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# Physicochemical Studies of Metal Complexes and It's Biologically Active Ligands

**Ajay M Patil[1*], Atish R. Mehetre[2], Sandeep N. Sampal[3] and Sunil R. Mirgane[4]**

*[*1]Department of Chemistry, Pratishthan College Paithan, Aurangabad-431107, INDIA*
*[2]Department of Chemistry, Shivaji Arts, Commerce and Science College Kannad, Aurangabad-431103, INDIA*
*[3]Department of Kalikadevi Arts, Commerce and Science College, Shirur (Kasar), Beed-413249, INDIA*
*[4]Department of Chemistry, J E S College, Jalna-431203, INDIA*

*[*] Correspondence: E-mail: patilam4@gmail.com*

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**ABSTRACT: 1,3,4 Thiadiazole moieties containing Ligand and their metal complex of Cu(II), Zn(II), Cd (II) was prepared by using substituted Salicyladehyde and 5-amino-1,3,4-thiadiazole-2-thiol derivatives. The ligand and its metal complexes were characterized and analyzed by different spectroscopic techniques (UV, $^{1}$HNMR FT-IR, $^{13}$C-NMR, HRMS), Magnetic Susceptibility and molar conductance, elemental analysis. The transition metal complexes show moderate to excellent antifungal activity against *A. Niger* and *F. Oxysporum* and antibacterial activity against *S. aureus* and *B. subtilis* using Kirby-Bauer disc diffusion method. The synthesis of new potential metal based drug.**

Keywords: Antifungal activity; antibacterial activity; Metal Complexes; Salicyladehyde; Thiadiazole.

**INTRODUCTION:** Schiff base is a condensation of aldehyde with primary amine important in organic synthesis and pharmacological applications[1]. 1,3,4 Thiadiazole is important compound because of their biological, pharmaceutical, and analytical applications[2]. 1,3,4 Thiadiazole acts as a ligands. Enhance biological activity by forming complexes[3]. The Most of the heterocyclic moieties has biological activity that depends on their orientation and their Structure[4].The aldehyde are ortho-substituted with (-OH) hydroxyl group, which acts as a bidentate donor ligand for transition metal ions[5].Schiff base is very important because of their structural resemblance and flexibility with naturally occurring biological and chemical substance.Imine group >C=N- (azomethine) also helps to determine the transformation and recemisation in biological systems[6].during last few years more intensely focus on Variable Thiadiazole derivative because of their potent biological properties like anti-inflammatory[7], analgesic[8],antituberculosis[9], antihypertensive[10],antimicrobial[11],anticonvulsants[12], antioxidant[13], antifungal[14], anticancer[15], antidepressant[16]. We now report the synthesis and characterization and biological analysis of 1, 3, 4 Thiadiazole containing ligand and its Cu (II), Zn (II) and Cd (II) Metal Complexes.

## MATERIALS AND METHODS:

**Experimental:** All the chemical of analytical grade. All salts are metal nitrates i.e. $Cu(NO_3)_2.3H_2O$,$Zn(NO_3)_2$ $.6H_2O$,$Cd(NO_3)_2.4H_2O$ were purchased from Sigma-Aldrich and used without further purification. 3,5-dichloro-2-hydroxybenzaldehyde and 5-amino-1,3,4-thiadiazole-2-thiol from Sigma-Aldrich and Alfa Aesar used without further purification. Distilled Ethanol used for synthesis of metal complexes and ligand diethyl ether (Sigma-Aldrich). IR Spectra recorded on Perkin Elmer Spectrometer in range 4000-400 $cm^{-1}$ KBr pellets. $^{1}$H and $^{13}$CNMR Spectra were recorded on BRUKER AVANCE III HD NMR 500 MHz spectrophotometer. Room Temperature magnetic moments by Guoy's methodin B.M.Electronic Spectra using DMSO on Varian Carry 5000 Spectrometer. Molar Conductance measurements in dry DMSO having $1\times10^{-3}$ concentration on Systronics conductivity bridge at room temperature. Elemental analysis (C,H,N) were carried out by using perkin Elmer 2400 elemental analyser. Mass Spectra were recorded on Bruker IMPACT HD.

**Biological Activity:** Schiff Base and their metal complexes evaluated in vitro their antibacterial activity against two Gram-Positive bacteria,viz, *B. Subtilis*; *S.*

*aureus*, Two fungal strains *A. niger and F. oxysporum* by Kirby-Bauer disc diffusion method [17].The fungal and bacterial strains sub-cultured on PDA and Nutrient Agar. The stock solution (1 mg $mL^{-1}$) was prepared in DMSO solution. The stock solution again diluted by using sterilized water to dilution in 500 ppm. The bacteria were subculture in agar medium and disc were kept incubated for 37°C at 24 hrs. The standard antibacterial drug Miconazole and Ciprofloxacin was also screen under same condition for comparison. Activity was measure and calculated by zone of inhibition (mm) surrounding discs. The experimental value compare with standard drug value Miconazole for the Antifungal activity and Ciprofloxacin for the antibacterial activity.

**Synthesis of Schiff base Ligand:** The mixture of 1:1 3,5-dichloro-2-hydroxybenzaldehyde (1.91g,0.01mol) with 5-amino-1,3,4-thiadiazole-2-thiol (1.33g, 0.01 mol) dissolved in ethanol. Then add Few drops of glacial acetic acid was added .The resultant mixture stirred for 3-4 hrs the colored precipitate of Ligands was obtained. Then wash with Ethanol recrystallized with Ethanol and Ether then dried in air. The purity of compound was checked by TLC using Silica Gel method (Fig.1).

**Synthesis of Metal Complexes:** The metal complexes were prepared by mixing of $Cu(NO_3)_2.3H_2O$,$Zn(NO_3)_2.6H_2O$,$Cd(NO_3)_2.4H_2O$ with (30 ml) ethanolic solution of Ligand in (metal: ligand) 1:2 ratio. The resulting mixture refluxed on water bath for 5-6hr.A colored product obtain washed with ethanol, filtered, and recrystalised with ethanol (Fig.2).

**RESULTS AND DISCUSSION:** The ligand (Fig.1) and its transition metal complexes of 2,4-dichloro-6-(5-mercapto-1,3,4-thiadiazol-2-yl)imino methyl phenol are stable at room temperature in solid state.The ligand is soluble in organic solvent DMSO,DMF and metal complexes is easily soluble in DMSO.The synthesized complexes having 1:2 metal to ligand stoichiometric ratio. The physical and analytical data shown in Table 1.Spectral data shows formation of ligand and its metal complexes.

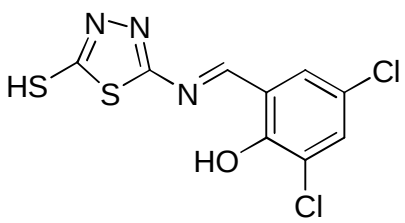


**Figure1: Structure of Schiff base Ligands.**

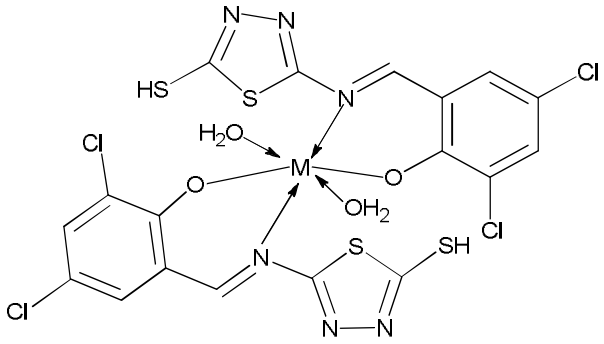


**Figure 2: Proposed Structures of metal complexes M: Cu (II),Zn (II) and Cd (II).**

**IR Spetra**: The IR spectra of 2, 4-dichloro-6-(5-mercapto-1, 3,4-thiadiazol-2-yl)imino methyl phenol (HL) Schiff base ligand and its complexes are listed in Table 2.The Infrared Spectra of the complexes are compared with the free ligand in order to determine the coordination sites that may be involved in a chelation. There are some important peaks in the spectra of the ligand, which is different in metal complexes helps to prove that formation of metal complexes IR spectra of 2,4-dichloro-6-(5-mercapto-1,3,4-thiadiazol-2-yl)imino methyl phenol (HL) Schiff base ligand having the most characteristic bands at 3316-3330$cm^{-1}$ ν(O-H), 1638-1652 cm-1 ν(C=N, azomethine) and 1258-1272 $cm^{-1}$ ν(C-O). The ligand spectra showed bands at 3314-3304 and 1340-1350 $cm^{-1}$ due to the deformation and stretching of the phenolic -OH[18] these are not present in the spectra of the complexes indicates the deprotonation of the hydroxyl group(-OH) and co-ordination through phenolic oxygen. The band 1,640–1,650 $cm^{-1}$ due to the azomethine (-C=N-) group of the Schiff bases have shifted to lower frequency (1,612–1,636 $cm^{-1}$) after complexation, indicating the bonding of nitrogen of the azomethine group (-C=N-) to the metal ions and this can be explained by the donation of electrons from the nitrogen to the empty d-orbital of the metal ion present in the complexes[19,20]. The phenolic λ(C–O) stretching vibration that appeared at 1,260–1268 $cm^{-1}$ in Schiff bases shift towards higher frequency (20–32 $cm^{-1}$) in the metal complexes. This shift confirms that involvement of oxygen in the C–O–M bond. The appearance of broad bands around (3,375–3,460 $cm^{-1}$) in the spectra of complexes may be due to water molecules coordinated to metal in the metal complexes[21]. New bands appearing in the low frequency range 528–575 cm-1 and 464–482 $cm^{-1}$ are due to ν(M–O) and ν(M–N), respectively. The ν(C–S–C) at 75–758 $cm^{-1}$ of the Thiadiazole ring remain unchanged suggested that Thiadiazole group not coordinate to the metal ion by

neither sulphur nor nitrogen atom of Thiadiazole ring of ligand [22].

**$^{1}$H NMR and $^{13}$C NMR Spectra:** The $^{1}$H-NMR spectra of ligand were recorded in Dimethyl Sulphoxide solution using TMS as a standard (Table 3). The spectra of ligand shows singlet at δ 7.19-7.90 ppm due to aromatic proton while azomethine (-C=N-) proton resonate at singlet δ 8.90 ppm the phenolic -OH has signal singlet at δ 11.22 ppm and Thiadiazole containing (–SH) group shows singlet at δ 13.44 ppm[23] .$^{13}$C-NMR of Ligand**,** peak appeared at δ158-164 ppm imine group (-C=N-),peak 187.52 ppm Due to carbon sulphur C-SH bonding in Thiadiazole.121.96-135.53 ppm because of aromatic carbon,158-172 ppm peak because of (Table 3) Ar-OH group[24].

**Mass Spectra**:Mass Spectra of ligands shows peak at m/z 305 which is M+H peak at 100% intensity this peak support to the structure formation of ligand.

**Magnetic Susceptibility and molar conductance:** The magnetic susceptibility seen at room temperature.Synthesized metal complexes of Copper (II) is paramagnetic in nature, Zinc(II) and Cadmium (II) is Diamagnetic in nature. Molar conductance of metal complexes was observed at room temperature at $1\times10^{-3}$M DMSO Solution. The studies show negligible molar conductance value in range 8-12 $ohm^{-1}cm^{2}mol^{-1}$results shows in table 4. it is observed that all metal complexes are non-electrolytic in nature[25,26].

**Electronic absorption Spectra**: The electronic spectral data of the ligands and metal complexes in DMSO sol. are given in Table 4. The geometry and nature of the ligand field around the metal ion has been conclude from the electronic spectral data of metal complexes and ligand. The band appearing at 220-312 is due to transition of benzene ring of the ligand. The other band due to free ligands 320-382 nm due to transition for phenolic -OH and azomethine moieties(-C=N-).These band shifts longer wavelength due to formation of ligand to metal complexes[27,28] The spectra of the complexes display band 424-500 nm assigned to charge transfer transition from ligands to metal[23].The magnetic moment value for Cu(II) complexes is 1.80 B.M is near to octahedral complex spectra shows two band at 360 nm and 560 nm shows that octahedral geometry of Cu (II) complex[29].Electronic spectra of Zn (II) complexes shows band 265 nm,370-430 nm did not show d-d transition suggest octahedral geometry[30].Elctronic spectra of Cd(II) shows two peak at 325 nm and 307-360 ligand to metal donation with diamagnetic suggest octahedral geometry[31].

**Antimicrobial activity:** Antimicrobial activity In vitro of the ligand and their corresponding metal complexes on two gram positive *bacteria S. aureus and B.Subtlis* two fungi *A. niger* and *F. Oxysporum* was carried out. All of the tested compounds showed good to moderate biological activity against test microorganism. The bactericidal and fungicidal investigation data of the ligand and Metal complexes are summarized in Table 5. The investigation shows that Cu(II) shows more The bactericidal and fungicidal activity than Zn (II) and Cd (II) Complexes and Ligand hence activity of metal complexes increases due to chelation increase in delocalization of π electron on chelating ring and enhance the penetration of complexes in lipid membrane and blocks the binding site enzymes of microorganism there are other factors i.e,solubility,lipophilicity/hydrophilicity,Conductivity and M-L bond length that increases the activity of complexes[32-37].

**Table 1: Analytical Data and physical properties of ligand and its metal complexes.**

| Comp. | Empirical Formula | Mol. Wt. | Color | M.P (°C) | Yield (%) | Elemental Analysis/ Found (Calc.) | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | C | H | N | S | M |
| Ligand(HL) | $C_9H_5Cl_2N_3OS_2$ | 306 | Dark Yellow | 118$_o$C | 72% | 35.89 (35.30) | 1.69 (1.65) | 13.63 (13.72) | 20.21 (20.94) | -- |
| Cu(II) Complex | $C_{18}H_{12}Cl_4CuN_6O_4S_4$ | 709 | green | >300 | 69% | 30.10(30.45) | 1.78(1.70) | 11.80(11.84) | 17.98 (18.07) | 8.85 (8.95) |
| Zn(II) Complex | $C_{18}H_{12}Cl_4ZnN_6O_4S_4$ | 711 | Lemon Yellow | >300 | 71% | 30.41 (30.37) | 1.65(1.70) | 11.75(11.81) | 18.12(18.02) | 9.23(9.19) |
| Cd(II) Complex | $C_{18}H_{12}Cl_4CdN_6O_4S_4$ | 758 | Gray | >300 | 68% | 28.40(28.49) | 1.65 (1.59) | 11.02(11.08) | 17.02 (16.90) | 14.35(14.81) |

**Table 2: Infrared Spectra of the Schiff base and Complexes in $Cm^{-1}$.**

| Compound | νOH/$H_2O$ | νC-O | νC=N | νM-N | νM-O | νC-S-C | ν-C=N-N=C | νN-N |
|---|---|---|---|---|---|---|---|---|
| Ligand | 3319 | 1265 | 1645 | ___ | ___ | 752 | 1467 | 1028 |
| Cu(II) Complex | 3410 | 1280 | 1633 | 470 | 569 | 758 | 1433 | 1028 |
| Zn(II) Complex | 3401 | 1290 | 1610 | 480 | 575 | 756 | 1436 | 1033 |
| Cd(II) Complex | 3460 | 1274 | 1611 | 482 | 555 | 755 | 1443 | 1030 |

**Table 3: $^1$H NMR Signals (δ, ppm) and their assignments.**

| Compound | $^1$H NMR Signals (δ,ppm) and their assignments |
|---|---|
| Ligand(HL) | 11.22 (s,1H,Ar-OH), 8.90(s,1H,CH=N),7.19-7.90 (s,2H,Ar-CH), 13.44 (s,1H,SH) |

**Table 4: Electronic spectral Magnetic and Molar conductance Data.**

| Compounds | Wavelength in nm | Magnetic moment μeff (BM) | Molar conductance ($ohm^{-1}$ $cm_2$ $mol^{-1}$) |
|---|---|---|---|
| Ligands(HL) | 280,372 | -- | 6.68 |
| $C_{18}H_{12}Cl_4CuN_6O_4S_4$ | 270-320,360,560 | 1.80 | 8.2 |
| $C_{18}H_{12}Cl_4ZnN_6O_4S_4$ | 265,370-430 | Diamagnetic | 10.2 |
| $C_{18}H_{12}C_{l4}CdN_6O_4S_4$ | 265,307-360 | Diamagnetic | 12 |

**Table 5: Antimicrobial activity of ligand and its Metal Complexes.**

| Compounds | Antibactrial Activity | | | | Antifungal Activity | | | |
|---|---|---|---|---|---|---|---|---|
| | *S.aureus* | | *B.subtilis* | | *A.niger* | | *F.oxysporum* | |
| | Diameter of inhibition Zone in mm | % Activity Index | Diameter of inhibi-tion Zone in mm | % Activity Index | Diameter of inhibi-tion Zone in mm | % Activity Index | Diameter of inhibi-tion Zone in mm | % Activity Index |
| | 500ppm | 500ppm | 500ppm | 500ppm | 500ppm | 500ppm | 500ppm | 500ppm |
| Ligands(HL) | 22 | 65 | 21 | 64 | 20 | 65 | 18 | 67 |
| Cu | 26 | 76 | 25 | 76 | 23 | 74 | 22 | 81 |
| Zn | 21 | 62 | 23 | 70 | 18 | 58 | 16 | 59 |
| Cd | 20 | 59 | 22 | 67 | 19 | 61 | 14 | 52 |
| Ciprofloxacin (Standard) | 34 | 100 | 33 | 100 | -- | -- | --- | -- |
| Micona-zole(Standard) | -- | -- | -- | | 31 | 100 | 27 | 100 |

**CONCLUSION:** In the present work our efforts to synthesize and characterize some novel metal Complexes from conventional methods. These Ligands and Metal Complexes were characterized by physico-chemical and spectral analyses. The synthesized Schiff base ligand binds metal ions in bidentate manner,with N and O donor site of azomethine-N and deprotonated phenolic-O.the antimicrobial activity data showed that Most of the metal complexes is more biologically active compared to those parent ligand against all pathogenic Bacteria and Fungi. Such studies may help to decrease emerging problems in drug resistance in health sciences over the world.

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