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# Synthesis and Antifungal Studies of New Metal Complexes of 1, 3, 4-Oxadiazole derivatives (CODMHQ)

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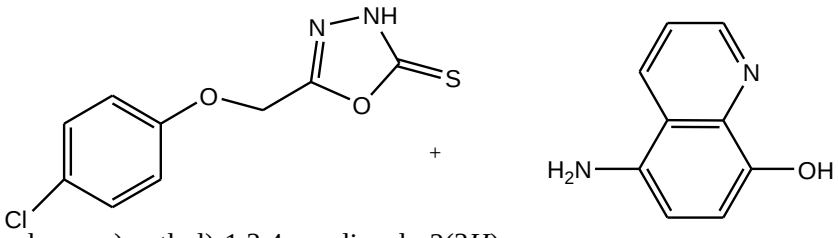
## ABSTRACT

Mannich reaction between 5-amino-8-quinolinol (AMQ) and 5-(4-chloro phenoxy methyl acetyl)-1,3,4-oxadiazole-2(3H)-thione (POD) in the presence of formaldehyde was gave 5-((4-chlorophenoxy)methyl)-3-(((8-hydroxyquinolin-5-yl)amino)methyl)-1,3,4-oxadiazole-2(3H)-thione (CODMHQ), which 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 the product were prepared and characterized by metal-ligand (M:L) ratio, IR and reflectance spectroscopies and magnetic properties. The antifungal activity of that synthesized compound and its metal chelates was screened against various fungi. The results show that all these samples are good antifungal agents.

**Keywords**: - 5-((4-chlorophenoxy)methyl)-3-(((8-hydroxyquinolin-5-yl)amino)methyl)-1,3,4-oxadiazole-2(3H)-thione**,** Spectroscopies study, Magnetic moment, Antifungal properties.

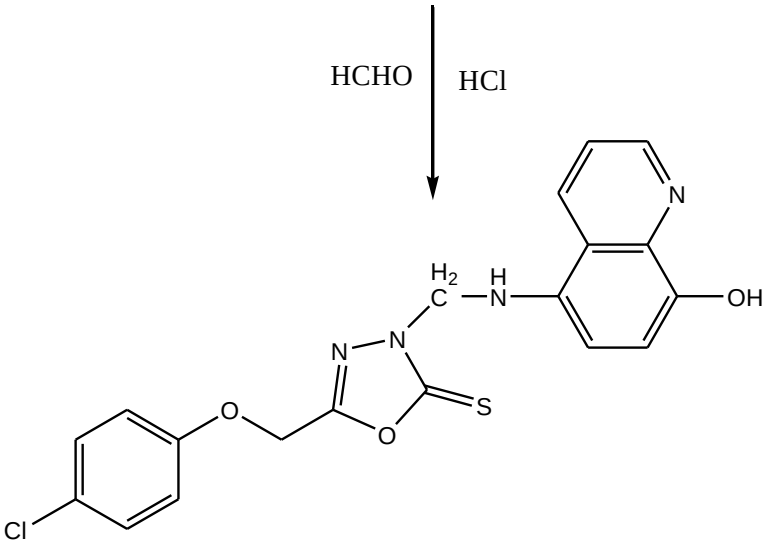
## I. INTRODUCTION

In recent year extensive study of 1,3,4-oxadiazole and their derivatives show diverse biological activities like antituberculotic, anti-inflammatory, analgesic, antibacterial and antifungal activity [1-10]. 8-Hydroxyquinoline is well known as an analytical reagent [11,12]. It's various derivatives [13] 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 [14-15]. One of the derivative say 5-amino-8- hyroxyquinolinol (AHQ) can be synthesize easily and studied extensively for number of derivatives [16]. Some of the ions exchanging resins are also reported with good potentiality [17-23]. The reaction of these derivatives with AHQ has not been reported so far. Hence such type of heterocyclic ring and 8-HQ into one molecule may afford good biological active compound. The present communications discuss about synthesizes, characterization and microbicidal properties of 5-((4-chlorophenoxy)methyl)-3-(((8-hydroxyquinolin-5-yl)amino)methyl)-1,3,4-oxadiazole-2(3H)-thione (CODMHQ). (scheme1)

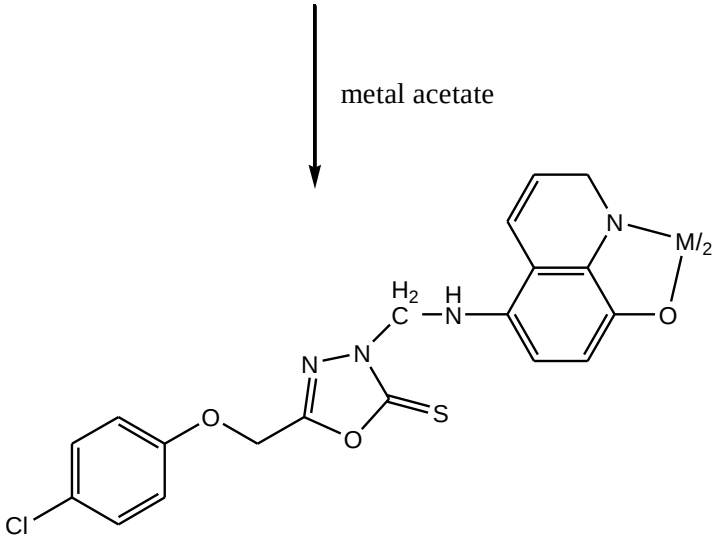


5-((4-chlorophenoxy)methyl)-1,3,4-oxadiazole-2(3*H*)-thione

5-aminoquinolin-8-ol




5-((4-chlorophenoxy)methyl)-3-(((8-hydroxyquinolin-5-yl)amino)methyl)-1,3,4-oxadiazole-2(3*H*)-thione




CODMHQ matel chelate

where M = $Cu^{+2}$ ,$Co^{+2}$, $Ni^{+2}$, $Mn^{+2}$, $Zn^{+2}$

scheme 1

## II. Experimental

5-amino-8-hyroxyquinolinol (AHQ) was prepared according to method reported in literature [16]. 5-(4-chlorophenoxy)methyl)-1,3,4-thiadiazol -2-amine was prepared by reported method[24-25]. All other chemicals used were of laboratory grade.

### Synthesis of 3-[(8-hydroxy Quinolin-5-yl) –amino methyl]-5-(4-cholro phenyloxy acetyl)-1,3,4-oxadiazole-2(3H)-thione

5-amino-8-quinolinol **(AMQ)**, (0.01 mole), 5-(4-chloro phenyloxy acetyl)-1,3,4-oxadiazole-2(3H)-thione (0.01 mole), formaldehyde (0.03 mole) and few drops of concentrated hydrochloric acid in iso propanol (50 ml) were suspended. This mixture was warmed on the steam bath for about ten hours till the reaction product was monitored by TLC. Finally, iso propanol was distilled out and water was added to extract product into aqueous layer. Methylene dichloride (50 ml) was charged to extract impurities and finally aqueous layer basify using 10% NaOH solution and extract product in methylene dichloride (2 X 50 ml). Finally, organic layer dried over sodium sulphate ($Na_2SO_4$) and distilled out atmospherically and finally apply vacuum to get a product. Yield of the ligand compound is 78% and having m.p- 175°C. (Uncorrected)

| | |
|---|---|
| Molecular Formula | $C_{19}H_{15}N_4O_3SCl$ |
| Molecular Weight | 414.5 gm/mole |

**Analysis**:

| Ligand No. | %C | | %H | | %N | | %S | |
|---|---|---|---|---|---|---|---|---|
| | Cal. | Found | Cal. | Found | Cal. | Found | Cal. | Found |
| CODHQM | 55.00 | 55.00 | 3.61 | 3.60 | 13.51 | 13.50 | 7.72 | 7.70 |

CODMHQ = %Cl = 8.56 (Cal.), 8.50 (Found)

| Ligands | Frequencies $cm^{-1}$ | | | | |
|---|---|---|---|---|---|
| | -OH | Aromatic | 8-HQ Moiety | -NH- | $-CH_2-$ |
| CODHQM | 2700-3800 | 1500<br>1600<br>3033 | 1470<br>1578<br>1630 | 3400 | 1448<br>2850<br>2920 |

**IR Spectrum ($cm^{-1}$) of Ligand CODMHQ**

**NMR Signals**: δ ppm 6.88-8.92 (m, 10H Ar-H), 5.56 (OH) , 4.48(N-$CH_2$),4.12(O-$CH_2$)

**Synthesis of metal chelates of CODMHQ:**

The metal chelates of CODMHQ 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.

**Preparation of CODMHQ solution:**

CODMHQ (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 CODMHQ. It was diluted to 100 ml.

**Table-1: ANALYSIS OF PODMHQ LIGAND AND ITS METAL CHELATES**

| Metal Chelates | Molecular formula | M.Wt Gm/mole | Yield % | Elemental analysis | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | %Metal | | %C | | %H | | %N | | % S | | % Cl | |
| | | | | Cald. | Found | Cald. | Found | Cald. | Found | Cald. | Found | Cald. | Found | Cald. | Found |
| $C_{38}H_{28}N_8O_6S_2Cl_2Cu^{+2}.2H_2O$ | 926.5 | 68 | 6.85 | 6.80 | 49.21 | 49.20 | 3.45 | 3.50 | 12.08 | 12.00 | 6.90 | 6.90 | 7.66 | 7.70 | 8.68 |
| $C_{38}H_{28}N_8O_6S_2Cl_2Co^{+2}.2H_2O$ | 922 | 67 | 6.40 | 6.40 | 49.45 | 49.50 | 3.47 | 3.50 | 12.14 | 12.10 | 6.94 | 6.94 | 7.70 | 7.72 | 9.72 |
| $C_{38}H_{28}N_8O_6S_2Cl_2Ni^{+2}.2H_2O$ | 918 | 68 | 6.00 | 6.00 | 49.67 | 49.70 | 3.48 | 3.50 | 12.20 | 12.20 | 6.97 | 7.00 | 7.73 | 7.80 | 8.84 |
| $C_{38}H_{28}N_8O_6S_2Cl_2Mn^{+2}.2H_2O$ | 922 | 69 | 6.40 | 6.40 | 49.45 | 49.50 | 3.47 | 3.50 | 12.14 | 12.10 | 6.94 | 6.90 | 7.70 | 7.70 | 8.70 |
| $C_{38}H_{28}N_8O_6S_2Cl_2Zn^{+2}.2H_2O$ | 928 | 70 | 7.00 | 7.00 | 49.13 | 49.10 | 3.44 | 3.40 | 12.06 | 12.00 | 6.90 | 6.90 | 7.65 | 7.90 | 9.65 |

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

## III. MEASUREMENTS

The elemental contents were determined by Thermo Finigen Flash1101 EA (Itally) the metals were determined volumetrically by Vogel's method [26]. 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 CODMHQ 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[27].

## IV. RESULTS AND DISCUSSION

The synthesis of 5-((4-chlorophenoxy)methyl)-3-(((8-hydroxyquinolin-5-yl)amino)methyl)-1,3,4-oxadiazole-2(3H)-thione (CODMHQ) was performed by a simple nucleophilic substitution reaction of 5-(chlorophenoxymethyl)-1,3,4-oxadiazole-2(3H)-thione (CPOD) and 5-amino-8-hyroxyquinolinol (AHQ). The resulted CODMHQ ligand was an amorphous brown powder. The C,H,N contents of CODMHQ (Table-1) are consistent with the structure predicted (Scheme-1). The IR spectrum of CODMHQ comprises the important bands due to 8-quinolinol. The bands were observed at 1640, 1575, 1475, and 755 $cm^{-1}$.

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

| Metal Chelates | $\mu_{eff}$ (BM) | Electronic spectral data ($cm^{-1}$) | Transition |
|---|---|---|---|
| CODMHQ-$Cu^{2+}$ | 2.56 | 23453<br>13215 | Charge transfer<br>$^2B_{1g} \rightarrow {}^2A_{1g}$ |
| CODMHQ-$Ni^{2+}$ | 3.72 | 22598<br>15372 | $^3A_{1g} \rightarrow {}^3T_{1g}(P)$<br>$^3A_{1g} \rightarrow {}^3T_{1g}(F)$ |
| CODMHQ-$Co^{2+}$ | 4.78 | 23735<br>19105<br>8925 | $^4T_{1g}(F) \rightarrow {}^4T_{2g}(F)$<br>$^4T_{1g}(F) \rightarrow {}^4T_{2g}$<br>$^4T_{1g}(F) \rightarrow {}^4T_{2g}(P)$ |
| CODMHQ-$Mn^{2+}$ | 5.56 | 23235<br>19035<br>16842 | $^6A_{1g} \rightarrow {}^6A_{2g}\ {}^4E_g$<br>$^6A_{1g} \rightarrow {}^4T_{2g}$ (4G)<br>$^6A_{1g} \rightarrow {}^4T_{1g}$(PG) |
| CODMHQ-$Zn^{2+}$ | Diamag. | | |

The broad band due to –OH group appeared at 3650 $cm^{-1}$. In this band the inflections are observed at 2970, 2930 and 2850$cm^{-1}$.While the latter two might be attributed to asymmetric and symmetric vibration of $CH_2$ of AHQ. The NMR spectrum of CODMHQ in DMSO indicates that the singlet of 2 H at 4.48 for N-$CH_2$ and 4.12

O-$CH_2$ group. While the singlet at 5.56 δ ppm due to –OH group. The aromatic protons are appeared in multiplicity at 6.88-8.92 δ. The vigorous oxidations of CODMHQ yield 8-hydroxy quinoline-5-carboxylic acid m.p. 215°C. Thus the structure of CODMHQ is confirmed as shown in Scheme-I.

The metal and C,H,N contents of metal chelates of CODMHQ (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 CODMHQ. The other bands are almost at their respectable positions as appeared in the spectrum of parent-CODMHQ 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 $Cu^{2+}$ chelates shows two broad bands around 13215 and 23453 $cm^{-1}$. 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. 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 23735 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 [28]. The spectrum of $Mn^{2+}$ polymeric chelate comprised two bands at 19035$cm^{-1}$ and 23235$cm^{-1}$. 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 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 distinct bands at 11980-11400 and 17710-17520 $cm^{-1}$ 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 2.99-3.3 B.M are consistent with the above moiety [28]. Many work done by our laboratory [29-36].

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

| Sample | Zone of inhibition of fungus at 1000 ppm (%) | | | |
|---|---|---|---|---|
| | *Asperginus niger* | *Botrydeplaia thiobromine* | *Nigrospora Sp.* | *Rhisopus Nigricans* |
| CODMHQ | 56 | 70 | 64 | 68 |
| CODMHQ-$Cu^{2+}$ | 78 | 85 | 85 | 82 |
| CODMHQ-$Zn^{2+}$ | 67 | 83 | 84 | 86 |
| CODMHQ-$Ni^{2+}$ | 77 | 82 | 72 | 80 |
| CODMHQ-$Co^{2+}$ | 78 | 84 | 77 | 77 |
| CODMHQ-$Mn^{2+}$ | 72 | 81 | 81 | 76 |

The examination of antifungal activity of CODMHQ ligand and it's 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.

## V. REFERENCES


[1]. A. Husain, M. Ajmal, Acta Pharm., 2009,59,223.

[2]. H.Kumar, S. A. Javed, S.A.Khan, M. Amir, European Journal of Medicinal Chemistry,2008,43,2688e2698.

[3]. K.Manjunatha,B.Poojary,P.L.Lobo,J.Fernandes, N.S.Umari,European Journal of Medicinal Chemistry,2010,45,5225e5233.

[4]. M.Akhter, A.Husain,B. Azad, M.Ajmal,European Journal of Medicinal Chemistry,2009,44,2372.

[5]. B. Jayashankar, K. M. Lokanath Rai , N. Baskaran, H.S. Sathish,European Journal of Medicinal Chemistry, 2009,44,3898.

[6]. T.Chandra, N.Garg, S.Lata, K.K.Saxena, A.Kumar, European Journal of Medicinal Chemistry,2010,45,1772.

[7]. A.S. Aboraia, H.M. Abdel-Rahman,N. M. Mahfouz and M.A. EL-Gendy, Bioorganic & Medicinal Chemistry,2006,14,1236.

[8]. L.Jin, J.Chen, B.Song, Z.Chen, S.Yang, Q.Li,D.Hu and R.Xu, Bioorganic & Medicinal Chemistry Letters,2006,16,5036.

[9]. Q.Zheng, X.Zhang, Y.Xu,K.Cheng, Q.Jiao, H.Liang Zhu,Bioorganic & Medicinal Chemistry,2010,18,7836.

[10]. K.A.Kumar, P.Jayaroopa,G.V.Kumar, International Journal of ChemTech Research,2012,4(4)4,1782.

[11]. M.M.Raikhshtat,S.B.Savvin and L.A. Gribov,Zh Anal. Khim.,1979,34,1886.

[12]. L.A.Gribov, S.B.Savvin and M.M.Raikhshtat,Zh. Anal. Khim.,1980,35,1469.

[13]. K.A. Oster and M.J.Golden,J. Am. Phrm. Assoc. Sci. Ed., 1947,37,283.

[14]. K.A. Oster and M.J.Golden,Exp. Med. Surg.,1949,37.

[15]. J.P. Philips, Chem. Review,1984,56, 271.

[16]. J.H. Barkhater and R.I.Teib, J.Org.Chem.,1968,26,4078.

[17]. A.Kenichiro, T. Zaaea and T. Sakurasaaea, seni Gakkaiski,2001,57,229.

[18]. T.D. Portanna, B.P.Anana, and Z.A.Rajvin,Visakamol soedin,1975,17,120.

[19]. L.Katshutoshi and L.Hideki,Japan patent,1998,1017953.

[20]. W.Abraham, K.Rami and P.Abrahaks,U.S.Patent,1976,4317887.

[21]. A.D.Dunya, S.J.Sukhina, V.G.Sinyavskii and Y.P. Kabrak,Ukr. Khim zh., 1982, 48,1087.

[22]. C. Xiamren,F.Yushi, L.Hisann, H.Kazuhisa and A.Kusabbura, Anal. Sci, 1955,11,313.

[23]. Patel,D.K and Singh,A.,E-journal of chemistry,6(4),1017(2009).

[24]. K. K. Oza, H. S. Patel, Bulgarian Chemical Communications,2010,42(2),103.

[25]. P.Mishra, V. Jatav and S.K. Kashaw, J. India Chem. Soc., 2006,83,1165.

[26]. A.I.Vogel,Textbook of Quantitative Chemical Analysis, ELBS 5th Edn. London, 1996.

[27]. W.R. Baily and E.G. Scott, Diagnostic Microbiology, The C. V. Moshy Co. St. Lovis,1966, 257.

[28]. B.R.Patil, Oriental J.Chem.,2006,18,547.

[29]. Kaushik Joshi, Haresh Ram, Bhavesh Dodiya, Hardik Bhatt, Chemistry & Biology Interface, , 2022, 12, 1, 7-14.

[30]. Kaushik Joshi, Hardik Bhatt and Nikunj Dave, Asian J. of Chemical Sciences, 2022 11(1): 10-16.

[31]. K. A. Joshi, H. B. Bhatt and K. M. Kapadiya, Current Chemistry Letters, 2021, (10) 479–488.

[32]. K. A. Joshi, H.P.Pandya, journal of advance scientific research 2020,11(4), 55-60.

[33]. Kaushik A. Joshi, Chauhan V., Journal of advance scientific research , 2020, 11(1), 44-49.
[34]. K. A. Joshi, N R Makwana, International journal for innovative research in multidisciplinary field, 2019.Issue 7, 16-21.
[35]. Kaushik A. Joshi, Haresh K. Ram, International Journal of Applied Chemistry, 201713(1),135-140.
[36]. Arun Vaghasiya, Kaushik Joshi, Jatin Upadhiyay, IJRAR, 2021, 8 (2), 706-711.

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