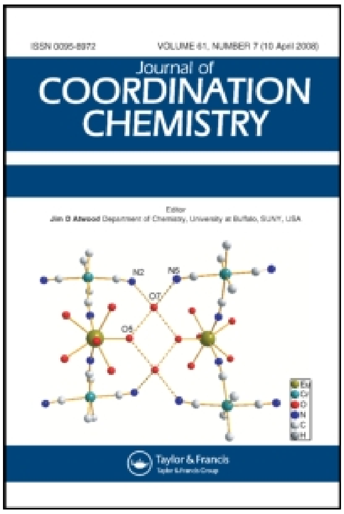

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Structural and Microbial Studies of some Transition Metal Complexes of 7-Substituted-8-Hydroxyquinoline-5-Sulphonic Acid Ligands

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STRUCTURAL AND MICROBIAL STUDIES OF SOME TRANSITION METAL COMPLEXES OF 7-SUBSTITUTED-8-HYDROXYQUINOLINE-5-SULPHONIC ACID LIGANDS

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The reaction of 7-substituted derivatives of the ligand 5-sulpho-8-hydroxyquinoline (7-X-HL), (X = H, NH_2, NO_2 and I), with some biologically important transition metal ion such as {Cr(III), Fe(III), Mn(II), Fe(II), Co(II), Ni(II), and Cu(II)} was investigated. The formation of ML_n (n = 1, 2) complexes of the ligand Na[7-I-HL] has been established by conductometric titrations in 10% (v/v) ethanol-water. The complexes of the ligands with all of the above transition metal ions which have been synthesized were characterized by elemental analyses, molecular weight determinations, X-ray diffraction (XRD), magnetic moments (μ_{eff}), and thermal analyses (DTA and TG). The data suggest the composition of these complexes, which have an octahedral coordination. The general formula is $Na_2[ML_2(H_2O)_2] \cdot 4H_2O$ where M(II) = Mn, Fe, Co, Ni and Cu. The thermal analyses of the complexes show that for $Na_3[ML_3] \cdot 6H_2O$ where M(III) = Cr and Fe all water molecules are lattice water. The antibacterial activity of these ligands and their divalent transition metal complexes has been determined on gram-positive (*Sarcina lutea*) and gram-negative (*Escherichia coli*) bacteria at 37°C, and antifungal activity has been determined on common fungi *viz*. (*Aspergillus niger*, and *Candida albicans*) at 30°C. A considerable increase in the biocidal activity of these ligands on being coordinated with transition metal ions has been reported. These compounds can be recommended to use for the chemotherapy of candidiaces and other fungal skin diseases.

Keywords: Antifungal; Antibacterial; Quinoline ligands; Transition metal

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INTRODUCTION

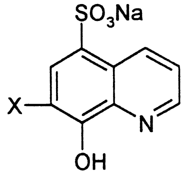
Evidence for the importance of steric factors in the fungitoxic mechanisms of 8-hydroxyquinoline and its 5- and 7-halogenated analog [1], synergistic antifungal action of 8-hydroxyquinoline and its bischelate with copper(II) [2], showed that no satisfactory investigation has been done since it is considered a collagen inhibitor [3]. Manufacturing of mono- or di-halo-8-hydroxyquinoline used as antiseptic is done on a large scale [4, 5], and a new 7-substituted aminomethyl-5-substituted sulfonamide-8-hydroxy-quinoline has been synthesized in view of their biological interest [6]. Some studies have been carried out on the structure of solid transition metal complexes [7, 8], and potentiometrically on the complex formation of metal ions and with some 8-hydroxyquinoline azo dyes [9], such as ferron [10] (7-iodo-5-sulpho-8-hydroxyquinoline), 5-nitroso-8-hydroxyquinoline [6], 2-methyl derivative-8-hydroxyquinoline [11], oxine [12, 13] (8-hydroxyquinoline), sulphoxine [14] (5-sulpho-8-hydroxyquinoline), 7-amino-sulphoxine [15] (7-amino-5-sulpho-8-hydroxyquinoline), and mixed ligand complexes with N, N and N, O ligands [16, 17].

The object of the present study is to complement the existing data and study the formed complexes of several M(II) and M(III) ions with 7-substituted derivatives (H, NH_2, NO_2 and I)-5-sulpho-8-hydroxyquinoline ligands. Insight into the possible structure was gained from conductometric titrations, molecular weight determinations, magnetic moments (μ_{eff}), X-ray diffraction (XRD), and thermal analyses (DTA and TG) of these complexes. The microbial activity of the above ligands and their divalent transition metal complexes against some common bacteria and fungi are also described.

EXPERIMENTAL

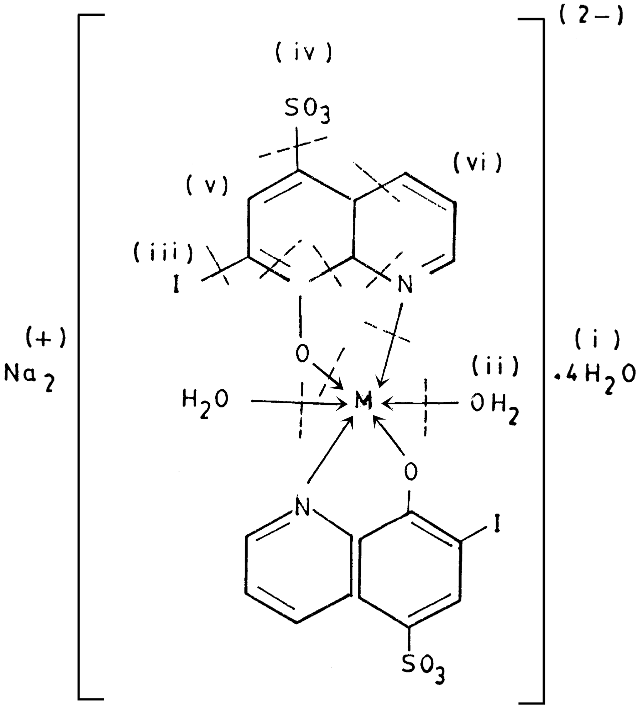
Materials

The ligand 5-sulpho-8-hydroxyquinoline (sulphoxine) (L) was prepared as described by Chawla [18]. 7-Amino-5-sulpho-8-hydroxyquinoline (7-amino-sulphoxine) (L^1) was prepared as described by Yanni [5]. 7-Nitro-5-sulpho-8-hydroxyquinoline (7-nitro-sulphoxine) (L^2) was prepared by nitration of sulphoxine ligand as described [35]. 7-Iodo-5-sulpho-8-hydroxyquinoline (ferron) (L^3) was prepared as described by Giermasinshi [4]. The different [7-X-HL] ligands are represented by the following structure:



(7-substituted-8-hydroxyquinoline-5-sulphonic acid, sodium salt), Na[7-X-HL], (X = H, NH_2, NO_2 and I)

The chromium(III), manganese(II), iron(II, III), cobalt(II), nickel(II), and copper(II) salts were the metal nitrates of AR grade and their solutions were prepared in carbonate-free double-distilled water.



The decomposition sequence of $Na_2[ML_2 \cdot 2H_2O] \cdot 4H_2O$ where M = Mn(II), Fe(II), Co(II), Ni(II), and Cu(II) complexes by heat; (i) hydrated water, (ii) coordinated water, (iii) iodine, (iv) sulphonic group, (v) C_5H_3 fragment, (vi) C_3H_3N fragment.

Instruments

X-ray Diffraction (XRD) data of the prepared solid complexes were recorded using a Philips X-ray diffractometer model PW 1140/90 and Ni-filtered Cu K_α radiation. The X-ray patterns of powdered samples were recorded automatically with a scanning speed of 2° per minute, and the scanning angular range (2θ) was from $6-60°$. All the diffraction patterns were measured at room temperature (25°C). The "$d \times 10^{-1}$ nm" spaces were calculated and compared with data of their relative intensities given in the ASTM cards. DTA was carried out using α-Al_2O_3 as the inert standard. An Ether Transitrol type 994 programmed temperature controller was used to permit a linear rate of heating of 12.0°C min.$^{-1}$ and a model B Cambridge recorder was used for recording the temperature differences. TG was carried out in static air at a heating rate of 10°C min.$^{-1}$ using a type 750/770 Stanton-Redcroft thermobalance connected to a BD9 Kipp and Zonnen two-channel automatic recorder. A YSI model 32M conductance meter [Yellow Spring Co. USA] was used to measure the conductance. The measuring range was from 0.0 to 200.0 microsiemens with a maximum error of $\pm 0.2\%$. A model YSI 3417 cell was used with a cell constant $K = 100/m$. This bridge has a limiting accuracy of $\pm 0.1 \times 10^{-6}$ Ohm^{-1}. Conductometric titrations were carried out at 25.0°C. All titrations were carried out twice to test reproducibility. Molecular weights of metal complexes were determined by a cryoscopic method in dimethylsulfoxide (DMSO). Magnetic measurements were carried out at room temperature (25°C) by Gouy's method using $Hg[Co(SCN)_4]$ as a calibrant. The values were corrected for diamagnetism by applying Pascal's constants. Elemental analyses of C, N and H were done at the Microchemical Analysis Center using a Perkin Elmer 2400 CHN Analyzer at Ain Shams University, Cairo, Egypt. The metal ion content was determined by complexometric titration after decomposition of the complex in the conventional manner [19].

Preparation and Analyses of the Chelate Complexes

The metal complexes were prepared by the addition of a concentrated solution of the ligand (7-X-HL), (0.30 mol) dissolved in 50 mL distilled water ($NaHCO_3$ was added to neutralize the sulphonic group in the ligand), to a hot 20 mL aqueous solution of the metal nitrate (0.10 mol). The mixed solution was left overnight at room temperature and a colored precipitate was obtained which was filtered and washed with hot benzene to dissolve any unreacted ligand and dried at 110°C. The iron(III) complex separated first as a dark viscous liquid that solidifies by adding dry diethyl ether. Dissolving in a small portion of ethyl alcohol or dioxane purified all solid complexes which were reprecipitated by dropwise addition of hot distilled water. The dried complexes, which were obtained in yields of 80–95%, were stored in a vacuum desiccator.

RESULTS AND DISCUSSION

Stability Constants of M(II) and M(III) Complexes of 7-X-5-sulpho-8-hydroxyquinoline [M : 7-X-HL], (X = H, NH_2, NO_2 and I)

The procedure employed for the potentiometric pH measurements has been described in detail elsewhere [20]. Equilibrium constants involving the ligand and its divalent and trivalent transition metal chelates were calculated from potentiometric data using the Calvin-Bjerrum titration technique as described by Irving and Rossotti [21, 22]. The potentiometric equilibrium curve in 1 : 10 molar ratio of metal ion to ligand at ionic strength $= 0.100\,\mu$ using KNO_3 at 25.0°C, shows well-separated curves. From the metal-ligand formation curves for M(II) and M(III) ions, values of $\log K_1$, $\log K_2$ and $\log K_3$ were obtained directly by interpolation at $n_A = 0.5$, 1.5 and 2.5, respectively, where

pK_{a1} = first protonation constant of ligand,
pK_{a2} = second protonation constant of ligand,
$\log K_1$ = equilibrium constant for the formation of M : L (1 : 1) complex,
$\log K_2$ = equilibrium constant for the formation of M : L (1 : 2) complex,
$\log K_3$ = equilibrium constant for the formation of M : L (1 : 3) complex and
$\log \beta_n$ = overall stability constant values of complex.

These values along with ionic radii (r Å) of M(II) and M(III) ions are reported in Table I. The overall stability constant values were found to follow the order: Fe(III) > Cr(III) > Ni(II) > Co(II) ≅ Cu(II) > Fe(II) > Mn(II). The $\log \beta_n$ values of these complexes followed the Irving-Williams order with Cu(II) complexes, an exception to this order which may be attributed to the occurrence of the distorted octahedral/square planar arrangements [23].

Conductometric Study

Despite the wide application of conductance measurements as a tool for end point detection of acid-base reactions, little attention has been given to

TABLE I Protonation constants (pK_a's) of the 7-X-HL ligands and the overall stability constants ($\log \beta_n$) of their complexes with different metal ions from potentiometric measurements[a]

Metal ion *ligand* pk_a		*Cr*(III)	*Fe*(III)	*Mn*(II)	*Fe*(II)	*Co*(II)	*Ni*(II)	*Cu*(II)
	(r Å) [28]	0.63	0.64	0.80	0.74	0.72	0.69	0.72
7-H-H_2L [14]	Log K_1	9.90	9.80	10.00	11.30	12.45	12.50	11.50
$pK_{a1} = 8.47$	Log K_2	8.60	8.50	9.00	10.40	10.95	11.50	10.00
$pK_{a2} = 3.98$	Log K_3	7.80	7.60	–	–	–	–	–
	Log β_n	26.30	25.90	19.00	21.70	23.40	24.00	21.50
7-NH_2-H_2L^1 [15]	Log K_1	10.10	10.00	10.35	11.55	12.00	12.45	12.03
$pK_{a1} = 9.00$	Log K_2	9.00	8.93	9.30	11.00	11.00	12.25	11.07
$pK_{a2} = 2.03$	Log K_3	7.62	7.70	–	–	–	–	–
	Log β_n	26.72	26.63	19.65	22.55	23.00	24.70	23.10
7-NO_2-H_2L^2	Log K_1	12.20	12.10	8.45	9.10	10.10	9.40	9.00
$pK_{a1} = 5.75$	Log K_2	9.00	9.00	6.80	7.80	7.90	7.70	8.00
$pK_{a2} = 3.28$	Log K_3	5.10	5.00	–	–	–	–	–
	Log β_n	26.30	26.10	15.25	16.90	18.00	18.10	17.00
7-I-H_2L^3 [10]	Log K_1	8.00	11.79	8.50	9.53	–	10.11	11.90
$pK_{a1} = 7.10$	Log K_2	6.88	9.41	7.31	8.21	–	8.71	7.30
$pK_{a2} = 2.72$	Log K_3	6.69	5.62	–	–	–	–	–
	Log β_n	21.57	26.82	15.89	17.74	–	18.82	19.20

[a] Values of the stability constants of some metal ions with different 7-X-HL. Ligands listed above were determined in the literature [10, 14, 15].

complex formation. A few conductometric titrations of metal chelates with EDTA in non-aqueous media [24], and conductometric determination of some metal ions using 8-hydroxyquinoline (oxine) as a reagent [25] have been found in the literature. In the present investigation the ligand ferron (7-iodo-5-sulpho-8-hydroxyquinoline, sodium salt), Na[7-I-HL], was used as a titrating agent for the determination of the molar ratio of ligand to metal. This investigation is a representative example for the other ligands and is done in ethanol-water (10% v/v) to overcome the problems of the chelate and free metal ion solubility.

Shape of the Titration Curves

The shape of the titration curves depends on the viscosity, dielectric constant, solvation, ion-pair association and proton transfer. The conductometric titrations of 10^{-3} mol of a divalent transition metal(II) nitrate (Mn, Fe, Co, Ni, Cu, and Zn) with 10^{-2} mol ligand Na[7-I-HL] *i.e.* $[HL^-]$, in ethanol-water (10% v/v) show a break in the conductance curve at the M : L ratio of 1 : 1. The reaction may be represented by Eq. (1).

$$M^{2+} + 2\,NO_3^- + HL^- \longrightarrow [H]^+ + 2\,NO_3^- + [ML(H_2O)_4]^\circ \tag{1}$$

Another break was observed at the M : L ratio 1 : 2. The reaction may be represented by Eq. (2).

$$[ML(H_2O)_4]^{\circ} + HL^{-} \longrightarrow [H]^{+} + [ML_2(H_2O)_2]^{2-} \qquad (2)$$

These complexes were found for all metal ions used (Fig. 1). The conductance values slightly increase after the equivalence point due to the

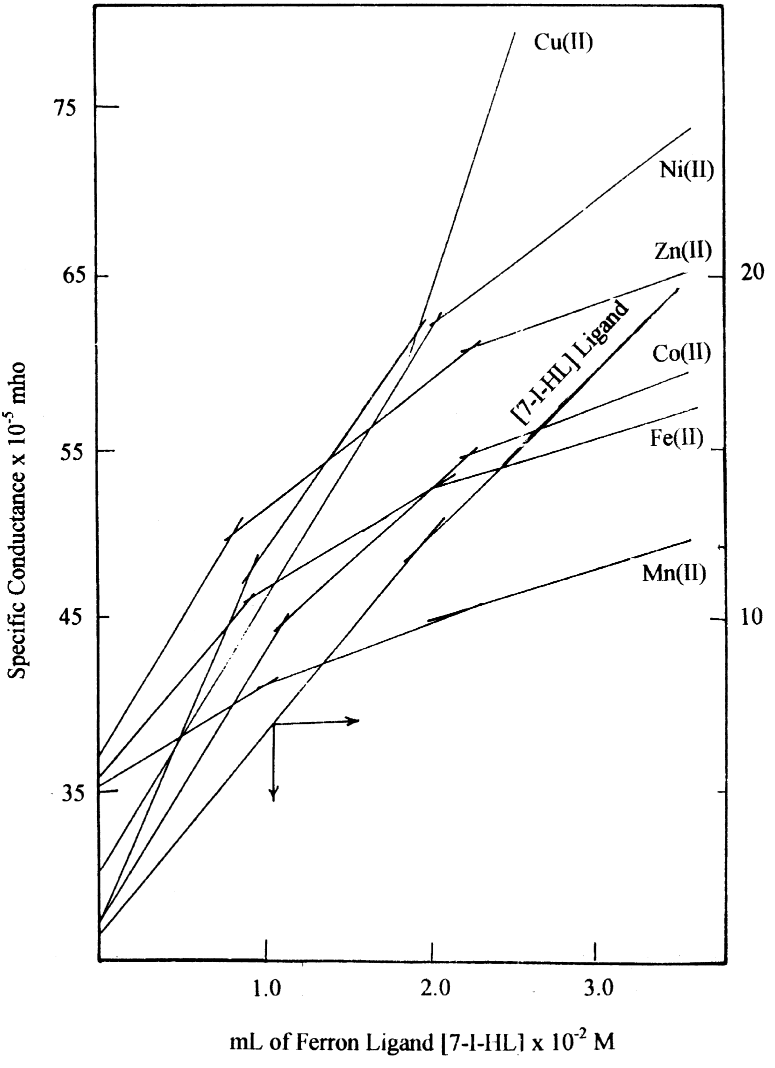


FIGURE 1 Conductometric titration curve of 10^{-3} M aqueous divalent transition metal ion solution with 10^{-2} M ferron ligand [7-I-HL] in ethanol-water (10% v/v).

partial dissociation of the ligand solution added. The reaction may be represented by Eq. (3).

$$HL^- \longrightarrow [H]^+ + L^{2-} \tag{3}$$

Furthermore, there is an important straight-line relationship between the specific conductance value of the 1 : 2 metal complexes $[ML_2(H_2O)_2]^{2-}$ and the ionic radii (r Å) of the metal ions as shown in Figure 2. From this relation one may deduce the specific conductance value of any 1 : 2 metal complex $[ML_2(H_2O)_2]^{2-}$ if its ionic radius is known.

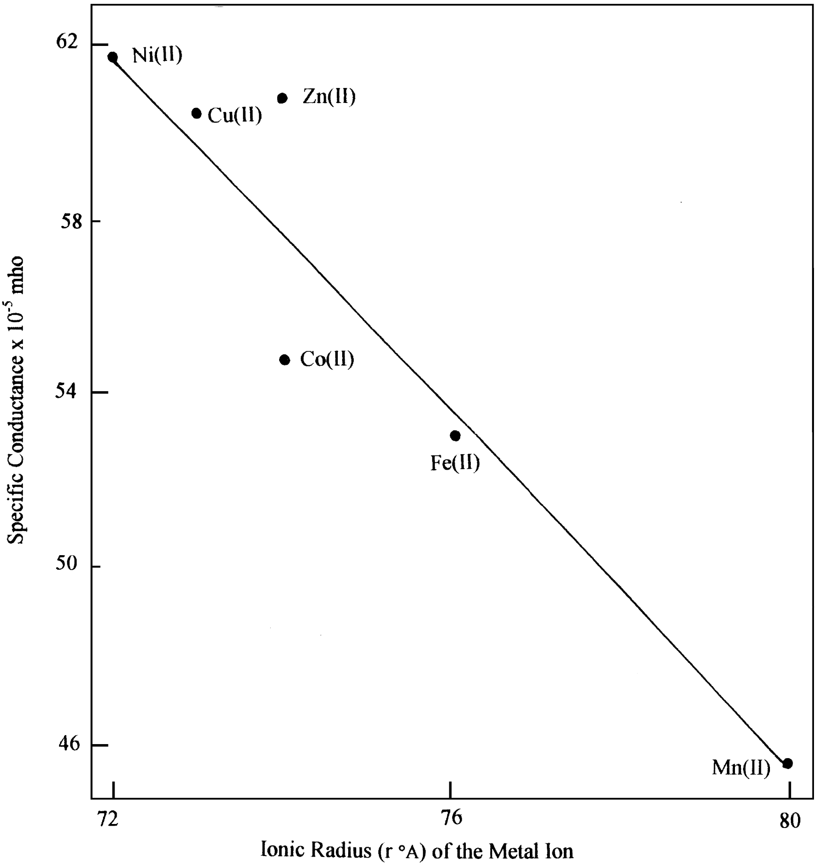


FIGURE 2 Plot of the specific conductance for 1 : 2 metal complexes $Na_2[ML_2(H_2O)_2]$ and the ionic radius (r Å) of the metal ions.

Thermal Analysis (TG and DTA)

Thermal analyses of $Na_2[ML_2(H_2O)_2] \cdot 4H_2O$ complexes where M(II) = Co and Ni, and L^3 = 7-iodo-5-sulpho-8-hydroxyquinoline, sodium salt, (ferron), represented here as examples while the data of the other complexes are available on request, confirmed the coordinated water molecules and lattice water very clearly. The TG of the Ni(II) complex revealed that the weight loss percentage equals 8.0% at the temperature range 120–160°C (calculated percentage loss is 7.5%) and represents four lattice water molecules. The weight loss percentage of 4.0% for the temperature range 160–250°C (calculated percentage loss is 3.8%) represents the two coordinated molecules. All water has disappeared at 260°C where the percentage loss is 12.0%. In case of the Co(II) complex the water molecules (coordinated and lattice) disappeared in the temperature range 50–170°C.

In the DTA curves all lost water molecules are represented as endothermic peaks as well as the evolution of iodine, while the loss of the sulphonic group is exothermic. All the decomposition steps are similar for the Co(II) and Ni(II) complexes. The thermal stability sequence for the complexes may be given as Ni(II) > Co(II), which is in accord with the covalence sequence for the M-O bond [26, 27]. The TG and DTA of the Co(II) and Ni(II) complexes are given in Table II, and represented in Figure 3. From the results of the TG investigation it is clear that the weight loss due to the decomposition of the complexes by heat occurs in following sequence: (i) hydrated water, (ii) coordinated water, (iii) iodine, (iv) sulphonic group, (v) C_5H_3 fragment, (vi) C_3H_3N fragment and the remaining material after decomposition is sodium carbonate and metal oxide.

X-ray Diffraction Data (XRD)

The X-ray diffraction data of the prepared solid powdered complexes were taken over the range $2\theta = 6-60°$ and show that all of the divalent metal complexes are crystalline solids with a similar structure *i.e.*, isostructural. The strongest lines in the X-ray patterns assume almost the same position for all of the M(II) complexes. Low symmetry, a large size of unit cells and various degrees of crystallinity characterize all crystalline complexes (Tab. III). The trivalent metal complexes (Fe and Cr) do not give any diffraction data when copper is used as target, this may be because they are isomorphous compounds. Also, the results show that the principal "*d*" lines

TABLE II Thermal analysis (TG and DTA) for $Na_2[CoL_2(H_2O)_2] \cdot 4H_2O$ represented by A, and $Na_2[NiL_2(H_2O)_2] \cdot 4H_2O$ represented by B

	TGA				*DTA*		
Step	*Temp. range °C*	*Total loss, %*	*Different loss, % Found (Calcd.)*	*Fragments lost*	*Temp. °C*	*Type of reaction*	*Fragments lost*
I	50 – 170 A	11.0	11.0 (11.3)	$-6H_2O$	185	Endo.	H_2O molecules
	50 – 250 B	12.0	12.0 (11.3)	$-6H_2O$	215	Endo.	H_2O molecules
II	170 – 455 A	36.0	25.0 (13.3)	– I	275	Endo.	Iodine atom
	250 – 380 B	33.0	21.0 (13.3)	– I	250	Endo.	Iodine atom
III	455 – 495 A	41.0	5.0 (13.3)	– I	420	Endo.	Iodine atom
	380 – 455 B	44.0	11.0 (13.3)	– I	345	Endo.	Iodine atom
IV	495 – 670 A	48.0	7.0 (8.4)	$1-SO_3$	635	Exo.	SO_3^- group
	455 – 475 B	58.0	14.0 (16.8)	$2-SO_3$	535	Exo.	SO_3^- groups
V	670 – 680 A	60.0	12.0 (8.4)	$1-SO_3$	650	Exo.	SO_3^- group
VI	680 – 715 A	73.0	13.0 (13.2)	$2-C_5H_3$			$-C_5H_3$ fragment
	475 – 520 B	74.0	16.0 (13.2)	$2-C_5H_3$			$-C_5H_3$ fragment
VII	715 – 980 A	81.0	8.0 (11.1)	$2-C_3H_3N$			$-C_3H_3N$ fragment
	520 – 980 B	81.0	7.0 (11.1)	$2-C_3H_3N$			$-C_3H_3N$ fragment
		Total loss = 81.0%	Total loss = 81.0 (79.0)%				Remaining Materials (A) $Na_2CO_3 + CoO$ (B) $Na_2CO_3 + NiO$ = 19.0 (18.8)%

L^3 = 7-iodo-5-sulpho-8-hydroxyquinoline, sodium salt (ferron, sodium salt); $(C_9H_5INO_4S \cdot Na)$, M. wt. = 373.

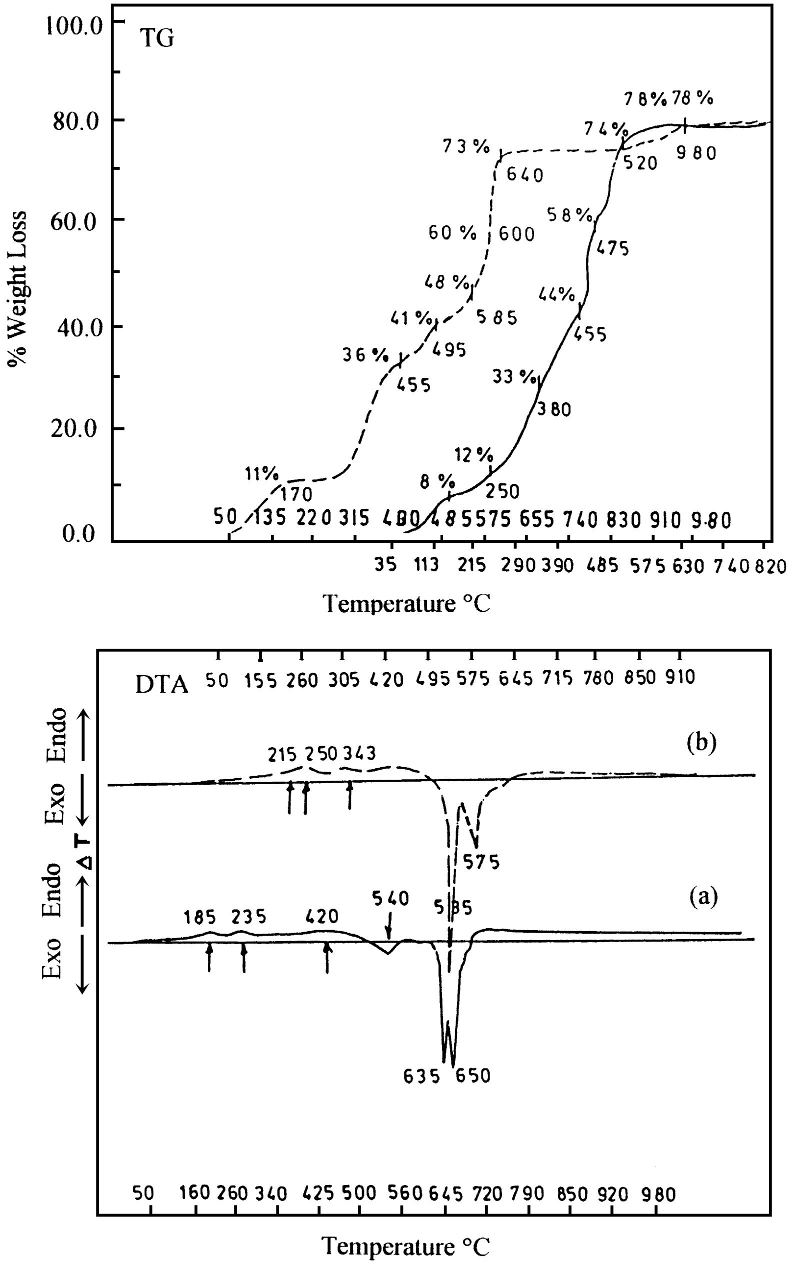


FIGURE 3 TG and DTA curves for (a) —— $Na_2[Co(7\text{-}I\text{-}HL)_2(H_2O)_2] \cdot 4H_2O$ complex and (b) ---- $Na_2[Ni(7\text{-}I\text{-}HL)_2(H_2O)_2] \cdot 4H_2O$ complex.

TABLE III Molecular weights, analytical data, melting points, magnetic moments, % yields and main lines in the X-ray diffraction powder patterns for the transition metal complexes*

Complex molecular weight		*Elemental analyses found (calculated)*				*M.p.*	μ_{eff}	%	*XRD*		
found (calculated)	*Color*	*C %*	*H %*	*N %*	*M %*	°*C*	*B.M.*	*yield*	*"d" [intensity]*		
$Na_3[CrL_3] \cdot 6H_2O$ 890 (897.4)	Violet	36.10 (36.10)	3.00 (3.00)	4.70 (4.68)	5.79 (5.79)	> 200 dec.	3.98	80	–	–	–
$Na_3[FeL_3] \cdot 6H_2O$ 896 (901.2)	Dark-Green	36.00 (35.95)	3.00 (3.00)	4.70 (4.66)	6.20 (6.19)	> 200 dec.	6.00	80	–	–	–
$Na_2[NiL_2(H_2O)_2] \cdot 4H_2O$ 650 (659.1)	Green	32.80 (32.79)	3.60 (3.64)	4.22 (4.25)	8.90 (8.91)	> 180 dec.	3.00	95	3.72 [1.0]	3.22 [0.5]	4.91 [0.5]
$Na_2[CuL_2(H_2O)_2] \cdot 4H_2O$ 654 (663.9)	Green	32.50 (32.55)	3.60 (3.62)	4.20 (4.22)	9.55 (9.57)	> 200 dec.	1.85	88	3.42 [1.0]	4.92 [0.7]	3.73 [0.5]
$Na_2[CoL_2(H_2O)_2] \cdot 4H_2O$ 650 (659.3)	Orange	32.80 (32.76)	3.60 (3.64)	4.30 (4.25)	8.98 (8.95)	> 195 dec.	4.80	82	3.21 [1.0]	3.32 [0.7]	3.11 [0.5]
$Na_2[FeL_2(H_2O)_2] \cdot 4H_2O$ 647 (656.2)	Light-Green	32.90 (32.92)	3.70 (3.66)	4.30 (4.27)	8.50 (8.50)	> 190 dec.	5.20	90	3.12 [1.0]	3.31 [0.7]	3.41 [0.6]
$Na_2[MnL_2(H_2O)_2] \cdot 4H_2O$ 645 (655.3)	Yellow	33.00 (32.96)	3.60 (3.66)	4.30 (4.27)	8.39 (8.38)	> 200 dec.	5.90	88	3.10 [1.0]	4.92 [0.9]	3.21 [0.7]
$Na_3[CrL^1_3] \cdot 6H_2O$ 933 (944.4)	Violet	34.30 (34.31)	3.20 (3.18)	8.90 (8.89)	5.77 (5.79)	> 210 dec.	3.85	82	–	–	–
$Na_3[FeL^1_3] \cdot 6H_2O$ 940 (948.2)	Dark-Green	34.20 (34.17)	3.18 (3.16)	8.90 (8.86)	5.90 (5.88)	> 210 dec.	5.95	83	–	–	–
$Na_2[NiL^1_2](H_2O)_2] \cdot 4H_2O$ 680 (689.1)	Green-Blue	31.30 (31.34)	3.80 (3.77)	8.10 (8.12)	8.55 (8.52)	> 200 dec.	2.99	90	3.65 [1.0]	3.20 [0.5]	4.85 [0.4]
$Na_2[CuL^1_2](H_2O)_2] \cdot 4H_2O$ 685 (693.9)	Dark-Green	31.30 (31.13)	3.80 (3.75)	8.10 (8.07)	9.10 (9.15)	> 210 dec.	1.80	85	3.38 [1.0]	4.88 [0.8]	3.68 [0.5]
$Na_2[CoL^1_2(H_2O)_2] \cdot 4H_2O$ 680 (689.3)	Red-Orange	31.30 (31.34)	3.80 (3.77)	8.12 (8.12)	8.52 (8.56)	> 195 dec.	4.75	80	3.18 [1.0]	3.28 [0.7]	3.10 [0.6]

$Na_2[FeL^1_2(H_2O)_2] \cdot 4H_2O$ 678 (686.2)	Green	31.50 (31.48)	3.80 (3.79)	8.20 (8.16)	8.15 (8.13)	$>$ 190 dec.	5.15	89	3.09 [1.0]	3.28 [0.8]	3.38 [0.6]
$Na_2[MnL^1_2(H_2O)_2] \cdot 4H_2O$ 677 (685.3)	Yellow Orange	31.50 (31.52)	3.80 (3.79)	8.20 (8.17)	8.00 (8.03)	$>$ 200 dec.	5.85	80	3.08 [1.0]	4.88 [0.9]	3.17 [0.6]
$Na_3[CrL^2_3] \cdot 6H_2O$ 1023 (1033.4)	Dark-Violet	31.40 (31.35)	2.34 (2.32)	8.11 (8.13)	5.00 (5.03)	$>$ 210 dec.	3.90	80	–	–	–
$Na_3[FeL^2_3] \cdot 6H_2O$ 1030 (1037.2)	Dark-Green	31.20 (31.24)	2.32 (3.31)	8.12 (8.10)	5.40 (5.38)	$>$ 200 dec.	5.90	85	–	–	–
$Na_2[NiL^2_2(H_2O)_2] \cdot 4H_2O$ 730 (739.1)	Green-Blue	28.80 (28.83)	2.69 (2.67)	7.50 (7.47)	7.88 (7.84)	$>$ 190 dec.	3.03	92	3.73 [1.0]	3.33 [0.4]	4.93 [0.4]
$Na_2[CuL^2_2(H_2O)_2] \cdot 4H_2O$ 690 (699.9)	Green	30.90 (30.86)	2.90 (2.86)	8.02 (8.00)	9.10 (9.07)	$>$ 195 dec.	1.82	90	3.34 [1.0]	5.00 [0.6]	3.62 [0.5]
$Na_2[CoL^2_2(H_2O)_2] \cdot 4H_2O$ 740 (749.3)	Dark-Orange	28.90 (28.82)	2.69 (2.67)	7.47 (7.47)	7.90 (7.87)	$>$ 190 dec.	4.80	87	3.24 [1.0]	3.32 [0.5]	3.13 [0.4]
$Na_2[FeL^2_2(H_2O)_2] \cdot 4H_2O$ 738 (746.2)	Dark-Green	29.00 (28.95)	2.70 (2.68)	7.50 (7.50)	7.50 (7.48)	$>$ 190 dec.	5.10	93	3.15 [1.0]	7.62 [0.7]	3.44 [0.6]
$Na_2[MnL^2_2(H_2O)_2] \cdot 4H_2O$ 737 (745.3)	Orange	29.00 (28.98)	2.70 (2.68)	7.52 (7.51)	7.40 (7.38)	$>$ 195 dec.	5.80	88	3.13 [1.0]	4.91 [0.9]	3.32 [0.8]

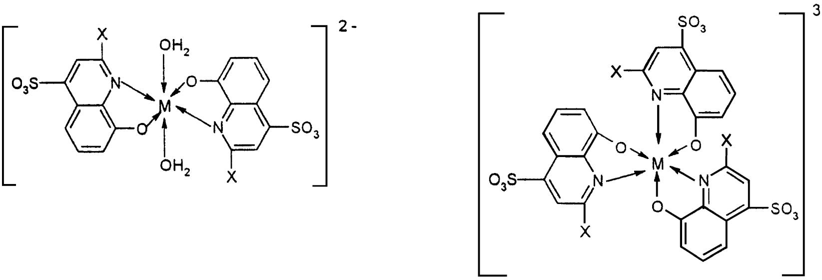
L = 5-sulpho-8-hydroxyquinoline (Sulphoxine); ($C_9H_7NO_4S$), M. wt. = 224.2.
L^1 = 7-amino-5-sulpho-8-hydroxyquinoline (7-amino-sulphoxine); ($C_9H_8N_2O_4S$), M. wt. = 239.2.
L^2 = 7-nitro-5-sulpho-8-hydroxyquinoline (7-nitro-sulphoxine); ($C_9H_6N_2O_6S$), M. wt. = 270.2.
* Results of L^3 = 7-iodo-5-sulpho-8-hydroxyquinoline, sodium salt (ferron, sodium salt); ($C_9H_5INO_4S \cdot Na$), M. wt. = 373 are reported in Ref. [7].

decrease in the reverse order of ionic radii of metal ions (r Å) and follow the Irving-Williams order [23].

Magnetic Susceptibility Measurements

The magnetic moments (μ_{eff}) of the prepared complexes calculated from the corrected magnetic susceptibilities are given in Table III. All of the iron(III) complexes show a high-spin d^5 octahedral configuration having $^6A_1$ ($t_{2g}^3\,e_g^2$) as the ground state as confirmed by their magnetic moment values which were found in the range 5.90 – 6.00 B.M. Some complexes show lower magnetic moments such as the Mn(II) complex (5.80 – 5.90 B.M.), this may be due to the effect of the ligands which are considered to be strong ligands with respect to the spectrochemical series. The iron(II) complex shows a value of, 5.10 – 5.20 B.M., which is expected for an octahedral high-spin d^6 configuration. The magnetic moment values of copper(II) complexes were found in the range of 1.80 – 1.85 B.M. indicating a spin-only value with octahedral geometry [28]. This was further confirmed by the electronic spectra of the ferron complexes [7], in which a band was observed in the range of 14,000 cm^{-1} probably due to the $^2E_g \rightarrow {}^2T_{2g}$ transition. There are two bands which can be assigned to the $^2B_{1g} \rightarrow {}^2E_g$ and $^2B_{1g} \rightarrow {}^2B_{2g}$ transitions within the energy level diagram of Cu^{2+} ion by considering highly distorted octahedral arrangements through tetragonal elongation leading finally to a situation similar to square planar due to the strong splitting of the Jahn-Teller unstable octahedral group state term $^2B_{1g}$ and consequently overlapping with splitting ^2E_g to a spectral pattern that is characteristic of square planar coordination.

The magnetic moments of all of the nickel complexes found in the range 2.99 – 3.03 B.M., which indicates octahedral geometry of the complexes. This geometry was further confirmed by the electronic spectra of the nickel ferron complex [7]. Three bands around 11,000, 18,000, and 27,000 cm^{-1} were probably due to three spin-allowed transitions, $^3A_{2g} \rightarrow {}^3T_{2g}$ (F), $^3A_{2g} \rightarrow {}^3T_{1g}$ (F), and $^3A_{2g} \rightarrow {}^3T_{1g}$ (P), respectively, in an octahedral environment [28]. All of the cobalt complexes are proposed to have octahedral geometry as confirmed by their magnetic moment values, which were found in the range 4.75 – 4.80 B.M. Three bands observed in the electronic spectra of the cobalt ferron complex [7] around 8,000, 15,000 and 18,000 cm^{-1} may be assigned to the $^4T_{1g} \rightarrow {}^4T_{2g}$(F), $^4T_{1g} \rightarrow {}^4A_{2g}$ (F) and $^4T_{1g} \rightarrow {}^4T_{1g}$ (P) transitions respectively. The suggested formulas for these complexes are given in Table III, with all of the complexes described as octahedral. The proposed structures are:



M(II) = Mn, Fe, Co, Ni and Cu

M(III) = Cr and Fe

FIGURE 4 The proposed structures of the $Na_2[ML_2(H_2O)_2] \cdot 4H_2O$ and $Na_3[ML_3] \cdot 6H_2O$ complexes, where L = Na[7-X-HL].

Microbial Activity

All the prepared divalent transition metal complexes and the 7-substituted-5-sulpho-8-hydroxyquinone ligands [M : 7-X-HL], (X = H, NH_2, NO_2 and I) were screened for their antimicrobial activity on both *Sarcina lutea* (gram-positive) and *Escherichia coli* (gram-negative) bacteria at 37°C and on two common fungi, *Aspergillus niger* and *Candida albicans* at 30°C by the serial dilution method [29]. A comparative study of the minimum inhibitory concentration values indicated that the ligands, Na[7-X-HL], and their corresponding divalent transition metal complexes are active against the bacteria and fungi used. The proper temperature, pH and the necessary nutrients and growth media free from other microorganisms have been provided for the preparation of cultures of pathogenic bacteria and fungi, using aseptic technique [30]. The culture media used for the slant and broth were sterilized by a moist heat sterilization method as reported [31]. The incubating period for bacteria was 24 hours at 37°C, while for fungi was 48 hours at 30°C. From closed and comparative study (Tab. IV), it is concluded that the antimicrobial activity of all ligands are enhanced when they are chelated with divalent transition metal ions. It has been found [32] that 8-hydroxyquinoline (HL*) is a strong inhibitor of the copper(II) containing cresolase enzyme present in a wide variety of fungi. It has been indicated [33], that the 1 : 2 [Metal-HL*] chelate penetrates the cell and dissociates into a 1 : 1 half-chelate. The 1 : 1 half-chelate would then become a toxic entity by combining and blocking the metals on enzymes. The charged complexes $Na_2[ML_2(H_2O)_2] \cdot 4H_2O$ may be active moieties at the site of action, reinforcing the total activity. This mechanism is also supported by other workers [34]. The growth inhibition capacity of

TABLE IV Antimicrobial activity of the 7-substituted-5-sulpho-8-hydroxyquinoline ligands (7-X-HL) and their divalent transition metal complexes $Na_2[ML_2(H_2O)_2] \cdot 4H_2O^a$

Ligand/Complex	*Bacteria*		*Fungi*	
albicans	*S. lutea*	*E. coli*	*A. niger*	*C.*
L	280.2	281.1	288.2	208.4
L^1	285.5	281.8	292.5	217.9
L^2	200.0	200.3	201.8	191.0
L^3	210.3	205.6	210.0	198.9
$Na_2[CuL_2(H_2O)_2] \cdot 4H_2O$	90.0	98.2	65.5	88.1
$Na_2[NiL_2(H_2O)_2] \cdot 4H_2O$	80.2	83.4	50.2	69.0
$Na_2[CoL_2(H_2O)_2] \cdot 4H_2O$	63.6	50.0	37.3	51.7
$Na_2[FeL_2(H_2O)_2] \cdot 4H_2O$	95.3	94.2	65.3	88.0
$Na_2[MnL_2(H_2O)_2] \cdot 4H_2O$	98.6	102.0	87.1	88.5
$Na_2[CuL^1_2(H_2O)_2] \cdot 4H_2O$	95.0	103.0	70.2	92.1
$Na_2[NiL^1_2(H_2O)_2] \cdot 4H_2O$	85.8	88.6	54.2	74.2
$Na_2[CoL^1_2(H_2O)_2] \cdot 4H_2O$	67.3	56.0	43.8	57.7
$Na_2[FeL^1_2(H_2O)_2] \cdot 4H_2O$	99.3	99.0	81.3	93.0
$Na_2[MnL^1_2(H_2O)_2] \cdot 4H_2O$	102.0	108.1	93.0	93.2
$Na_2[CuL^2_2(H_2O)_2] \cdot 4H_2O$	20.1	22.0	15.4	17.8
$Na_2[NiL^2_2(H_2O)_2] \cdot 4H_2O$	16.0	16.3	9.1	11.0
$Na_2[CoL^2_2(H_2O)_2] \cdot 4H_2O$	10.7	10.0	7.2	7.6
$Na_2[FeL^2_2(H_2O)_2] \cdot 4H_2O$	20.5	28.1	19.3	18.0
$Na_2[MnL^2_2(H_2O)_2] \cdot 4H_2O$	20.6	30.0	25.0	18.4
$Na_2[CuL^3_2(H_2O)_2] \cdot 4H_2O$	30.3	38.0	25.6	28.0
$Na_2[NiL^3_2(H_2O)_2] \cdot 4H_2O$	26.1	27.1	15.0	19.0
$Na_2[CoL^3_2(H_2O)_2] \cdot 4H_2O$	19.6	15.0	12.2	12.2
$Na_2[FeL^3_2(H_2O)_2] \cdot 4H_2O$	30.9	38.8	28.4	28.4
$Na_2[MnL^3_2(H_2O)_2] \cdot 4H_2O$	32.5	42.2	37.2	28.6

L = 5-sulpho-8-hydroxyquinoline (Sulphoxine).
L^1 = 7-amino-5-sulpho-8-hydroxyquinoline (7-amino-sulphoxine).
L^2 = 7-nitro-5-sulpho-8-hydroxyquinoline (7-nitro-sulphoxine).
L^3 = 7-iodo-5-sulpho-8-hydroxyquinoline (ferron).
[a] Values are minimum inhibitory concentrations in μmol/L.

7-substituted-5-sulpho-8-hydroxyquinone complexes follows the order: Co(II) > Ni(II) > Cu(II) > Fe(II) > Mn(II), which is almost the same order as the overall stability constants of these complexes found in this study. The growth inhibition capacity of the ligands Na[7-X-HL] follows the order: $-X = NO_2 > I > H > NH_2$. This is the order of the values of the Hammet substitution constant (σ_{meta}) with respect to the sulphonic group in the 5-position of the ligands, where (σ_{meta}) for the above ligands is +0.71, +0.35, 0.00, −0.16 respectively [35]. The highest activity was observed for *Aspergillus niger* fungi and this may be attributed to the polar character of the NO_2 and I groups, {electron-withdrawing substitutents}. These groups are helpful in its easy distribution in the affected colonies whereby giving ample opportunity for the compounds to react with the microorganisms. On the other hand the $-X=H$ and NH_2 derivatives were found to be less active against all microorganisms and this may be due to the electron-repelling character of these groups (Tab. IV). In view of the above, the mechanism which explains the comparable activity of the charged divalent transition metal complexes, $Na_2[ML_2(H_2O)_2]\cdot 4H_2O$, to that of free ligands, Na[7-X-HL], may be due to the dissociation of complexes at the site of action as below:

$$Na_2[ML_2(H_2O)_2] \xrightarrow{K_1} Na[ML(H_2O)_4] + Na[HL] \xrightarrow{K_2} [M(H_2O)_6]^{2+} + Na[HL]$$

The anionic complex 1 : 1, [M : L], thus formed may also be active at the site of action, which increases the activity of the 1 : 2, [M : L], and reinforces the total activity. This mechanism is supported by other workers [36].

From the present work, it is clear that the 7-substituted-5-sulpho-8-hydroxy-quinoline ligands, Na[7-X-HL], are very active against *Aspergillus niger* and *Candida albicans* fungi, therefore, these compounds can be recommended for chemotherapy of candidiaces and other fungal skin diseases.

CONCLUSIONS

From the conductometric titrations, thermal analyses (DTA and TG), X-ray diffraction (XRD), magnetic moments (μ_{eff}), elemental analyses, molecular weight determinations, IR and reflectance spectra one may conclude that the ligand coordinates to the metal through the quinoline nitrogen and phenolic oxygen atoms to form intramolecular five-member chelating rings and the remaining coordination sites are occupied by water molecules for the divalent metal ions or with another ligand for the trivalent metal ions.

From the microbial studies it is clear that the growth inhibition capacity of the 7-substituted-5-sulpho-8-hydroxyquinoline ligands, Na[7-X-HL] and the 7-substituted-5-sulpho-8-hydroxyquinone complexes follows the order: Co(II) > Ni(II) > Cu(II) > Fe(II) > Mn(II), which is almost the same order as the overall stability constants of these complexes. They are very active against *Aspergillus niger* and *Candida albicans* fungi, therefore, these complexes can be recommended to be used for the chemotherapy of candidiaces and other fungal skin diseases.

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