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Synthesis, characterization and antimicrobial activity of metal chelates of 5-((5-((pyridin-4-yloxy)methyl)-1,3,4-thiadiazol-2-ylamino)methyl) quinolin -8-ol (PYHQ)

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ABSTRACT

5-Chloromethyl-8-quinolinol was condensed stoichiometrically with 5-((pyridin-4-yloxy)methyl)-1,3,4-thiadiazol -2-amine(PY) in the presence of sodium bicarbonate. The resulting 5-((5-((pyridin-4-yloxy)methyl)-1,3,4-thiadiazol-2-ylamino) methyl) quinolin -8-ol (PYHQ) was characterized by elemental analysis and spectral studies. The transition metal chelates viz. Cu^{2+}, Ni^{2+} , Co^{2+} , Mn^{2+} and Zn^{2+} of PYHQ were prepared and characterized by metal-ligand (M:L) ratio, IR and reflectance spectroscopies and magnetic properties. The antifungal activity of PYHQ and its metal chelates was screened against various fungi. The results show that all these samples are good antifungal agents.

Keywords: Thiadiazol -2-amine(PY) ,8-hydroxyquinoline, IR/NMR Spectroscopies, Magnetic moment, Metal Chelates, Antifungal properties.

INTRODUCTION

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 [4-6]. One of the derivative say 5-chloromethyl 8-quinolinol (CMQ) can be synthesize easily and studied extensively for number of derivatives [7]. Some of the ions exchanging resins are also reported with good potentiality [8-17]. The reaction of CMQ with heterocyclic derivatives has also been reported recently [18]. The heterocyclic compound say derivatives of 2-amino-1,3,4-thiadiazole have interesting wide range of biological activity, antimicrobial agents [19-25]. The reaction of these derivatives with CMQ has not been reported so far. Hence such type of heterocyclic ring and 8-HQ into one molecule may afford good biological active compound. Hence one of the author [AS] publish the initial

work.[26] In continuous of this work the present paper deals with syntheses, characterization, chelating and microbicidal properties of 5-((5-((pyridin-4-yloxy)methyl)-1,3,4-thiadiazol-2-ylamino) methyl) quinolin -8-ol (PYHQ) (scheme : 1).

MATERIALS AND METHODS

5-Chloromethyl-8-quinolinol (CMQ) hydrochloride was prepared according to method reported in literature [6]. 5-((pyridin-4-yloxy)methyl)-1,3,4-thiadiazol -2-amine was prepared by reported method.[19,27] All other chemicals used were of laboratory grade.

Synthesis of 5-((5-((pyridin-4-yloxy)methyl)-1,3,4-thiadiazol-2-ylamino) methyl) quinolin -8-ol (PYHQ):

Synthesis of PYHQ: In a round bottom flask, to a suspension of 5-chloromethyl-8-quinolinol (CMQ) hydrochloride (23 g, 0.1 mol) in THF (100ml), 5-((pyridin-4-yloxy)methyl)-1,3,4-thiadiazol -2-amine(PY) (24.9gm ,0.12mol) was added gradually at room temperature. Sodium bicarbonate (16.8 g 0.2 mole) was added in the mixture and the mixture was refluxed on water bath for 3 hrs. The resulting solid mass was filtered off, washed with boiling water and the 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 up to 230°C.

Analysis:

		C%	H%	N%	S%
Elemental Analysis					
	Calculated:	59.16	4.14	19.17	8.78
$C_{18}H_{15}N_5O_2S$ (365)	Found:	59.1	4.1	19.1	8.7

IR Spectral Features (cm^{-1}): 3420 (NH), 2980 (CH_2), 1260, 1070(ether), 2850, 1630, 1575, 1500, 1470 (aromatic).

NMR Signals: δ ppm 7.32-9.2 (m, 9H Ar-H), 5.8 (OH) , 4.6(N-CH_2),5.35(O-CH_2)

Synthesis of metal chelates of PYHQ:

The metal chelates of PYHQ with Cu^{2+}, Co^{2+}, Zn^{2+}, Mn^{2+}, and Ni^{2+} metal ions were prepared in two steps. All the metal chelates were prepared in an identical procedure. The details are given as follows.

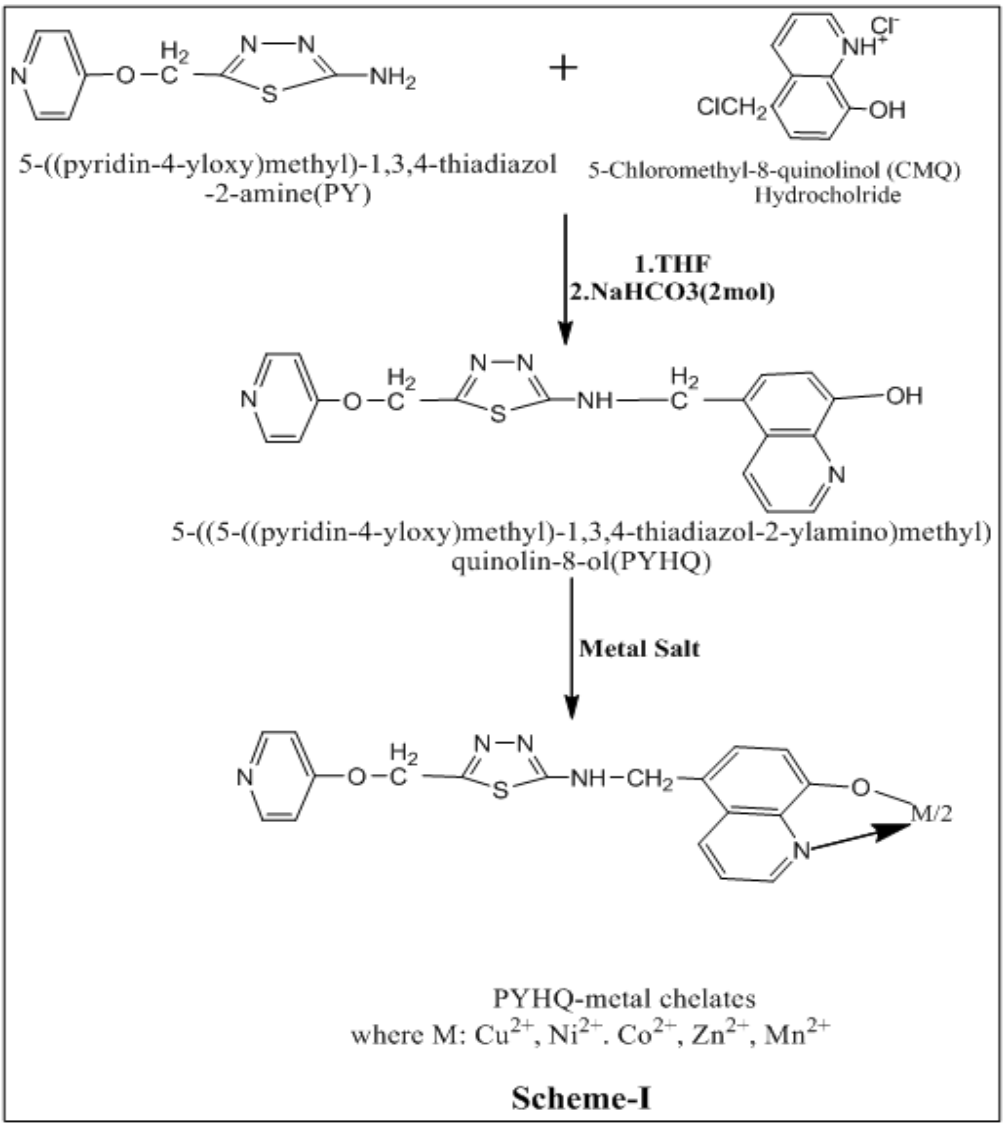
Preparation of PYHQ solution:

PYHQ (0.05 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 PYHQ. It was diluted to 100 ml.

Synthesis of PYHQ-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 PYHQ solution (i.e. containing 0.01 M PYHQ) 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.



Scheme-I

Measurements

The elemental contents were determined by Thermo Finigen Flash1101 EA (Itally) the metals were determined volumetrically by Vogel's method [28]**.** To a 100 mg chelate sample, each 1 ml of 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 spectrometer. NMR spectrum of PYHQ was recorded on 60 MHz NMR spectrophotometer. Magnetic susceptibility measurement of the synthesized complexes was carried out on Gouy Balance at room temperature. Mercury tetrathiocynatocobalate (II) $Hg[Co(NCS)_4]$ was used as a calibrant. 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 [29].

RESULTS AND DISCUSSION

The synthesis of 5-((5-((pyridin-4-yloxy) methyl) -1,3,4-thiadiazol-2-ylamino) methyl) quinolin-8-ol (PYHQ) was performed by a simple nucleophilic substitution reaction of 5-((pyridin-4-yloxy) methyl)-1,3,4-thiadiazol-2-amine (PY) and 5-chloro methyl-8-quinolinol hydrochloride (CMQ). The resulted PYHQ ligand was an amorphous dark brown powder. The C, H, N contents of PYHQ (Table-1) are consistent with the structure predicted (Scheme-1). The IR spectrum of PYHQ comprises the important bands due to 8-quinolinol. The bands were observed at 1635, 1575, 1470, and 755 cm^{-1}.

The broad band due to –OH group appeared at 3850-2720 cm^{-1}. In this band the inflections are observed at 2970, 2930 and 2850cm^{-1}.While the latter two might be attributed to asymmetric and symmetric vibration of CH_2 of CMQ. The NMR spectrum of PYHQ in DMSO indicates that the singlet of 2 H at 2.6 δ ppm of N-CH_2-Ar group.

Table-1: ANALYSIS OF PYHQ LIGAND AND ITS METAL CHELATES

Empirical Formula	Mol. Cal. gm/mole	Yield (%)	Elemental Analysis									
			C%		H%		N%		S%		M%	
			Cald	Found	Cald	Found	Cald	Found	Cald	Found	Cald	Found
$C_{18}H_{15}N_5O_2S$	365	85	59.16	59.1	4.14	4.1	19.17	19.1	8.78	8.7	---	---
$C_{36}H_{28}N_{10}O_4S_2Cu^{2+}2H_2O$	827.54	72	52.20	52.1	3.86	3.8	16.91	16.9	7.73	7.7	7.67	7.6
$C_{36}H_{28}N_{10}O_4S_2Co^{2+}2H_2O$	822.94	73	52.49	52.4	3.88	3.8	17.01	16.9	7.77	7.7	7.16	7.1
$C_{36}H_{28}N_{10}O_4S_2Ni^{2+}2H_2O$	822.71	68	52.50	52.4	3.88	3.8	17.01	16.9	7.77	7.7	7.13	7.1
$C_{36}H_{28}N_{10}O_4S_2Mn^{2+}2H_2O$	818.94	78	52.75	52.7	3.90	3.8	17.09	17.0	7.81	7.7	6.71	6.7
$C_{36}H_{28}N_{10}O_4S_2Zn^{2+}2H_2O$	829.38	70	52.08	52.0	3.85	3.8	16.88	16.8	7.71	7.6	7.88	7.8

While the singlet at 5.8 δ ppm due to –OH group. The aromatic protons are appeared in multiplicity at 7.02-8.9 δ. The vigorous oxidation of PYHQ yield 8-hydroxy quinoline-5-carboxylic acid m.p. 235°C[30]. Thus the structure of PYHQ is confirmed as shown in Scheme-I.

The metal and C,H,N contents of metal chelates of PYHQ (Table-I) 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.

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 PYHQ. The other bands are almost at their respectable positions as appeared in the spectrum of parent-PYHQ 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.

TABLE-2: SPECTRAL FEATRUES AND MAGNETIC MOMENT OF PYHQ METAL CHELATES

Metal Chelates	μ_{eff} (BM)	Electronic spectral data (cm^{-1})	Transition	IR spectral features common for all (cm^{-1})	
PYHQ-Cu^{2+}	2.13	23266 15972	Charge transfer $^2B_{1g} \rightarrow {}^2A_{1g}$	1650 1565 1500 1460	Quinoline moiety
PYHQ-Ni^{2+}	3.36	22596 15370	$^3A_{1g} \rightarrow {}^3T_{1g}(P)$ $^3A_{1g} \rightarrow {}^3T_{1g}(F)$	2920 2850 1450	CH_2
PYHQ-Co^{2+}	4.68	22737 15278 8924	$^4T_{1g}(F) \rightarrow {}^4T_{2g}(F)$ $^4T_{1g}(F) \rightarrow {}^4T_{2g}$ $^4T_{1g}(F) \rightarrow {}^4T_{2g}(P)$	1100 500	C-O-M & O-M bands
PYHQ-Mn^{2+}	5.45	23880 18354 16838	$^6A_{1g} \rightarrow {}^6A_{2g}\ {}^4E_g$ $^6A_{1g} \rightarrow {}^4T_{2g}$ (4G) $^6A_{1g} \rightarrow {}^4T_{1g}$(PG)	710 750	Ar-Cl
PYHQ-Zn^{2+}	Diamag.		---------	------	------

TABLE-3: ANTIFUNGAL ACTIVITY OF PYHQ LIGAND AND ITS METAL CHELATES

Sample	Zone of inhibition of fungus at 1000 ppm (%)						
	AN	AF	AA	AK	BT	N	RN
PYHQ	70	69	73	75	62	60	57
PYHQ-Cu^{2+}	89	90	87	89	89	83	82
PYHQ-Zn^{2+}	79	89	91	88	81	72	66
PYHQ-Ni^{2+}	82	77	85	87	87	80	78
PYHQ-Co^{2+}	77	82	82	89	70	83	79
PYHQ-Mn^{2+}	76	86	82	86	86	77	77

BT= Botrydeplaia thiobromine N= Nigrospora Sp.RN= Rhisopus Nigricans
AN= Asperginus niger AF= Aeprogines funigalus AA= anida Albicans
AK= Andida krusegios candida grabrataHO5

Magnetic moments of metal chelates are given in Table-2. The diffuse electronic spectrum of Cu^{2+} chelates shows two broad bands around 13215 and 23455 cm^{-1}. The first band may be due to a $^2B_{1g} \rightarrow {}^1A_{1g}$ transition. 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[31,32]. 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 23745 and 19105 cm^{-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^{2+} metal chelate [33,34]. The spectrum of Mn^{2+} polymeric chelate comprised two bands at 19035cm^{-1} and 23235cm^{-1}. The latter does not have a very long tail. These bands may be assigned to $^6A_{1g} \rightarrow {}^4T_{2g(G)}$ 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 measuremet of magnetic moment it is difficult to attach any significance to this. As the spectrum of the metal chelate of Ni^{2+} show two distinct bands at 11985-11405 and 17715-17525 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 µeff values in the range 3.01-3.3 B.M are consistent with the above moiety[35,36].

The examination of antifungal activity of PYHQ 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.

REFERENCES

[1] M.M Raikhshtat, S.B Savvin, and L.A. Gribov, *Zh Anal. Khim.*, **1979,**34, 1886.
[2] L.A Gribov, S.B Savvin and M.M. Raikhshtat, *Zh. Anal. Khim.*, **1980,**35,1469.
[3] K.A Oster, and M.J. Golden, *J. Am. Phrm. Assoc. Sci. Ed.*, **1947,**37,283.
[4] K.A Oster, and M.J. Golden, *Am. Pharm. Assoc. Sci. Ed.*, **1947,**37,283.
[5] J.P.Philips, *Chem. Review*, **1984,**56, 271.
[6] A.D.Patel, N.K.Prajapati, S.P.Patel and G.R.Patel,*Der Chemica Sinica*,**2011**,2(2):130.
[7] J.H.Barkhater,. and R.I.Teib, *J.Org.Chem.*,**1968**, 26,4078.
[8] W, Abraham, K, Rani, and P, Abrahaks, *U.S.Patent* **1976,**4317887.
[9] L Katshutoshi,. and L, Hideki, *Japan patent* **1998,**1017953.
[10] T.D, Portanna, B.P Anana, and Z.A. Rajvin, *Visakamol soedin*, **1975,**17, 120.
[11] A.Kenichiro, T Zaaea, and T.Sakurasaaea, *seni Gakkaiski*,**2001,**57, 229.
[12]A.D.Dunya, S.J. Sukhina, V.G, Sinyavskii and Y.P. Kabrak, *Ukr. Khim zh.*, **1982,** 48, 1087.
[13]C.Xiam ren, F.Yushi, L.Hisann, H.Kazuhisa, And A. kusabbura, *Anal. Sci* **1955,**11,313.
[14]A.W.Abraham, D. Abraham, And K. Rami, *S.African patent* 1976,7704289.
[15] J Den,*appl.poly.sci* **1979,**2414425.
[16] J.Dem, *Reactive polymers ion exchange sorbent*, 2,301 (1984).
[17]B.Autkelav, E.E. Eegochin, B.A Mukhidinava, and S.R.Ratikav, *Vyokomal soedin ser. A* **1978,**220 491.
[18] I.M.Vohra, *Phd. Thesis, VNSGuni. Surat*,**2006**.
[19] A.K.Padhy, V.L.Nag and C.S. Panda, *Indian J. Chem., Sect. B*, **1999,**38,998.
[20] K. S. Chukwuka, J. O. Ikheloa, I. O. Okonko, J. O. Moody, T. A. Mankinde, *Advances in Applied Science Research*, **2011**, 2(4), 37.
[21] S. Sharma, J. Ramani, J. Bhalodia, N. Patel, K. Thakkar and R. Patel, *Advances in Applied Science Research*, **2011**, 2(4), 374.
[22] M. I. Fazal Mohamed, S. Arunadevi, M. Koperuncholan and M. Seeni Mubarak, *Der Chemica Sinica*, **2011**, 2(2), 52.
[23] A. Prasada, K. S. Nimavatb and K. B. Vyas, *Der Pharmacia Sinica*, **2011**, 2(4), 26.
[24] Dhanalakshmi, D. Sathis Kumar, M. Sravan Prasad, V. Koli, B. Pawan Kumar and A. Harani, *European Journal of Experimental Biology*, **2011**, 1(1), 103.
[25] S. K. Jain and P.Mishra, *European Journal of Experimental Biology*, **2011**, 1 (2):1-6
[26] D.K Patel and A.Singh,*E-journal of chemistry*,**2009**,6(4),1017.
[27] P.Mishra,V. Jatav and S.K. Kashaw, *J. India Chem. Soc.*, **2006,**83,1165.
[28] B.R.Patil et. *Oriental J.Chem.* **2006,**18, 547.
[29] B.J. Hathway and A. A. G. Tomilson, *Coord. Chem. Rev.*,**1970.**
[30] B.R.Patil et. *J.Ind. Council of Chemistry*,**2006**, **23**, 01.
[31] B.J. Hathway and A.A.G. Tomilson, *Coord. Chem. Rev.*, **1980,**5,1.
[32] H.B. Pancholi and M.M. Patel, *J. Polym. Mater.*, **1996,13**, 261-267.
[33] R. Papplardo, *J. Chem. Phys.*, **1960,**33, 613 ()
[34] J. Lewis and R. S. Wilkins,"Modern Coordination Chemistry", New york,**1960,** 290.
[35] C. furlani and G. Morpurgo, *Theoret. Chim. Acta*, **1965,**1, 1181.

[36] C. K. Jorgenson, *Acta. Chem. Scand*., **1955,**9, 1362.