulting in interference with the normal cell process [48]. The results show that the Cu(II) complexes exhibit higher activity against the fungus compared with other analogous complexes containing M(II) ions. The activity of Cu(II) complexes may be attributed to its higher stability constant [6,7].

Since the complexes have the different donating atoms (N,N,O) and (O,N,O), and containing metals with the same oxidation state M(II), therefore the more effective factors that influence the antifungal activity are the donating atoms and the nature of the central atoms [6,7].

On comparison with the standard antifungal drug Amphotricene B (inhibition zone 1.70 cm), the results indicate that, the tested complexes exhibited moderate activity against the fungal strains and weaker than the standard Amphotericin B.

4. Conclusion

In this study we have reported the synthesis and structural characterization of the tridentate quinoxaloylhydrazones Schiff bases ligands (LHP and LHS) and their complexes with transition metals (Mn(II), Co(II), Ni(II), Cu(II), Zn(II), Cd(II), Hg(II) and Tin(II)). The ligand to metal stoichiometry and the nature of bonding were ascertained on the basis elemental analysis, IR spectra, electronic absorption spectra, magnetic moment measurements and conductivity data. The results show that the ligands behave as tridentate with NON donor sequence. The complexes were characterized by physico-chemical measurements which led to the proposal of octahedral geometry for Mn(II), Co(II) and Cu(II) complexes. The biological activity tests for the ligands and their complexes show enhancement of the ligands activity against the tested organism on chelation with metals. But, it is still weak to be compared with standard drug.

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