

# METAL COMPLEXES OF SCHIFF BASE DERIVED FROM SULFAMERAZINE: SYNTHESIS, SPECTRAL CHARACTERIZATION, THERMAL AND BIOLOGICAL ACTIVITIES

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## ABSTRACT

New Schiff base ligand and its chelates of cobalt, nickel and copper derived from sulfamerazine and 5-bromo-2-hydroxy benzaldehyde have been synthesised. Microanalytical data, molar conductance and magnetic susceptibility values have been obtained and IR,  $^1\text{H}$  NMR,  $^{13}\text{C}$  NMR, UV-Visible, CV and EPR spectral studies have been carried out to suggest the tentative structure for the complexes. The antibacterial activities of the ligand and its metal complexes were also evaluated and some of them were found to show promising activity.

**Keywords:** Sulfamerazine, synthesis, conductance, condensation, biological activity.

## 1. INTRODUCTION

Biologically relevant metal complexes have several requirements in terms of their synthetic design. Various biological aspects of the metal based drugs/ligands entirely depend on the ease of cleaving the bond between the metal ion and the ligand<sup>1</sup>. As a consequence, it is essential to understand the relationship between ligand and the metal in biological system. Historically, medicinal inorganic chemistry is rich in metal based drugs including Paul Erlich's organoarsenic compound for the treatment of syphilis, antiarthritic gold preparations etc. The pharmacological activity of metal complexes is highly dependent on the nature of the metal ions and the donor sequence of the ligands because different ligands exhibit different biological properties. The wide range of coordination numbers and geometries, available redox states of the metal ion and ligand itself offers variety of reactivities. N-substituted sulfonamides are still the most widely used antibacterial agents in the world and it is well documented that toxicological

and pharmacological properties are enhanced when sulfonamides are administered in the form of their metal complexes. The potential therapeutic activities<sup>2-5</sup> of sulfadruugs and their metal complexes have spurred the study of the coordination chemistry of these ligands. The principle subject of this study is to synthesise a new series of sulfonamide based Schiff base metal complexes, which were further investigated for their biological activities.

## 2. EXPERIMENTAL

### 2.1. Materials and Measurements

All chemicals and reagents used were of analytical reagent grade (AR) except ethanol which was purified prior to use<sup>6</sup>. Conductance measurements were carried out using Elico conductivity bridge and dip type conductivity cell. Elemental analyses were recorded with a Elemental Vario EL III model. IR spectra were studied as KBr pellets on a SHIMADZU 8000 FTIR spectrophotometer in the range of 4000-400 $\text{cm}^{-1}$ . UV-Vis-NIR spectra were recorded on a Varian, Cary 5000

spectrophotometer in the range of 175-3300nm.  $^1\text{H}$  and  $^{13}\text{C}$ -NMR spectra of compounds were recorded with a Bruker Spectrospin Avance DPX-400 using TMS as internal standard and  $\text{DMSO-d}_6$  as solvent. Magnetic susceptibility measurements were carried out on solid compounds using Gouy balance at room temperature. Melting points of the ligands and their metal complexes were determined by open capillary method using Silicon bath electric melting point apparatus and uncorrected. Thermal analyses (TG and DTG) were carried out by using Perkin Elmer, Diamond TG/DTA. The metal contents of the complexes were determined by ICP-AES technique using Thermo electron IRIS INTERPID II XSP DUO model. The EPR studies were carried out in Bruker EMX Plus model at room temperature. The cyclic voltammetric studies were performed using Versa STAT MC model. Cyclic voltammograms of complexes in the concentration of  $10^{-3}\text{mol L}^{-1}$  in DMF were recorded in an electrochemical cell, equipped with a Pt,Ag/AgCl and glassy carbon (GC) as counter, reference, and working electrode respectively. Tetra butyl ammonium perchlorate (TBAP) was used as supporting electrolyte and its concentration was  $10^{-1}\text{mol L}^{-1}$ . In vitro antibacterial and antifungal activity were carried out at Periyar college of Pharmaceutical sciences, Tiruchirappalli.

## 2.2. Synthesis of the Schiff base

The Schiff base ( $\text{HL}^1$ ) was synthesised by the condensation of sulfamerazine(0.7mmol) and 5-bromo-2-hydroxy benzaldehyde(0.7mmol) in equimolar ratio by dissolving in ethanol. The solution was refluxed for three hours. The precipitates formed was cooled and collected by suction filtration. It was washed thoroughly with ethanol (80% yield).

## 2.3. Synthesis of the metal complexes

To a hot DMF-ethanolic solution of the ligand (0.2mmoles) an ethanolic solution of metal acetate (0.1mmole) was mixed keeping ligand-metal ratio 2:1. The reaction mixture was then refluxed for 6 hours. The precipitate formed was cooled and collected through suction filtration and washed with small amount of ethanol and dried.

## 3. RESULTS AND DISCUSSION

The structure of the Schiff base  $\text{HL}^1$  is established by elemental analysis, FT-IR,  $^1\text{H}$ ,  $^{13}\text{C}$  NMR spectroscopy, UV-Visible and molar conductance measurements. The Schiff base was further used for the complexation reaction with  $\text{Co}^{2+}$ ,  $\text{Ni}^{2+}$  and

$\text{Cu}^{2+}$  metal ions using the respective metal acetates. The newly synthesised Schiff base ligand and its complexes are brightly coloured and very stable at room temperature. They are insoluble in organic solvents like ethanol, methanol and chloroform and soluble in solvents like DMF, Dioxane and DMSO. The analytical data of all the compounds are presented in Table 1. They show very low molar conductance indicating their non-electrolytic nature<sup>6</sup>. The analytical data indicates 1:2 metal ligand stoichiometry.

The IR spectra (Table -2) of the ligand shows a medium broad band centered at  $3379\text{cm}^{-1}$  due to intra-molecular hydrogen bonded  $\nu(\text{O-H})$ <sup>7</sup>. In the spectra of metal complexes, this band disappears indicating deprotonation and the involvement of the phenolic oxygen in bonding with metal ions. The strong band at  $1628\text{cm}^{-1}$  is assigned to the azomethine  $\nu(\text{C=N})$  stretching vibration observed in the ligand and this band undergoes a shift ( $\sim 20\text{cm}^{-1}$ ) in the complexes indicating the participation of the azomethine nitrogen in coordination<sup>8</sup>. The characteristic bands due to sulfonamide oxygen, amido nitrogen are almost unaffected in the metal complexes. The new bands observed in the region of  $450\text{--}488\text{cm}^{-1}$  and  $572\text{--}578\text{cm}^{-1}$  in the metal complexes can be attributed to  $\nu(\text{M-O})$ <sup>9</sup> and  $\nu(\text{M-N})$ <sup>10</sup> bonds respectively.

$^1\text{H}$  NMR spectra of the free ligand was recorded in  $\text{DMSO-d}_6$ . The formation of Schiff base ligand is revealed by the appearance of the azomethine proton ( $-\text{CH=N}-$ ) signal at 8.918 ppm<sup>11</sup>. The ligand exhibit signals for methyl protons, aromatic protons,  $-\text{NH}$  group and phenolic  $-\text{OH}$  group at 2.32, 6.8 to 8.05, 11.6 and 12.43ppm respectively<sup>12</sup>. In  $^{13}\text{C}$  spectrum of ligand, the appearance of singlet at 159.2 ppm confirms the presence of azomethine carbon<sup>13</sup> and the carbon atoms of methyl group and aromatic groups were found to be in their expected region.

The electronic spectra of the ligand and its complexes are summarized in the Table 2. The ligand shows two bands in UV visible region. The bands at  $36,232\text{cm}^{-1}$  and  $28,901\text{cm}^{-1}$  may be due to  $\pi \rightarrow \pi^*$  and  $n \rightarrow \pi^*$  transition<sup>14</sup>. The electronic spectrum of the  $\text{Co(II)}$  complex gives three bands at  $15,987\text{cm}^{-1}$ ,  $17,345\text{cm}^{-1}$  and  $22,564\text{cm}^{-1}$ . The bands observed are assigned to the transition  $^4\text{T}_{1g}(\text{F}) \rightarrow ^4\text{T}_{2g}$ ,  $^4\text{T}_{1g}(\text{F}) \rightarrow ^4\text{A}_{2g}(\text{F})$  and  $^4\text{T}_{1g}(\text{F}) \rightarrow ^4\text{T}_{2g}(\text{P})$  respectively suggesting that there is an octahedral geometry around  $\text{Co(II)}$ <sup>15</sup>. The magnetic moment value of 4.69 B.M. for  $\text{Co(II)}$  complex at room temperature suggests the high spin six-coordinated octahedral arrangement

around the metal ion<sup>16,17</sup>. The Ni (II) complex has the magnetic moment value of 3.71 B.M. suggests tetrahedral structure<sup>18</sup>. The diffused reflectance spectrum shows three bands at 4083 cm<sup>-1</sup>, 6002 cm<sup>-1</sup> and 16077 cm<sup>-1</sup> which are assigned to  $^3T_1 \rightarrow ^3T_2 (v_1)$ ,  $^3T_1 \rightarrow ^3A_2 (v_2)$  and  $^3T_1 (F) \rightarrow ^3T_1 (P) (v_3)$  respectively<sup>19</sup>. The  $\mu_{\text{eff}}$  value of the Cu(II) complex is 1.89B.M. which indicates a distorted octahedral geometry<sup>20,21</sup> around the metal ion. Only one broad band is observed at 16,285 cm<sup>-1</sup> in the electronic spectrum of the Cu (II) complex and is assigned to  $^2E_g \rightarrow ^2T_{2g}$  transition which is in conformity with octahedral geometry<sup>22</sup>.

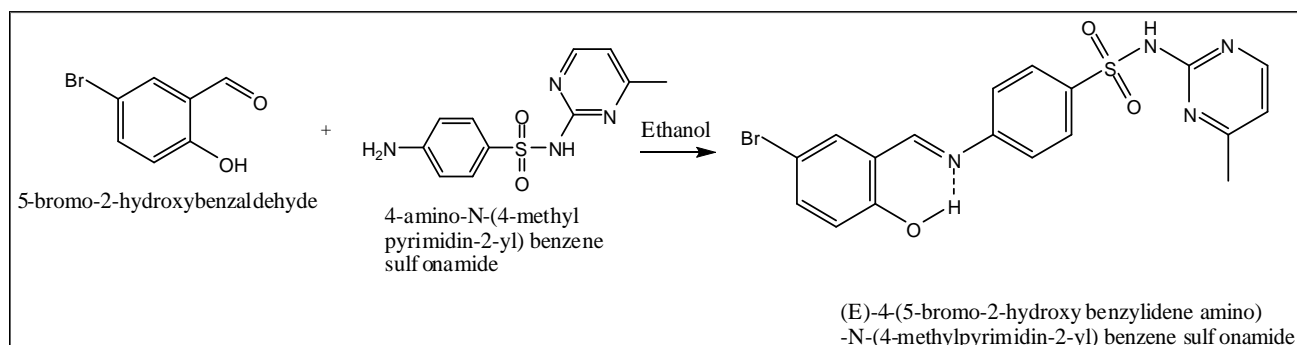
The ESR spectra of copper complex provide information about the metal ion environment. The ESR spectra of the Cu(II) complex recorded at room temperature is shown in Figure 3. The spectrum exhibit an isotropic signal without any hyperfine splitting, with  $g_{\text{iso}} = 2.11$  due to the tumbling motion of the molecules. The value obtained in the present study when compared to the g value of a free electron, 2.0023, indicates an increase in the covalent nature of the bonding between the metal ion and ligand molecule<sup>23</sup>.

The TGA curve for copper complex is given in Figure-4. The thermogram of copper shows a weight loss of 3.61% (calculated 3.62%) in the temperature range 85-115°C attributed to loss of two molecules of lattice water<sup>24</sup>. The second weight loss was noticed in the temperature range 180-210°C. The corresponding weight loss observed 3.65% (calculated 3.62%) is consistent with the elimination of two coordinated water molecules<sup>25</sup>. The third weight loss is in the temperature range of 240-470°C (observed 40.89%, calculated 44.91%) is due to the

decomposition of one molecule of the ligand. The fourth weight loss starts in the temperature range of 480°C may be due to the step by step decomposition of another molecule of the ligand and metal. A similar trend was observed for cobalt complex (Figure-5) also which contains no lattice water, but it contain two coordinated water molecules inside the sphere. The thermogram (Figure-6) of nickel shows no weight loss up to the temperature of ~300°C which infers the absence of lattice/ coordinated water. The weight loss occurs near 317°C and 394°C may be due to the step by step decomposition of the two molecules of the ligand.

#### 4. BIOLOGICAL ACTIVITY

The synthesised ligand and its metal complexes were tested against two gram-positive (*S. aureus*, *Bacillus subtilis*) and two gram-negative (*E.coli*, *Klebsiella sp.*) bacterial strains by disc diffusion method. The results were compared with those of the standard drug ciproflaxin. All the complexes showed a wide range of activities and the nickel complex is significantly active against all bacterial strains whereas cobalt complex shows less activity. The antifungal activity of the compounds was tested against *A.niger* and *Candida albicans* and the standard used was nystatin. Majority of the synthesised compounds showed good antifungal activity against these fungal strains (Table-3). When compared to the cobalt and copper complexes, nickel complex exhibits promising activity. It is observed that the antimicrobial activities of all the complexes are found to be increased after chelation.



Scheme 1: Preparation of ligand

**Table 1: Analytical data of the Schiff base and its metal (II) complexes**

| Compound No. | Molecular formula   | M.Wt. | M.Pt.°C | Yield % | Elemental analysis Calculated (Observed) % |                |                  |                |                |
|--------------|---|-------|---------|---------|--|----------------|------------------|----------------|----------------|
|              |   |       |         |         | C  | H              | N                | S              | M              |
| 1            | HL <sup>1</sup> / C <sub>18</sub> H <sub>15</sub> BrN <sub>4</sub> O <sub>3</sub> S   | 447   | 207     | 80      | 48.33<br>(48.18)                           | 3.38<br>(3.79) | 12.52<br>(12.52) | 7.16<br>(7.33) | -              |
| 2            | [Co(L <sup>1</sup> ) <sub>2</sub> (H <sub>2</sub> O) <sub>2</sub> ]/<br>[Co(C <sub>18</sub> H <sub>14</sub> BrN <sub>4</sub> O <sub>3</sub> S) <sub>2</sub> (H <sub>2</sub> O) <sub>2</sub> ]   | 987   | 256     | 49      | 43.78<br>(44.04)                           | 3.27<br>(3.15) | 11.35<br>(11.6)  | 6.5<br>(6.17)  | 5.97<br>(5.7)  |
| 3            | [Ni(L <sup>1</sup> ) <sub>2</sub> ]/<br>[Ni(C <sub>18</sub> H <sub>14</sub> BrN <sub>4</sub> O <sub>3</sub> S) <sub>2</sub> ]   | 951   | 271     | 52      | 45.45<br>(44.97)                           | 2.97<br>(2.52) | 11.78<br>(11.56) | 6.74<br>(6.28) | 6.17<br>(6.33) |
| 4            | [Cu(L <sup>1</sup> ) <sub>2</sub> (H <sub>2</sub> O) <sub>2</sub> ] <sub>2</sub> H <sub>2</sub> O/<br>[Cu(C <sub>18</sub> H <sub>14</sub> BrN <sub>4</sub> O <sub>3</sub> S) <sub>2</sub> (H <sub>2</sub> O) <sub>2</sub> ] <sub>2</sub> H <sub>2</sub> O | 992   | 251     | 66      | 43.58<br>(43.87)                           | 3.25<br>(3.51) | 11.29<br>(11.05) | 6.46<br>(6.62) | 6.40<br>(6.12) |

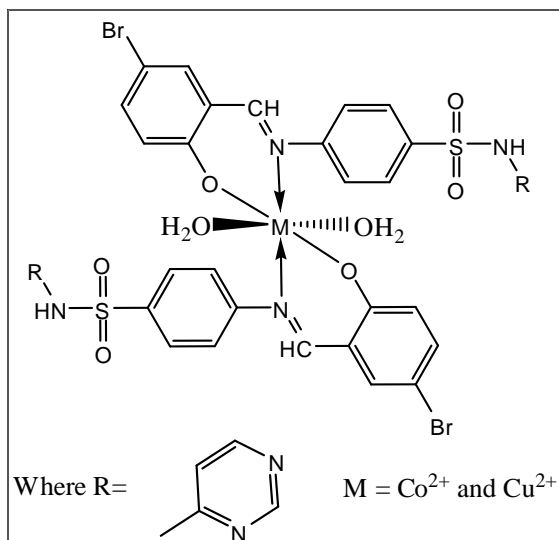
**Table 2: Conductivity, magnetic and spectral data of the Schiff base and its metal (II) complexes**

| Comp<br>ound<br>no | $\Omega m$<br>( $\Omega^{-1}$<br>cm <sup>2</sup><br>mol <sup>-1</sup> ) | BM<br>( $\mu_{eff}$ ) | $\Lambda_{max}$ (cm <sup>-1</sup> ) |   | Infrared spectral data (cm <sup>-1</sup> ) |                |                          |                |                |                |                |                             |
|--------------------|---|-----------------------|-------------------------------------|---|--|----------------|--------------------------|----------------|----------------|----------------|----------------|-----------------------------|
|                    |   |                       |                                     |   | N<br>(C=N)                                 | $\nu$<br>(C-O) | $\nu$ (SO <sub>2</sub> ) | $\nu$<br>(S-N) | $\nu$<br>(O-H) | $\nu$<br>(M-N) | $\nu$<br>(M-O) | $\nu$<br>(H <sub>2</sub> O) |
| 1                  | -   | -                     | 36,232<br>28,901                    | $\pi \rightarrow \pi^*$<br>$n \rightarrow \pi^*$  | 1628                                       | -              | 1330,<br>1157            | 969            | 3379           | -              | -              | -                           |
| 2                  | 9.96  | 4.69                  | 22,564<br>17,345<br>15,987          | <sup>4</sup> T <sub>1g</sub> (F) → <sup>4</sup> T <sub>2g</sub> (P)<br><sup>4</sup> T <sub>1g</sub> (F) → <sup>4</sup> A <sub>2g</sub> (F)<br><sup>4</sup> T <sub>2g</sub> (F) → <sup>4</sup> T <sub>2g</sub> | 1606                                       | 1367           | 1330,<br>1155            | 974            | -              | 827            | 488            | 3481                        |
| 3                  | 9.83  | 3.71                  | 16,077<br>6,002<br>4,083            | <sup>3</sup> T <sub>1</sub> (F) → <sup>3</sup> T <sub>1</sub> (P)<br><sup>3</sup> T <sub>1</sub> → <sup>3</sup> A <sub>2</sub><br><sup>3</sup> T <sub>1</sub> → <sup>3</sup> T <sub>2</sub>                   | 1610                                       | 1342           | 1329,<br>1153            | 975            | -              | 827            | 491            | -                           |
| 4                  | 9.94  | 1.89                  | 16,285                              | <sup>2</sup> E <sub>g</sub> → <sup>2</sup> T <sub>g</sub>   | 1606                                       | 1381           | 1323,<br>1159            | 975            | -              | 825            | 459            | 3408                        |

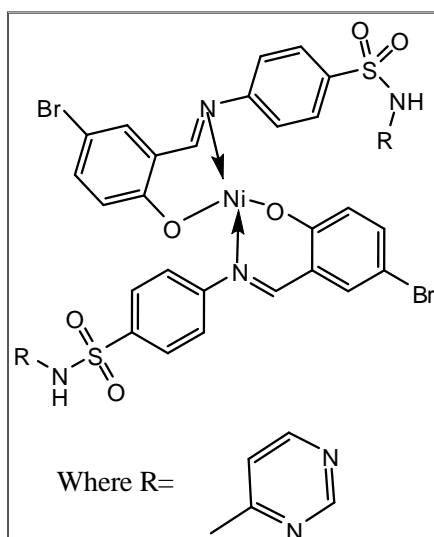
**Table 3: Antimicrobial activity of HL<sup>1</sup> and its complexes**

| Compound  | Gram +ve                 |                   | Gram -ve |                        | Fungi   |                  |
|---|--------------------------|-------------------|----------|------------------------|---------|------------------|
|   | Staphylococcus<br>aureus | Bacillus subtilis | E.coli   | Pseudomonas aeruginosa | A.niger | Candida albicans |
| HL <sup>1</sup>   | 16                       | 13                | 16       | 15                     | 11      | 12               |
| [Co(L <sup>1</sup> ) <sub>2</sub> (H <sub>2</sub> O) <sub>2</sub> ]                               | 13                       | 15                | 16       | 16                     | 17      | 16               |
| [Ni(L <sup>1</sup> ) <sub>2</sub> ]   | 20                       | 23                | 16       | 20                     | 23      | 19               |
| [Cu(L <sup>1</sup> ) <sub>2</sub> (H <sub>2</sub> O) <sub>2</sub> ] <sub>2</sub> H <sub>2</sub> O | 16                       | 20                | 20       | 16                     | 20      | 16               |
| Standard  | 35                       | 40                | 38       | 35                     | 35      | 32               |

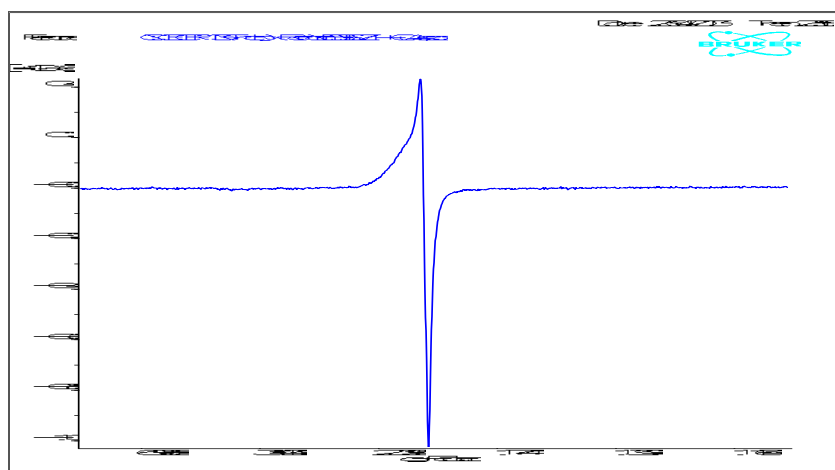
Standard - Ciprofloxacin 5 $\mu$ g/disc for bacteria ; Nystatin 100 units / disc for fungi;



**Fig. 1: Structure of octahedral complexes**



**Fig. 2: Structure of Nickel (tetrahedral) complex**



**Fig. 3: EPR spectrum of copper complex**

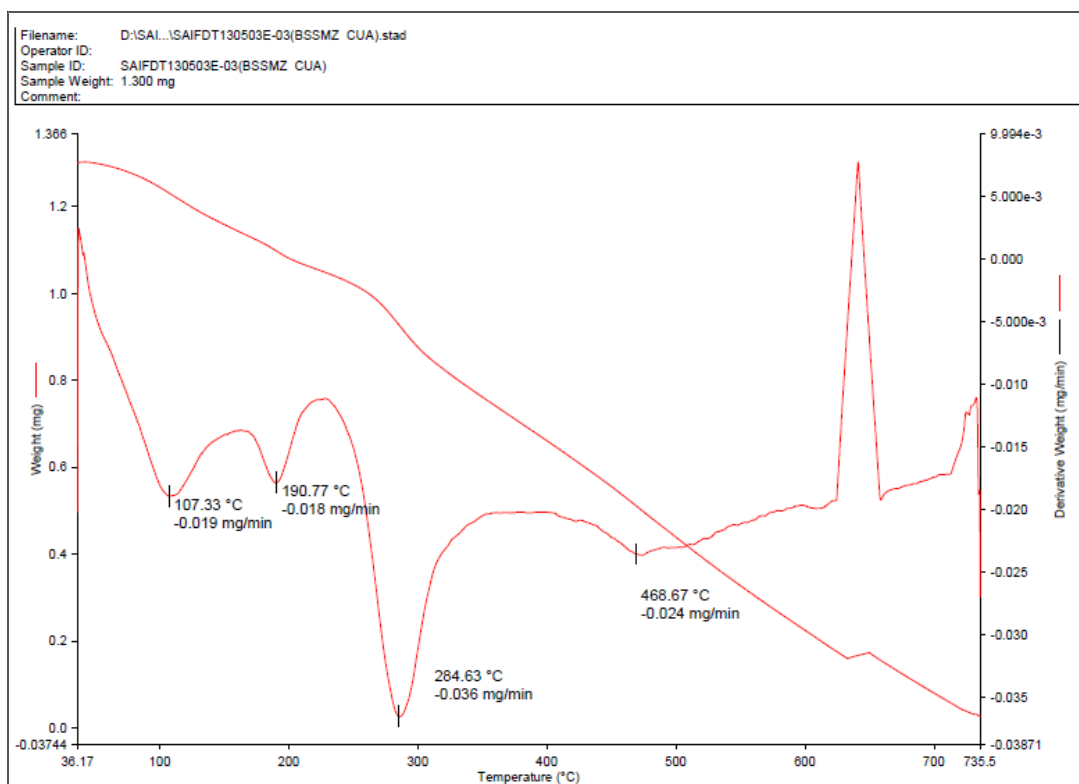


Fig. 4: Thermogram of copper complex

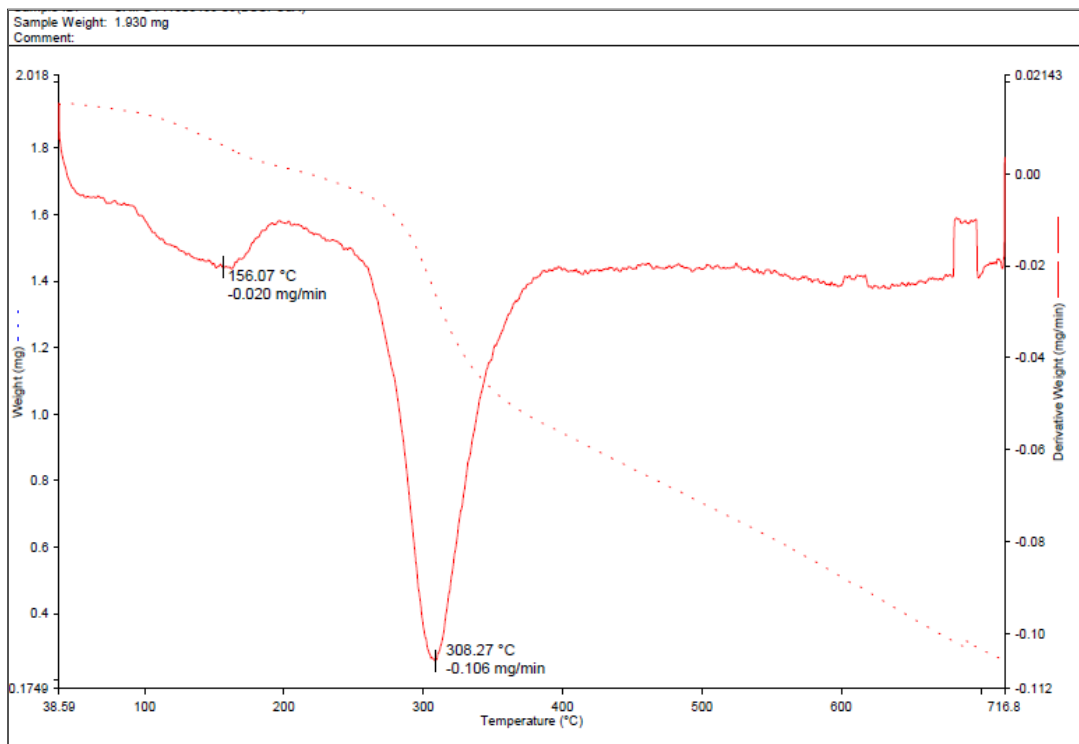


Fig. 5: Thermogram of cobalt complex

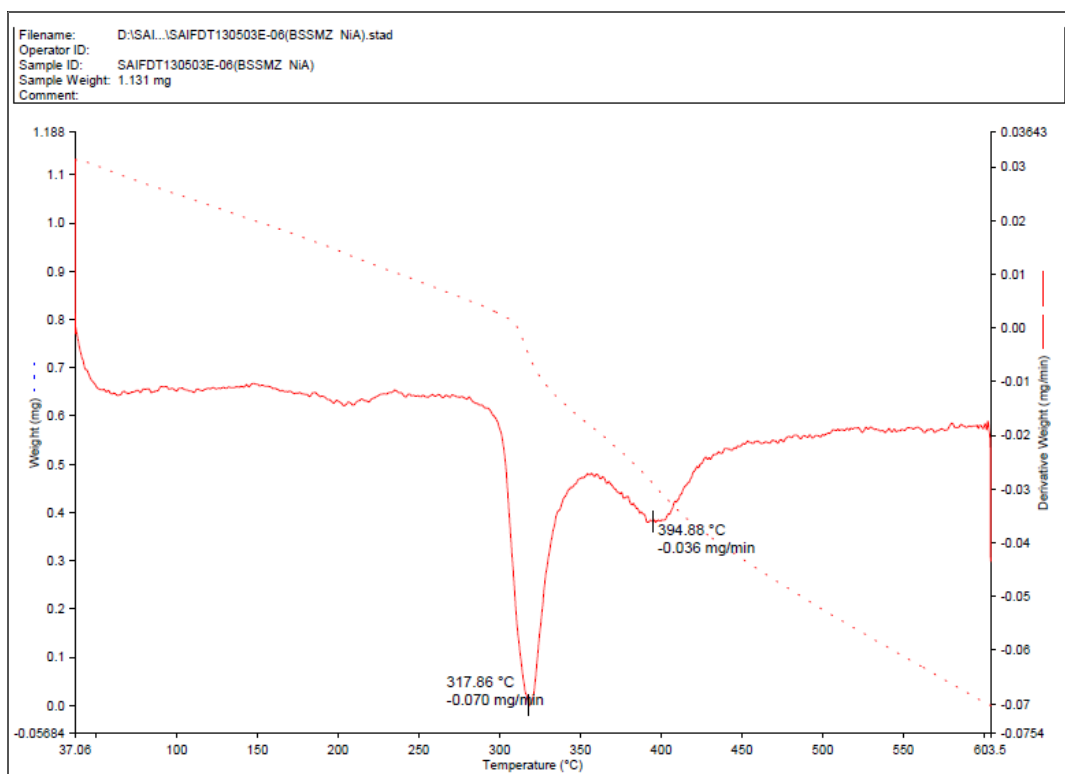


Fig. 6 Thermogram of nickel complex



Fig. 7: Antimicrobial activity of the complexes against *A. niger*

## CONCLUSION

A new Schiff base ligand has been synthesised by 1:1 condensation of sulfamerazine and 5-bromo-2-hydroxy benzaldehyde. From the satisfactory micro analytical and various spectral data, it is concluded that the ligand acts as a bidentate

ligand and its structure is shown in the Scheme-1. The metal chelates of the ligand have been structurally characterized and have the stoichiometry of 1:2 metal, ligand ratio for all the complexes. It is tentatively proposed that the Schiff base ligand coordinates through the



nitrogen of the azomethine group and the phenolato oxygen, forming a stable chelate structure. From the TG/DTA analysis it is noted that the cobalt and copper complexes have lattice/coordinated water and for nickel no such water is present inside or outside the sphere. On the basis of the above discussions, it is concluded that cobalt and copper complexes exhibit six-coordinated octahedral geometry as shown in the Figure-1 whereas the nickel complex exhibit tetrahedral geometry Figure-2. Biological studies of the complexes reveal that these complexes show better activity compared to that of the ligand.

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