

## In-vitro antibacterial, antifungal activity of some transition metal complexes of thiosemicarbazone Schiff base (HL) derived from N<sup>4</sup>-(7'-chloroquinolin-4'-ylamino) thiosemicarbazide

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### Abstract

The synthetic, spectroscopic, and biological studies of Cu(II), Ni(II), Zn(II), Co(II), Mn(II), Fe(III) and Cr(III) complexes of N<sup>4</sup>-(7'-chloroquinoline-4'-ylamino)-N<sup>1</sup>-(2-hydroxy-benzylidene)thiosemicarbazone (HL) obtained by the reaction of N<sup>4</sup>-(7'-chloroquinolin-4'-ylamino)thiosemicarbazide with 2-hydroxybenzaldehyde. The structures of the complexes were determined on the basis of the elemental analyses, spectroscopic data (IR, electronic, <sup>1</sup>H and <sup>13</sup>C NMR and Mass spectra) along with magnetic susceptibility measurements, molar conductivity and thermogravimetric analyses. Electrical conductance measurement revealed the non-electrolytic nature of the complexes. The resulting colored products are mononuclear in nature. On the basis of the above studies, only one ligand was suggested to be coordinated to each metal atom by thione sulfur, azomethine nitrogen and phenolic oxygen to form mononuclear complexes in which the thiosemicarbazone behaves as a monobasic tridentate ligand. The ligand and its metal complexes were tested against Gram +ve bacteria (*Staphylococcus aureus*), Gram -ve bacteria (*Escherichia coli*), fungi (*Candida albicans*) and (*Fusarium solani*). The tested compounds exhibited significant activity.

### Introduction

The synthesis and structural investigations of thiosemicarbazone and their metal complexes are of considerable centre of attention because of their potentially beneficial pharmacological properties and a wide variation in their modes of bonding and stereochemistry [1–3]. Thiosemicarbazones that are most widely studied are sulfur and nitrogen consisting ligands [4,5]. Besides, thiosemicarbazones have emerged as an important sulfur containing ligands in the last two decades [6–9]. The real impetus towards coordination chemistry is the wide range of biological properties depending on parent aldehyde or ketone including antitumour [10,11], antibacterial, and antifungal [12,13] as well as their physicochemical effects [14,15]. In addition of this, they have been screened for their medical properties because they possess some cytotoxic effect. They also stabilize

uncommon oxidation states, generate a different coordination number in transition metal complexes in order to participate in various redox reactions [16,17]. It is well known that several metal ions enhance and modify the biological activities of thiosemicarbazones [13]. Much attention has been drawn towards the chemistry of transition metals [18–22] in different coordination spheres. Due to different oxidation states of transition metals and their reactivity depends upon stability of oxidation states. In view of this ruthenium (III), thiosemicarbazones with nitrogen and sulphur as donor atoms have been found to be very efficient catalysts in the oxidation of alcohols and alkenes [23]. With the growing interest of thiosemicarbazones [24–27], the present work was undertaken in order to investigate the ligational behaviour of the thiosemicarbazone derived from N<sup>4</sup>-(7'-chloroquinolin-4'-ylamino)thiosemicarbazide with

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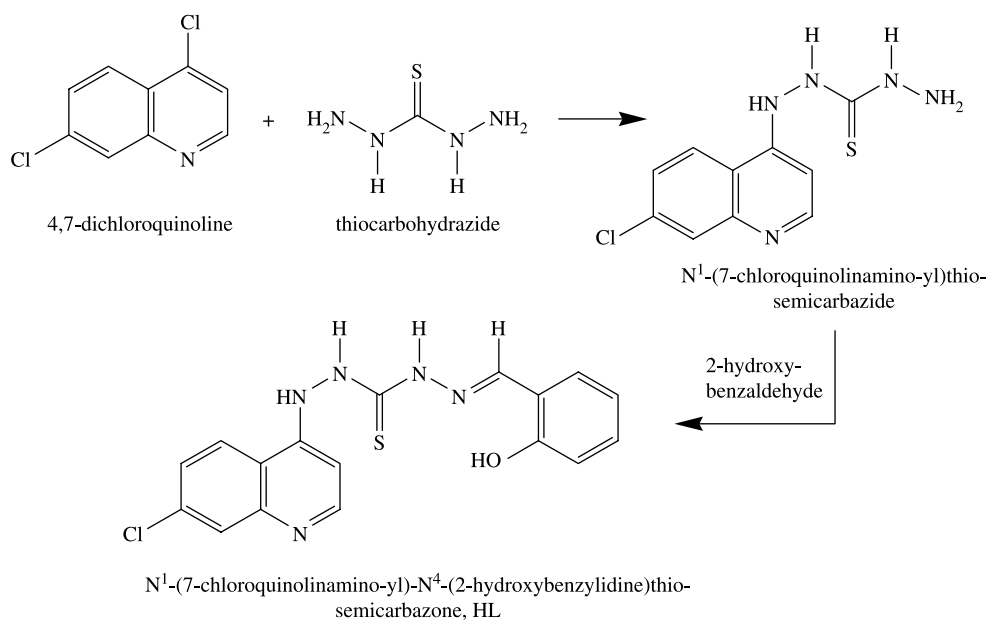


Figure 1. Scheme for the synthesis of the HL ligand.

2-hydroxy-benzaldehyde (Figure 1) towards metal ions, Cu(II), Ni(II), Zn(II), Co(II), Mn(II), Fe(III) and Cr(III) as well as their biological activity in inhibiting the growth of some pathogenic bacteria.

## Experimental

### Materials

Reagent grade chemicals were used without further purification. CuCl<sub>2</sub>·2H<sub>2</sub>O, CoCl<sub>2</sub>·6H<sub>2</sub>O, NiCl<sub>2</sub>·6H<sub>2</sub>O, MnCl<sub>2</sub>·4H<sub>2</sub>O, ZnCl<sub>2</sub>, FeCl<sub>3</sub>·6H<sub>2</sub>O, CrCl<sub>3</sub>·6H<sub>2</sub>O and Li(OH)·H<sub>2</sub>O were obtained from BDH. Hydrazine hydrate, 4,7-dichloroquinoline, and carbon disulphide, were either from BDH or Mercks solvents used were reagent grade.

### Synthesis of the ligand

**Synthesis of thiocarbohydrazide, (TCH), (I).** The preparation was carried out according to the previously reported method [28,29]. Carbon disulphide (5 mL) was added gradually to 20 mL hydrazine hydrate (90%). The reaction mixture was refluxed for 30 min. The reaction mixture was cooled in a water bath for further 30 min. and the formed yellow precipitate was filter off and washed several times with ethanol followed by diethyl ether. The white crystals were then re-crystallized from the least amount of water then dried over anhydrous CaCl<sub>2</sub> and collected (yield 80%, m.p. 171°C<sub>2</sub>).

**Synthesis of N<sup>1</sup>-(7'-chloroquinolin-4'-ylamino)thiosemicarbazide, (II).** A hot solution of 4,7-dichloroquinoline

(2 g, 10 mmol dissolved in 20 mL ethanol) was added to thiocarbohydrazide (TCH) (I) (1 g, 10 mmol) dissolved in the least amount of ethanol-water mixture (10/5 v/v). The reaction mixture was left under stirring while it is hot for 30 min and then allowed to cool. The formed deep yellow crystals were filter off, washed several times with hot ethanol and finally dried over anhydrous CaCl<sub>2</sub> for 24 hr. (yield 65%, m.p. 245°C) (Figure 1).

**Synthesis of N<sup>1</sup>-(7'-chloroquinolin-4'-ylamino)thiosemicarbazone, (HL).** The ligand HL was prepared by adding 2-hydroxybenzaldehyde (1.12 g, 10.1 mmol, dissolved in 10 mL absolute ethanol) to the thiocarbazide (II), (0.2 g, 10 mmol dissolved in 10 mL absolute ethanol). The reaction mixture was stirred thoroughly and refluxed for 2 h, golden orange crystals precipitated which were filtered and washed with few drops of ethanol (yield 85%, m.p. 265°C). The proposed chemical structure (Figure 1) of the ligand, HL, is known to be in good agreement with the ratios concluded from analytical data (Table I).

### Synthesis of the metal complexes

A general method has been used for the preparation of the complexes using stoichiometric reaction of the metal salts and the corresponding Schiff base in presence of Li(OH) in molar ratio (M:L:Li(OH) = 1:1:1). Lithium hydroxide (0.1 g, 2.4 mmol) was dissolved in 5 mL methanol was added drop-wise to a stirred solution of the ligand (0.7 g, 2.4 mmol dissolved in 5 mL methanol). Metal salt solution (2.4 mmol dissolved in 10 mL methanol) was added

Table I. Physicochemical parameters of ligand and its complexes.

Compound <sup>a</sup> (F. wt.)	Colour	Yield (%)	M.p. (°C)	Elemental analysis, found/(Calcd) %						U <sub>M</sub> (Ohm cm <sup>2</sup> mol <sup>-1</sup> )
				C	H	N	Cl	S	M	
HL C <sub>17</sub> H <sub>14</sub> N <sub>5</sub> ClOS (371.5)	Deep orange-yellow	85	265	55.21 (54.91)	4.32 (3.77)	19.11 (18.84)	9.83 (9.56)	8.831 (8.61)	—	—
(1)[(L)Cu(Cl)].H <sub>2</sub> O C <sub>17</sub> H <sub>15</sub> N <sub>5</sub> Cl <sub>2</sub> O <sub>2</sub> SCu (488.5)	Green	33	277	42.11 (41.76)	3.32 (3.07)	14.63 (14.33)	14.91 (14.53)	7.02 (6.55)	14.67 (13.20)	13.4
(2)[(L)Ni(Cl)(OH <sub>2</sub> ) <sub>2</sub> ].2H <sub>2</sub> O C <sub>17</sub> H <sub>21</sub> N <sub>5</sub> Cl <sub>2</sub> O <sub>5</sub> SNi (537)	Pale yellow	25	270	38.41 (38.01)	4.11 (3.91)	13.44 (13.04)	13.64 (13.23)	5.45 (5.96)	10.62 (10.94)	15.0
(3)[(L)Zn(Cl)(OH <sub>2</sub> ) <sub>2</sub> ].2H <sub>2</sub> O C <sub>17</sub> H <sub>21</sub> N <sub>5</sub> Cl <sub>2</sub> O <sub>5</sub> SZn (543)	Yellow	55	264	37.23 (37.54)	4.21 (3.86)	13.22 (12.88)	13.49 (13.07)	6.11 (5.89)	12.44 (12.04)	11
(4)[(L)Co(Cl)(OH <sub>2</sub> ) <sub>2</sub> ].H <sub>2</sub> O C <sub>17</sub> H <sub>19</sub> N <sub>5</sub> Cl <sub>2</sub> O <sub>4</sub> SCo (519)	Yellowish green	47	250 (decomp)	39.75 (39.31)	4.00 (3.66)	13.81 (13.49)	14.01 (13.68)	6.54 (6.17)	11.68 (11.37)	12.6
(5)[(L)Mn(Cl)(OH <sub>2</sub> ) <sub>2</sub> ].H <sub>2</sub> O C <sub>17</sub> H <sub>19</sub> N <sub>5</sub> Cl <sub>2</sub> O <sub>4</sub> SMn (515)	Deep brown	34	260 (decomp)	39.22 (39.61)	3.45 (3.69)	13.82 (13.59)	14.10 (13.79)	6.51 (6.21)	10.93 (10.68)	18.4
(6)[(L)Fe(Cl) <sub>2</sub> (OH <sub>2</sub> ) <sub>2</sub> ].2H <sub>2</sub> O C <sub>17</sub> H <sub>19</sub> N <sub>5</sub> Cl <sub>3</sub> O <sub>4</sub> SFe (551.5)	Reddish brown	44	264 (decomp)	37.32 (36.99)	3.25 (3.45)	12.92 (12.69)	19.71 (19.31)	6.22 (5.80)	10.35 (10.15)	18.5
(7)[(L)Cr(Cl) <sub>2</sub> (OH <sub>2</sub> ) <sub>2</sub> ].2H <sub>2</sub> O C <sub>17</sub> H <sub>19</sub> N <sub>5</sub> Cl <sub>3</sub> O <sub>4</sub> SCr (547.5)	Green	75	255 (decomp)	37.53 (37.26)	3.82 (3.47)	13.12 (12.79)	19.11 (19.45)	5.44 (5.84)	9.26 (9.50)	13.6

<sup>a</sup>L = [C<sub>17</sub>H<sub>13</sub>N<sub>5</sub>ClOS]<sup>-</sup>

Table II. Characteristic IR bands ( $\text{cm}^{-1}$ ) of HL and its metal complexes.

Compound	$\nu(\text{C}=\text{N})$	$\nu(\text{N}-\text{H})$	$\nu(\text{N}-\text{N})$	$\nu(\text{C}=\text{S})$	$\nu(\text{M}-\text{N})$	$\nu(\text{M}-\text{O})$	$\nu(\text{M}-\text{S})$	$\nu(\text{OH})$	Other bands
HL $\text{C}_{17}\text{H}_{14}\text{N}_5\text{ClOS}$ (371.5)	1570 s	3270 m	1120 s	876 s	—	—	—	3530 m, br	$\delta(\text{COH})_{\text{br}}$ , 1355
(1) $(\text{L})\text{Cu}(\text{Cl})\cdot\text{H}_2\text{O} \cdot \text{C}_{17}\text{H}_{15}\text{N}_5\text{Cl}_2\text{O}_2\text{SCu}$ (488.5)	1520 s	3265 m	1136 s	820 s	450 w	560 m	360 w	—	$\nu$ (3436); $\delta$ (930, 770) (coordinated $\text{H}_2\text{O}$ )
(2) $(\text{L})\text{Ni}(\text{Cl})(\text{OH}_2)_2\cdot 2\text{H}_2\text{O} \cdot \text{C}_{17}\text{H}_{21}\text{N}_5\text{Cl}_2\text{O}_5\text{SNi}$ (537)	1525 m	3278 s	1137 w	825 s	460 w	555 m	365 w	—	$\nu$ (3440); $\delta$ (935, 770) (coordinated $\text{H}_2\text{O}$ )
(3) $(\text{L})\text{Zn}(\text{Cl})(\text{OH}_2)_2\cdot 2\text{H}_2\text{O} \cdot \text{C}_{17}\text{H}_{21}\text{N}_5\text{Cl}_2\text{O}_5\text{SZn}$ (543)	1520 m	3270 s	1125 w	850 s	430 w	545	350 w	—	$\nu$ (3435); $\delta$ (930, 775) (coordinated $\text{H}_2\text{O}$ )
(4) $(\text{L})\text{Co}(\text{Cl})(\text{OH}_2)_2\cdot \text{H}_2\text{O} \cdot \text{C}_{17}\text{H}_{19}\text{N}_5\text{Cl}_2\text{O}_4\text{SCo}$ (519)	1530 m	3270 m	1125 w	845 m	445 w	555 m	355 w	—	$\nu$ (3435); $\delta$ (930, 775) (coordinated $\text{H}_2\text{O}$ )
(5) $(\text{L})\text{Mn}(\text{Cl})(\text{OH}_2)_2\cdot \text{H}_2\text{O} \cdot \text{C}_{17}\text{H}_{19}\text{N}_5\text{Cl}_2\text{O}_4\text{SMn}$ (515)	1527 m	3265 m	1136 s	820 m	445 w	545 w	360 w	—	$\nu$ (3440); $\delta$ (938, 770) (coordinated $\text{H}_2\text{O}$ )
(6) $(\text{L})\text{Fe}(\text{Cl})_2(\text{OH}_2)_2\cdot 2\text{H}_2\text{O} \cdot \text{C}_{17}\text{H}_{19}\text{N}_5\text{Cl}_3\text{O}_4\text{SFe}$ (551.5)	1530 m	3278 s	1130 w	840 s	455 w	540 w	365 w	—	$\nu$ (3426); $\delta$ (930, 770) (coordinated $\text{H}_2\text{O}$ )
(7) $(\text{L})\text{Cr}(\text{Cl})_2(\text{OH}_2)_2\cdot 2\text{H}_2\text{O} \cdot \text{C}_{17}\text{H}_{19}\text{N}_5\text{Cl}_3\text{O}_4\text{SCr}$ (547.5)	1520 m	3270 s	1137 s	825 m	450 w	555 m	355 w	—	$\nu$ (3435); $\delta$ (930, 775) (coordinated $\text{H}_2\text{O}$ )

s: strong; w: weak; m: medium; br.: broad

gradually to the stirred solution of the lithium salt of the ligand. The precipitated solid complex was filtered off, washed with 50% (v/v) methanol-water mixture to remove any traces of the unreacted starting materials, then washed with diethyl ether and dried in vacuum desiccator over  $\text{CaCl}_2$ . The obtained solid metal complexes and their colours are shown in Table I. The complexes are stable solid, and some of them decomposed above  $250^\circ\text{C}$  without melting. They are insoluble in common organic solvents such as ethanol, methanol, chloroform and acetone. However, they are soluble in DMSO and DMF.

#### Physical measurements and analyses

Carbon, hydrogen, nitrogen and sulfur microanalyses were carried out at the analytical center of King Khalid University, Assir, Abha, Saudi Arabia using a Perkin Elmer 2400 Series Analyzer. Analyses of the metals followed decomposition of their complexes with concentrated nitric acid. The resultant solution was diluted with distilled water, filtered to remove the precipitated ligand. The solution was then neutralized with aqueous ammonia solution and the metal ions titrated with EDTA. Electronic spectra were recorded for the solutions of the ligand in ethanol, and for metal complexes as Nujol Mull on a Shimadzu UV-vis spectrophotometer model 1601 in the range 190–1100 nm. IR spectra were recorded as KBr discs using a FT-IR 4000 Perkin Elmer Spectrometer. The  $^1\text{H}$  NMR spectra were recorded at room temperature on Bruker WP 250 (250 MHz) spectrometer in  $\text{DMSO-d}_6$ . The  $^{13}\text{C}$  NMR spectra were recorded at ambient temperature on Bruker 250 WM (62.9 MHz) spectrometer in  $\text{DMSO-d}_6$ . Chemical shifts are given in ppm downfield from TMS. The halide content was then determined by titration using diphenyl carbazone as an indicator. Magnetic susceptibilities of the complexes were measured by the Gouy's method at room temperature using a model MK1 Johnson Matthey. Alpha products magnetic susceptibility balance. The effective magnetic moments were calculated using the relation ( $\mu_{\text{eff}} = 2.828 (\chi_m T)^{\frac{1}{2}}$  B.M. where  $\chi_m$  is the molar susceptibility corrected using Pascal's constants for diamagnetism of all atoms in the compounds. The TG-DTA measurements were carried out on a Shimadzu thermo gravimetric analyzer in dry nitrogen atmosphere and a heating rate of  $10^\circ\text{C}/\text{min}$  using the TA-50 WS1 program. Mass spectra were recorded at 70 eV and  $300^\circ\text{C}$  on a MS 5988 Hewlett-Packard mass spectrometer. Conductivity measurements were measured in DMF solutions of the complexes ( $10^{-3}$  M) using a model LBR, WTWD-812 Wilhelm Conductivity meter fitted with a model LTA 100 cell.

### Pharmacology

The in-vitro evaluation of antimicrobial activity was performed according to the diffusion technique on solid media [30]. Bacteria including *Staphylococcus aureus*, *Escherichia coli* were grown in nutrient broth at 37°C for 24 h. *Candida albicans* and *Fusarium solani* were grown in malt broth at 28°C for 48 h. Sterile (5 mm) diameter sensitivity discs were impregnated with different conc. of the ligand/complex (50 µg or 100 µg/mL) dissolved in DMSO. Discs of each tested compound were laid onto nutrient agar for bacteria or potato dextrose agar for fungi. Plates are surface spread with 0.2 mL of logarithmic phase bacteria or fungi cultures. A 0.5 mL spore suspension (10<sup>8</sup> spores/mL) for bacteria or for filamentous fungi was also spread onto potato dextrose agar plates. The plates were then incubated for 24 h at 37°C for bacteria and for 48 h at 28°C for fungi. Additionally antibiotic discs for cephalosporin and streptomycin were tested as positive control. The results were recorded by measuring the zones of growth inhibition surrounding the discs.

## Results and discussion

### Chemistry

The thiosemicarbazone Schiff base ligand, HL is expected to act as a heptadentate ligand, the possible coordination sites being quinoline nitrogen, phenolic oxygen, imine nitrogen, thio-keto sulfur and azomethine nitrogen. A study and comparison of the IR spectra of the ligand and its metal complexes imply that the Schiff base behave as monobasic tridentate ligands with phenolic-oxygen, azomethine-nitrogen, and the thio-keto sulfur as ONS ligand. The present thiosemicarbazone ligand exists as the thio-keto form since it has  $\text{-NH-C=S}$  thio amide group; although, in many instances, thiol form or equilibrium mixture of both forms has been observed in thiosemicarbazones. All the complexes are insoluble in common organic solvents such as ethanol, methanol, chloroform or acetone. However, they are soluble in DMSO and DMF. They are amorphous powder, stable at room temperature and do not show any decomposition on standing for two months. The molar conductance of the complexes in DMF lies in the range 18.5-11  $\Omega^{-1} \text{cm}^2 \text{mol}^{-1}$  (Table I). The values are too low to account for any dissociation, therefore the complexes are considered to be nonelectrolytes [31].

**Infrared spectra.** The binding mode of the ligand to metal ions was further elucidated by analysis of the IR spectra (Table II) of the ligand and its metal complexes formation. A study and comparison of infrared spectra of free ligand and its metal complexes, Table II, imply that the Schiff base behaves as

monobasic tridentate ligand and the metal ion is coordinated through the deprotonated oxygen atom of the phenolic, the nitrogen atom of the azomethine and the sulfur atom of thio-keto groups.

The disappearance of the absorption bands associated with the stretching  $\nu(\text{O-H})$  of the phenolic groups (observed at 3530  $\text{cm}^{-1}$  in the free ligand) in all the spectra of the metal complexes, indicates a loss of phenolic proton on complexation and thus forming a metal-oxygen bond. The  $\delta(\text{COH})_{\text{ip}}$  mode [32-34] which appeared at 1355  $\text{cm}^{-1}$  in the spectrum of the ligand, was not observed in the spectra of the complexes and thus supported the suggestion that the ligand coordinate to the metal through its deprotonated form. The presence of coordinated water was suggested by the very broad absorption centered around  $\sim 3430 \text{cm}^{-1}$  in the infrared spectra. Bands at  $\sim 930$  and  $\sim 770 \text{cm}^{-1}$  may be attributed to rocking and wagging modes of the coordinated water [32-35].

Furthermore, the band observed at  $\sim 3270 \text{cm}^{-1}$  region in the free ligand have been assigned to  $\nu(\text{NH})$  vibrations. Practically no effect on this frequency after complexation indicating the noninvolvement of this group in coordination with the metal ion. The most notable change in the ligand spectral features when coordinated to metal ion is the observed C=N red shift. The  $\nu(\text{C=N})$  band [32-34] at 1570  $\text{cm}^{-1}$  in the ligand spectrum exhibited a red shift of 50-40  $\text{cm}^{-1}$  in the spectra of the complexes. This finding may be taken as evidence for participation of the C=N group in coordination to the metal ions.

The intensity of the medium band at 1120  $\text{cm}^{-1}$  assigned for  $\nu(\text{N-N})$  in spectrum of the ligand, remains unchanged in all the spectra of the complexes, however, it shifted to the higher frequency [34-38]. The strong band observed at 876  $\text{cm}^{-1}$  in the spectrum of HL, is mainly due to the stretching vibrations of (C=S), is shifted towards lower frequency and occurred at 850-820  $\text{cm}^{-1}$ . in the corresponding spectra of the metal complexes indicating the coordination of the thio-keto sulphur to metal atom [34].

The bands observed at 1586-17400  $\text{cm}^{-1}$  assigned for  $\nu(\text{C=C}) + \nu(\text{C=N})$  of the quinoline ring and at 577-462 and 478-700  $\text{cm}^{-1}$  due to in- and out-plane quinoline ring deformations, respectively, and that observed in the spectrum of the ligand at 827-1013  $\text{cm}^{-1}$  due to the quinoline ring breathing remain unchanged in frequency and band intensities revealing the noninvolvement of the quinolinic-nitrogen atom in the coordination with the metal ion.

The possibility of thione-thiol tautomerism ( $\text{H-N-C=S}$ ), ( $\text{C=N.SH}$ ) in the HL ligand has been ruled out for no band around 2700-2500  $\text{cm}^{-1}$ , characteristic of thiol group is observed in the infrared absorption [32-34]. The new bands observed in the regions 560-540, 460-445 and 365-355  $\text{cm}^{-1}$  are



Table III. Magnetic moment, electronic spectral data for HL and its metal complexes.

Compound	$\mu_{eff}$ , B.M.	$\pi \rightarrow \pi^*$ , $n \rightarrow \pi^*$ and charge transfer transitions (nm)	$d \rightarrow d$ transitions (nm)
HL $C_{17}H_{14}N_5ClOS$ (371.5)	—	279, 300, 353, 364, 382, 309	—
(1) [(L)Cu(Cl)] $\cdot H_2O$ $C_{17}H_{15}N_5Cl_2O_2SCu$ (488.5)	1.78	240, 311, 325, 348	665
(2) [(L)Ni(Cl)(OH $_2$ ) $_2$ ] $\cdot 2H_2O$ $C_{17}H_{21}N_5Cl_2O_5SNi$ (537)	2.85	240, 315, 327, 348, 355	768, 670 (sh)
(3) [(L)Zn(Cl)(OH $_2$ ) $_2$ ] $\cdot 2H_2O$ $C_{17}H_{21}N_5Cl_2O_5SZn$ (543)	—	279, 300, 353, 364, 385, 319	—
(4) [(L)Co(Cl)(OH $_2$ ) $_2$ ] $\cdot H_2O$ $C_{17}H_{19}N_5Cl_2O_4SCo$ (519)	5.2	239, 315, 327, 350, 359	656, 477
(5) [(L)Mn(Cl)(OH $_2$ ) $_2$ ] $\cdot H_2O$ $C_{17}H_{19}N_5Cl_2O_4SMn$ (515)	5.39	245, 315, 330, 352, 365	469–853
(6) [(L)Fe(Cl) $_2$ (OH $_2$ ) $_2$ ] $\cdot 2H_2O$ $C_{17}H_{19}N_5Cl_3O_4SFe$ (551.5)	5.8	233, 315, 327, 350, 355, 396	722
(7) [(L)Cr(Cl) $_2$ (OH $_2$ ) $_2$ ] $\cdot 2H_2O$ $C_{17}H_{19}N_5Cl_3O_4SCr$ (547.5)	3.8	233, 315, 327, 350, 355, 396	592, 396

tentatively assigned to  $\nu(M-O)$ ,  $\nu(M-N)$  and  $\nu(M-S)$  (metal-ligand) stretching bands, respectively [34].

In conclusion, the infrared spectral studies suggest the monobasic tridentate nature of the ligand with ONS coordination sites. This was accounted for as the ligand contains phenolic OH, azomethine and ketonic-oxygen or thio-keto groups.

*Magnetic moments and electronic spectral data of the metal complexes.* The electronic spectra and magnetic moments of the metal complexes are listed in Table III. Generally, in all spectra of metal complexes, the absorption bands due to  $\pi-\pi^*$  and  $n-\pi^*$  transitions that observed in the spectrum of the free ligand have shifted to lower frequencies due to the coordination of the ligand with metal ions.

The spectra of the Cu(II) complex (1) (Table III) showed absorption bands at 240, 311, 325, and 348 nm attributed to ligand absorptions and a band at 665 nm is due to the  $d \rightarrow d$  transition within the Cu(II) cation in square-planar geometry [35–40]. The magnetic moments value, 1.78 B.M. reveals the presence of one unpaired electron and shows no copper-copper interaction. The square-planar geometry is achieved by the coordination of HL molecule as monobasic tridentate ligand, to the copper(II) ion. The shift of the  $d \rightarrow d$  absorption band to lower energy than that expected for square-planar geometry, at 550 nm for square-planar N,N'-ethylenebis(salicylideneimine)-copper(II), Cu(acacen) [39] may be due to the distortion of the square-planar geometry towards tetrahedral [35–39].

The electronic spectrum of the Ni(II) complex (2), Table III, showed a main band at 768 nm and a shoulder at 670 nm. The main band may be due to the  $^3A_{1g} \rightarrow ^3T_{1g}$  electronic transition in an octahedral geometry. The  $^3A_{2g} \rightarrow ^3T_{1g}$  transition may be overlapped by the ligand transition, which appeared at 355 nm [35–39]. The third transition due to  $^3A_{2g} \rightarrow ^3T_{2g}$  would be out of the range of the used spectrophotometer. The magnetic moment of the complex is 2.85 B.M. which agrees with the presence of Ni(II) ion in an octahedral geometry [36–39]. This indicates that the Ni(II) ion coordinated to ONS sites in an octahedral geometry [36–39]. The Ni(II) ion complete its six-coordination sphere by two water molecules and chloride ion.

Octahedral, tetrahedral and square-planar cobalt (II) complexes show magnetic moment between 4.7–5.2, 4.2–4.8 and 2.2–2.9 B.M., respectively [25,27]. The  $\mu_{eff}$  value measured for the present Co(II) complex (4), (Table III), is 5.2 B.M. which indicates that Co(II) ion is present in an octahedral geometry. The electronic spectrum of the complex showed two d-d transitions in the range 656 nm and shoulder at 477 nm due to the electronic transitions  $^4T_{1g} \rightarrow ^4A_{2g}$  and  $^4T_{1g}(F) \rightarrow ^4T_{1g}(P)$ , respectively, [37–39]

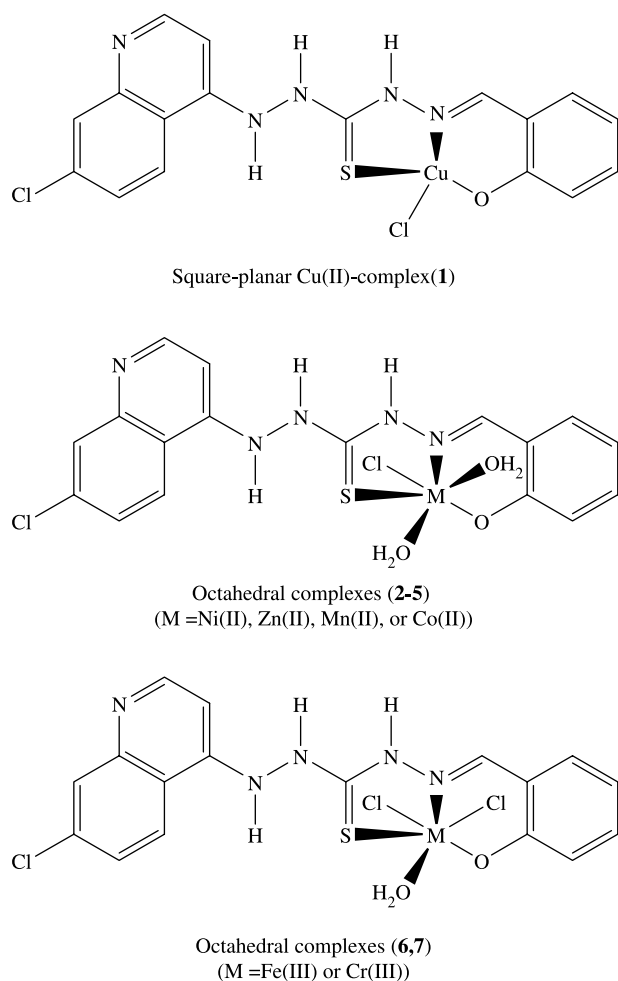


Figure 2. Suggested structures for the metal complexes.

indicating an octahedral configuration around Co(II) ion. The  ${}^4T_{2g}(F) \rightarrow {}^4T_{1g}(F)$  electronic transition would be observed in near IR. This region is out of the range of our Uv-vis spectrophotometer.

The spectrum of the Mn(II) complex (5) showed a series of weak bands in the range 469–853 nm. These bands are both Laporte and spin-forbidden. However, due to instantaneous distortion of the octahedral structures around the metal cation, weak bands sometimes do appear [37–39]. The magnetic moment of the complex is 5.39 B. M.

On the other hand, the electronic spectra of Fe(III) complex (6) showed broad bands 577 nm and at 722 nm. The former band may be due to the spin forbidden transition  ${}^6A_{1g} \rightarrow {}^4T_{2g}$ , which may gain intensity as a result of the vibronic mechanism in the octahedral field around ferric ion. The second bands may be attributed to  ${}^6A_1 \rightarrow {}^4T_1$  transitions [25]. In addition, a third absorption band with high intensity observed at 396 nm assigned for charge transfer transition. The magnetic moment of the complex is 5.9 B. M [36–39].

The spectrum of the Cr(III) complex (7) showed two broad bands at 592 and 396 nm besides the bands

Table IV.  ${}^1H$  and  ${}^{13}C$  NMR spectral data ( $\delta_{ppm}$ ) of the ligand HL and its Zn(II) complex.

${}^1H$ NMR ( $\delta$ )	${}^{13}C$ NMR ( $\delta$ )	${}^1H$ NMR ( $\delta$ )	${}^{13}C$ NMR ( $\delta$ )
[s, 1H] (a)	145.7	[s, 1H] (a)	C1
[s, 1H] (b)	120.5	[s, 1H] (b)	C2
[s, 1H] (c)	127.3	[s, 1H] (c)	C3
[s, 1H] (d)	130.9	[s, 1H] (d)	C4
[s, 1H] (e)	129.4	(e) disappeared	C5
[m, 9H] (f & g)	7.7–8.48	[m, 9H] (f & g)	C6
	2.0		C7
	4.0		C8
	11.67		C9
	7.52		C10
	9.83		C11
	7.7–8.48		C12
	165.5		C13
	176.5		C14
	150.5		C15
	123.5		C16
	151.3		C17
	117.7		
	118.0		C7
	132.5		C8
	123.5		C9
	129.6		C10
	116.5		C11
	159.7		C12
	161.3		C13
	169.3		C14
	150.5		C15
	123.5		C16
	123.5		C17
	116.5		
	162.6		
	117.7		

Table V. Thermal analyses data for Zn(II) complex.

Compound M.F. (M.wt.)	Dissociation stages	Temp range in TG°C	Weight loss found (Calcd.) %	Decomposition assignment
[(L)Zn(Cl)(OH) <sub>2</sub> ] <sub>2</sub> ·2H <sub>2</sub> O C <sub>17</sub> H <sub>21</sub> N <sub>5</sub> Cl <sub>2</sub> O <sub>5</sub> SZn (543)	Stage I	120-150	7.26 (6.63)	2 mol outer sphere water
	Stage II	180-210	7.66 (6.63)	2 mol coordinated water
	Stage III	250-350	20.13 (19.61)	HCl, HCN, NHCNH <sub>2</sub>
	Stage IV	660-760	15.57 (15.00)	Formation of ZnO

due to the ligand adsorptions. The observed bands at 592 and 396 nm may be due to  ${}^4A_{2g} \rightarrow {}^4T_{2g}$  and  ${}^4A_{2g} \rightarrow {}^4T_{1g}$  electronic transitions, respectively [35,39]. The  ${}^4A_{2g} \rightarrow {}^4T_{1g}(P)$  transition would be in the UV region and overlapped by ligand transitions. The expected value for  $\mu_{eff}$  of a single Cr(III) ion in its octahedral complexes is 3.80 B.M. The spectrum of the diamagnetic Zn(II) complex (3) is dominated only by the ligand bands [37]. Base on the above results, the structures in (Figure 2) are suggested for the metal complexes.

<sup>1</sup>H and <sup>13</sup>C NMR. Coordination of thiosemicarbazone, HL, in the metal complexes are further confirmed by <sup>1</sup>H and <sup>13</sup>C NMR spectra [40,41] (Table IV). The <sup>1</sup>H NMR spectrum of diamagnetic Zn(II) (3), showed the disappearance of the signal due to the proton of the phenolic OH group, appeared at  $\delta$  9.83 ppm in the ligand spectrum. This is attributed to its involvement in coordinating the zinc cation. Significant azomethine proton signal, due to CH=N, was observed at  $\delta$  7.52 ppm in ligand, and in complexes it has shown a change as a downfield shift and occurred at  $\delta$  8.22 ppm, indicating involvement of nitrogen in coordination. The proton peak of N—H group at  $\delta$  2.4 and 11.67 ppm remains the same in the ligand, and in the complexes it suggested that deprotonation do not occur and it has also shown keto form of the ligand. The signal due to the S—H (thiol) is not observed in the expected range 2-3 ppm [34,40] indicating that the ligand exist in the thione form. The multiplets as strong bands in region  $\delta$  7.7-8.24 ppm were assigned to aromatic and quinoline ring protons, which also shifted down field in the complexes.

The <sup>13</sup>C NMR spectra revealed the presence of expected number of signals corresponding to different types of carbon atoms present in the compounds. The spectrum of the ligand exhibit a strong band at  $\delta$  176 ppm and are assigned as C=S group [41]. This band undergoes upfield shift of  $\delta$  7.2 ppm and occurs at  $\delta$  169.3 ppm. This has shown involvement of thione sulfur in coordination. The signal due to azomethine carbon occurred at  $\delta$  165.5 ppm as downfield peak, and on complexation it has shown shift to  $\delta$  161.3 ppm due to the resonance and also have given proof that nitrogen is involved in coordination. The O—C (C6) absorbs at  $\delta$  159.7 ppm in the ligand and on complexation and it has shown downfield shift to  $\delta$  162.6 ppm due to the resonance and also have given proof that nitrogen is involved in coordination. Due to the deshielding of the directly attached electronegative oxygen atom.

*Mass spectra.* The mass spectrum of the ligand, HL, showed its molecular ion at m/e 372 15%) which coincide with formula weight. The base peak observed



Table VI. Antimicrobial activity of the Schiff base HL and its metal complexes.

Compound	Microbial species			
	(a)	(b)	(c)	(d)
HL C <sub>17</sub> H <sub>14</sub> N <sub>5</sub> ClOS (371.5)	+++	++	+++	+++
(1)[(L)Cu(Cl)].H <sub>2</sub> O C <sub>17</sub> H <sub>15</sub> N <sub>5</sub> Cl <sub>2</sub> O <sub>2</sub> SCu (488.5)	+++	+++	++	+++
(2)[(L)Ni(Cl)(OH <sub>2</sub> ) <sub>2</sub> ].2H <sub>2</sub> O C <sub>17</sub> H <sub>21</sub> N <sub>5</sub> Cl <sub>2</sub> O <sub>5</sub> SNi (537)	+++	+++	++	++
(3)[(L)Zn(Cl)(OH <sub>2</sub> ) <sub>2</sub> ].2H <sub>2</sub> O C <sub>17</sub> H <sub>21</sub> N <sub>5</sub> Cl <sub>2</sub> O <sub>5</sub> SZn (543)	+++	++	++	+++
(4)[(L)Co(Cl)(OH <sub>2</sub> ) <sub>2</sub> ].H <sub>2</sub> O C <sub>17</sub> H <sub>19</sub> N <sub>5</sub> Cl <sub>2</sub> O <sub>4</sub> SCo (519)	+++	+++	+++	+++
(5)[(L)Mn(Cl)(OH <sub>2</sub> ) <sub>2</sub> ].H <sub>2</sub> O C <sub>17</sub> H <sub>19</sub> N <sub>5</sub> Cl <sub>2</sub> O <sub>4</sub> SMn (515)	++	+++	+++	+++
(6)[(L)Fe(Cl) <sub>2</sub> (OH <sub>2</sub> ) <sub>2</sub> ].2H <sub>2</sub> O C <sub>17</sub> H <sub>19</sub> N <sub>5</sub> Cl <sub>3</sub> O <sub>4</sub> SFe (551.5)	+++	+++	++	++
(7)[(L)Cr(Cl) <sub>2</sub> (OH <sub>2</sub> ) <sub>2</sub> ].2H <sub>2</sub> O C <sub>17</sub> H <sub>19</sub> N <sub>5</sub> Cl <sub>3</sub> O <sub>4</sub> SCr (547.5)	+++	+++	+++	++++
Cephalosporin <sup>a</sup>	+++	+++	+++	+++
Streptomycin <sup>b</sup>	++++	+++	+++	++

(a) = *S. aureus*, (b) = *E. coli*, (c) = *Candida. Albicans* and (d) = *Fusarium solani*. Inhibition zone diameter in mm (% growth): +, 8-10 (36-45%); ++, 10-16 (45-73%); +++, 16-19 (73-86%); +++++, 19-22 (86-100%). Percent growth values are relative to growth zone (22 mm) with 100% growth.

<sup>a</sup>Standard antifungal and <sup>b</sup>antibacterial agents.

at m/e 142 corresponded to the ion [C<sub>9</sub>H<sub>6</sub>N<sub>2</sub>]<sup>+</sup>. The metal complexes, melted or decomposed at relatively low temperature (250-300°C) and soluble in DMF and DMSO indicating the non-polymeric nature of the complexes which consequently confirmed the noninvolvement of nitrogen atoms of the quinoline moiety. Moreover, mass spectrum of Zn(II) complex, (3), which was chosen as representative example of this type of complexes, show a peak at m/e = 543 (8.5%) corresponding to the molecular ion, [C<sub>17</sub>H<sub>21</sub>N<sub>5</sub>Cl<sub>2</sub>O<sub>5</sub>SZn]<sup>+</sup>. The base peak appeared at m/e = 331 (100%) corresponded to the formation of a fragment [C<sub>16</sub>H<sub>14</sub>N<sub>2</sub>O<sub>2</sub>Zn]<sup>+</sup>. Metastable ion(s) is/are not observed [34,41].

**Thermal analyses.** Generally, there is less known about the thermal properties of transition metal complexes of thio-carbazones [42-45]. In the present work, we report herein the thermal decomposition data of a representative complex, [(L)Zn(Cl)(OH<sub>2</sub>)<sub>2</sub>].2H<sub>2</sub>O, (3), that is, presented in Table V. Analyses of thermogravimetric curve suggest that, the complex contain two molecules of lattice water, which is evident by loss in weight at 120-150°C. A second decomposition step was observed at 180-210°C, in which the complex loss two coordinated water molecules. After that, the complex loss one molecule HCl, one molecule HCN and NH-C-NH<sub>2</sub> in one step at 250-350°C. There is no change up to ~400°C after that the rest of the organic ligand began to decompose at ~550°C. Finally, at ~760°C, metal oxide, ZnO, formed [42-45].

#### Antimicrobial activities results

A number of authors [3,46-49] were interested to investigate the biological and medicinal properties of

transition metal complexes of thiosemicarbazones. Thomas and Parmeswaran [46] studied the antitumour activities of Mn(II), Co(II), Ni(II), and Cu(II) chelates of anthracene-9-carboxaldehyde thiosemicarbazone. Murthy and Dharmaraja [47] reported the cytotoxic activity of phenylglyoxal bis(thiosemicarbazone) against *Ehrlich ascites* carcinoma cells. These compounds were also screened for antimicrobial activity on *Bsubtilis* and *E. coli*. They inhibited the bacterial growth considerably.

The Schiff base, HL and its metal complexes reported were evaluated for antimicrobial activity against one strain Gram + ve bacteria (*S. aureus*) (a), Gram - ve bacteria (*E. coli*) (b), fungus (*C. albicans*), (c), fungus *F. solani*, (d). The results of the antimicrobial screening are presented in Table VI. Generally, the thio-keto Schiff base HL and its metal complexes were found to be biologically active. However, remarkable antimicrobial activity was shown for the metal complex, which is expected as it contains sulfur and nitrogen atoms. The results show, also, that all metal complexes exhibit antimicrobial activity to one or more strain and enhanced it comparing with the parent Schiff base.

It is known that chelation [25-28,50] tends to make the ligand act as a more powerful and potent bactericidal agent. A possible explanation for this increased activity upon chelation is that in the complex, the positive charge of the metal is partially shared with the donor atoms present on the ligand and there is an electron delocalization over the whole chelate ring. This, in turn, increase the lipophilic character of the metal chelate and favours its permeation through the lipid layers of the bacterial membranes. Generally, it is suggested that the complexes deactivate various cellular enzymes, which play a vital role in various metabolic pathways of these microorganisms. Other factors such as solubility,

conductivity and dipole moment, which affected by the presence of metal ions, may also be possible reasons for increasing the biological activity of the metal complexes as compared to the ligand from which they are derived.

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