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Synthesis, Characterization and Antimicrobial Activity of Metal Chelates of 5-[4-(3-Chloro phenyl)piperazinyl-methylene]-8-hydroxy Quinoline

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5-Chloro methyl-8-quinolinol was condensed with 4-3(3-chloro phenyl piperazine in presence of sodium bicarbonate. The resulting 5-[4-(3-chloro phenyl)piperazinyl methylene]-8-quinolinol (CPPQ) was characterized by elemental analysis and spectral studies. The transition metal chelates *viz.*, Cu^{2+}, Ni^{2+}, Co^{2+}, Mn^{2+}, Zn^{2+} and Cd^{2+} of CPPQ were prepared and characterized by metal-ligand (M:L) ratio, IR and reflectance spectroscopies and magnetic properties. The antifungal activity of CPPQ and its metal chelates was screened against various fungi. The results show that all these samples are good antifungal agents.

Key Words: 8-Hydroxy quinoline, Magnetic moment, Metal chelates, Antifungal properties.

INTRODUCTION

8-Hydroxyquinoline or 8-quinolinol is well known as an analytical reagent[1,2]. It's various derivatives[3] are also useful in pharmaceuticals. Several azo dyes based on 8-quinolinol are also reported for dyeing of textiles as well as their chelating properties[4,5]. One of the areas in which the derivative based on replacement of chloro group of 5-chloro methyl-8-quinolinol (CMQ) can be synthesize easily. Various derivatives based on CMQ have also been reported in literature[5]. The literature survey reveals that the reaction of CMQ with 4-substituted piperazine derivatives has not been reported so far. The present paper deals with synthesis, characterization and chelating properties of 5-[4-(3-chlorophenyl)piperazinyl methylene]-8-quinolinol (CPPQ) towards transition metal ions.

EXPERIMENTAL

5-Chloromethyl-8-quinolinol (CMQ) hydrochloride was prepared according to method reported in literature[5]. 8-Quinolinol and 4-(3-chlorophenyl)piperazine were used as pure grade. All other chemicals used were of laboratory grade of purity.

Synthesis of 5-[4-(3-chlorophenyl)piperazinyl methylene]-8-quinolinol

Synthesis of CPPQ: In a round bottom flask, to a suspension of 5-chloromethyl-8-quinolinol (CMQ) hydrochloride (23 g, 0.1 mol) in THF (100 mL), 4-(3-chloro phenyl)piperazine (10.0 g, 0.1 mol) was added gradually at room temperature. Sodium bicarbonate (16.8 g) was added in the mixture and the mixture was refluxed on water bath for 3 h. The resulting solid mass was filtered off, washed with boiling water and then air-dried. It was dark green amorphous powder. It was insoluble in common organic solvent but soluble only in formic acid and DMSO. It did not melt upto 230ºC.

Synthesis of metal chelate of CPPQ: The metal chelates of CPPQ were prepared in two steps. All the metal chelates were prepared in an identical procedure. The details are given as follows.

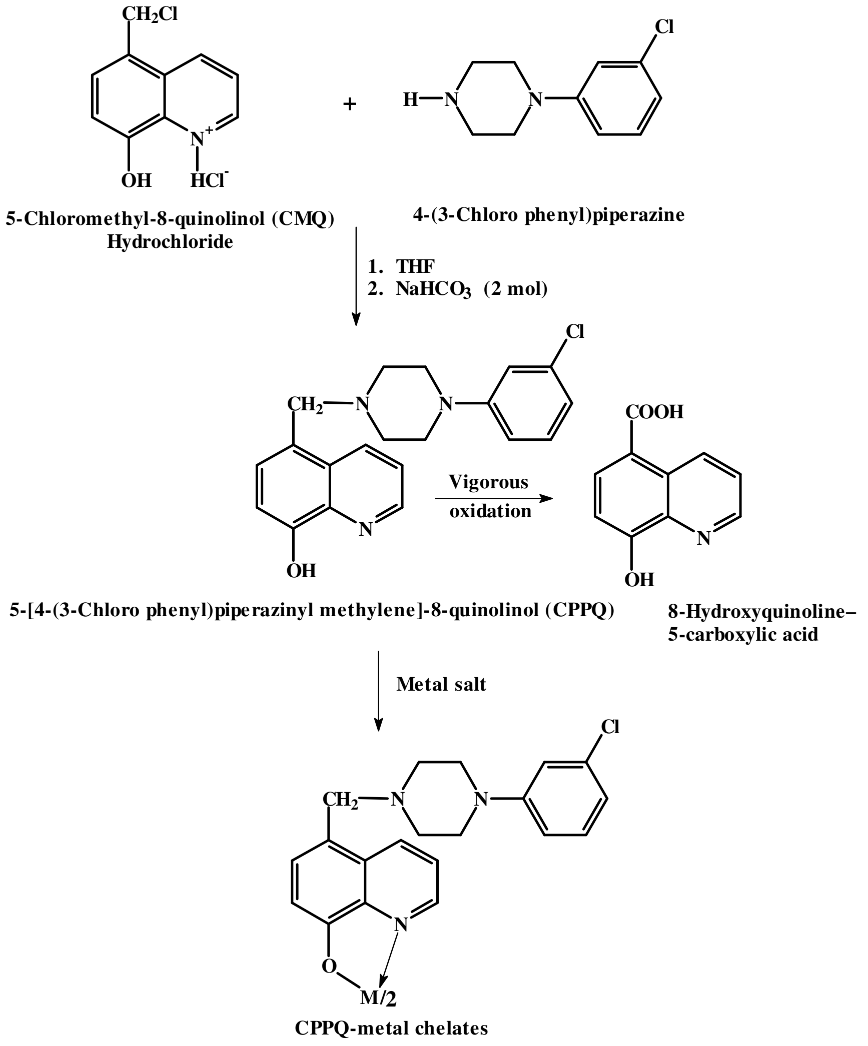
Preparation of CPPQ solution: CPPQ (17.7 g, 0.05 mol) was taken in 500 mL beaker. Formic acid was added upto slurry formation. To this slurry water was added till the complete dissolution of CPPQ. It was diluted to 100 mL.

Synthesis of CPPQ-metal chelates: In a solution of metal acetate (0.005 mol) in acetone:water (50:50 v/v) mixture (40 mL), the 20 mL of above mentioned CPPQ solution (*i.e.* containing 0.01 M CPPQ) was added with vigorous stirring at room temperature. The appropriate pH was adjusted by addition of sodium acetate for complete precipitation of metal chelate. The precipitates were digested on a boiling water bath. The precipitates of chelate were filtered off, washed by water and air-dried.

The elemental contents of C, H, N were determined by thermoanalyzer, the metals were determined volumetrically by Vogel's method[1]. To a 100 mg chelate sample, each 1 mL of analaR HCl, H_2SO_4 and $HClO_4$ were added and then 1 g of $NaClO_4$ was added. The mixture was evaporated to dryness and the resulting salt was dissolved in double distilled water and diluted to the mark. From this solution the metal content was determined by titration with standard EDTA solution. Infrared spectra of the synthesized compounds were recorded on Nicolet 760 FT-IR spectrometers. NMR spectrum of CPPQ was recorded on 60 MHz NMR spectrophotometer. Magnetic susceptibility measurement of the synthesized complexes was carried out on Gouy balance at room temperature. The electronic spectra of complexes in solid were recorded on at room temperature. MgO was used as reference. Antifungal activity of all the samples was monitored against various fungi, following the method reported in literature[6].

RESULTS AND DISCUSSION

The synthesis of 5-[4-(3-chlorophenyl)piperazinyl methylene]-8-quinolinol (CCPPQ) was performed by a simple nucleophilic substitution reaction of 4-(3-chlorophenyl)piperazine and 5-chloromethyl-8-quinolinol hydrochloride (CMQ). The resulted CPPQ ligand was an amorphous dark brown powder. The C, H, N contents of CPPQ (Table-1) are consistent with the structure predicted (**Scheme-I**). The IR spectrum of CPPQ comprises the important bands due to 8-quinolinol. The bands were observed at 1630, 1575, 1500, 1470 and 750 cm^{-1}.



where M: Cu^{2+}, Ni^{2+}, Co^{2+}, Zn^{2+}, Mn^{2+} or Cd^{2+}

Scheme-I

The broad band due to -OH group appeared at 3800-2700 cm^{-1}. In this band the inflections are observed at 2950, 2920 and 2850 cm^{-1}. While the latter two might be attributed to asymmetric and symmetric vibrations of CH_2 of piperazine moiety as well as from CMQ protion. The NMR spectrum of CPPQ in DMSO indicates that the doublet between 2.1 to 2.40 δ ppm due to CH_2 groups of piperazine moiety. The singlet of 2 H at 2.6 δ ppm of $N–CH_2–Ar$ group. While the singlet at 3.8 δ ppm due to -OH group. The aromatic protons are appeared in multipilicity at 7.2 δ. The vigorous oxidation of CPPQ yield 8-hydroxy quinoline-5-carboxylic acid m.p. 230ºC[7]. Thus the structure of CPPQ is confirmed as shown in **Scheme-I**.

The metal and C, H, N contents of metal chelates of CPPQ (Table-1) are also consistent with the predicted structure. The results show that the metal:ligand (M:L) ratio for all divalent metal chelate is 1:2.

TABLE-1
ANALYSIS OF CPPQ LIGAND AND ITS METAL CHELATES

m.f. (m.w.)	Yield (%)	Calculated (Found)			
		Elemental analysis (%)			M
		C	H	N	
$C_{20}H_{21}N_3OCl$	85	67.70	5.92	11.84	–
(354.50)		(67.65)	(5.90)	(11.80)	–
$C_{40}H_{40}N_6O_2Cl_2\cdot Cu^{2+}\cdot 2H_2O$	70	59.51	5.45	10.41	7.87
(806.54)		(59.50)	(5.40)	(10.40)	(7.85)
$C_{40}H_{40}N_6O_2Cl_2\cdot Ni^{2+}\cdot 2H_2O$	65	59.87	5.48	10.47	7.32
(801.69)		(59.85)	(5.45)	(10.45)	(7.30)
$C_{40}H_{40}N_6O_2Cl_2\cdot Co^{2+}\cdot 2H_2O$	70	59.85	5.48	10.47	7.34
(801.93)		(59.80)	(5.40)	(10.40)	(7.35)
$C_{40}H_{40}N_6O_2Cl_2\cdot Mn^{2+}\cdot 2H_2O$	75	60.15	5.51	10.52	6.88
(797.98)		(60.10)	(5.50)	(10.50)	(6.85)
$C_{40}H_{40}N_6O_2Cl_2\cdot Zn^{2+}\cdot 2H_2O$	65	59.37	5.44	10.39	8.08
(808.39)		(59.53)	(5.40)	(10.35)	(8.05)
$C_{40}H_{40}N_6O_2Cl_2\cdot Cd^{2+}\cdot 2H_2O$	75	56.11	5.14	9.81	13.14
(855.41)		(56.10)	(5.10)	(9.80)	(13.10)

The infrared spectra of all the chelates are identical and suggest the formation of all the metalocyclic compound by the absence of band characteristic of free -OH group of parent CPPQ. The other bands are almost at their respectable positions as appeared in the spectrum of parent-CPPQ ligand. However, the band due to (M–O) band could not be detected as it may appeared below the range of instrument used. The important IR spectral data are shown in Table-2.

Magnetic moments of metal chelates are given in Table-2. The diffuse electronic spectrum of Cu^{2+} chelate shows two broad bands around 13000 and 23000 cm^{-1}. The first band may be due to a $^2B_{1g} \rightarrow {}^2A_{1g}$ transition,

TABLE-2
SPECTRAL FEATURES AND MAGNETIC MOMENT OF CPPQ-METAL CHELATES

Metal chelates	μ_{eff} (BM)	Electronic spectral data (cm^{-1})	Transition	IR spectral features common for all (cm^{-1})	
CPPQ-Cu^{2+}	2.10	23250 15875	Charge transfer $^2B_{1g} \rightarrow {}^2A_{1g}$	1650 1565 1500 1460	Quinoline moiety
CPPQ-Ni^{2+}	3.36	22580 15375	$^3A_{1g} \rightarrow {}^3T_{1g}(P)$ $^3A_{1g} \rightarrow {}^3T_{1g}(F)$	2920 2850 1450	CH_2
CPPQ-Co^{2+}	4.60	22724 15260 8935	$^4T_{1g}(F) \rightarrow {}^4T_{2g}(F)$ $^4T_{1g}(F) \rightarrow {}^4T_{2g}$ $^4T_{1g}(F) \rightarrow {}^4T_{2g}(P)$	1100 500	C–O–M & O–M bands
CPPQ-Mn^{2+}	5.48	23860 18345 16820	$^6A_{1g} \rightarrow {}^4A_{2g}\,{}^4E_g$ $^6A_{1g} \rightarrow {}^4T_{2g}(4G)$ $^6A_{1g} \rightarrow {}^4T_{1g}(PG)$	710-750	Ar–Cl
CPPQ-Zn^{2+}	Diamag.		–	–	–
CPPQ-Cd^{2+}	Diamag.		–	–	–

while the second band may be due to charge transfer. The first band shows structures suggesting a distorted octahedral structure for the Cu^{2+} metal chelates[8-10]. The higher value of the magnetic moment of the Cu^{2+} chelate supports the same. The Co^{2+} metal chelate gives rise to two absorption bands at 23800 and 19040 cm^{-1}, which can be assigned $^4T_{1g} \rightarrow {}^2T_{2g}$, $^4T_{1g} \rightarrow {}^4T_{1g}(P)$ transitions, respectively[11,12]. These absorption bands and the μ_{eff} value indicate an octahedral configuration of the Co^{2+} metal chelate[11,12]. The spectrum of Mn^{2+} polymeric chelate comprised two bands at 19010 cm^{-1} (asymm.) and 23300 cm^{-1}. The latter does not have a very long tail. These bands may be assigned to $^6A_{1g} \rightarrow {}^4T_2(G)$ and $^6A_{1g} \rightarrow {}^4A_{2g}(G)$ transitions, respectively. The high intensity of the bands suggests that they may have some charge transfer character. The magnetic moment is found to be lower than normal range. In the absence of low temperature measurement of magnetic moment it is difficult to attach any significance to this. As the spectrum of the metal chelate of Ni^{2+} show two distint bands at 11960-11450 and 17700-17400 cm^{-1} are assigned as $^3A_{2g}(F) \rightarrow {}^3T_{1g}(F)$ and $^3A_{2g}(F) \rightarrow {}^3T_{1g}(F)$ transition, respectively suggested the octahedral environment for Ni^{2+} ion. The observed μ_{eff} values in the range 3.01-3.2 B.M. are consistent with the above moiety[8,9,13].

The examination of antifungal activity of CPPQ ligand and its all chelates (Table-3) reveals that the ligand is moderately toxic against fungi, while all the chelates are more toxic than ligand. Among all the chelates the Cu^{2+} chelate is more toxic against fungi.

TABLE-3
ANTIFUNGAL ACTIVITY OF CPPQ LIGAND AND ITS METAL CHELATES

Sample	Zone of inhibition of fungas at 1000 ppm (%)						
	PE	BT	N	T	RN	AN	TL
CPPQ	55	54	53	63	63	67	70
CPPQ-Cu^{2+}	83	78	77	83	81	84	85
CPPQ-Zn^{2+}	75	64	63	77	83	83	84
CPPQ-Ni^{2+}	80	77	75	75	73	81	80
CPPQ-Co^{2+}	65	76	75	73	78	79	85
CPPQ-Mn^{2+}	79	75	73	75	80	77	83
CPPQ-Cd^{2+}	80	85	89	80	85	75	85

PE = *Penicillium expansum*; BT = *Botrydepladia thiobromine*; N = *Nigrospara* sp.; T = *Trichothesium* sp.; RN = *Rhizopus nigricans*; AN = *Aspergillus niger*; TL = *Trichoderma lignorum.*

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