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Synthesis, characterization and antifungal activity of metal complexes of 8-hydroxyquinoline based azo dye

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ABSTRACT

Novel metal complexes of ligand 1-(4-((8-hydroxyquinolin-5-yl)diazenyl)phenyl)-2-(4-methyl-piperazin-1-yl)ethanone (APEHQ) were prepared using transition metal salts and characterized by physic chemical parameters and various spectroscopic techniques. The geometry of the metal complexes was carried out by electronic spectral analysis and magnetic measurement studies. Novel ligand APEHQ was synthesized using diazotized 1-(4-aminophenyl)-2-(piperazin-1-yl)ethanone (APE) with 8-hyroxyquinoline (HQ) and was duly characterized. The antifungal activity of APEHQ and its metal complexes was screened against various fungi. Results showed that the metal complexes were found more active as compared to ligand.

Keywords: *metal complex; spectral study; antifungal activity*

INTRODUCTION

Tremendous work based on the synthesis and development of metal complexes of 8-hydroxyquinolines (8HQs) [1–4]. Various strategies can be envisaged to synthesize or modify metal complex structures by exploiting the reactivity of this heterocycle with their derivatives by various researchers [5–7]. 8-hydroxyquinoline and its derivatives were also reported to have promising bioactivities, including anticancer [8–9], antibacterial [10–11], antidyslipidemic and antioxidative properties [12], vasorelaxing properties [13], antivirus and antiplatelet [14–15] activities. There has also been interest in the use of azo dye a biologically active compound. The coupling reaction of diazo derivative of 1-(4-aminophenyl)-2-(piperazin-1-yl)ethanone with HQ has not been reported so far. We therefore decided to undertake a study of metal complexes from APEHQ containing a combination of the azo dye and 8-HQ structures in single molecular framework. Our prime intention was to synthesize metal complexes and to study their antifungal activity. Our synthetic approach in the different phases of this work, viz.: (1) Synthesis of the ligand 1-(4-((8-hydroxyquinolin-5-yl)diazenyl)phenyl)-2-(4-methyl-piperazin-1-yl) ethanone (APEHQ); (2) Synthesis of metal complexes by use of a variety of metal(II) acetates, e.g. Mn(II), Co(II), Ni(II), Cu(II) and Zn(II) metal ions is summarized in Fig. 1 and details of the procedures and the results obtained are discussed below.

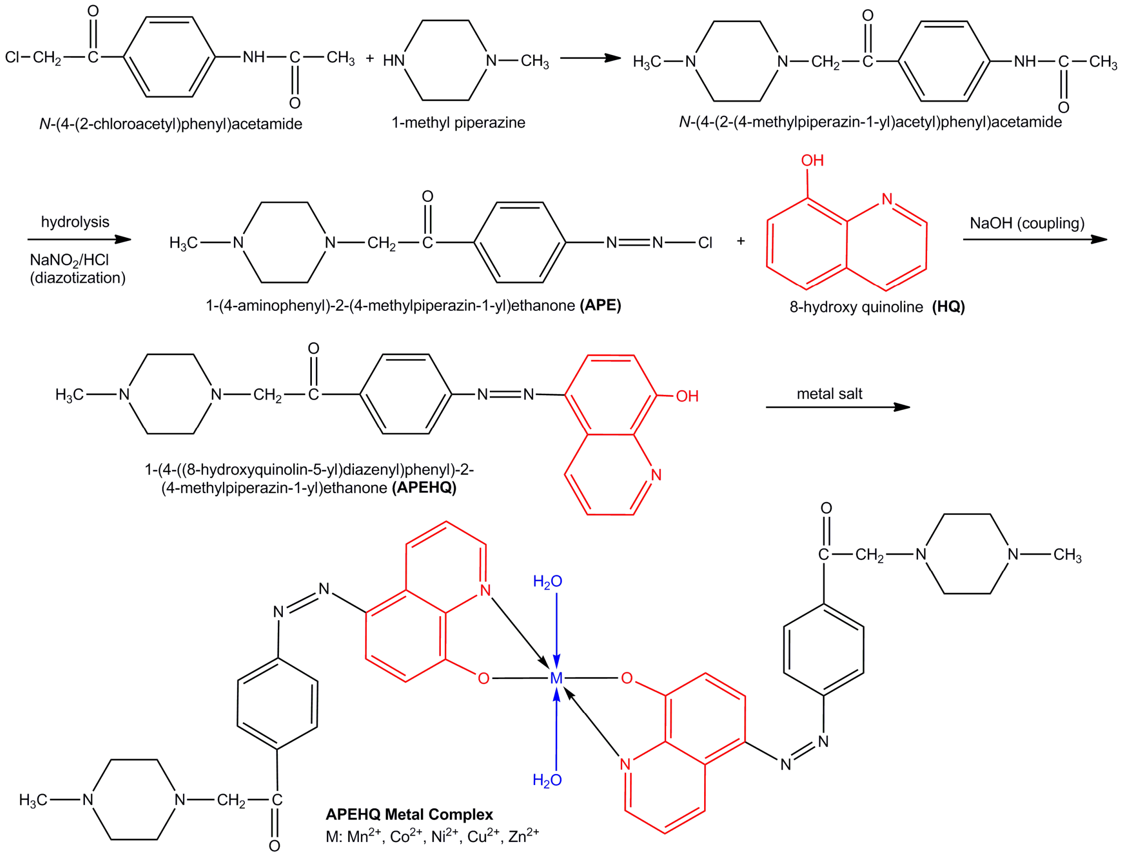

Figure 1 Synthesis of ligand and its metal complexes

MATERIALS AND METHODS

All common reagents and solvents were used of analytical grade and were used without further purification. Alumina supported pre-coated silica gel 60 F254 thin layer chromatography (TLC) plates were purchased from the E. Merck (India) Limited, Mumbai and were used to check purity of compounds and, to study the progress of the reaction whereby TLC plates were illuminated under Ultraviolet light (254 nm), evaluated in I_2 vapors and visualized by spraying with Draggendorff's reagent. Infrared spectra (FT–IR) were obtained from KBr pellets in the range of 4000–400 cm^{-1} with a Perkin Elmer spectrum GX spectrophotometer (FT–IR) instrument. ^1H NMR and ^{13}C NMR spectra were acquired at 400 MHz on a Bruker NMR spectrometer using DMSO-d_6 as a solvent as well as TMS an internal reference standard. Micro analytical (C, N, H) data was obtained by using a Perkin–Elmer 2400 CHN elemental analyzer. The solid diffuse electronic spectra were recorded on a Beckman DK–2A spectrophotometer with a solid reflectance attachment. MgO was employed as a reference. Magnetic moments [16] were determined by the Gouy method with mercury tetra thiocyanetocobaltate (II), $[HgCo(NCS)_4]$ as calibrant (Xg = 1644×10^{-6} cgs units at 20 $^{\circ}C$), by Citizen Balance (at room temperature). Molar susceptibilities were corrected using Pascal's Constant [17]. The thermogravimetric studies were carried out with a model Perkin Elmer thermogravimetry analyzer at a heating rate of 10 $^{\circ}C$ min^{-1} in the temperature range 50–700 $^{\circ}C$ in air. The metal content of the coordination polymers was carried by decomposing a weighed amount of each coordination polymers with $HClO_4$, H_2SO_4 and HNO_3 (1:1.5:2.5) mixture followed by standard EDTA titration method [18]. The melting point was checked by the standard open capillary method. The 4-chloro acetamido phenacylchloride (APC) was prepared by reported method [19].

Synthesis of 1-(4-aminophenyl)-2-(4-methylpiperazin-1-yl)ethanone (APE)

The mixture of 4-chloro acetamido phenacyl chloride (APC) (0.1 mole), 1-methyl piperazine (0.1 mole) and K_2CO_3 (0.1mole) in acetone were refluxed at room temperature for 5h. The resultant product was filtered and hydrolyzed by

50:50 HCl: ethanol mixture. The obtained product was purify and recrystallized, designated as 1-(4-aminophenyl)-2-(4-methyl-piperazin-1-yl)ethanone (APE).

Synthesis of 1-(4-((8-hydroxyquinolin-5-yl)diazenyl)phenyl)-2-(4-methyl-piperazin-1-yl) ethanone (APEHQ)

A solution of sodium nitrite (0.01M) is added drop wise to a stirred and cold solution of 1-(4-aminophenyl)-2-(piperazin-1-yl)ethanone (APE) (0.01mole) in 50% HCl. The reaction mixture was allowed to keep in ice-bath. These diazonium salts poured with stirring into a cold solution of 8-hydroxyquinoline (0.01mole) in sodium hydroxide solution. The reaction mixture was kept in ice-bath for 30minutes. The separated 68% yield of dark brown product was filtered and washed with ethanol, purify and recrystallized, designated as 1-(4-((8-hydroxyquinolin-5-yl)diazenyl)phenyl)-2-(piperazin -1-yl) ethanone (APEHQ). Yield 68%; M. Wt. 389g; M.P. 231–232 ˚C; Elemental Analysis Calculated for $C_{22}H_{23}N_5O_2$: C 67.18, H 5.64, N 18.65%; Found: C 67.16, H 5.60, N 18.56%; ^{1}HNMR (DMSO–d_6, δ ppm): 8.09–8.27 (m, 4H, Ar–H), 6.89–8.92 (m, 5H, Quinoline), 5.56 (s, 1H, –OH), 3.74(s, 2H, N–CH_2), 2.40–2.68 (t, 8H, –CH_2–), 2.03 (s, 3H, –CH_3); FT–IR (KBr, cm^{-1}): 3650(–OH),3420 (–NH–), 2980 (–CH_2–), 1725 (–C=O), 2850, 1630, 1470 (aromatic), 1640, 1575, 1475 and 755 (8-Hydroxyquinoline).

Synthesis of metal complexes of APEHQ

The metal complexes of APEHQ with Cu(II), Co(II), Zn(II), Mn(II), and Ni(II) metal ions were prepared in two steps. All the metal complexes were prepared in an identical procedure. APEHQ (0.01 mol) was taken in 500 ml beaker and formic acid (85% v/v) was added up to slurry formation. To this slurry water was added till the complete dissolution of APEHQ. It was diluted to 100 ml of water. In a solution of metal acetate (0.001 mol) in acetone: water (50:50 v/v) mixture (40 ml) the 20 ml of above mentioned APEHQ solution (i.e. containing 0.01 M APEHQ) was added with vigorous stirring at room temperature. The appropriate pH was adjusted by addition of sodium acetate for complete precipitation of metal complexes. The precipitates were digested on a boiling water bath. The precipitates of metal complexes were filtered off, washed by water and air-dried. Synthesized metal complexes were characterized by various spectroscopic techniques and by physico chemical parameters.

RESULTS AND DISCUSSION

The synthesis of 1-(4-((8-hydroxyquinolin-5-yl)diazenyl)phenyl)-2-(4-methyl-piperazin-1-yl)ethanone(APEHQ) was performed by a simple diazotization reaction of 1-(4-aminophenyl)-2-(4-methyl-piperazin-1-yl)ethanone (APE) and 8-hyroxyquinolinol (HQ). The resulted APEHQ ligand was an amorphous yellow powder. The C, H, N contents of APEHQ (Table-1) are consistent with the structure predicted (Figure-1). The IR spectrum of APEHQ comprises the important bands due to 8-quinolinol. The bands were observed at 1640, 1575, 1475, and 755 cm^{-1}.

Table 1: Physicochemical parameters of ligand and its metal complexes

Empirical Formula	Mol. Wt. gm/ mole	Yield (%)	Elemental Analysis							
			C%		H%		N%		M%	
			Cald	Found	Cald	Found	Cald	Found	Cald	Found
$C_{22}H_{23}N_5O_2$	375	68	67.18	67.16	5.64	5.62	18.65	18.63	-	-
$C_{42}H_{40}N_{10}O_4Cu(II)2H_2O$	847.54	74	59.47	59.45	5.19	5.17	16.52	16.51	7.50	7.49
$C_{44}H_{44}N_{16}O_4Co(II)2H_2O$	842.94	72	59.79	59.78	5.22	5.20	16.61	16.60	6.99	6.97
$C_{42}H_{40}N_{10}O_4Ni(II)2H_2O$	842.71	70	59.81	59.79	5.22	5.21	16.61	16.59	6.97	6.96
$C_{42}H_{40}N_{10}O_4Mn(II)2H_2O$	838.94	76	60.08	60.06	5.24	5.23	16.69	16.68	6.55	6.53
$C_{42}H_{40}N_{10}O_4Zn(II)2H_2O$	849.38	72	59.34	59.32	5.18	5.16	16.48	16.46	7.70	7.68

Table 2: Spectral features and magnetic moment of metal complexes

Metal Chelates	μ_{eff} (BM)	Electronic spectral data (cm^{-1})	Transition
APEHQ-Cu(II)	2.53	23450 13212	Charge transfer $^2B_{1g}\rightarrow{}^2A_{1g}$
APEHQ-Ni(II)	3.71	22595 15369	$^3A_{1g}\rightarrow{}^3T_{1g}(P)$ $^3A_{1g}\rightarrow{}^3T_{1g}(F)$
APEHQ-Co(II)	4.77	23732 19103 8922	$^4T_{1g}(F)\rightarrow{}^4T_{2g}(F)$ $^4T_{1g}(F)\rightarrow{}^4T_{2g}$ $^4T_{1g}(F)\rightarrow{}^4T_{2g}(P)$
APEHQ-Mn(II)	5.56	23234 19032 16840	$^6A_{1g}\rightarrow{}^6A_{2g}\,{}^4E_g$ $^6A_{1g}\rightarrow{}^4T_{2g}$ (4G) $^6A_{1g}\rightarrow{}^4T_{1g}(PG)$
APEHQ-Zn(II)	Diamag.		---------

The broad band due to –OH group appeared at 3650 cm^{-1}. In this band the inflections are observed at 2970, 2980 and 2850cm^{-1}.While the latter two might be attributed to asymmetric and symmetric vibration of CH_2 of AHQ. The NMR spectrum of APEHQ in DMSO indicates that the singlet of 2 H at 3.74 for N-CH_2 group. While the singlet at 5.56 δ ppm due to –OH group. The aromatic protons are appeared in multiplicity at 8.09-8.27 δ. The vigorous oxidations of APEHQ yield 8-hydroxy quinoline-5-carboxylic acid m.p. 215°C. Thus the structure of APEHQ is confirmed as shown in Scheme-I.

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

Table 3: Antifungal activity of ligand and its metal complexes

Sample	**Zone of inhibition of fungus at 1000 ppm (%)**			
	Asperginus niger	***Botrydeplaia thiobromine***	***Nigrospora Sp.***	***Rhisopus Nigricans***
APEHQ	55	71	66	66
APEHQ-Cu$^{(II)}$	77	86	87	80
APEHQ-Zn$^{(II)}$	66	84	86	84
APEHQ-Ni$^{(II)}$	76	83	74	78
APEHQ-Co$^{(II)}$	77	85	79	75
APEHQ-Mn$^{(II)}$	71	82	83	74

The infrared spectra of all the chelates are identical and suggest the formation of the entire metalocyclic compound by the absence of band characteristic of free –OH group of parent APEHQ. The other bands are almost at their respectable positions as appeared in the spectrum of parent-APEHQ ligand. However, the band due to (M-O) band could not be detected as it may appear 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$^{(II)}$ chelates shows two broad bands around 13212 and 23450 cm^{-1}. The first band may be due to a $^2B_{1g} \rightarrow {}^1A_{1g}$ transition. While the second band observed was due to the charge transfer. The first band shows structures suggesting a distorted octahedral structure for the Cu$^{(II)}$ metal chelates. The higher value of the magnetic moment of the Cu$^{(II)}$ chelate supports the same. The Co$^{(II)}$ metal chelate gives rise to two absorption bands at 23732 and 19103cm^{-1}, which can be assigned $^4T_{1g}\rightarrow {}^2T_{2g}$, $^4T_{1g}\rightarrow {}^4T_{1g}$(P)transitions, respectively. These absorption bands and the µeff value indicate an octahedral configuration of the Co$^{(II)}$ metal chelate [19]. The spectrum of Mn$^{(II)}$ polymeric chelate comprised two bands at 19032cm^{-1} and 23234 cm^{-1}. The latter does not have a very long tail. These bands may be assigned to ^{6} $A_{1g}\rightarrow {}^4T_{2g(G)}$ and ^{6} $A_{1g}\rightarrow {}^4A_{2g(G)}$ 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 measuremet of magnetic moment it is difficult to attach any significance to this. As the spectrum of the metal chelate of Ni$^{(II)}$ show two distinct bands at 15369 and 22595 cm^{-1} are assigned as $^3A_{1g}\rightarrow {}^3T_{1g}$(F) and $^3A_{1g}\rightarrow {}^3T_{1g}$(P) transition, respectively suggested the octahedral environment for Ni$^{(II)}$ ion. The observed µeff values in the range 2.53-5.56 B.M are consistent with the above moiety [19].

The examination of antifungal activity of APEHQ 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$^{(II)}$ chelate is more toxic against fungi.

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