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# Synthesis, Characterization and Antimicrobial Properties of Transition Metal Complexes of Aniline and Sulphadiazine Schiff Bases as Mixed Ligands

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## ABSTRACT

*Novel Cu(II), Mn(II), Fe(II) and Zn(II) metal complexes of Schiff bases were synthesized from the condensation reaction between salicylaldehyde and aniline (L1) and sulphadiazine (L2) and characterized by FTIR and UV-Visible spectroscopy. Conductivity, melting point and solubility measurements were also carried out. It was observed that these complexes were non-toxic, non-electrolytic and stable solids. The IR and results showed that the involvement of the azomethine nitrogen in coordination with the metals. The complexes were also screened against various microorganisms; they showed strong potency against the micro-organisms.*

**Keywords:** Schiff bases; Aniline; Sulphadiazine; Transition metal complexes; Antimicrobial properties

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## INTRODUCTION

Coordination compounds of sulphur, oxygen and nitrogen have been reported for their antimicrobial activities [1]. Most of these compounds are formed from Schiff bases, which are fundamental materials for synthesis of various Schiff base ligands used as chiral auxiliaries in asymmetric synthesis. The development of these ligands resulted in an enhanced research activity in the field of coordination chemistry. The chemistry of Schiff bases has led to important discoveries in the chemical and medical industries. Multi-dentate complexes of Iron and Nickel showed high activities of ethylene oligomerization and polymerization [2-4]. Also, they are reported to show a variety of biological activities including antibacterial, antifungal, anticancer and herbicidal activities [5,6]. Metal complex Schiff bases have also been used in oxidation reactions [6] owing to their ability to coordinate (as ligands), with various metals and stabilize them in various oxidation states, enabling them as useful in catalytic transformations [7,8], catalytic activity in hydrogenation of olefins and transfer of amino acids [9], their ability to form complexes with major metals. Transition metal complexes of Schiff bases derived from salicylaldehyde have been studied and reported for antitumor, antibacterial and antifungal activities [10].

Spectroscopic techniques like the Fourier-Transform Infra-red (FTIR) spectroscopy [11-14], Ultra-violet/visible spectroscopy (UV-Vis) [11-14], proton and carbon-13 nuclear magnetic resonance spectroscopy ($^{1}$H-and $^{13}$C-NMR) [10,13,14], magnetic moment measurements [13], thermographic analysis (TGA) [14], molar conductivity [13], magnetic susceptibility measurements [13] and elemental analysis [13,14] have been used in characterizing metal complexes. Antimicrobial studies reveal the potency of synthesized compounds against pathogens, this is necessary as the search for new drugs that combat drug resistant pathogens remains ongoing [3,7,15].

This project was aimed at synthesizing metal complexes of Cu(II), Mn(II), Fe(II) and Zn(II) ions using sulfadiazine and aniline mixed ligands, to characterize the synthetized transition metal complexes as well as the complexing agents (ligands) using characterization techniques such as FTIR, UV/Vis spectroscopic and to determine the medical value of the synthesized ligands and their respective transition metal complexes by carrying out necessary antimicrobial studies.

## MATERIALS AND METHODS

All reagents and solvents [sulfadiazine, aniline, salicyaldehyde, ethanol, dionized water and the salts of Cu(II), Mn(II), Fe(II) and Zn(II)] are of analytical grade and they were used as supplied without further purification.

### Preparation of Ligands

### Synthesis of Schiff base ligand (n-salicylideneaniline) using aniline and salicyaldehyde

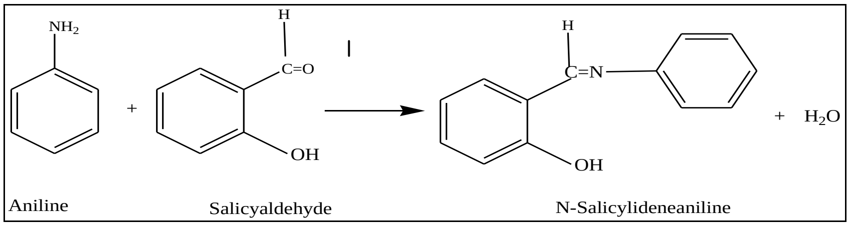

**Figure 1: Synthesis of Aniline Schiff Base Ligand, L1**

The ligand was prepared using the same methods as in Maurya and co-workers [16].

An ethanolic solution of salicyaldehyde was prepared by dissolving 4 ml of salicyaldehyde (0.04 mol) in 40 ml of ethanol and it was added to an ethanolic solution of aniline prepared by dissolving about 4 ml of aniline (0.04 mol) in 30 ml ethanol. The resulting solution was refluxed with stirring for 4 hours, the solution turned yellow after about 30 min of stirring; it was cooled in an ice bath and filtered to obtain a yellow solution which turned oily after concentration on water bath. The oily yellow solution was left overnight to obtain crystals of the Schiff base. The crystal was washed with ethanol and dried in a desiccator (Figure 1).

### Synthesis of sulphadiazine Schiff base ligand using salicyaldehyde and sulphadiazine ligand

### Equation of reaction

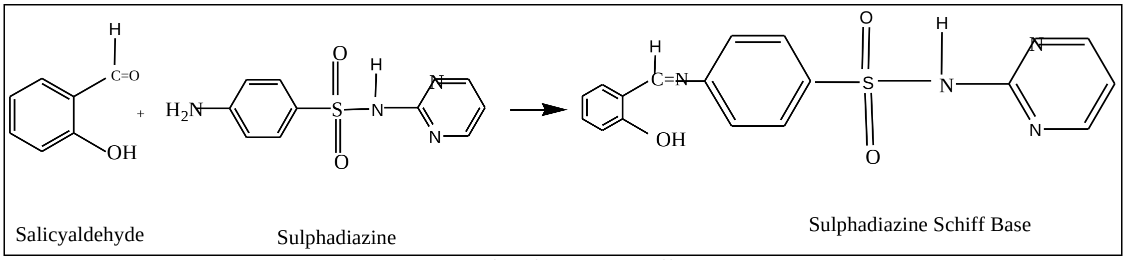

**Figure 2: Synthesis of Sulfadiazine Schiff Base Ligand, L2**

An ethanolic solution of salicyaldehyde (0.04 mol) was prepared by dissolving about 4 ml of salicyaldehyde in 40 ml of ethanol and it was added dropwisely to an ethanolic solution of sulphadiazine which was prepared by dissolving 10.01 g (0.04 mol) of sulphadiazine in 40 ml ethanol (the sulphadiazine was stirred till it dissolves). The resulting solution was stirred under reflux for 6 hours during which the solution turned yellow. Then the solution was cooled on an ice bath and yellow crystals formed were filtered out, washed with ethanol and dried over silica gel in a desiccator (Figure 2).

### Synthesis of the metal complexes

0.001 mol (0.3544 g) sulphadiazine Schiff base was dissolved in 15 ml ethanol in a beaker (the sulphadiazine Schiff base solution was stirred with heating using a magnetic stirrer to help it dissolve), 0.001 mol (0.1973 g) of aniline Schiff base was also dissolved in 15 ml of ethanol in a beaker, then the aniline solution was added in a drop wise manner to an hot ethanolic solution of the metal salt (0.1596 g $CuSO_4$, 0.1615 g NiSO4 followed by the addition of the sulphadiazine Schiff base solution also in a drop wise manner. The resulting mixture was refluxed with stirring for 5 hours. The mixture was then allowed to cool and the precipitate formed was filtered and dried over silica gel in a dessicator (Figure 3).

## Equation of reaction

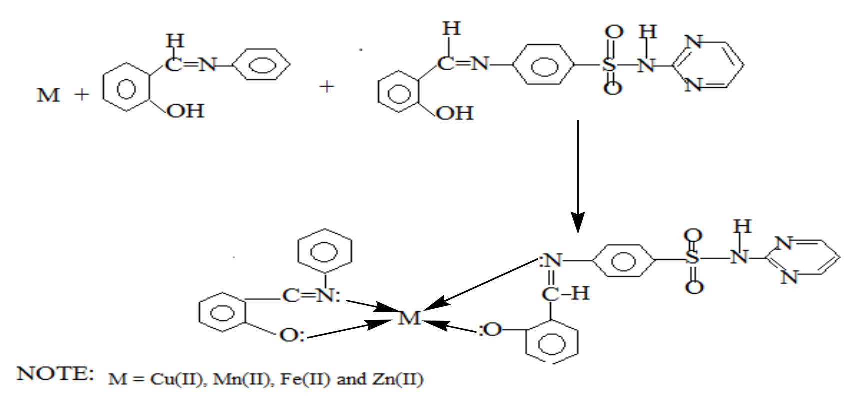

**Figure 3: Synthesis of Metal Complexes**

## Evaluation of Antibacterial Activity

The investigated compounds were tested, *in vitro* against *Pseudomonas aeruginosa* and *Staphylococcus aures*. This was carried out by the disk diffusion techniques, using agar nutrient as the medium. The stock solutions (5 and 10 Mm) of new compounds were prepared by dissolving the compounds in DMSO. In a typical procedure, a well was made on the agar medium inoculated with microorganisms. The well was filled test solution using a micropipette and the plate was incubated for 24 h at 37°C. During this period, the test solution diffused and the growth of the inoculated microorganism was affected. The results were recorded by measuring the growth inhibition surrounding the disk.

# RESULTS

All synthesized ligands and their corresponding metal complexes show appreciable solubility in dimetyl sulphoxide **(**DMSO) and partially soluble in other organic solvents such as diethyl ether, hexane, methanol among others.

## **Conductivity Measurement** (Table 1)

**Table 1: The conductivities and melting points of the Schiff base ligands and the metal complexes**

| Compound/complex | Conductivity (× $10^{-6}$) (µseccm$^{-1}$) | Melting points (°C) |
|---|---|---|
| N-Salicylideneaniline (L1) | 17 | 125 |
| N-Salicylidenesulphadiazine (L2) | 20 | 250 |
| [CuL1L2]$SO_4$ | 18 | 242 |
| [MnL1L2] | 16 | 253 |
| [FeL1L2]$SO_4$ | 20 | 252 |
| [ZnL1L2]$Cl_2$ | 22 | 245 |

## **IR Spectroscopy** (Table 2)

**Table 2: IR results showing the bands of schiff base ligands and metal complexes and their corresponding functional groups**

| Compound/Complex | υC=N | υC-O | υ$SO_{2(as)}$ | υN-H | υ$SO_{2(s)}$ |
|---|---|---|---|---|---|
| N-Salicylideneaniline (L1) | 1613 | 1273 | - | - | - |
| N-Salicylidenesulphadiazine (L2) | 1618 | 1277 | 1338 | 3030 | 1187 |
| [CuL1L2]$SO_4$ | 1616 | 1276 | 1336 | 3030 | 1187 |
| [MnL1L2] | 1649 | 1261 | 1324 | 3038 | 1151 |
| [FeL1L2]$SO_4$ | 1649 | 1261 | 1324 | 3038 | 1151 |
| [ZnL1L2]$Cl_2$ | 1620 | 1278 | 1337 | 3029 | 1164 |

### Electronic Absorption Spectra

The UV-Vis electronic spectra of the ligands and corresponding metal complexes were recorded in ethanol between 200-600 nm at room temperature. The electronic spectra of the synthesized metal complexes and the ligands are shown in Table 3.

**Table 3: The electronic spectra of the ligands and synthesized metal complexes and their corresponding transitions**

| **Compound/Complex** | **$\lambda_{max}$ value (nm)** | **Assignment** |
|---|---|---|
| **N-Salicylideneaniline (L1)** | 224<br>264<br>298<br>338 | ICT<br>π-π*<br>π-π*<br>n-π* |
| **N-Salicylidenesulphadiazine (L2)** | 230<br>270<br>344 | ICT<br>π-π*<br>n-π* |
| **[CuL1L2]$SO_4$** | 232<br>274<br>342 | ICT<br>π-π*<br>n-π* |
| **[MnL1L2]** | 232 | ICT |
|  | 272 | π-π* |
|  | 352 | n-π* |
| **[FeL1L2]$SO_4$** | 268 | π-π* |
| **[ZnL1L2]$Cl_2$** | 232 | ICT |
|  | 272 | π-π* |
|  | 346 | n-π* |

### Antimicrobial Studies

The antimicrobial studies of the free ligands and their metal complexes were recorded in dimethyl sulphoxide against ten bacteria and ten fungi isolates, using Muller Hinton agar media. The results are given in the Tables 4-7.

**Table 4: Results of zones of inhibition in (mm) of the compounds against various bacteria isolates**

| **Test organisms** | **L1** | **L2** | **[CuL1L2]$SO_4$** | **[MnL1L2]** | **[Fe(L1)(L2)]$SO_4$** | **[ZnL1L2]$Cl_2$** | **Ampicillin** | **DMSO** |
|---|---|---|---|---|---|---|---|---|
| *Escherichia coli* | 13 | 10 | 17 | 11 | 7 | 12 | 15 | NI |
| *Pseudomonas aeruginosa* | 11 | NI | 14 | NI | 8 | 8 | 12 | NI |
| *Proteus vulgaris* | 12 | 9 | 12 | NI | NI | 10 | 11 | NI |
| *Klebsiella pneumonia* | NI | 8 | 12 | 9 | NI | 11 | 11 | NI |
| *Salmonella thypii* | NI | 11 | 13 | 11 | NI | 10 | 11 | NI |
| *Bacillus cereus* | NI | 10 | 12 | 9 | 8 | 9 | 10 | NI |
| *Staphulococcus aureus* | NI | 13 | 15 | 10 | 8 | 10 | 12 | NI |
| *Streptococci feacalis* | NI | 12 | 16 | NI | 7 | 10 | 12 | NI |
| *Bacillus subtillis* | 8 | 10 | 11 | 9 | 8 | 8 | 10 | NI |
| *Staphylococcus epidermidis* | 14 | 11 | 13 | 10 | 7 | 7 | 9 | NI |

Key: NI=No inhibition, L1=N-Salicylideneaniline, L2=N-Salicylidenesulphadiazine

**Table 5: Results of the zones of inhibition in (mm) of the compounds against various fungi isolates**

| Test organisms | L1 | L2 | [CuL1L2]SO$_4$ | [MnL1L2] | [Fe(L1)(L2)]SO$_4$ | [ZnL1L2]Cl$_2$ | Mycotine | DMSO |
|---|---|---|---|---|---|---|---|---|
| *Aspergillus niger* | 13 | 15 | 14 | NI | NI | 11 | 11 | NI |
| *Candida albicau* | 16 | 14 | 17 | 12 | 9 | 12 | 15 | NI |
| *Mucor hiemalis* | 11 | 13 | 12 | 9 | NI | 9 | 11 | NI |
| *Fusarium oxysporium* | 11 | 13 | NI | 9 | NI | NI | 9 | NI |
| *Candida krusei* | 14 | 14 | 15 | 11 | 10 | 11 | 14 | NI |
| *Rhizopus stolonifer* | 11 | 12 | NI | 9 | 9 | 9 | 13 | NI |
| *Aspergillus flavus* | 12 | 11 | 13 | NI | NI | 9 | 10 | NI |
| *Mternaria infectoria* | 10 | 11 | 14 | 9 | 9 | 9 | 12 | NI |
| *Aspergillus fumigutus* | 11 | 10 | 14 | 9 | 9 | 11 | 11 | NI |
| *Fusarium solani* | 10 | 10 | 12 | 9 | 9 | 10 | 10 | NI |

Key: NI=No inhibition, L1=N-Salicylideneaniline, L2=N-Salicylidenesulphadiazine

**Table 6: Minimum inhibitory concentration (mg/ml) (bacteria)**

| Name of test organisms | L1 | L2 | [CuL1L2]SO$_4$ | [MnL1L2] | [Fe(L1)(L2)]SO$_4$ | [ZnL1L2]Cl$_2$ | Ampicillin |
|---|---|---|---|---|---|---|---|
| *Escherichia coli* | 10 | 20 | 5 | 20 | 20 | 20 | 5 |
| *Pseudomonas aeruginosa* | 10 | NI | 5 | NI | 20 | 20 | 10 |
| *Proteus vulgaris* | 10 | 20 | 10 | NI | NI | 20 | 5 |
| *Klebsiella pneumonia* | NI | 20 | 10 | 20 | NI | 20 | 5 |
| *Salmonella thypii* | NI | 20 | 10 | 20 | NI | 20 | 5 |
| *Bacillus cereus* | NI | 20 | 10 | 20 | 20 | 20 | 5 |
| *Staphulococcus aureus* | NI | 10 | 5 | 20 | 20 | 20 | 5 |
| *Streptococci feacalis* | NI | 20 | 5 | NI | 20 | 20 | 5 |
| *Bacillus subtillis* | 20 | 20 | 10 | 20 | 20 | 20 | 5 |
| *Staphylococcus epidermidis* | 10 | 20 | 10 | 20 | 20 | 20 | 5 |

Key: NI=No inhibition, L1=N-Salicylideneaniline, L2=N-Salicylidenesulphadiazine

**Table 7: Minimum inhibitory concentration (mg/ml) (fungi)**

| Name of test organisms | L1 | L2 | [CuL1L2]SO$_4$ | [MnL1L2] | [Fe(L1)(L2)]SO$_4$ | [ZnL1L2]Cl$_2$ | Mycotine |
|---|---|---|---|---|---|---|---|
| *Aspergillus niger* | 10 | 10 | 10 | NI | NI | 20 | 10 |
| *Candida albicau* | 10 | 20 | 20 | 20 | 20 | 20 | 5 |
| *Mucor hiemalis* | 20 | 20 | 20 | 20 | NI | 20 | 10 |
| *Fusarium oxysporium* | 20 | 20 | NI | 20 | NI | NI | 10 |
| *Candida krusei* | 20 | 20 | 20 | 20 | 20 | 20 | 5 |
| *Rhizopus stolonifer* | 20 | 20 | NI | 20 | 20 | 20 | 10 |
| *Aspergillus flavus* | 20 | 20 | 20 | NI | NI | 20 | 10 |
| *Mternaria infectoria* | 20 | 20 | 20 | 20 | 20 | 20 | 10 |
| *Aspergillus fumigutus* | 20 | 20 | 20 | 20 | 20 | 20 | 10 |
| *Fusarium solani* | 20 | 20 | 20 | 20 | 20 | 20 | 10 |

Key: NI=No inhibition, L1=N-Salicylideneaniline, L2=N-Salicylidenesulphadiazine

## DISCUSSION

### Physical Parameters

The results suggested that the complexes are basically non-polar compounds. They dissolve in solvents with relatively low dielectric constant. The molar conductivity measurement which was taken at 0.001g/20ml in DMSO also support this, their conductivities are also appreciably low, indicating that they are non-electrolytes. The Schiff base ligands are soluble in DMSO. The metal complexes are soluble in methanol and DMSO, partially soluble in hexane and diethyl ether, insoluble in chloroform. Their melting points are within the range of 242°C -253°C, indicating that they are all thermally stable up to 240°C.

## Spectroscopic Studies

### Infra-red spectroscopy

The infrared spectra for the compounds were taken in the range 500-4000 $cm^{-1}$, indicating the regions of absorption due to the υO-H, υC=N, υN-H, υC-O, υ$SO_{2(}$s and as) for symmetric and asymmetric bands, υM-N etc. vibrations. Stretching modes found in the ligands and their complexes have been identified. Comparison of the metal complex spectra with those for the free ligands themselves was most useful in rationalizing the infrared results and assigning of various stretching modes.

The IR spectra of the ligands showed an intense band in the region 1613-1618 $cm^{-1}$, assigned to υC=N. This band shows a shift in the spectra of all the metal complexes, indicating that azomethine nitrogen participated in coordination with metals. The elevation in stretching frequency may be tentatively attributed to an increase of the C=N bond order as a result of the M-N bond formation in the complexes. The bands appearing between 1520 and 1600 $cm^{-1}$ are been assigned to aromatic υC=C while those appearing at 1323-1338 $cm^{-1}$ have been assigned to υ$SO_2$ asymmetric. Phenolic C-O stretching band is found in the range 1261-1277 $cm^{-1}$. Further evidence for bonding by nitrogen and oxygen atoms is provided by far IR spectra of complexes.

All the IR data suggest that the metal was bonded to the Schiff bases through the phenolic oxygen and the imino-nitrogen. On the basis of these studies presented in Table 3, the positive shift of IR vibration of free ligand on complexation confirms that the ligands act as N-donor and O-donor bases.

### UV-visible spectroscopy

The Schiff base ligand shows two type of transitions, π-π* and n-π*. These transitions are also present in the spectra of the complexes, but they shifted to lower intensity, confirming the co-ordination of the ligand to the metal ion. The lower wavelengths for the Schiff bases (224 nm-230 nm). These values were assigned to *π-π* transition* of Schiff base. The longer wavelengths (264 nm-298 nm) are assigned to n-π*. The wavelength range 296-390 nm is assigned to intra charged transfer (ICT). The electronic absorption spectral bands of the complexes are summarized in Table 3.

### Antimicrobial studies

The ligands and their metal complexes were positive against some of the selected bacteria and fungi isolates at various concentrations respectively. The two ligands and copper complex show high antifungal activities at MIC of 20 mg/ml with three exceptions from the ligands in which their activities were at 10 mg/ml. Their antibacterial activities are not as profound as that of the antifungal activities; the L1 ligand is active against only 5 of the bacteria, and L2 ligand against 9 bacteria. The complexes were active against 7 bacteria respectively. The result shows that the complexes have lower antibacterial activities than the free ligands, except for Cu(II) complex. The highest activity from the complexes was that of the copper complex against *Escherichia coli* (17 mm), *Streptococci faecalis* (16 mm), *Staphylococcus aureus* (15mm), *Pseudomonas aeruginosa* (14 mm), *Staphylococcus epidermidis* (13 mm) and *Salmonella thypii* (13 mm), all higher than that of the common antibacterial compound (Ampicillin). It also gave better inhibitory results than ampicillin against other bacteria. L2 gave better inhibitory potentials than ampicillin against *Staphylococcus aureus* and *Staphylococcus epidermidis.* L1 gave better inhibition than ampicillin only against *Staphylococcus epidermidis* and *Proteus vulgaris*.

The result also shows that the complexes have lower antifungal activities than the free ligands, except for Cu(II) complex. The highest activity from the complexes was that of the copper complex against *Candida albicau* (17mm), *Candida Krusei* (15 mm), *Aspergillus fumigutus* (14 mm), *Aspergillus niger* (14 mm) and *Mternaria infectoria* (14 mm), all higher than that of the common antifungal compound (Mycotine). It also gave better inhibitory results than mycotine against other fungi. L1 gave better inhibitory potentials than mycotine against all the fungi except against *Rhizopus stolonifer* and *Mternaria infectoria.* L2 gave better inhibitory potentials than mycotine against all the fungi except against *Candida albicau, Rhizopus stolonifera, Mternaria infectoria* and *Aspergillus fumigutus*.

## CONCLUSION

The bidentate Schiff base ligands are coordinated to the metals through the phenolic oxygen that is deprotonated and the azomethine nitrogen. Also, the ligands coordinate to the metal complex through the same atoms, sulphate ions are still retained in the inner sphere of the metal complex causing an octahedral geometry for the complex. The new complexes are chelate complexes, hence; very stable. In their antimicrobial studies, the complexes are strongly active against most of the selected bacteria and fungi.

Due to the strong potency of some of the ligands and complexes against some of the selected test pathogens, the possibility of using the synthesized ligands and their metals complexes as modern-day drugs to combat drug resistant diseases or pathogens by pharmaceutical industries is recommended.

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