

Synthesis, Spectral Studies and Antibacterial Activities of 8-Hydroxyquinoline Derivative and its Metal Complexes

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Received 7 May 2013 / Accepted 7 June 2013

Abstract: 1-(8-Hydroxy quinolin-2-yl-methyl) thiourea ligand (HTF) was synthesized from 8-hydroxyquinoline and thiourea with formaldehyde by condensation method in *N,N*-dimethyl formamide medium. The metal complexes Zn(II), Cu(II), Ni(II) and Co(II) were prepared using the 1-(8-hydroxy quinolin-2-yl-methyl) thiourea as ligand. The ligand and its metal complexes were characterized by elemental analysis, FT-IR, UV-Visible, cyclic voltammetry, Mass spectra and NMR spectroscopy. The ligand and its metal complexes possess antibacterial activity for certain bacteria such as *Staphylococcus aureus*, *Escherichia coli*, *Pseudomona aeruginosa* and *C.tropicalis*.

Keywords: 8-Hydroxyquinoline derivative, Antibacterial screening, Thiourea derivative, Cyclic Voltammetry

Introduction

8-Hydroxyquinoline is a long known molecule which due to its metal complexation ability frequently is used for analysis or metal precipitation¹. Recently aluminum complexes with 8-hydroxyquinoline derived ligands were introduced as molecular components for organic light emitting diodes². Zinc(II) complexes show luminescence as well, which typically is red shifted compared to the corresponding Al(III) compounds³. The coordination chemistry of simple 8-hydroxyquinolines with zinc(II) ions is very versatile. Although mainly 2:1 complexes are obtained, 3:1 complexes can also be formed⁴. In case of 2:1 complexes different structures could be observed in the solid state. For example, with unsubstituted 8-hydroxyquinoline an octahedral compound was obtained which bears two water molecules binding trans to a square planar bis(quinolinato) zinc moiety⁵. The anhydrous 8-hydroxyquinolate complex of zinc(II) is made up from four 2:1 complex units which are connected by bridging quinolate oxygen atoms⁶. Recently the trinuclear zinc complex was described which possesses some interesting photophysical properties. Liphophilic 8-hydroxyquinoline

derivatives (like the commercially available kelex 100)⁷ are used for metal extraction purposes. On the other hand sterically less demanding 7-nonyl-8-hydroxyquinoline forms a dimeric complex with pentacoordinated zinc atoms⁸. Recently the groups of pierre, Secrratrice, Bradshaw and Hiratani developed di and tritopic 8-hydroxyquinoline derivatives for the selective extraction or sensitizing of metal ions⁹. In supramolecular chemistry of 8-hydroxyquinoline derivatives can be used for the formation of hydrogen bonded networks^{10, 11} as well as of metallo-supramolecular aggregates⁴. To manipulate the self-assembly properties of the 8-hydroxyquinoline derivatives we recently introduced amide or urea substituents as additional hydrogen bond donor/acceptor units¹¹. Here hierarchical self-assembly¹² can take place leading first to an 8-hydroxyquinoline dimer or a metal complex. Some complexes of 8-hydroxyquinoline and its derivatives are used as the emitting elements in electroluminescent devices^{13,14}.

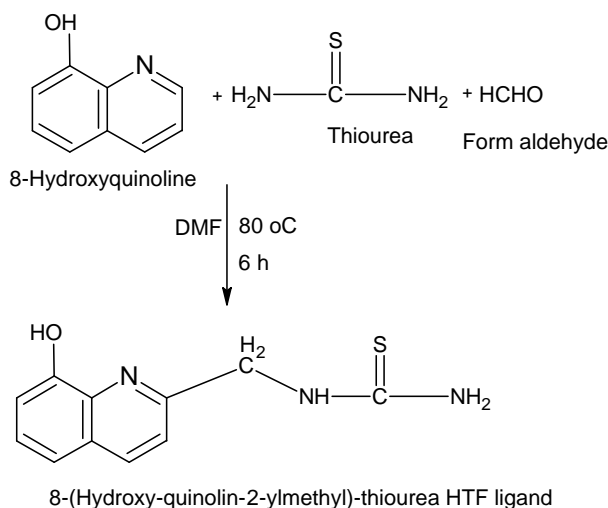
In the present study 8-hydroxyquinoline derivatives and their metal complexes from thiourea and formaldehyde have been prepared and characterized by spectral studies. Their antibacterial activity has also been investigated.

Experimental

8-Hydroxyquinoline and thiourea were procured from Merck, India and purified by rectified spirit. Formaldehyde (37%) was of AR grade. Merck and used as received. Double distilled water was used for all the experiments. All other chemicals and metal salts were of analytical grade and used without further purification.

1-(8-Hydroxy quinolin-2-yl-methyl)thiourea

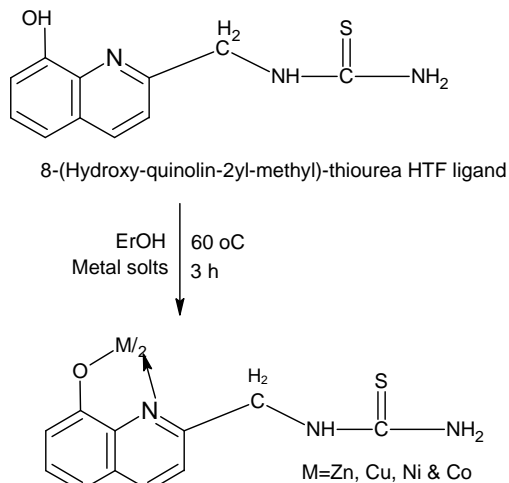
The compound was synthesized by the refluxation of 8-hydroxyquinoline (0.1 mole) with thiourea (0.1 mole) and formaldehyde (0.1 mole) using dimethyl formamide as the reaction medium at 60 °C for 6 h. The reaction mixture was then cooled, poured into crushed ice with constant stirring and kept in refrigerator overnight. The yellow colour precipitate was formed and separated out. The separated precipitate was several times washed with water and dried. The compound was recrystallised using ethanol. The yield of the compound was found 92.75% and the reaction route was shown in Scheme 1.



Scheme 1. Reaction route of HTF ligand

Synthesis of metal complexes

The ligand (0.1 mole) was dissolved in ethanol and the metal nitrates of Zn(II), Cu(II) (0.1 mole) and metal chlorides of Ni(II), Co(II) (0.1 mole) were dissolved separately in ethanol and filtered off. The resultant solution were mixed together with constant stirring and refluxed for 3 h. The organic metal complexes obtained were separated and washed with water. Moreover the organic metal complexes were dried in an air oven at 40 °C for 3 h. The reaction scheme for the preparation of the organic metal complexes is shown in Scheme 2.



Scheme 2. Reaction route for HTF metal complexes

Spectral analysis

The elemental analysis of the compound and their metal complexes has been carried out to identify the composition of each element (Model Vario EL III, Germany). The metal contents were determined volumetrically by Vogel's methods¹⁵. The FT-IR spectrum of the synthesized ligand and their metal complexes had been scanned in KBr pellets on a Bruker (Model Tensor 27) spectrophotometer to identify the linkages and functional groups. Cyclic Voltammetry studies have been used for the identification of various metal ions present in the complexes. The UV-Visible spectrum of the synthesized ligand and metal complexes were recorded in Cary Eclipse varian (Model U.3400) UV-Visible spectrophotometer and the ¹H NMR spectrum using CDCl₃-d₆ solvent Bruker 400 MHz, ¹³C NMR spectrum was also recorded for the ligand using Bruker 100 MHz. Mass spectra were obtained using Voyager DETM PRO Biospectrometry Workstation (Applied Biosystems). All the electrochemical measurements were carried out using conventional two compartments and three electrode electrochemical analyzer (CHI model 643B, Austin, USA).

Antibacterial screening

Biological assay depends upon a comparison of the inhibition of growth of microorganism by measuring the concentration of the sample which is to be examined with the known concentration of standard antibiotic. Disc diffusion method has involved for antibacterial activity. In this study the ligand and its metal complexes were tested for their effect on certain human pathogenic bacteria such as *Staphylococcus aureus*, *Escherichia coli*, *Pseudomonas aeruginosa* and *C. tropicalis*.

Results and Discussion

The synthesized compound and its metal complexes were soluble in solvents like methanol, ethanol, acetone, chloroform, *N-N*-dimethyl formamide, tetrahydrofuran and dimethyl sulphoxide. The physical and analytical data of the synthesized compound and its metal complexes are given in Table 1. Based on the analytical data the molecular formula of the synthesized ligand and its metal complexes are found to be in good agreement with the calculated elemental values of C, H, N, and metal.

Table 1. Physical and analytical data of the HTF ligand and their metal complexes

Compd.	Empirical Formula	Molecular Weight	Colour	Yield, Melting % Point, °C		% Found (Calculated)				
						C	H	N	S	M
Ligand (HTF)	C ₁₁ H ₁₁ N ₃ OS	233	Light Yellow	92.75	51	56.54 (56.65)	4.68 (4.72)	17.56 (18.02)	13.65 (13.73)	-
HTF-Zn	C ₁₁ H ₁₀ N ₃ OS-Zn	297.7	yellow	56.11	156	44.28 (44.33)	3.57 (3.69)	13.94 (14.10)	10.57 (10.74)	21.86 (22.06)
HTF-Cu	C ₁₁ H ₁₀ N ₃ OS-Cu	295.54	Brownish green	62.27	280	44.53 (44.66)	3.63 (3.72)	14.08 (14.21)	10.38 (10.82)	21.29 (21.49)
HTF-Ni	C ₁₁ H ₁₀ N ₃ OS-Ni	290.69	Light green	67.03	289	45.23 (45.40)	3.61 (3.78)	14.32 (14.44)	10.89 (11.00)	19.95 (20.18)
HTF-Co	C ₁₁ H ₁₀ N ₃ OS-Co	290.93	Dark green	61.90	324	45.32 (45.37)	3.60 (3.78)	14.28 (14.43)	10.84 (10.99)	19.91 (20.25)

Spectral analysis

FT-IR spectra are the most powerful tool for identifying the functional groups. The FT-IR spectrum of the 1-(8-hydroxy quinolin-2-yl-methyl) thiourea ligand (HTF) and its metal complexes are depicted in Figure 1 and the frequency data are presented in Table 2. In the ligand spectrum a broad band appeared in the region of 3390.34 cm⁻¹ is assigned to the hydroxyl group present in 8-hydroxyquinoline aromatic ring¹⁶. A peak appeared at 2920.55 cm⁻¹ is assigned to CH₂ group vibration in the aromatic ring. A band appeared in the region of 1571.36 cm⁻¹ is assigned for C=N present in aromatic ring. A strong band appeared in the range of 1382.85 cm⁻¹ and 1127.28 cm⁻¹ is assigned for C-N and C=S moiety of thiourea.

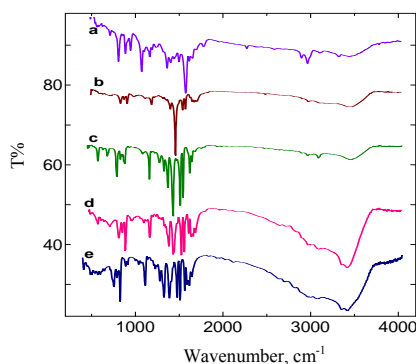


Figure 1. FT-IR spectra obtained for (a) HTF-ligand, (b) HTF-Zn, (c) HTF-Cu, (d) HTF-Ni and (e) HTF-Co complexes

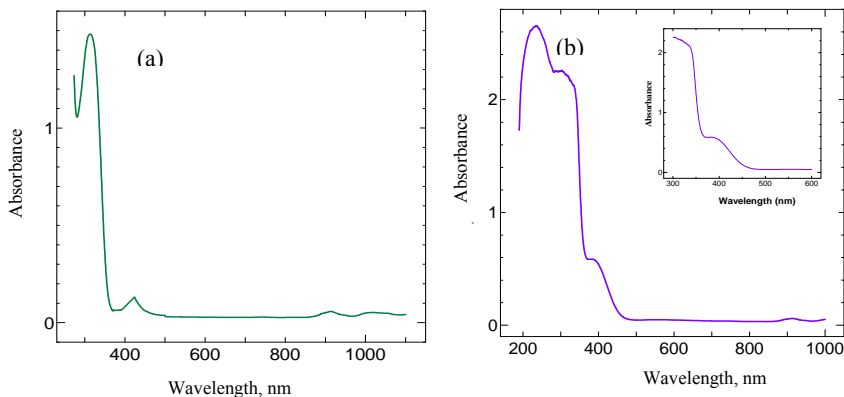
Table 2. FT-IR spectral data of the HTF ligand and their metal complexes

Compound	Observed frequencies (cm ⁻¹)					
	ν -OH	ν C-N (aromatic)	ν CH ₂	ν C=S	ν C=N	ν C-O-M
HTF-ligand	3390.34	1382.85	2920.55	1127.28	1571.36	-
HTF-Zn	3405.67	1384.64	2925.48	1106.94	1556.27	1033.66
HTF-Cu	3405.67	1384.64	2958.27	1110.8	1573.63	1033.66
HTF-Ni	3374.82	1375.00	2927.41	1101.15	1579.41	1033.66
HTF-Co	3343.96	1378.85	2940.91	1108.87	1577.49	1033.66

A weak band appearing in the region 3084.93 cm⁻¹ is attributed to CH₂ linkage present in the synthesized 1-(8-hydroxy quinolin-2-yl-methyl) thiourea ligand (HTF)¹⁷. In the spectra of metal complexes a sharp band appearing compared to its ligand in the region of 3300-3400 cm⁻¹ due to the coordination of the ligand with the metal ions through the oxygen atom of phenolic group of 8-hydroxyquinoline and may also be due to the coordination of water molecules. A band appearing in the region of 1101.15-1127.28 cm⁻¹ is assigned to C=S stretching vibrations. The band in the range of 1033.66 cm⁻¹ are assigned to the C-O-M in the respective metal complexes¹⁸. The band ranges from 1375.00-1384.64 cm⁻¹ are due to C-N stretching vibrations of the metal complexes.

Electronic spectra and magnetic moments

The electronic spectra provide the information about the electronic structure of the synthesized ligand and its metal complexes. The UV-Visible spectrum clearly shows the electronic absorption of HTF ligand and its metal complexes which are shown in Figure 2. The electronic spectra of all the metal complexes exhibited different bands in the region 250-300 nm and 450-490 nm. The band appearing in the range of 250-300 nm is assigned as $\pi \rightarrow \pi^*$ transition of the ligand where as the band at 450-490 nm is assigned to chromophores metal complexes which is clear evidence the metal ion coordination with nitrogen and oxygen atom present in 1-(8-hydroxy quinolin-2-yl-methyl) thiourea ligand. The electronic spectrum of HTF-Co complex exhibited the absorption at 20,630 cm⁻¹. The electronic transition of HTF-Co observed between $^2E_g \rightarrow ^2T_{2g}$. The structure of HTF-Co was assigned as square bipyramidal environment with a magnetic moment of 1.79 BM. The absorption bands occurred at 19,867 cm⁻¹ is assigned as $^3A_{2g} \rightarrow ^3T_{1g}$ for tetrahedral HTF-Ni complex with a magnetic moment value of 3.10 BM.



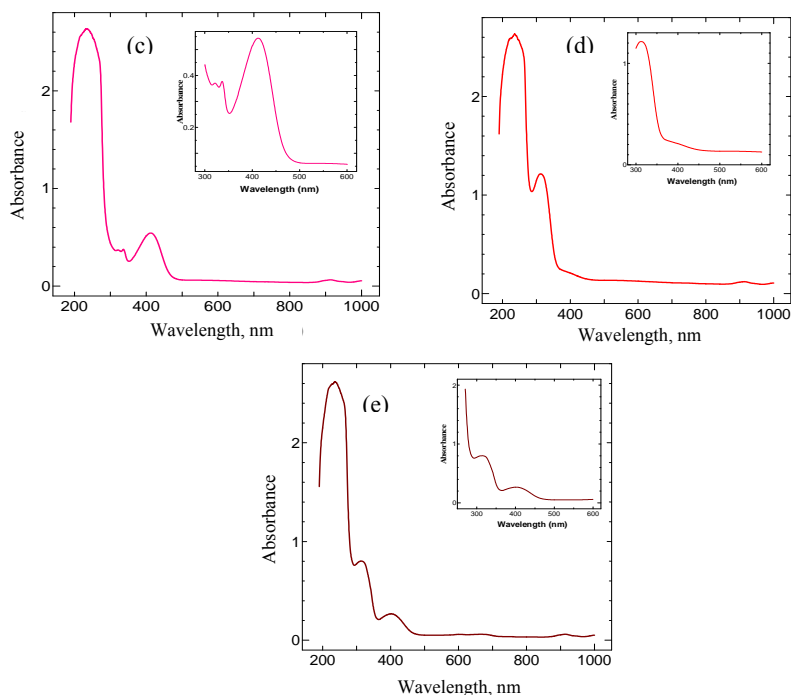


Figure 2. UV-Visible absorption spectra obtained for (a) HTF-ligand, (b) HTF-Zn, (c) HTF-Cu, (d) HTF-Ni and (e) HTF-Co complexes.

NMR spectral analysis

The ^1H NMR spectrum of the HTF ligand and its metal complexes are shown in Figure 3 and the spectral data are presented in Table 3. The signal at 8.6 ppm is assigned to the OH group of 8-hydroxyquinoline ring and this downfield shift is due to intramolecular hydrogen bonding between OH of 8-hydroxyquinoline ring. The signal at 8.86 ppm is assigned to NH_2 group of thiourea moiety. The signal in the region of 7.1-7.6 ppm is assigned to all the aromatic protons of the 8-hydroxyquinoline ring¹⁹. The signal appearing in the region of 3.4 ppm is due to methylene protons attached with 8-hydroxyquinoline ring. The signal obtained at 2.3 ppm is attributed to NH group in thiourea moiety.

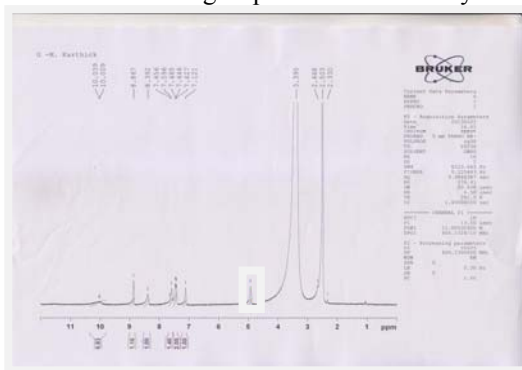
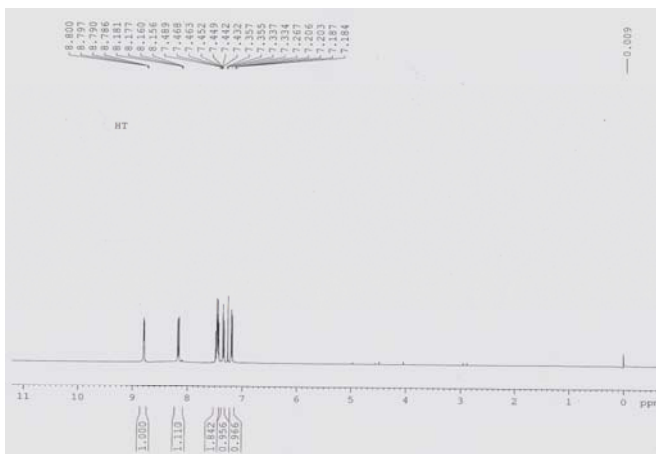


Figure 3. ^1H -NMR spectrum obtained for HTF-ligand

Table 3. ^1H NMR spectral data of the ligand and their complexes

	Chemical Shifts, ppm		
	Aromatic protons	CH_2 attached with 8-HQ	NH_2 of thiourea moiety
HTF-ligand	7.1-7.6	2.3-5.0	8.86
HTF-Zn	7.1-7.4	4.0	8.80
HTF-Cu	7.1-7.4	4.0	8.80
HTF-Ni	7.1-7.4	4.0	8.80
HTF-Co	7.1-7.4	4.0	8.80

The ^1H NMR spectra of the organic metal complexes show multiplet in the range at 7.1-7.4 ppm are assigned to the aromatic protons. The signal observed in the region 4.0 ppm is due to methylene protons. The signal obtained in the region of 8.6 ppm is assigned to OH group of HTF ligand and its complexes which is completely vanished from its parent ligand gives a clear evidence for the bond formation of metal ion with the ligand through the oxygen atom of the -OH group in the quinoline ring (Figure 4).

**Figure 4.** ^1H -NMR spectrum obtained for HTF-Ni complex

The ^{13}C NMR spectrum of the HTF ligand is shown in Figure 5. The observed chemical shifts are assigned on the basis of the literature²⁰. The spectrum shows the corresponding peaks at 109.96, 117.8, 127.8, 128.5, 136.1 and 130.3 ppm with respect to C1 to C9 of the 8-hydroxyquinoline ring. The peak appeared at 56.2 ppm is assigned to CH_2 group is attached with 8-hydroxyquinoline ring. The peak is assigned at 180.0 ppm is assigned $\text{C}=\text{S}$ which is present in thiourea moiety. The mass spectrum of the synthesized HTF-ligand shows molecular ion peak at m/z 233 indicating the molecular weight of HTF-ligand.

Electrochemical behavior of HTF ligand and its metal complexes

The electrochemical behaviour of HTF-ligand and its metal complexes were examined by cyclic voltammetry based on the literature²¹⁻²³. Cyclic voltammogram(CV) of the HTF-ligand and its metal complexes are shown in Figure 6. Figure 6a shows the CV obtained for the HTF-ligand in DMF solution using GCE as a working electrode. It shows three pairs of oxidation along with one shoulder oxidation wave. The redox wave I at -0.72 V corresponds to the quinoline redox. The redox wave II at 0.65 V corresponds to the aldehyde redox wave. The oxidation wave at 0.45 V is due to the amine oxidation. Figure 6b shows the quinone redox wave at -0.82 V and one broad oxidation wave at 0.21 V corresponding to the metal

redox wave $\text{Zn}^{\text{II}}/\text{Zn}^{\text{I}}$. The absence of oxidation wave at 0.63 V indicates that the metal ion forms a bond on keto group. Figure 6c shows the CV for HTF-Cu complex. It shows a redox wave at -0.72 V indicating the presence of quinoline moiety in metal complex. Further, it shows a weak oxidation wave at 0.14 V corresponding to $\text{Cu}^{\text{II}}/\text{Cu}^{\text{I}}$ metal centre²⁴. This clearly reveals the formation of HTF-Cu complex. Based on the results, the following structures are assigned to the complexes prepared (Scheme 2). These structures are in agreement with the structures proposed by Markus Albrecht *et al.*¹⁵.

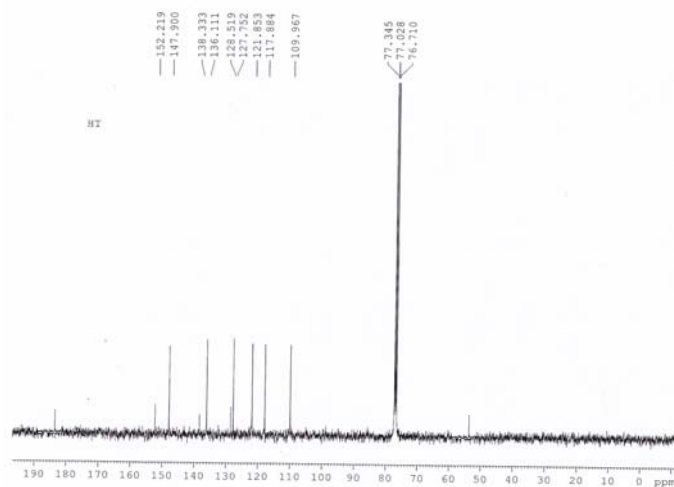
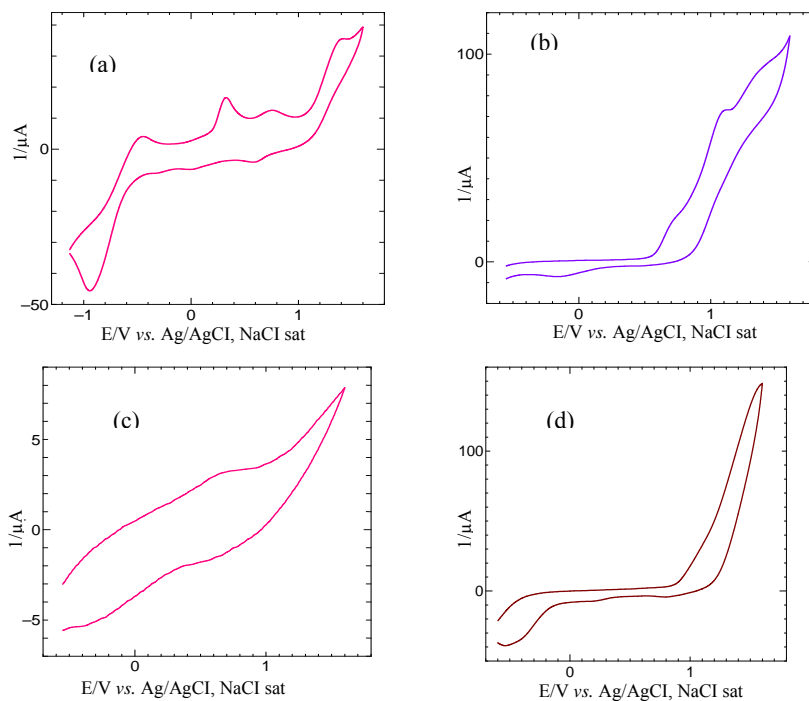


Figure 5. ^{13}C -NMR spectrum obtained for HTF-ligand



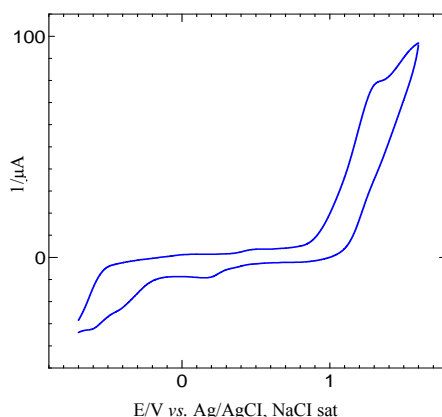


Figure 6. CVs obtained for (a) HTF-ligand, (b) HTF-Zn, (c) HTF-Cu, (d) HTF-Ni and (e) HTF-Co complexes

Antimicrobial screening

The results of microbial screening of the HTF ligand and its metal complexes are presented in Table 4.

Table 4. Antibacterial activity of HTF-ligand and its metal complexes

Compound	Zone inhibition, mm			
	<i>E.coli</i>	<i>S.aureus</i>	<i>P.aeruginosa</i>	<i>C.tropicalis</i>
HTF-ligand	14	16	22	11
HTF-Zn	15	17	22	14
HTF-Cu	16	18	24	13
HTF-Ni	15	17	22	13
HTF-Co	16	15	19	11
Standard (Ciprofloxacin)	15	15	20	12
Control(DMF)	-	-	-	-

Antibacterial activity

The 1-(8-hydroxy quinolin-2-yl-methyl) thiourea ligand and its metal complexes show good inhibition against the growth of pathogenic bacterial strains. A good result was obtained for the HTF-Cu, HTF-Co complexes against *S.aureus*, *E.coli*, *P.aeruginosa* and *C.tropicalis*. HTF-Cu and HTF-Co complexes show higher activity against *S.aureus* when compared to the 1-(8-hydroxy quinolin-2-yl-methyl) thiourea ligand and other complexes. The 1-(8-hydroxy quinolin-2-yl-methyl) thiourea ligand, HTF-Zn, HTF-Cu, HTF-Ni complexes show activity against *E.coli*.

Conclusion

Four number of metal complexes have been prepared using a synthesized 1-(8-hydroxy quinolin-2-yl-methyl) thiourea ligand involving 8-hydroxyquinoline and thiourea with formaldehyde. The synthesized ligand and its four metal complexes show higher bacterial activity against *S.aureus*, *E.coli*, *P.aeruginosa* and *C.tropicalis*. The activity of ligand and its metal complexes are greater than the standard chosen for the study.

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