



METAL CHELATES OF FE (II) WITH LIGAND 2-AMINO-1,4-NAPHTHOQUINONE AND 2-AMINO-3-CHLORO-1,4-NAPHTHOQUINONE-1-OXIME SYNTHESIS, CHARACTERIZATION AND ANTIMICROBIAL ACTIVITY

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ABSTRACT Ligand 2-amino-1,4-naphthoquinone (ANQ) and 2-amino-3-chloro-1,4-naphthoquinone-1-oxime (ACNQO) with metal chelates of Iron (Fe) were synthesized. Fe (ANQ)₂ and Fe (ACNQO)₂ these metal complexes have been categorized by analytical modern techniques such as mass spectroscopy, elementary analysis, electronic spectra, FTIR, thermogravimetric analysis. These chelates are colored by nature and up to 700°C thermally stable. Ligand and metal chelate were tested for antimicrobial activity on fungi by Agar Well Diffusion, gram-positive and gram-negative bacteria. The results and Method are compared to Cisplatin as standard.

KEYWORDS : X-ray diffraction, Antimicrobial activity, 2-amino-1,4-naphthoquinone, 2-amino-3-chloro-1,4-naphthoquinone 1-oxime.

I. INTRODUCTION

The excellent biological applications which include antimalarial, antineoplastic agents larvicides, antitubercular, herbicide antibacterial, and fungicides having the compound like 2-amino-1,4-Naphthoquinones, 2-amino-3-chloro-1,4-Naphthoquinones have an active amino group in the 2-position. So, researches always focused on these molecules, derivatives, metal complexes. Iron (Atomic number 26, atomic weight 55.845, Electron configuration: [Ar] 3d⁶4s²) is silvery white metal having physical properties like malleable, ductile, soft in nature. Ligand 2-amino-1,4-naphthoquinone & 2-amino-3-chloro-1,4-naphthoquinone-1-oxime are ability to take the electron and form the stable complex on other hand to complete the Octet rule Fe is easily donate the two electrons in outermost valence shell, so it gives two electrons and form a stable complex, hence synthesis and characterization of these molecules were selected for research. Synthesis of ligand 2-amino-1,4-naphthoquinone & 2-amino-3-chloro-1,4-naphthoquinone-1-oxime are reported in various methods. This paper summarizes the synthesis and characterization with modern analytical tools of Fe metal chelates with ligands 2-amino-1,4-naphthoquinone-1-oxime & 2-amino-3-chloro-1,4-naphthoquinone, also microbiological activities are studied and reported.

II. MATERIALS USED FOR SYNTHESIS AND SYNTHESIS PROCESS

From 1, 4 naphthoquinones the ligand 2-amino-1,4-naphthoquinone was synthesized. 1,4 naphthoquinone which was supplied by Fluca chemicals and ligand 2-amino-3-chloro-1,4-naphthoquinone-1-oxime was synthesized from 2-amino-3-chloro-1,4-naphthoquinone which was supplied by Sigma-Aldrich.

2.1. Synthesis:

2.1.1 Synthesis of 2-amino-1,4-naphthoquinone from 1,4-naphthoquinone:

In 40 ml tetrahydrofuran and 10 ml of water forms 50 ml mixture in this mixture dissolved about 2.0 gm 1,4-naphthoquinone. To this solution 2.5 gm of Sodium Azide (Saturated) in 5ml water was added. 15ml of glacial acetic acid was added in the reaction mixture to acidify the reaction mixture to getting pH 2.6. This reaction mixture was stirred for 6 hours at room temperature. Evaporate the solution to obtain the red-brown solid. Purification and recrystallization were done with the help of Dichloromethane solvent.

2.1.2: Synthesis of 2-amino-3-chloro-1,4-naphthoquinone-1 oxime from 2-amino-3-chloro-1,4-naphthoquinone:

In 40 mL of water 5.0 gm of Sodium hydroxide was dissolved, to which slowly added about 4.1 gm of 2-amino-3-chloro-1,4-naphthoquinone. To this mixture a solution 40 ml distilled water with 2 gm hydroxyl amine hydrochloride was added. This entire mixture was stirred and warmed at 50-60°C for one hour on water bath. After one hour the reaction mixture was cooled to room temperature followed by cooled to about 5°C in an ice bath. Further to this solution cooled distilled water was added, which was subsequently neutralize with newly made dilute Hydrochloric acid. Dilute hydrochloride acid was added till

precipitation is formed. Filter the precipitate and washed with the cold water. Solid was obtained; the solid was dried on hot plate.

2.2.3 Synthesis of Fe chelate with 2-amino-1,4-naphthoquinone:

Ligand solution: Dissolved 0.346 gm of 2-amino-1,4-naphthoquinone (2×10^{-3} mole) in 20 mL of methanol and shake well to form a clear solution (Ligand solution), further reflux the solution in round bottom flask 2-neck for 15-20 minutes on water bath.

Metal solution: Dissolved 0.278 gm of Ferrous sulphate heptahydrate (1×10^{-3} mole) in 10 mL water in beaker, stirred well to form clear solution.

Drop wise metal solution was added in ligand solution under reflux condition maintained the temperature of solution about 60°C. Then this reaction mixture was heated for half hour under reflux condition on water bath. pH of solution was checked and further adjusted to 5.5 to 6.5 with dilute Ammonia solution. Reflux the reaction mixture, continue the heating and checked the pH of solution, if require the pH of solution was adjusted. Continued the reflux for two hours, After reflux, cool the solution to room temperature to form the solid and filtered the solution to get the solids. The solid was dried on hot plate.

2.1.4 Fe chelate with 2-amino-3-chloro-1,4-naphthoquinone-1-oxime:

Ligand solution: Dissolved 0.415 gm of 2-amino-3-chloro-1,4-naphthoquinone (2×10^{-3} mole) in 20 mL of methanol and shake well to form a clear solution (Ligand solution), further reflux the solution in round bottom flask 2-neck for 15-20 minutes on water bath.

Metal solution: Dissolved 0.278 gm of Ferrous sulphate heptahydrate (1×10^{-3} mole) in 10 mL water in beaker, stirred well to form clear solution.

Drop wise metal solution was added in ligand solution under reflux condition maintained the temperature of solution about 60°C. Then this reaction mixture was heated for half hour under reflux condition on water bath. pH of solution was checked and further adjusted to 5.5 to 6.5 with dilute Ammonia solution. Reflux the reaction mixture, continue the heating and checked the pH of solution, if require the pH of solution was adjusted. Continued the reflux for two hours, cool the solution at room temperature to form the solid and filtered the solution to get the solids. The solid was dried on hotplate.

III. INTERPRETATION OF ANALYTICAL DATA

3.1 Instrumental analysis:

The produced compound was subjected to structural clarification by elemental analysis, FTIR, Thermogravimetry analysis, X-ray diffraction, electronic spectra, Mass spectroscopy, and metal content by ICP-MS.

3.1.1 Fourier-transform infrared spectroscopic study:

FTIR studied was done to evaluation functional groups and confirmation of the structure. FTIR spectra was recorded on Perkin

Elmer instrument in KBr matrix with range 4000-400cm⁻¹. Typical functional groups identifications by IR spectroscopy of ligand and metal complex are summarized in Table-1.

Table-1: Typical functional groups by IR spectroscopy of ligand and metal complex,

Compound → Functional group ↓	Typical IR frequencies (cm-1) ↓	Experimental IR frequencies (cm-1)			
		ACNQO	ANQ	Fe (ACNQO) ₂	Fe (ANQ) ₂
M-O	700-500	--	--	526,, 556, 572	703, 696, 725
M-N	700-500	--	--	623, 647	649, 622
C-Cl	850-550 S	770	--	670S	--
C-H	900-700 B	861, 835, 811, 797, 788, 782, 770, 749, 722, 710	906, 874, 860, 850, 832, 821, 803, 798, 779, 754, 726	960	725, 757, 796, 876,
	1465-1365 B	1470, 1434, 1421, 1396, 1391, 1379, 1369, 1360	1478, 1442, 1419, 1395, 1365	1301, 1310, 1402, 1472	1342, 1377, 1420,
C=C	995-790 B	994, 967, 926, 861, 835, 811, 797	986, 919, 906, 874, 860, 850, 832, 821, 803, 798	960	877, 962, 988,
	1670-1600 S	1675, 1668, 1660, 1653, 1634, 1617, 1603	1662, 1615, 1609, 1605, 1600	1648, 1660	1660
C-N	1342-1266	1340, 1327, 1315, 1296, 1281, 1270,	1320, 1270	1247, 1280, 1301, 1310	1343, 1316, 1277
N-O	1550-1500 S	1497	--	1524, 1492	--
C=N	1690-1640 S	1675, 1668, 1660, 1653	--	1659, 1649	--
C=O	1870-1650 S	1864, 1830, 1675, 1668, 1660, 1653	1866, 1842, 1686, 1662	1660, 1648, 1832,	1844, 1681, 1660, 1925
N-H	3500-2800 S	3456, 3273, 3098	3398, 3390	3170	3232
O-H	3700-3584 B	3671, 3612	--	3650 broad	--

B=Bending, S=Stretching, M=Metal,

For IR frequency evaluation study, Gaussian 09 software was used. Experimental IR frequencies are matches with literature values.

3.1.2 UV spectrophotometric study (Electronic spectroscopy):

Electronic spectroscopic study was conducted to evaluate the UV spectrum of metal chelate and co-relation with ligand. In DMSO solvent UV spectra had been recorded on Shimadzu instrument for metal chelates and Methanol solvent is used for UV scan of ligand. In UV spectroscopy, a beam of UV-Visible light is passed through the

sample solution; a molecule absorbs the UV or visible radiations and goes to excited. The electron moves from occupied molecular orbital to unoccupied molecular orbital. Hence this spectroscopy is also called as electronic spectroscopy.

Energy transitions are observed as $\pi \rightarrow \pi^*$, $\sigma \rightarrow \sigma^*$, $\pi \rightarrow \pi^*$, $\sigma \rightarrow \pi^*$, $\sigma \rightarrow \sigma^*$.

Table 2: Experimental λ_{max} observed

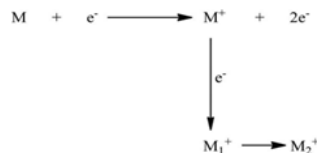
$\lambda \rightarrow$ Compound ↓	λ_{max1}	λ_{max2}	λ_{max3}
Fe (ACNQO) ₂	227 nm	274	310
Fe (ANQ) ₂	253 nm	354	--

Observed λ_{max} are due to energy transitions of metal complex.

3.1.3 Mass spectroscopic study:

Evaluation of mass to charge ratio of ions Mass spectroscopy is widely used. For evaluation of mass of molecules in pharmaceuticals industries these techniques are used.

Mass spectroscopy was used for evaluation of mass to charge ratio i.e., m/z of ligand and metal complex. In this technique sample is converted in vapour phase and high energy electron is bombarded to knock out an electron. Thus, a positively charged ion is produced which is called as molecular ion i.e., M⁺



Where,
M⁺ = molecular ion
M₁⁺ and M₂⁺ = Fragment ions

Further based on ionization M+1, M+2 ions formed.

The ions are analysed under the electric and magnetic field and verified to give a mass spectrum. Molecular weight of ligand and metal chelate was evaluated by shimadzu mass spectrometer instrument and results are reported in Table 3.

Table 3: Molecular weights of ligand and metal complex

Mass spectroscopic data → Compound ↓	Theoretical molecular weight	Experimental data		
		m/z	M+1	M+2
ACNQO	222.63	223	224	225
ANQ	173.17	174	175	--
Fe (ACNQO) ₂	499.08	500	501	502
Fe (ANQ) ₂	402.18	402	403	--

Above data is depicted that the experimental data correlates to Theoretical molecular weights.

3.1.4 Elemental analysis

To evaluate the elements like Carbon, Hydrogen and Nitrogen CHN analysis was done. In CHN analysis sample under goes the process of flashly burning and further get oxidized into simple compounds which are detected by thermal conductivity detector or infra-red spectroscopy. Analysis of ligand and metal complexes were carried out by Perkin Elmer instrument and data is reported in Table 4. The results compared with the theoretical values.

Table 4: Result of Elemental analysis (CHN)

CHN analysis → Compound ↓	Carbon (%)		Hydrogen (%)		Nitrogen (%)	
	Theoretical	Experimental	Theoretical	Experimental	Theoretical	Experimental
ACNQO	53.95	52.99	3.17	3.25	12.58	13.46
ANQ	69.36	69.36	68.67	4.07	4.13	8.09
Fe (ACNQO) ₂	48.13	44.41	2.42	2.87	11.23	11.05
Fe (ANQ) ₂	59.73	54.42	3.51	2.87	6.97	5.96

Results of elemental analysis represented that the experimental values

are good agreements with the theoretical values of ligand and metal complexes.

3.1.5 Metal analysis by ICP MS: Inductively coupled plasma mass spectrometry (ICP-MS) With the help of ICP MS % Metal content was analysed (Inductive couple plasma mass spectroscopy) and compared with the theoretical values and summarized the data Table 5.

Table 5: Result of Metal content by ICPMS

Metal content → Compound ↓	% Metal content	
	Theoretical	Experimental
Fe (ACNQO) ₂	11.19	11.01
Fe (ANQ) ₂	13.89	13.33

Experimental results of metal contents are matches with the theoretical contents.

3.1.6 Thermogravimetric study:

In TGA (thermogravimetric) analysis sample exposed to temperature and measures the properties like phase conversions, adsorption, absorptions or desorption.

All metal complexes were studied for TGA. The metal complexes were studied for % weight loss against the temperatures.

Fig-1 and 2 indicates the TGA for Cd (ACNQO)₂ and Cd (ANQ)₂.

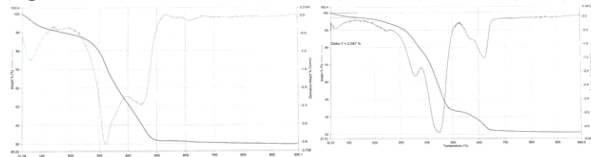


Fig-1: TGA for Fe (ACNQO)₂, Fig-2: TGA for Fe (ANQ)₂

The results of TGA indicated that there is thermal decomposition with weight loss. Fe (ACNQO)₂ shows the decomposition at higher temperature (about 500°C) where as Fe (ANQ)₂ shows decomposition at 400-630°C.

Thermogravimetric analysis data for Fe (ACNQO)₂ shows that first major weight loss was observed at the temperature about 300°C. Second weight loss was observed at temperature 500°C. Thermogravimetric analysis data for Fe (ANQ)₂ shows that first weight loss was observed at the temperature about 300°C; Second weight loss was observed at temperature 450°C. Third weight loss was observed at temperature 620°C.

3.1.7 X-ray diffraction study:

X-ray diffractions study is widely used to identify the crystalline / amorphous nature of compounds. Also, it is used for determination of crystalline form of different type of compounds. This technique has a vast application in pharmaceutical industry and academic fields.

Metal complexes were studied for X-ray diffraction and found that all ligands and metal complexes were observed as "Crystalline in nature". Fe (ACNQO)₂ & Cd (ANQ)₂ belong to Rhombohedral and hexagonal group respectively.

Fig 5. : Molecular Structure of ligand (ACNQO & ANQ)

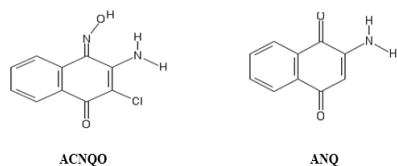
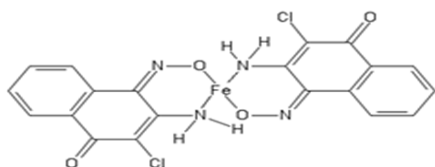
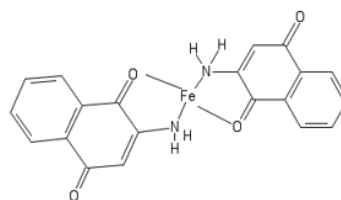


Fig 6: Molecular structure for Metal complexes (Fe (ACNQO)₂, Fe(ANQ)₂)



Fe (ACNQO)₂



Fe (ANQ)₂

3.1.8 Microbiological study

Microbiological activities of ligand and metal chelates was evaluated and compared with Cisplatin drug and data was summarized. Antimicrobial activity of test material by Agar Well Diffusion Method. Media: Nutrient Agar for Bacterial cultures and Chloramphenicol Yeast Glucose Agar for fungal cultures. Cultures against which activity was tested: Bacterial cultures: Bacillus subtilis NCIM 2063, Staphylococcus aureus NCIM 2079, Escherichia coli NCIM 2065, Proteus vulgaris NCIM 2813. Fungal Culture: Aspergillus niger NCIM 501, Candida albicans NCIM 3471. Incubation temperature: 37°C, Incubation time: 24 Hrs.

Procedure: Antibacterial activity of the test material was performed by Agar Well Diffusion Method. Specified organisms were prepared separately of a 24 hours old culture. Sterile nutrient agar plates and for fungal cultures sterile Chloramphenicol Yeast Glucose agar were prepared for bacterial culture. Each type of micro-organism a 0.2 ml of culture was spread with sterile swabs on different plates. Four or five wells were prepared in the agar with 8.0 mm cork borer on each plate. The test material was prepared in Dimethyl Sulfoxide (DMSO) as a stock solution. A 50 µl of the stock solution was added in each well. The stock solution was added. Cisplatin was used as standard (Std). The plates were incubated at 37°C for 24 hours. After incubation the zone of inhibition was measured in millimetre (mm). Antibacterial activity against specified organisms in terms of Zone of inhibition in mm calculated and compared. Data indicated that Cadmium metal complex with both ligands shows good antibacterial activities when compared with standard Cisplatin.

IV. CONCLUSIONS:

Ligand 2-amino-1,4-naphthoquinone (ANQ) and 2-amino-3-chloro-1,4-naphthoquinone 1-oxime (ACNQO) were synthesized and also metal chelates were synthesized. These ligands and metal complexes were characterized by elemental analysis, FTIR, Electronic spectra, Mass spectroscopy, Thermogravimetry, Differential scanning calorimetry, X-ray diffraction and metal content by ICPMS. The metal chelates were found crystalline in nature. Microbiological activities were found good than standard Cisplatin which was used as standard. All results of structure elucidations show good agreement with the theoretical values. Thermal analysis depicted that the metal chelates are decomposed with high temperatures above 6000C.

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REFERENCES

- Shubhangi V.Kulkarni, Raghunath G. Sarawadekar and Avinash B. Pawar 'Synthesis and vibrational study of 2-amino, 3-chloro 1,4-naphthoquinone by DFT' International Journal of Chem Tech Research Vol.10 No.15, pp 239-246, 2017.
- A.D. Mandke, N.R. Gonenar, R.G. Sarawadekar and A.B. Pawar, International Journal of Chem Tech Research, Vol.10 No.9, pp 291-298, 2017.
- Sharma U., Katoch Deepali, SoodSwati, Neeral Kumar, Bikram Singh, Thakur Archana and Gulati Aravind, Synthesis and antifungal activity of 2-Amino -1,4- naphthoquinone using silica supported perchloric acid(HClO4-SiO2) as a mild, recyclable and highly efficient heterogeneous catalyst, Indian J. Chem., 2013, 52B, 1431-1440.
- N.G. Clark, The fungicidal activity of substituted 1,4-naphthoquinones part II:alkoxy, phenoxy and acyloxy derivatives, Pestic. Sci. 15, 235-240 (1984).
- E.M. Hodnett, C. Wongwiechintana, W.J. Dunn 3rd, P. Marrs, Substituted 1,4-naphthoquinones vs. the ascitic sarcoma 180 of mice, J. Med. Chem. 1983, 26, 570-574.
- Prescott B., Potential antimalarial agents. Derivatives of 2-chloro-1,4-naphthoquinone, J. Med. Chem. 1969,12, 181-182
- Camara, C.A.; Silva, T.M.S.; Silva, T.G.; Martins, R.M.; Barbosa, T.P.; Pinto, A.C.; Vargas, M.D. Molluscicidal activity of 2-hydroxy-[1,4]naphthoquinone and derivatives. An. Acad. Bras. Cienc. 2008, 80, 329-334.