



## TRANSITION METAL CHELATES OF AZO LIGAND CONTAINING SALICYLIC ACID: SYNTHESIS, CHARACTERIZATION AND BIOLOGICAL EVALUATION

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### ABSTRACT

A series of M(II)-azo ligand chelates with various transition metal ions were synthesized. The azo ligand i.e. 5-((5-(furan-2-yl)-1,3,4-oxadiazol-2-yl)diazanyl)-2-hydroxybenzoic acid were synthesized by coupling reaction between diazonium salt of 2-amino-5-(furan-2-yl)-1,3,4-oxadiazol and salicylic acid. The structure of azo ligand was established by IR, mass, elemental analysis and NMR spectral studies. The reflectance spectral study and magnetic measurement studies reveals that octahedral geometry for synthesized metal chelates. All the synthesized compounds were screened for their antifungal activity, which shows potent inhibitory action against all employed fungal strains.

### KEYWORDS

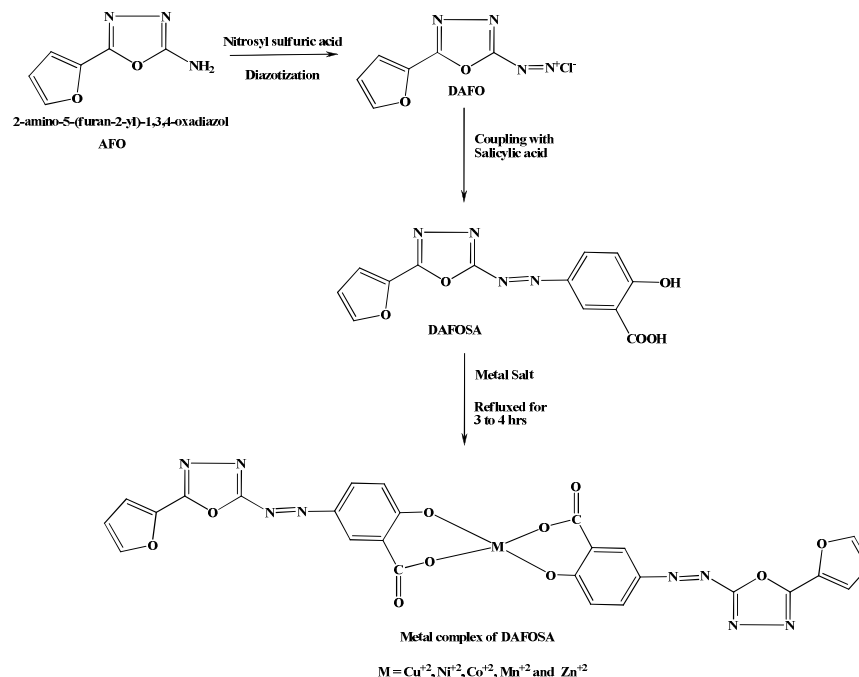
2-amino-5-(furan-2-yl)-1,3,4-oxadiazol, salicylic acid, diazotization reaction, spectral studies, Antifungal activity.

### INTRODUCTION

The azo compounds are applicable in various biological fields since several decades. Azo compounds are well used for their medicinal importance and pharmaceutical applications such as antibacterial, antifungal, antidiabetics, antiseptics, antineoplastics, antibacterial and antitumor. They are also involved in a many biological applications such as inhibition of DNA, RNA, carcinogenesis, protein synthesis and nitrogen fixation [1-5].

Recently, the study of coordination compounds of heterocyclic azo ligand has been made much progress. These compounds are known for their semi conducting catalytic properties, thermal stability, in protective coating, and also for some biological properties [6-8]. Such coordination compounds are mostly derived from bichelating ligands in which metal ions and chelating agents are coordinate alternatively. Azo derivatives of salicylic acid show good biological activities and also act as good metal chelating agent [9,10]. The area in which, the coordination compounds having different heterocyclic azo ligands have been reported by us in earlier articles. In extension of earlier work [11-13], the present article comprises the study of coordination compounds based on heterocyclic azo ligand containing salicylic acid with 1,3,4-oxidazole segment. Also the chelating and antifungal properties of

synthesized compounds were discussed in present communication. The synthetic routes are shown in **Scheme-1**.



**Scheme-1 Synthetic route for synthesized compounds**

## MATERIALS AND METHODS

2-amino-5-(furan-2-yl)-1,3,4-oxadiazol (**AFO**) was prepared by reported method [14]. All other chemicals and solvents used were of laboratory grade. The elemental contents were determined by Thermo Finigen Flash1101 EA (Italy) the metals were determined volumetrically by Vogel's method [15]. To a 100 mg chelate sample, each 1 ml of HCl, H<sub>2</sub>SO<sub>4</sub> and HClO<sub>4</sub> were added and then 1 g of NaClO<sub>4</sub> 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 **DAFOSA** was recorded on 400 MHz NMR spectrophotometer. Magnetic susceptibility measurement of the synthesized complexes was carried out on Gouy Balance at room temperature. Mercury tetrathiocyanatocobalate (II) Hg[Co(NCS)<sub>4</sub>] 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 and results are described in **Figure-1** [16].

### Synthesis of 5-((5-(furan-2-yl)-1,3,4-oxadiazol-2-yl)diazenyl)-2-hydroxybenzoic acid (**DAFOSA**):

2-amino-5-(furan-2-yl)-1,3,4-oxadiazol (**AFO**) (0.01mole) was dissolved in a mixture of H<sub>2</sub>SO<sub>4</sub> (12ml) and water (15ml) and cooled to 0°C in ice bath. To this solution a cold aqueous solution of sodium nitrite (0.04mole) was added. The diazonium salt solution of APO was filtered into a cooled solution of salicylic acid (0.01mole) at 0-5°C. The resulting solid azo dye was washed with water, dried and recrystallized from, MeOH. Yield: 72%, M.P.222-225°C (decompose) uncorrected.

**Analysis:**

## Elemental Analysis

	C%	H%	N%
$C_{13}H_8N_4O_5$ (300)			
Calculated:	52.01	2.69	18.66
Found :	51.9	2.6	18.6
IR Spectral Features:	3040	Ar C-H	
2950- 2850	Ar C-C		
( $cm^{-1}$ )	1632, 1570	Azo group	
	3425	-OH	
	1353	C-O-C	
	1710	CO of COOH	

NMR :  $\delta$  ppm 6.52-7.80 (m,6H, Ar-H), 5.27 (s,1H,OH), 11.35 (s,1H,OH of COOH).

**Synthesis of metal chelates of 5-((5-(furan-2-yl)-1,3,4-oxadiazol-2-yl)diazenyl)-2-hydroxybenzoic acid (DAFOSA):**

The metal chelates of **DAFOSA** with Cu(II), Ni(II), Co(II), Mn(II) and Zn(II) metal ions were prepared in two steps. All the metal chelates were prepared in an identical procedure.

**(i) Preparation of DAFOSA solution:**

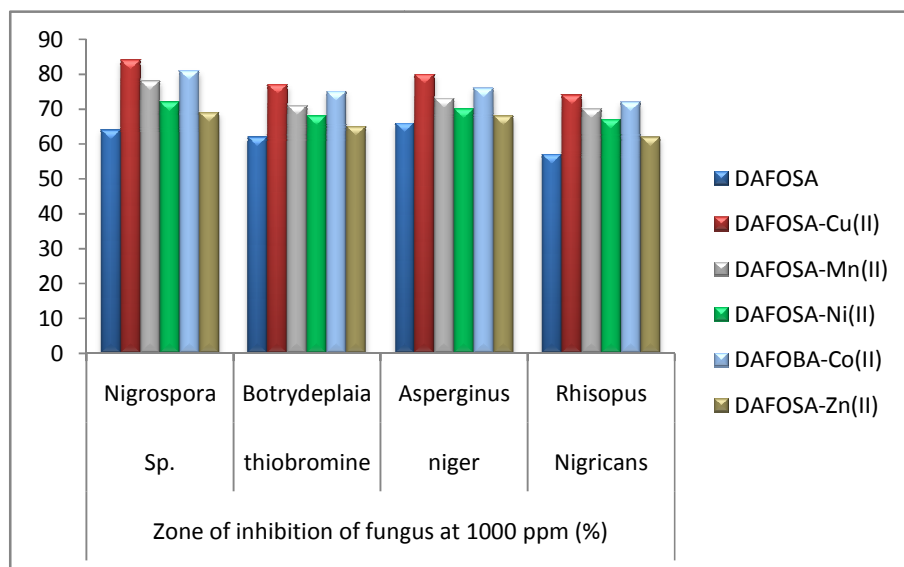
**DAFOSA** (0.05 mol) was taken in 500 ml beaker and formic acid (85% v/v) was added up to slurry formation. To this slurry water was added till the complete dissolution of **DAFOSA**. It was diluted to 100 ml.

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

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

Empirical Formula	Yield (%)	Elemental Analysis							
		C%		H%		N%		M%	
		Calcd	Found	Calcd	Found	Calcd	Found	Calcd	Found
<b>DAFOSA</b>	72	52.01	51.9	2.69	2.6	18.66	18.6	-	-
<b>(DAFOSA)<sub>2</sub>Cu(II)</b>	70	47.32	47.3	1.83	1.8	16.98	16.9	9.63	9.6
<b>(DAFOSA)<sub>2</sub>Ni(II)</b>	65	47.67	47.6	1.85	1.8	17.10	17.0	8.96	8.9
<b>(DAFOSA)<sub>2</sub>Co(II)</b>	67	47.65	47.6	1.85	1.8	17.10	17.0	8.99	8.9
<b>(DAFOSA)<sub>2</sub>Mn(II)</b>	64	47.94	47.9	1.86	1.8	17.20	17.1	8.43	8.4
<b>(DAFOSA)<sub>2</sub>Zn(II)</b>	62	47.18	47.1	1.83	1.8	16.93	16.9	9.88	9.8



**Figure-1 Antifungal activity of synthesized compounds**

## RESULTS AND DISCUSSION

All metal chelates are coloured, stable in air, and practically insoluble in water and most organic solvents but soluble in DMSO and DMF. The presence of -OH group at  $3624\text{ cm}^{-1}$  in the ligand is vanished in IR spectra of all metal chelates suggest coordination of metal with -OH group of 8-HQ. Also the all chelates shows lower value of CO compared to its parent ligand. The band at  $1710\text{ cm}^{-1}$  in azo ligand is attributed to the C=O of 8-HQ, which are shifted at  $\sim 1680\text{ cm}^{-1}$  in chelates. This shift suggests the coordination through the 8-HQ oxygen atom. The other bands such as azo group ( $1630, 1570\text{ cm}^{-1}$ ), C-O-C group ( $1353\text{ cm}^{-1}$ ), Ar C-H and Ar C-C are found almost identical in spectra of azo ligand and their metal chelates. The coordination further supported by weak bands found in the range  $520\text{-}550\text{ cm}^{-1}$  due to M-O bonding.

Reflectance spectra of Cu(II) chelate display two prominent bands. Low intensity broad band at  $14526\text{ cm}^{-1}$  corresponding to  ${}^2B_{1g} \rightarrow {}^1A_{1g}$  transition and high intensity band at  $23765\text{ cm}^{-1}$  due to symmetry forbidden ligand  $\rightarrow$  metal charge transfer transition. This supports the distorted octahedral Cu(II) chelate which was usually found in the  $d^9$  system. The magnetic moment value for Cu(II) chelate is 2.51 B.M., which is close to spin only value expected for an octahedral geometry. The reflectance spectra of the Ni(II) chelate exhibit bands at  $15545$  and  $22657\text{ cm}^{-1}$  assignable to  ${}^3A_{1g} \rightarrow {}^3T_{1g}(P)$  and  ${}^3A_{1g} \rightarrow {}^3T_{1g}(F)$ , transitions respectively. The value of the magnetic moment i.e. 3.65 B.M. may confirm the octahedral structure for Ni(II) chelate. For the Co(II) complex the reflectance spectra shows the bands at  $8955, 19067$  and  $23225\text{ cm}^{-1}$ , which may reasonably be assigned to  ${}^4T_{1g}(F) \rightarrow {}^4T_{2g}(F)$ ,  ${}^4T_{1g}(F) \rightarrow {}^4T_{2g}$  and  ${}^4T_{1g}(F) \rightarrow {}^4T_{2g}(P)$  transitions respectively of an octahedral geometry around the metal ion and shows the magnetic moment value of 4.68 B.M. The reflectance spectra of the Mn(II) chelate shows absorption bands at  $16632, 19525$  and  $23475\text{ cm}^{-1}$  assignable to  ${}^6A_{1g} \rightarrow {}^6A_{2g}$ ,  ${}^6A_{1g} \rightarrow {}^4T_{2g}$  and  ${}^6A_{1g} \rightarrow {}^4T_{1g}(PG)$  transitions, respectively, in an octahedral environment around the Mn(II) ion. The magnetic moment value of the Mn(II) chelate is 5.64 B.M. may be due to a high-spin  $d^5$ -system with an octahedral geometry [17-20].

The synthesized compounds were screened for their antifungal activities against employed strains using agar dilution method. Reviewing the antifungal results from **Figure-1**, the

chelates were found significantly active against all the fungal strains. Result obtained from **Figure-1** indicates all the synthesized compounds have been found to show significant activity. However, potency order is given as Cu(II)> Co(II)> Mn(II)> Ni(II)> Zn(II)> DAFOSA.

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