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Research Article

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Synthesis and description of transition metal complexes and antimicrobial studies

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ABSTRACT

Mixed ligand complexes of transition metal with 8-quinolinols and 5-Alkoxumethyl-8-quinolinol have been prepared. Structural, spectroscopic and thermal properties have been studied on the basis of infrared spectra, Mass spectra, NMR spectra, electronic spectra, and elemental analyses. Also their antibacterial activities against Gram – ve (Escherichia coli and Ps. Aeruginosa Bacillus subtilis) and Gram +ve (Becillus megaterium and S.taphylococcus aureus) and antifungal activities again Aspergillus niger and Trichothesium Sp. have been carried out. All the tested complexes show higher antibacterial activity as compared to free ligand.

Keywords: Transition metal Heterochelates, Oxine, spectroscopic and antimicrobial activity.

INTRODUCTION

8-Quinolinol (8Q) or its derivatives have been introduced as chelating groups. [1-3].The chelating properties of the compounds of the 8Q series are related to its biological activity [4]. 8-hydroxyquinoline (8Q) and its metalloquinolates have attracted great interest because their high thermal stability and good electroluminescence properties make them important prototypical electron transport and emitting materials for OLED devices [5-7].8-Hydroxyquinoline (8-quinolinol, oxine, 8Q) might be thought to function as a phenol, but of the 7 isomeric hydroxyquinolines only oxine exhibits significant antimicrobial activity, and is the only one to have the capacity to chelate metals. If the hydroxyl group is blocked so that the compound is unable to chelate, as in the methyl ether, the antimicrobial activity is destroyed. The relationship between chelation and activity of oxine has been investigated [8-10]. Oxine itself is inactive, and exerts activity by virtue of the metal chelates produced in its reaction with metal ions in the medium. Used by itself or as the sulfate (Chinosol) or benzoate in antiseptics, the effect is bacteriostatic and fungistatic rather than microbiocidal. Inhibitory action is more pronounced upon gram-positive than gram-negative bacteria; the growth-preventing concentrations for staphylococci being 10 ppm; for streptococci 20 ppm; for *Salmonella typhosa* and for *E. coli* 100 ppm. [11,12]. Certain halogen derivatives of 8-hydroxyquinoline have a record of therapeutic efficacy in the treatment of cutaneous fungus infections and also of amebic dysentery. Among these Kharadi et al. and others Previously synthesized, are 5-chloro-7-iodo-8-quinolinol (iodochlor-hydroxyquinoline,Vioform),5,7-diiodo-8-hydroxyquinoline(diiodohydroxyquinoline),andsodium7-iodo-8-hydroxy quinoline-5-sulfonate[13-19].Patel et al also reported the first series of complexes of transition metal with8-Quinolinol(8Q)and5-Mthoxymethyl-8-quinolinol.[20]

Copper 8-quinolinolate (copper oxinate), the copper compound of 8-hydroxyquinoline, is employed as an industrial preservative for a variety of purposes, including the protection of wood and textiles against fungus-caused rotting, and interior paints for food plants. It has 25 times greater antifungal activity than oxine [21-25].

In present work, we describes synthetic, characteristic, spectroscopic features of new mixed ligand complexes using different transition metal with 8-Quinolinol(8Q) and 5- Ethoxymethyl-8-quinolinol and also describe antimicrobial activities of newly synthesized compounds (Fig. 1).

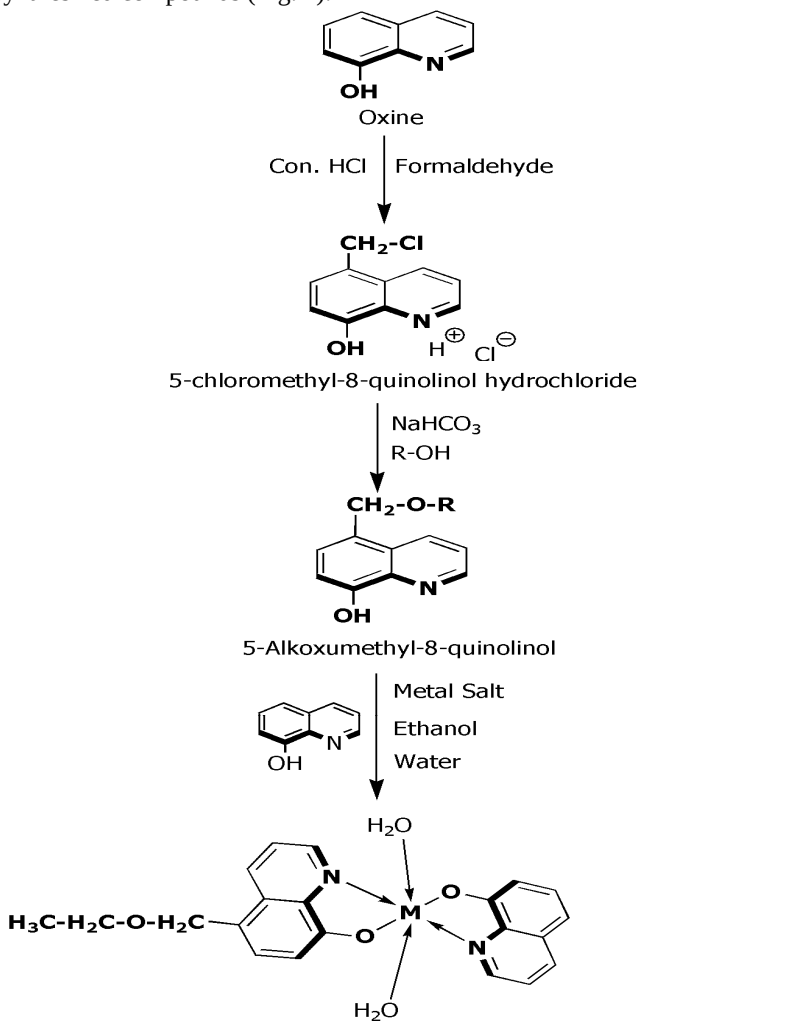

Figure 1. General synthesis of complexes.

EXPERIMENTAL SECTION

Reagent and solvents

All the chemicals used were of analytical grade. 8-hydrxyquinoline, Hydrochloric acid, Formaldehyde, Sodium bicarbonate, Ethyl alcohol and different metal salt was purchased from the E. Merck (India) Limited, Mumbai. ia). Luria broth and agar- agar were purchased from SRL, India. Acetic acid and EDTA were purchased from Sigma Chemical Co., India. The organic solvents were purified by recommended method [26].

Physical measurements

The metal content of the complexes were determined by the EDTA titration technique [27] after treating them with mixture of $HClO_4$, H_2SO_4 and HNO_3 (1:1.5:2.5). Elemental analysis was carried out using Perkin Elmer, USA 2400-

II CHN analyzer. The magnetic moments were obtained by the Gouy's method using mercury tetrathiocyanatocobaltate (II) as a calibrant (χ_g=16.44×10^{-6} c.g.s. units at 20 ^oC). Diamagnetic corrections were made using Pascal's constant [28]. A simultaneous TG/DTG had been obtained by a model 5000/2960 SDT, TA Instruments, USA at heating rate of 10 ^oC min^{-1} under N_2 atmosphere. The IR spectra were recorded on a FT-IR Nicolet 400D Spectrophotometer using KBr pellets. NMR spectra were recorded on a model Bruker Avance (400MHz).

Preparation of ligands

Synthesis of 5-(Ethoxymethyl-8-Quinolinol) (EMQ).

To a suspension of 2.3 gm. (0.01 mole) of 5-chloromethyl-8-Quinolinol (CMQ), ethanol (3 times.) and 0.84 gm. (0.01 mole) of sodium bicarbonate ($NaHCO_3$) added. The mixture was warmed on the steam bath with occasional shaking until most of the alcohol had been evaporated. The pale yellow solid was dissolved in water and made basic with 5 %ammonium hydroxide. The white solid was collected on a filter and dried to give 2.12 gm. Yield: 94%, M.p. 80 °C. FT-IR (KBr, cm-1): υ(-OH,) 3311, υ(-CN) 1198, 1H NMR (DMSO-d6 400 MHz): δ 4,75 (CH_2- protons), δ 1,05 (CH_3- protons), δ 7.1 to 7.64 (9H, m, aromatic protons), δ 8.6 (1H, s, OH- protons), Elemental analysis found (%):C, 70.82; H, 6.28, N, 6.80; calculated for $C_{12}H_{13}NO_2$ (203.00): C, 70.93; H, 6.40; N, 6.89 (Fig. 2).

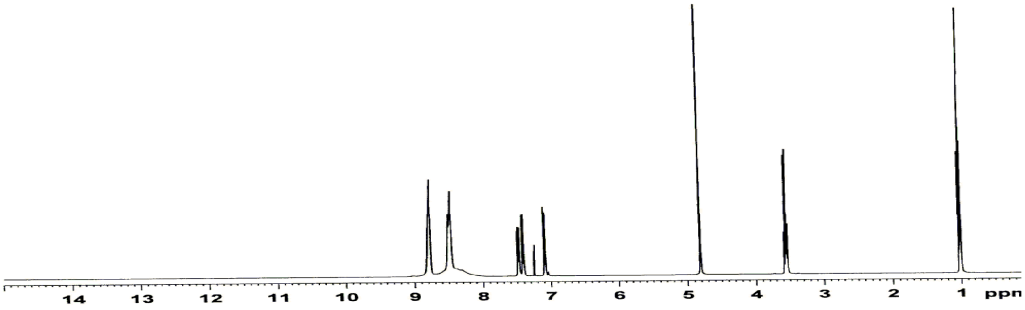

Fig:2 Preparation of Metal Complexes

(I) Formation of Cu^{2+} Complex

A water solution of Cu $(NO_3)_2.3H_2O$ was added to dimethyl formamide solution of ligand followed by addition of 8-HQ in ethanol; the pH was adjusted to 4.5-6.0 with dilute NaOH solution. The resulting solution was refluxed for 7 h and then heated over a steam bath to evaporate up to half of the volume. The reaction mixture was kept overnight at room temperature. A dark green colored crystalline product was obtained. The yield of a purified complex was 75%. The obtained product was washed with ether and dried over vacuum desiccator. Analytical and physical data are shown in Table 1

(II) Formation of Ni^{2+} Complex

Ni^{+2} complex was synthesized by same method used for Cu^{+2} complex. A light blue colored crystalline product was obtained. The yield of a purified complex was 70%.

(III) Formation of Co^{2+} Complex

Co^{+2} complex was synthesized by same method used for Cu^{+2} complex. A light brown colored crystalline product was obtained. The yield of a purified complex was 68%.

(IV) Formation of Mn^{2+} Complex

Mn^{+2} complex was synthesized by same method used for Cu^{+2} complex. A light pink colored crystalline product was obtained. The yield of complex was 65%.

(V) Formation of Zn^{2+} Complex

Zn^{+2} complex was synthesized by same method used for Cu^{+2} complex. A pale yellow colored powder product was obtained. The obtained product was washed with ether and dried over vacuum desiccators. The yield was 72%.

Table- 1 Analytical and physical parameters of ligand and complexes

Compounds	Molecular formula	M. wt gm/mole	Yield %	% Metal analysis		Elemental analysis					
				Cal.	Found	% C		% H		% N	
						Cal.	Found	Cal.	Found	Cal.	Found
HL-2	$C_{12}H_{13}NO_2$	203	94	---	---	70.93	70.82	6.40	6.28	6.89	6.80
(HL-2) Cu^{+2}	$C_{21}H_{22}N_2O_5Cu^{+2}$	445.96	75	14.25	13.85	56.56	56.12	4.97	4.83	6.28	6.14
(HL-2)Mn^{+2}	$C_{21}H_{22}N_2O_5Mn^{+2}$	437.35	65	12.56	12.32	57.67	57.51	5.07	5.01	6.41	6.35
(HL-2) Co^{+2}	$C_{21}H_{22}N_2O_5Co^{+2}$	441.34	68	13.35	12.92	57.15	57.10	5.02	4.92	6.35	6.21
(HL-2) Zn^{+2}	$C_{21}H_{22}N_2O_5Zn^{+2}$	447.82	72	14.61	14.43	56.32	56.19	4.95	4.79	6.26	6.19
(HL-2) Ni^{+2}	$C_{21}H_{22}N_2O_5Ni^{+2}$	441.10	70	13.31	12.98	57.18	56.99	5.03	4.84	6.35	6.23

Antimicrobial studies

Antifungal activity

The antifungal activity of the standard fungicide (Flucanazone), ligand and complexes were tested for their effect on the growth of microbial cultures and studied for their interaction with *Aspergillus niger and Trichothesium Sp*. using Czapek's agarmedium having the composition, glucose 20 g, starch 20 g, agar-agar 20 g and distilled water 1000 mL. To this medium was added requisite amount of the compounds after being dissolved in methanol so as to get the certain concentrations (50, 100 and 200 ppm). The medium then was poured into petri plates and the spores of fungi were placed on the medium with the help of inoculum's needle. These petri plates were wrapped in polythene bags containing a few drops of alcohol and were placed in an incubator at 30 °C. The controls were also run and three replicates were used in each case. The linear growth of the fungus was recorded by measuring the diameter of the fungal colony after 96 h and the percentage inhibition was calculated by the equation:

% Inhibition D (C – T/C) 100

Where C and T are the diameters of the fungal colony in the control and the test plates, respectively [29].

Antibacterial activity

Antibacterial activity was tested against Gram –ve (*Escherichia coli* and *Ps. Aeruginosa Bacillus subtilis)* and Gram +ve(*Becillus megaterium* and *S.taphylococcus aureus*) using the paper disc plate method [30,31]. Each of the compounds was dissolved in methanol and solutions of the concentrations (500 and 1000 ppm) were prepared separately. Paper discs of Whatman filter paper (No. 42) of uniform diameter (2 cm) were cut and sterilized in an autoclave. The paper discs soaked in the desired concentration of the complex solutions were placed aseptically in the petri dishes containing nutrient agar media (agar 20 g C beef extract 3 g C peptone 5 g) seeded with E. coli and B. subtilis bacteria separately. The Petri dishes were incubated at 37 °C and the inhibition zones were recorded after 24 h of incubation. The antibacterial activity of common standard antibiotic Streptomycin was also recorded using the same procedure as above at the same concentrations and solvent. The %Activity Index for the complex was calculated by the formula as under:

% Activity Index = D Zone of inhibition by test compound x 100 /Zone of inhibition by standard

RESULTS AND DISCUSSION

The toxic effect of all the complexes on fungi is shown in Table 3. The results give the following conclusions. All the complexes are toxic more or less to fungi. The substitution of phenyl rings does not have more effect on the fungicidal activity of complexes. In each series the Cu-complexes have much toxicity. This is expected because the copper salts are mostly used as fungicides. Most of the complexes inhibit the growth of the above organisms which cause decease in many plants. Cu^{+2} metal complexes are more toxic than others and the order for is $Cu^{+2} > Zn^{+2} > Co^{+2} > Ni^{+2} > Mn^{+2}$.

IR spectra

The important infrared spectral bands and their assignments for the synthesized ligands and complexes were recorded as KBr disks and are presented in Table 2. The IR data of the free ligands and its metal complexes were carried out within the IR range 4000–400 cm^{-1}.

In the 8-hydroxyquinoline complexes of divalent metals, the υ (C-O), appeared at 1120 cm^{-1} region and the position of the band slightly varies with the metal. The υ (C-O), observed in the free oxine molecule at 1090 cm^{-1} , shifted to higher frequencies in all the mixed ligand complexes giving a strong absorption band at 1110 cm^{-1} . This clearly indicates the coordination of 8-hydroxyquinoline in these complexes. In the investigated heterochelates, the band observed in the region 3400-3500, 1295-1300, 860-870 and 715-717 cm^{-1} are attributed to –OH stretching, bending, rocking and wagging vibrations, respectively due to the presence of water molecules. The evidence of complexes formation clear by appearance of new bands at 418–432 and 507–516 cm^{-1}, which are assigned to *ν*(M–N) and *ν*(M–O), respectively(Fig. 3) [32,33].

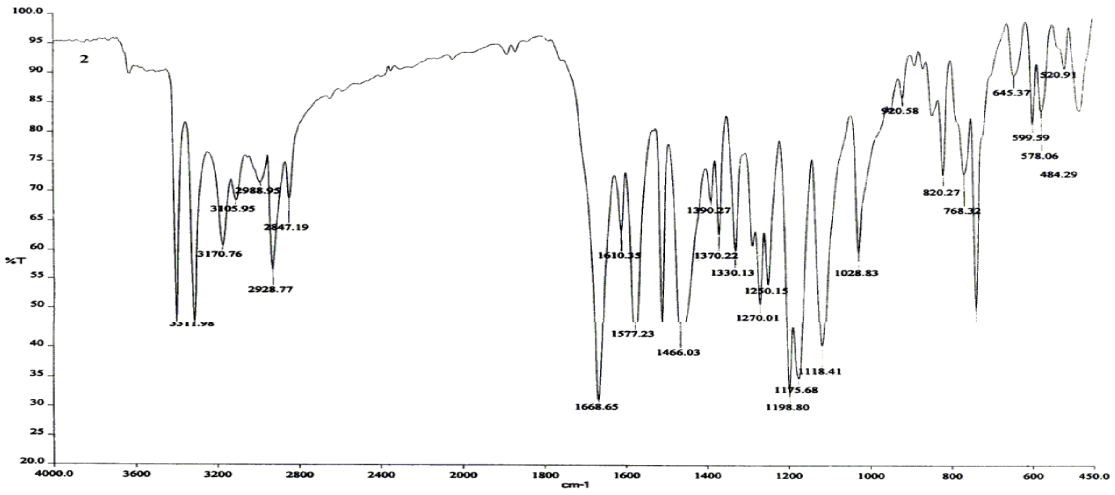

Figure 3. IR spectra of Cu (II) complex.

Reflectance spectra and magnetic measurements

In order to shed some light on the geometrical structure of the complexes, the reflectance spectra of the complexes were recorded in the solid phase at room temperature. The reflectance spectra of the Mn(II) complex shows absorption bands at ~14600, ~19720 and ~24400 cm^{-1} assignable to $^6A_{1g} \rightarrow {}^4T_{1g}$, $^6A_{1g} \rightarrow {}^4T_{2g}$ and $^6A_{1g} \rightarrow {}^4A_{1g}$, ^4E_g transitions, respectively, in an octahedral environment around the Mn(II) ion. The magnetic moment value of the Mn(II) complex is 6.02 B.M. due to a high-spin d^5-system with an octahedral geometry[34]. For the Co(II) complex, the reflectance spectra exhibits the bands of medium intensity at ~9300, ~18050 and ~18900 cm^{-1}, which may reasonably be assigned to $^4T_{1g}(F) \rightarrow {}^4T_{2g}(F)$, $^4T_{1g}(F) \rightarrow {}^4A_{2g}(F)$ and $^4T_{1g}(F) \rightarrow {}^4T_{1g}(P)$ transitions, respectively, of an octahedral geometry around the metal ion[26] and the magnetic moment value is observed to be of 4.06 B.M. The electronic spectra of the Ni(II) complex exhibits absorption bands at ~10200, ~17650 and ~23800 cm^{-1} assignable to $^3A_{2g}(F) \rightarrow {}^3T_{2g}(F)$, $^3A_{2g}(F) \rightarrow {}^3T_{1g}(F)$ and $^3A_{2g}(F) \rightarrow {}^3T_{1g}(P)$ transitions respectively, in an octahedral geometry[35]. The value of the magnetic moment (2.84 B.M.) may be taken as additional evidence for their octahedral structure [35–39]. The Cu(II) complex display a broad band at ~15440 cm^{-1} due to the $^2E_g \rightarrow {}^2T_{2g}$ transition and the magnetic moment value is 1.78 B.M., which is close to spin-only value (1.73 B.M.) expected for an unpaired electron, which offers the possibility of an octahedral geometry [40].

This improvement in activity of complexes is also be rationalized on the basis of their structure activity relationship:

A feasible manner for raise in biocidal activity may be explained on the basis of chelation theory or/and may be due to light of Overtone's concept. Chelation reduces the polarity of the metal ion considerably, mainly because of the partial sharing of its positive charge with donor groups and possible π-electron delocalization on the whole chelate ring. Polysaccharides and lipids are some important constituent of cell wall and membranes, Chelation can considerably reduce the polarity of the metal ion, which in turn increases the lipophilic character of the chelates. Thus, the interaction between metal ion and the lipid is favored. This may lead to the breakdown of the permeability barrier of the cell, resulting in interference with the normal cell processes. Presence of lypophilic and polar substituents are expected to enhance biocidal activity. Heterocyclic ligand with multifunctionality have greater chance of interaction either with nucleoside bases (even after complexation with metal ion) or with biologically essential metal ions present in the biosystem can be promising candidates as bactericides since they always look to

enact especially with some enzymatic functional groups, to achieve higher coordination number. Thus, the antibacterial property of metal complexes can not be ascribed to chelation alone but it is an intricate blend of all the above contributions.

CONCLUSION

The complexes were obtained as colored powdered materials and were characterized using IR spectra, electronic spectra, and magnetic measurements. The compounds were insoluble in ethanol, methanol, DMF, acetone, ether, hexane, chloroform, THF, and dichloromethane, and soluble in DMSO. The elemental analyses were in good agreement with the complexes. From the antimicrobial activity data, it is observed that the complexes exhibit higher activity than the free ligands, metal salt, and the control (DMSO). The increase in antimicrobial activity of the complexes may be due to the metal chelation. From comparative analysis as shown in Table 3 it is observed that all the metal complexes are more potent biocidal than the ligand. The zone of inhibition was measured (in mm) around the disc and the results are represented in Table 3. From the graph it is clear that Cu(2) is highly active among the complexes of the respective metal, this may be due to presence of ethoxy group of ligand whereas Cu(2) is most active among all which may be due to combine effect of Cu(2) and functional groups on the ligand.

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Abbreviation
8HQ = 8- Hydroxy Quinoline
HL_2 = 5-(Ethoxymethyl-8-Quinolinol) (EMQ).
D.D.Water = Double distilled water
LB = Luria broth

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