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Synthesis, characterization and antimicrobial activity of metal (Mn, Fe, Co, Ni, and Cu) chelates of 1, 2 naphthoquinone dioxime,

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Abstract: *Transition metal chelates of the type M [NQO]* $_2$ *where M = Mn, Fe, Co, Ni, Cu: NQO = 1, 2 napthoquinone dioxime have been synthesized. All chelates have been characterized by modern methods such as elemental analysis, FTIR, Electronic spectra and X-ray diffraction. The chelates of manganese and copper have shown triclinic structures. Scanning electron microscopy of chelates were carried out. Their particle sizes are in the range of 15-42 nm. The ligand and the metal chelates have been screened for antimicrobial activity on gram positive and gram negative bacteria and fungi and the results are compared with cisplatin as standard chemotherapy agent..*
Keywords: *1-2 naphthoquinone dioxime, X-ray diffraction, IR, SEM, Antimicrobial activity, Electronic spectra*

I. Introduction:

The structure of 1-2 naphthoquinone dioxime was examined by use of the HF (6 -31 G* level), density functional theory DFT (6 -31 G* level) & hybrid functional B3LYP. Using the optimized structure of the titled compound IR, NMR, and ultraviolet data was calculated and compared with experimental data.(1). The co-ordination chemistry of metal chelates of vic-dioximes has been studied well and is the subject of several reviews published in literature (2, 6). It is well known that the complex formation ability of the -C (C = NOH) – C (C = NOH) – is greatly influenced by the special arrangement of the oxime groups. The presence of mildly acidic hydroxyl groups and slightly basic nitrogen atoms makes oximes, dioximes amphoteric ligands, which form square planar, square-pyramidal or octahedral complexes with transition metal ions such as Co (III) and Ni (II) as the central atom (7). Al, Zn, Cu (II), Ni(II) and alkali metal salts of dioximes were reported and the authors concluded that the colour of the quinone oximes is not related to quinone oxime structure (8). Synthesis, characterization and antimicrobial activity of bivalent metal (Zn, Cd, Hg, Pb and Ag) chelates of 1, 2-naphthoquinone dioxime have been published by N.R. Gonawar et.al.(9)

In this paper we report synthesis of bivalent metal chelates of the type M $[NQO]_2$ where M = Mn, Fe, Co, Ni and Cu : NQO = 1, 2 napthoquinone dioxime and characterization by XRD, Mid IR, electronic spectra, Scanning electron microscopy and antimicrobial activity against microorganisms have been reported.

II. Materials and Methods

The ligand 1, 2-naphthoquinone dioxime is synthesized in laboratory as per the reported method (10). A stock solution of Mn (II), Fe (II), Co (II), Ni (II) and Cu (II) is prepared by using AR grade chemicals. Distilled water is used during synthesis.

2.1Preparation of metal chelates.

The chelates were prepared by mixing metal salt solution and ligand in 1: 1 proportion. The mixture was constantly stirred for one hour on magnetic stirrer. The pH of the mixture was maintained, in between 5.0 – 6.0 by adding ammonia solution to it. Warm the mixture on water bath for about 15 minutes. On cooling it was filtered and compounds are found to be coloured.

2.2 Instrumental Analysis.

Elemental analysis was carried out with a Perkin Elmer 2400 series for C, H, O & N. The IR spectra are recorded on a Shimadzu FTIR 8400 S model in a KBr matrix. The XRD patterns of all the samples are recorded on Bruker D_8 diffractometer in the diffraction angle range $(10\text{-}70)^0$ 2θ. SEM was carried out on a JEOL-3SM-5200 scanning electron microscopy.

Antimicrobial activity testing

Test organisms: The antimicrobial activity of ligands, metal salts and synthesized metal chelates is tasted against bacteria *Escherichia coli* (NCIM 2065), *Bacillus subtilis* (NCIM 2063), *Staphylococcus aureus* (NCIM 2079), *Proteus Vulgaris* (NCIM 2813), *P. aeruginosa* (NCIM 2200), *Aspergillius Niger* (NCIM 1196) and Candida *albicans* (NCIM 3471)] strains collected from NCL, Pune India. ESBL *Escherichia coli*, *Klebsiella Pneumoniae*. The causative agent Cisplatin is chosen as standard chemotherapy agent.

2.4Maintenance of culture:

The cultures of bacteria and fungi were maintained on Nutrient agent (Hymenia Laboratories Pvt Ltd. Ref. M 002-500G 99% Purity), Mueller-Hinton Agar (Himedia Laboratories Pvt. Ltd Ref. M 173 – 500G, 99% Purity) and subcultured accordingly and preserved at 4^{o} C. for 24 hours in incubator.

2.5Plating

The 100 µL cell suspension (108 cell / ml of bacteria & yeasts C. albicans and 100 µL of spore suspension of mold (A. niger) were spread on then. Agar (for bacteria) and Mueller-Hinton Agar for fungi were used. Then wells were bored in the media. In the wells DMSO (solvent), ligand, metal salts and metal chelates solutions were poured for each organism, and then incubated at 37^0C for 48 hrs. for bacteria and 30^0C for 5 days for fungi . The zone diameter of inhibition were measured in mm & recorded.

III. Results and discussion

3.1 Infrared Spectra

IR frequencies of 1-2naphthoquinone dioxime were calculated by RHF / 6-31G* and reported by N.R. Gonewar et. al. (1). In IR spectra of chelates M (NQO)2 where M = Mn (II), Fe (II), Co (II), Ni (II) and Cu (II) showed a weak γ (C – H) stretching at about 3000 – 3400 cm^{-1}. The functional group such as C = N and N – O is assigned. The data is given in table 8. It can be seen from the table that the spectrum of NQO can be compared with chelates of metals which clearly shows lower wave numbers for γ(C = N) band owing to elongation of this bond upon coordination. The absorption of γ (N – O) was found at higher wave numbers since this bond was significantly shortened in the chelates. The high position of γ (NO) frequencies indicates that nitroso atom of the oxime group coordinates to the centre (11,12). The data of frequencies are given in Table: 1,

Table: 1 Characteristic ν IR (cm^{-1}) bands of NQO and its metal chelates.

Sr.No.	Compound	C –H	C = N	N - O
1	NQO	3245	1594	1110
2	Mn $(NQO)_2$	3126	1501	1079
3	$Fe(NQO)_2$	3235	1541	1133
4	Co $(NQO)_2$	3235	1556	1134
5	$Ni(NQO)_2$	3235	1520	1165
6	Cu $(NQO)_2$	3237	1556	1157

3.2 Electronic Spectra (UV)

These bands are interpretated as benzenoid electron transfer (BET), quinonoid electron transfer (QET) and combination band respectively. The third combination band occurring in visible region is composed of n → π* transitions + L to M charge transfer band. The d – d bands which are expected in this region are not distinctly resolved most probably due to their overlapping in this combination band. The UV spectra of the ligand NQO and its metal chelates M (NQO) 2 where (M = Mn (II), Fe (II), Co (II), Ni (II) and Cu (II) were studied in a dimethyl sulphoxide (DMSO) solution and the data is complied in Table 2. NQO exhibits absorption bands at 253 nm, 307 nm and at 406 nm. These bands are assigned to π to π*. The band at 307 nm is originated from the π to π* of the orthoquinone oxime (13). The chelates, studied here show two bands which are due to π to π* transition and third one is due to n → π*. In the case of copper chelate, one more band is observed at 545 nm which can be assigned to combination of ligand to metal or metal to ligand transition with d-d transitions.

Table: 2 Electronic absorption data (λ nm) of metal chelates in DMSO in the range (200-800 nm).

Sr. No.	Compound	π – π* Transitions	π – π* Transitions	n → π* Transitions	Combination of L + d – d Transitions M to L+d–d
1	NQO	253	307	406	--
2	Mn-dioxime	262	318	456	--
3	Fe (II)- dioxime	288	320	464	--
4	Co (II)- dioxime	261	322	448	--
5	Ni (II)- dioxime	265	315	452	--
6	Cu (II)- dioxime	260	325	456	545

3.3 X-ray diffraction:

1, 2 naphthoquinone dioxime (NQO) crystallizes in the triclinic group and it has crystallographic parameters, a = 10.7684 A^o, b = 8.5280 Ao and c = 8.7887 A^o $\alpha = 101.464^o$, $\beta = 102.764^o$, $\gamma = 85.881^o$, Its volume is 771.106 $(A^o)^3$ and space group H-M symbol P1. Dmin = 2.853032 g/cm^3. The data was processed by using McMaille computer program for determination of cell parameters and space group (14). M. Nasakkala et.al. (15) have reported that NQO belongs to monoclinic, space group $P2_1/c$ (No.14), a = 7.082(12) A^0, b = 9.046(11) A^0, c = 13.845(11) A^0, $\beta = 100.2\ (1)^0$, Z=4 and D=1.432 g/cm^3.

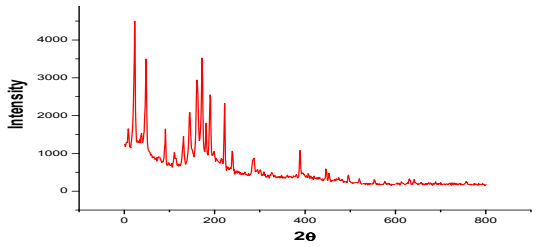


Fig. 1 X- ray diffraction of NQO

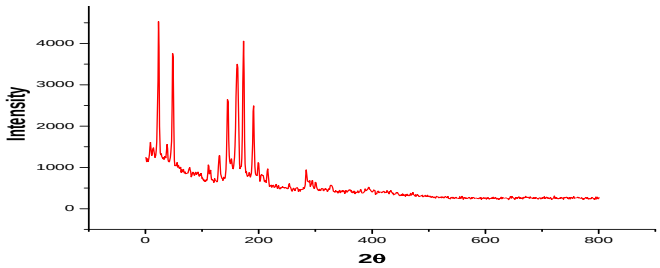


Fig. 2 X- ray diffraction of Mn(NQO)2

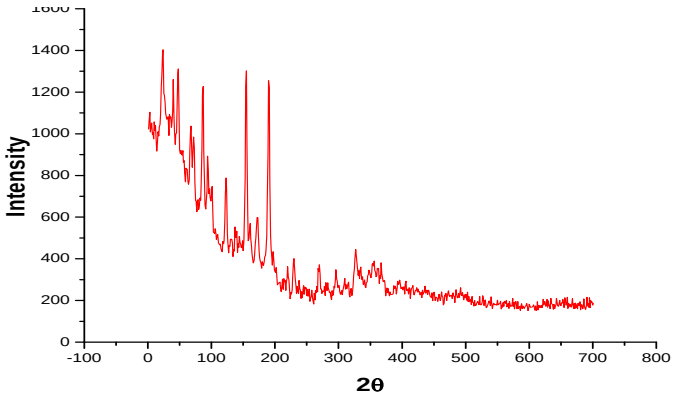


Fig. 3 X- ray diffraction of Cu(NQO)2

The metal chelate of Mn (NQO)2, shows data as per computer code referred above that it belongs to Triclinic, a = 8.1622, b = 8.8456 c = 9.9178 A^0, $\alpha = 102.267$, $\beta = 85.446$, $\gamma = 91.254$, volume = 697.49 $(A^O)^3$ and density calculated as 2.5136 g/cm^3 with Z = 2. Table-3 shows h,k,l data of Mn (NQO)2.

Table: 3 h k l values of Mn (NQO)2,

h	k	l	TH(Obs)	TH-ZERO	TH(Calc)	DIFF
0	1	-1	12.199	12.138	12.138	0.000
1	0	1	13.699	13.638	13.638	0.000
1	-2	1	22.998	22.937	22.937	0.000
2	-1	1	24.398	24.337	24.337	0.000
2	-1	-1	27.197	27.137	27.137	0.000
1	0	3	28.997	28.937	28.937	0.000

The metal chelate of Cu(NQO)2, shows data as per computer code referred above that it belongs to triclinic, a = 12.3738, b = 11.7092 c = 5.6439 A^0, α = 69.444, β = 71.352, γ = 67.132, volume = 689.383 $(A^O)^3$ and density calculated as 2.4178 g/cm^3 with Z = 2. Table-4 shows h,k,l data of Cu $(NQO)_2$.

Table: 4 h k l values of Cu $(NQO)_2$

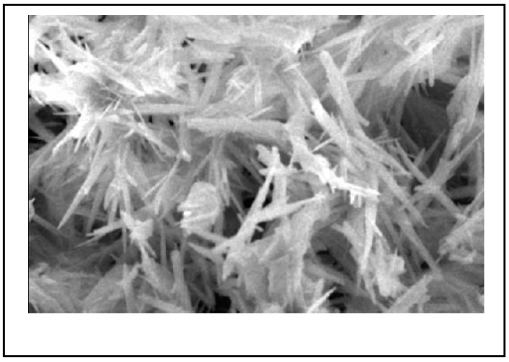
h	k	l	TH(Obs)	TH-ZERO	TH(Calc)	DIFF
0	2	0	17.004	17.034	17.031	0.003
2	1	1	18.547	18.577	18.578	-0.001
2	2	1	20.048	20.078	20.079	-0.001
2	2	0	19.378	19.378	19.377	0.001
1	-1	1	22.188	22.217	22.212	0.005
1	-2	-1	25.358	25.388	25.396	-0.008
2	1	-1	27.107	27.137	27.142	-0.005
1	-2	1	28.917	28.946	28.948	-0.001
1	-3	-1	31.367	31.396	31.391	0.005
3	1	-1	32.877	32.906	32.902	-0.001
3	-2	0	33.697	33.727	33.728	-0.001
0	3	-1	34.647	34.676	34.679	-0.003
1	1	-2	36.836	36.866	36.864	0.002

The particle sizes of Mn $(NQO)_2$ and Cu $(NQO)_2$ are found to be as 39.97 & 40.06 nm respectively which are calculated Scherer equation.

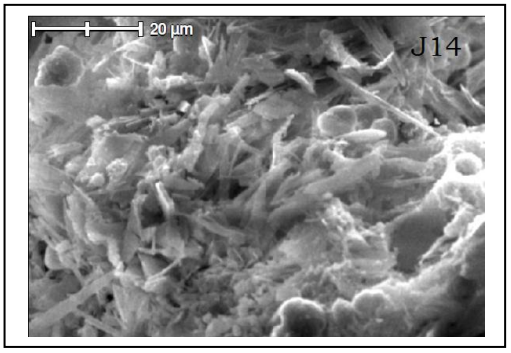
3.4 SEM studies

The scanning electron microscopy (SEM) of the ligand and their Mn (II), Fe (II), Co (II), Ni (II) and Cu (II) chelates was carried. In general, the average crystallite size of the metal chelates is smaller than the crystallite size of the parent ligand. These results of SEM investigations support the results obtained from XRD investigations. A careful examination of the SEM photographs (shown in Fig.4) of the ligand and their five metal chelates reveals that all the samples are heterogeneous mixtures of different particle size. The morphology can be explained as

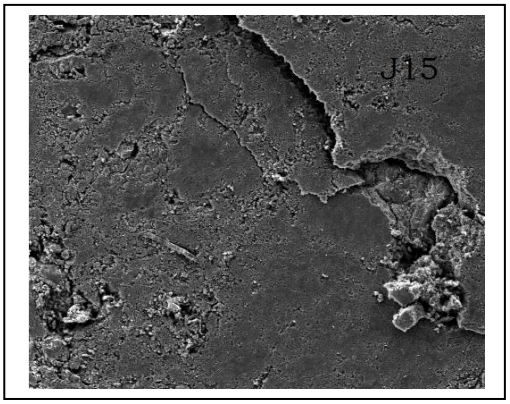
1. NQO shows needle like crystallite structure. Needles are entangled with each other**.**
2. Mn(NQO)2 shows fiber like structure intermixed with semi crystalline phase.
3. Fe (NQO)2 shows a continuous and homogeneous phase spread in mono planar film structure. The grain boundaries are merged together. A hair line crack seen which shows presence of traces.
4. Co (NQO)2 shows a nano granular structure of micro beads. These micro beads are held together in a compact phase to form a cloudy cluster like structure
5. Ni (NQO)2 shows a continuous phase planer structure with grain boundaries merged together. The phase shows distribution of Ni phase in a heterogeneous pattern.
6. Cu (NQO)2 is a cluster of well defined crystals grouped in a bunch of grape like structure.



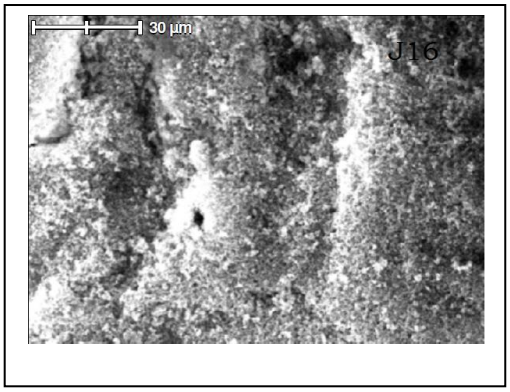
a)NQO



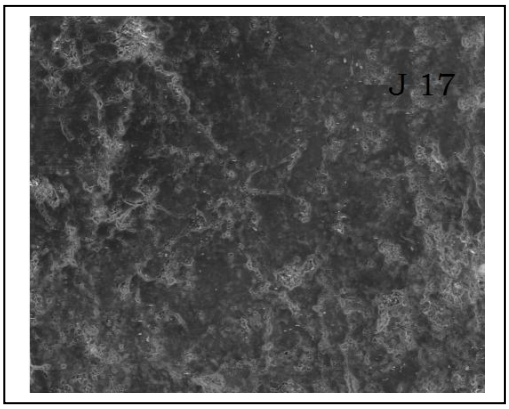
b) Mn(NQO)2



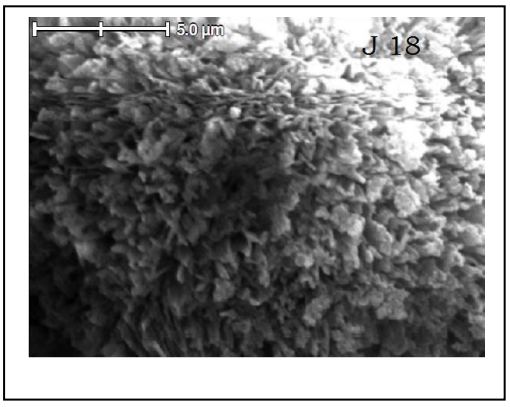
c) Fe (NQO)2



d) Co(NQO)2



e) Ni(NQO)2



f) Cu(NQO)2

Fig. 4. SEM photographes of ligand and its chelates

3.5 Antimicrobial activity

The antimicrobial activity of metal salts, ligands and their complexes were tested against bacteria and fungi like *Escherichia coli, Bacillus subtilis, Staphylococcus aureus, Proteus vulgaries, and Candida albicans.* The causative agent Cisplatin is chosen as standard chemotherapy agent.

The testing against growth of micro-organisms was carried out by using well diffusion method employing Mueller Hinton Agar (MHA) and culture in nutrient broth in each case of micro-organisms. The concentration of NQO and its metal chelates were chosen as 10^{-4}M. The plates were incubated at 37^0C for 24 hours in incubator. The clear zone of inhibition of growth for the organism was measured in mm^2 and the data is given in Table :3.

Table 5: Antimicrobial activities of 1, 2 naphthoquinone dioxime (NQO) and its metal chelates (Inhibition zone area in mm^2)

Sr. No.	Comp.	S.aureus	B.subtilils	*P.vulgaris*	*E.coli*	*C.albicans*
1	NQO	551.2	754.3	415.2	379.9	1074.6
2	Mn(NQO)2	471.1	706.5	362.8	314	1074.6
3	Fe(NQO)2	0	0	0	0	0
4	Co(NQO)2	433.5	415.2	200.9	188.5	153.8
5	Ni (NQO)2	0	153.8	0	0	0
6	Cu(NQO)2	200.9	254.3	143.06	86.5	143.06
7	Cisplatin	314.0	132.6	254.3	254.3	0

Antimicrobial Activity of the Ligands exhibit fairly good activity against the five microorganisms studied. Maximum activity is exhibited by NQO against *C. albicans* (1074.6 mm^2).

The activity of NQO shows decrease in most of the cases. For *B. subtilis*, the trend is not uniform. Here the activity of the ligand is increased from (154.30 mm^2 to 706.5 mm^2). For Ni (II) chelates it is slightly reduced to153.8 mm^2. The variations for this ligand are between zero (minimum) to 1074.6 mm^2 (maximum). Metal Chelates of NQO show decrease in activity from top to bottom. It can be expressed as

Mn > Fe > Co > Ni > Cu

The powerful antimicrobial activity of the three 1, 2 NQ dioximes and their chelates against the selected microorganisms may results due to the successful competition of these ligands with enzymes to interact with metals. Enzyme also can act as ligands because of the presence of $-NH_2$ groups in protein molecules. This competition might affect the metal enzyme activity which disturbs the life cycle of microorganisms causing their death or inhibit their growth. The results of metal chelates are comparable with cisplatin complex.

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