



(RESEARCH ARTICLE)



## Synthesis, characterization and anti-microbial activities of mixed ligand complexes of sulphamethoxazole-urea with cobalt (II) and zinc (II) ions in water-methanol medium

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### Abstract

Novel mixed ligand metal complexes of Zinc (II) and Cobalt (II) were respectively synthesized with sulphamethoxazole-urea in a water-methanol medium by refluxing method and characterized gravimetrically (using Mohr's method for chloride and sulfur determination); the purity of the complexes through melting point determination; the functional groups present by infrared spectroscopy. The results predicted the coordination of the metals to the ligand through the amide group and oxygen atom of the sulphamethoxazole-urea bidentate. Solubility tests revealed that metal complexes were soluble in dimethyl sulphoxide acetone and ethanol. The metal complexes synthesized were also screened for their activities against some bacteria (*Xanthomonas* sp, *E. coli*, *B. aureus*, *P. syringae*, *Staphylococcus* sp., *Bacillus aureus*, and *P. aureus*) and some fungi (*S. rolfsii*, *C. indimutium*, *C. capsicia*) using Agar Disc diffusion principle. The metal complexes of sulphamethoxazole (SMX) and mixed ligands show little sign of bacteria inhibition but are more effective on fungi. The results indicate that the mixed ligand metal complexes were more biologically active than the free ligand. The better biological activity resulted in the MLC of Zn.

**Keywords:** Cobalt (II); Zinc (II); Sulphamethoxazole-Urea; Spectroscopic Studies and Bioactivity Tests

### 1. Introduction

The use of metal complexes in medicine as a chemotherapeutic agent, magnetic resonance imaging contrast agent, rheumatic drugs are well established [1, 2, 3].

Also, Tumer *et al.* [4] stated that the study of transition metal complexes containing biologically important ligands is because some metal ions are active in many biological processes. Mixed ligand complexes with metal ions bound to two different and biologically important ligands have aroused interest as a model for metalloenzymes [5]. It is also well established that mixed ligand complexes play a decisive role in the activation of the enzyme and also the storage and transport of active substances [6].

Synthesis and crystal structures of the mixed ligands complexes of Co (II) and Zinc (II) with Carboxylic and Picolinic acids have also been characterized in the literature by other fellow researchers; the results of the analyzes have revealed that Co (II) complexes may be a potential compound for optical and blue light-emitting materials. However, the electronic spectra of Zn (II) complexes do not exhibit d-d electronic transition due to the filled d-orbital, while that of Co (II) complexes showed two peaks at 477 and 547nm assignable and in conformity with the octahedral arrangement [7].

The derivatives of SMX is sulfonamide bacteriostatic antibiotic. It is most often used as a synergetic drug while combined with trimethoprim in a 5:1 ratio in co-trimoxazole. Its primary activity is against susceptible forms

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of *Streptococcus*, *Staphylococcus aureus*, *Escherichia coli*, *Haemophilus influenza*, and oral anaerobes. This drug is very active and commonly used to treat urinary tract infections. In addition, it can be used as an alternative to amoxicillin-based antibiotics to treat sinusitis, toxoplasmosis, and pneumocystis pneumonia which are primarily common among patients with HIV [8]. It is most frequently prescribed antibiotics in nephrology and pneumocystis jirovecii infections [9, 10].

Moreso, bacterial resistance to SMX occurs by mutations in the enzymes involved in the folic acid synthesis that prevent the drug from binding. The most common side effect of SMX is gastrointestinal upset. Another symptom caused by SMX includes nausea, severe stomach or abdominal ache, headaches, and pains that can lead to megaloblastic anemia in some patients.

Mixed drug metal (II) complexes of trimethoprim (TMP) and Sulfamethoxazole (SMX) have been synthesized, characterized by percentage purity and electronic spectroscopy, room temperature, magnetic moment, and conductance measurements. The results obtained in this study indicated that the metal (II) complexes were all magnetically dilute and octahedral, covalent in nature, and anti-microbial active against *Bacillus spp*, *Escherichia albican*, *Streptococcus aureus*, and *Candida albican* [11].

Strategies currently being explored to tackle this problem include the structural modification of existing antimicrobial drugs to which resistance has developed and the development of entirely new classes of antimicrobial agents that work on different target sites [12]. Broad empirical screening of chemical entities for antimicrobial activity represents an alternative strategy for new technology to tackle antimicrobials [13]. Nitrogen-containing heterocyclic compounds play important antimicrobial roles. This research paper projects the synthesis, characterization, and antimicrobial evaluations of the mixed ligands complexes of SMX and urea with Cobalt (II) and Zinc (II) metals in a methanol-water medium.

## 2. Material and methods

### 2.1. Chemical reagents

Reagents purchased were of good analytical grades and used without further purification. These include Sulfamethoxazole (SMX) obtained as a gift from Chemopharma Laboratory, Lagos, Nigeria; Urea, Zinc (II) sulfate heptahydrate, Cobalt (II) chloride hexahydrate from Aldrich Chemical. The methods employed for the different analyses are presented under the write-up on experimental below.

### 2.2. Synthesis of Metal Complexes and Mixed Metal Complexes of Zinc and Cobalt with SMX

Equimolar concentrations of 0.506g of SMX (ligand) and 0.323g of zinc were carefully weighed and dissolved in a mixture of methanol and water 50% v/v. The colorless solutions mixture of SMX and zinc sulfate salt were agitated for 3hours on a magnetic stirrer, and the resultant colorless mixture was filtered using sintered glass porosity NO. 4. The white residue obtained was then put in the desiccators for four (4) days. The % yield at constant weight was calculated and recorded. The ratio 2:1 metal complexes were done by doubling the concentration of the ligand. The mixed ligand metal complexes were synthesized in ratio 1:1:1 by mixing equimolar concentrations of metal and SMX (ligand) on a magnetic stirrer for two hours followed by the urea (secondary ligand) then, stirring continued for another one hour. The reacting mixture was filtered, and the residue was re-collected and kept inside a desiccator for five days. It was repeated for ratio 1:2:1 by doubling the concentration of SMX.

Metal complexes of the Cobalt with SMX and its mixed ligand were synthesized at different ratios 1:1, 1:2, 1:1:1, and 1:2:1 as stated above in the zinc complexes.

### 2.3. Physical Properties Evaluation

Synthesized metal complexes were analyzed and characterized adopting the following techniques: Melting points using Mel-Temp electrochemical machine and sulfur content was analyzed using barium chloride; chloride content was analyzed using silver nitrate (Argentometre titrations; the % yield by weighing the red residue while complexometric titration method for the analysis of the metals.

### 2.4. Spectroscopic Properties Evaluation

Spectroscopic properties evaluation the electronic transition studies were conducted using UV-visible spectrophotometer were recorded on a Perkin-Elmer 250 spectrophotometer. FTIR (infrared) in the range 400-

4000nm on spectroscopy was employed to determine the functional properties of the metal complexes' ligand site of metal coordination to the ligand.

### 2.5. Evaluation of the Antimicrobial Activity of Metal Complexes

The bacteria used for the experiment include *Xanthomonas*, *Bacillus cereus*, *Escherichia coli*, *Staphylococcus aureus*, *Pseudomonas syringae*, *Bacillus subtilis*, and *Pseudomonas aeruginosa*. All bacteria were cultured aerobically at 37°C for 18-24hours in peptone water; antimicrobial testing on the nutrients agar plate. 0.2 g/ml concentration of each of the complexes prepared, and 0.5 ml each of the samples were introduced into the bore agar well and incubated for 24hours at 37°C; the control plate was set up using standard streptomycin sulfate at 0.05 g/ml.

Zone inhibition around the wells was measured and recorded then, the results obtained were quoted as the radii (mm) of the zones of inhibition around the wells.

### 2.6. Evaluation of Antifungal Activity of the Metal Complexes

The fungi used for this experiment include *Serc. Rolfsii*, *Collettriculum lindimutianum*; *Collettriculum capcia*. About 0.02 g/ml each of the samples were mixed with 15 ml of sterile molten potatoes dextrose agar nutrient (PDA), then cooled to 45°C before pour plated and allowed to solidify at ambient temperature.

The fungi formed were inculcated at the center of the plates, a 7 mm diameter distance from the edge of the needle to elucidate the available fungal. Benlate (a standard antifungal) was employed for the control at 0.005 g/ml DMF and methanol impregnated plates were equally prepared.

Another control plate without any treatment was also set up and inoculated as above. All the plates were incubated at 27°C for 144hours, while mycelial growth was measured and calculated in percentage (%).

$$\text{Percentage of inhibition} = \frac{x-y}{x} \times 100\%.$$

Where X = Non-treated (without sample); Y = Treated sample

## 3. Results

The results obtained from our interrogation, the physical and chemical properties, reactivity of the ligands and complexes used were itemized in the Tables below.

**Table 1** Analysis data for different Zinc (II) Mixed Ligand Complexes

| Complexes                                                             | Ratio (Zn:L:L') | Medium           | Colour | M. Pt. (°C) | %Yield | %S in the Complexes |
|-----------------------------------------------------------------------|-----------------|------------------|--------|-------------|--------|---------------------|
| [ZnLH <sub>2</sub> OSO <sub>4</sub> ]H <sub>2</sub> O                 | 1:01            | H <sub>2</sub> O | White  | 218-220     | 10.98  | 4.91                |
| [ZnL <sub>2</sub> H <sub>2</sub> OSO <sub>4</sub> ]H <sub>2</sub> O   | 1:02            | H <sub>2</sub> O | White  | 223-225     | 21.96  | 6.12                |
| [ZnLL'H <sub>2</sub> OSO <sub>4</sub> ]H <sub>2</sub> O               | 1:01:01         | H <sub>2</sub> O | White  | 206-208     | 16.47  | 11.15               |
| [ZnL <sub>2</sub> L'H <sub>2</sub> OSO <sub>4</sub> ]H <sub>2</sub> O | 1:02:01         | H <sub>2</sub> O | White  | 211-213     | 27.46  | 22.74               |

**Table 2** Analysis data for different Cobalt (II) Mixed Ligand Complexes

| Complexes                                                             | Ratio   | Medium           | Colour | M. Pt. (°C) | % Yield | % Cl in the Complexes |
|-----------------------------------------------------------------------|---------|------------------|--------|-------------|---------|-----------------------|
| [COLH <sub>2</sub> OCl]H <sub>2</sub> O                               | 1:01    | H <sub>2</sub> O | Pink   | 175-177     | 21.98   | 4.91                  |
| [CoL <sub>2</sub> H <sub>2</sub> OCl <sub>2</sub> ]H <sub>2</sub> O   | 1:02    | H <sub>2</sub> O | Pink   | 176-178     | 28.96   | 6.2                   |
| [CoLL'H <sub>2</sub> OCl]H <sub>2</sub> O                             | 1:01:01 | H <sub>2</sub> O | Purple | 178-200     | 39.47   | 11.15                 |
| [CoL <sub>2</sub> L'H <sub>2</sub> OCl <sub>2</sub> ]H <sub>2</sub> O | 1:02:01 | H <sub>2</sub> O | Purple | 201-213     | 41.46   | 22.7                  |

**Table 3** Solubility tests for different Zinc (II) Mixed Ligand Complexes

| Complexes                                                                         | Water | Ethanol | Toluene | Butanol | Propanol | Acetone | Chloroform | Benzene | Hexane |
|-----------------------------------------------------------------------------------|-------|---------|---------|---------|----------|---------|------------|---------|--------|
| [ZnLH <sub>2</sub> OSO <sub>4</sub> ] <sub>2</sub> H <sub>2</sub> O               | IS    | SS      | PS      | SS      | SS       | SS      | IS         | PS      | PS     |
| [ZnL <sub>2</sub> H <sub>2</sub> OSO <sub>4</sub> ] <sub>2</sub> H <sub>2</sub> O | IS    | SS      | PS      | SS      | SS       | SS      | IS         | PS      | PS     |
| [ZnLL'H <sub>2</sub> O] <sub>2</sub> H <sub>2</sub> O                             | IS    | SS      | PS      | SS      | SS       | SS      | IS         | PS      | PS     |
| [ZnL <sub>2</sub> L'H <sub>2</sub> O] <sub>2</sub> H <sub>2</sub> O               | IS    | SS      | PS      | SS      | SS       | SS      | IS         | PS      | PS     |

IS (Insoluble); SS (Soluble); PS (Partially soluble).

**Table 4** Solubility Tests for Cobalt (II) Mixed Ligand Complexes

| Complexes                                                                         | Water | Ethanol | Toluene | Butanol | Propanol | Acetone | Chloroform | Benzene | Hexane |
|-----------------------------------------------------------------------------------|-------|---------|---------|---------|----------|---------|------------|---------|--------|
| [CoLH <sub>2</sub> OSO <sub>4</sub> ] <sub>2</sub> H <sub>2</sub> O               | IS    | SS      | PS      | SS      | SS       | SS      | IS         | PS      | PS     |
| [CoL <sub>2</sub> H <sub>2</sub> OSO <sub>4</sub> ] <sub>2</sub> H <sub>2</sub> O | IS    | SS      | PS      | SS      | SS       | SS      | IS         | PS      | PS     |
| [CoLL'H <sub>2</sub> O] <sub>2</sub> H <sub>2</sub> O                             | IS    | SS      | PS      | SS      | SS       | SS      | IS         | PS      | PS     |
| [CoL <sub>2</sub> L'H <sub>2</sub> O] <sub>2</sub> H <sub>2</sub> O               | IS    | SS      | PS      | SS      | SS       | SS      | IS         | PS      | PS     |

IS (Insoluble); SS (Soluble); PS (Partially soluble).

**Table 5** Data of some IR Spectral Assignment (cm<sup>-1</sup>) and UV-Vis  $\lambda_{\max}$  (nm) of the Parent and Mixed Ligands with the Zn (II) Metal Complexes

| Complexes                                                                           | M-N | M-O | SO <sub>4</sub> <sup>2-</sup> | S=O        | -NH  | NH <sub>2</sub> | OH   | C=O        | UV-Vis. (nm) |
|-------------------------------------------------------------------------------------|-----|-----|-------------------------------|------------|------|-----------------|------|------------|--------------|
| [ZnLH <sub>2</sub> OSO <sub>4</sub> ] <sub>2</sub> H <sub>2</sub> O                 | 559 | 683 | 1093, 1146                    | 1405, 1500 | 1614 | 3207, 3394      | 3760 | -          | 285          |
| [ZnL <sub>2</sub> H <sub>2</sub> OSO <sub>4</sub> ] <sub>2</sub> H <sub>2</sub> O   | 559 | 683 | 1093, 1146                    | 1404, 1500 | 1614 | 3208, 3394      | 3754 | -          | 350          |
| [ZnLL'H <sub>2</sub> OSO <sub>4</sub> ] <sub>2</sub> H <sub>2</sub> O               | 560 | 684 | 1094, 1146                    | 1405, 1501 | 1614 | 3209, 3395      | 3760 | 1261, 1301 | 352          |
| [ZnL <sub>2</sub> L'H <sub>2</sub> OSO <sub>4</sub> ] <sub>2</sub> H <sub>2</sub> O | 559 | 682 | 1093, 1146                    | 1405, 1502 | 1617 | 3210, 3396      | 3760 | 1309       | 254          |
| L                                                                                   | -   | -   | -                             | 1470, 1502 | 1624 | 3144, 3372      | -    | -          | -            |
| L'                                                                                  | -   | -   | -                             | -          | -    | 3309            | -    | 1271       | -            |

L = Sulfamethoxazole; L' = Urea

**Table 6** Data of some IR Spectral Assignment (cm<sup>-1</sup>) and UV-Vis  $\lambda_{\max}$  (nm) of the Parent and Mixed Ligands with the Co (II) Metal Complexes

| Complexes                                                                           | M-N | M-O | M-Cl | S=O        | -NH  | NH <sub>2</sub> | OH-(OH <sub>2</sub> ) | C=O  | UV-Vis.(nm) |
|-------------------------------------------------------------------------------------|-----|-----|------|------------|------|-----------------|-----------------------|------|-------------|
| [CoLH <sub>2</sub> OSO <sub>4</sub> ] <sub>2</sub> H <sub>2</sub> O                 | 558 | 682 | 369  | 1405, 1500 | 1614 | 3469            | 3760                  | -    | 285         |
| [CoL <sub>2</sub> H <sub>2</sub> OSO <sub>4</sub> ] <sub>2</sub> H <sub>2</sub> O   | 554 | 685 | 415  | 1474, 1500 | 1614 | 3376            | 3760                  | -    | 350         |
| [CoLL'H <sub>2</sub> OSO <sub>4</sub> ] <sub>2</sub> H <sub>2</sub> O               | 559 | 683 | 372  | 1405, 1501 | 1615 | 3309, 3395      | 3754                  | -    | 352         |
| [CoL <sub>2</sub> L'H <sub>2</sub> OSO <sub>4</sub> ] <sub>2</sub> H <sub>2</sub> O | 559 | 683 | 374  | 1405, 1502 | 1615 | 3209, 3394      | 3760                  | -    | 254         |
| L                                                                                   | -   | -   | -    | 1470, 1502 | 1624 | 3144, 3372      | -                     | -    | -           |
| L'                                                                                  | -   | -   | -    | -          | -    | 3309            | -                     | 1271 | -           |

L = Sulfamethoxazole; L' = Urea

**Table 7** Antibacterial Zone of Inhibition after 24hrs of Incubation at 37°C (mm) for Zinc (II) Complexes

| Complexes                                                                           | Ratio   | <i>Xanthomonas</i> | <i>E. coli</i> | <i>B. cereus</i> | <i>P. syringae</i> , | <i>S. aureus</i> | <i>B. subtilis</i> | <i>P. aeruginosa</i> |
|-------------------------------------------------------------------------------------|---------|--------------------|----------------|------------------|----------------------|------------------|--------------------|----------------------|
| [ZnLH <sub>2</sub> OSO <sub>4</sub> ] <sub>2</sub> H <sub>2</sub> O                 | 1:01    | +                  | +++            | +                | ++++                 | ++               | ++++               | +                    |
| [ZnL <sub>2</sub> H <sub>2</sub> OSO <sub>4</sub> ] <sub>2</sub> H <sub>2</sub> O   | 1:02    | ++                 | ++             | ++               | +++                  | ++               | ++                 | +                    |
| [ZnLL'H <sub>2</sub> OSO <sub>4</sub> ] <sub>2</sub> H <sub>2</sub> O               | 1:01:01 | ++                 | +++            | ++               | ++++                 | ++               | +                  | ++                   |
| [ZnL <sub>2</sub> L'H <sub>2</sub> OSO <sub>4</sub> ] <sub>2</sub> H <sub>2</sub> O | 1:02:01 | ++                 | ++++           | +++              | ++++                 | ++               | ++++               | ++                   |
| Streptomycine                                                                       |         | +++++              | +++++          | +++++            | +++++                | ++++             | ++++               | ++++                 |
| Metronidazole                                                                       |         | ++++               | ++++           | ++++             | +++++                | ++++             | ++++               | ++++                 |
| Ciprofloxacin                                                                       |         | +++++              | ++++           | +++++            | +++++                | +++++            | +++++              | +++++                |
| Ligand                                                                              |         | +                  | +              | ++               | ++                   | ++               | ++                 | +                    |

Key to zone of inhibition: + = &lt; 5 mm; ++ = 5-10 mm; +++ = 10-15mm; ++++ = 15 -20mm; +++++ = &gt; 20mm

**Table 8** Antibacterial Zone of Inhibition after 24hrs of Incubation at 37°C (mm) for Cobalt (II) Complexes

| Complexes                                                             | Ratio   | <i>Xanthomonas</i> | <i>E. coli</i> | <i>B. cereus</i> | <i>P. syringae</i> , | <i>S. aureus</i> | <i>B. subtilis</i> | <i>P. aeruginosa</i> |
|-----------------------------------------------------------------------|---------|--------------------|----------------|------------------|----------------------|------------------|--------------------|----------------------|
| [CoLH <sub>2</sub> OCl] <sub>2</sub> H <sub>2</sub> O                 | 1:01    | +                  | +              | +                | +                    | ++               | ++                 | +                    |
| [CoL <sub>2</sub> H <sub>2</sub> OCl] <sub>2</sub> H <sub>2</sub> O   | 1:02    | +                  | ++             | ++               | +++                  | ++               | ++                 | +                    |
| [CoLL'H <sub>2</sub> OCl] <sub>2</sub> H <sub>2</sub> O               | 1:01:01 | ++                 | ++             | +++              | ++++                 | ++               | ++                 | ++                   |
| [CoL <sub>2</sub> L'H <sub>2</sub> OCl] <sub>2</sub> H <sub>2</sub> O | 1:02:01 | ++                 | ++             | +++              | ++++                 | ++               | ++++               | +++                  |
| Streptomycine                                                         |         | +++++              | +++++          | +++++            | +++++                | ++++             | ++++               | ++++                 |
| Metronidazole                                                         |         | ++++               | ++++           | ++++             | +++++                | ++++             | ++++               | ++++                 |
| Ciprofloxacin                                                         |         | +++++              | ++++           | +++++            | +++++                | +++++            | +++++              | +++++                |
| Ligand                                                                |         | +                  | +              | ++               | ++                   | ++               | ++                 |                      |

Zone of inhibition: + = &lt; 5 mm; ++ = 5-10 mm; +++ = 10-15mm; ++++ 15-20mm; +++++ = &gt; 20mm.

**Table 9** % Fungal Mycelial Growth Inhibition at 72hrs of Incubation at 25°C for Zinc (II) Complexes

| Zinc (II) Complexes                                                 | Ratio   | <i>Sclerotium rolfsii</i> | <i>Collentriculum lindimutiaum</i> | <i>Collentriculum capsicia</i> |
|---------------------------------------------------------------------|---------|---------------------------|------------------------------------|--------------------------------|
| [ZnLH <sub>2</sub> OSO <sub>4</sub> ] <sub>2</sub> H <sub>2</sub> O | 1:01    | 64                        | 74                                 | 39                             |
| [ZnLH <sub>2</sub> OSO <sub>4</sub> ] <sub>2</sub> H <sub>2</sub> O | 1:02    | 66                        | 72                                 | 48                             |
| [ZnLH <sub>2</sub> OSO <sub>4</sub> ] <sub>2</sub> H <sub>2</sub> O | 1:01:01 | 70                        | 75                                 | 57                             |
| [ZnLH <sub>2</sub> OSO <sub>4</sub> ] <sub>2</sub> H <sub>2</sub> O | 1:02:01 | 72                        | 76                                 | 58                             |
| L Sulfamethoxazole                                                  |         | 34                        | 29                                 | 23                             |
| L' Urea                                                             |         | 8                         | 6                                  | 8                              |
| Control (Benlote)                                                   |         | 98                        | 100                                | 99                             |

**Table 10** % Fungal Mycelial growth inhibition at 72hrs of incubation at 25°C for Cobalt (II) complexes

| Cobalt (II) Complexes                                   | Ratio   | <i>Sclerotium rolfii</i> | <i>Collentriculum lindimutiaum</i> | <i>Collentriculum capsicia</i> |
|---------------------------------------------------------|---------|--------------------------|------------------------------------|--------------------------------|
| [CoLH <sub>2</sub> OCl]H <sub>2</sub> O                 | 1:01    | 41                       | 23                                 | 20                             |
| [CoL <sub>2</sub> H <sub>2</sub> OCl]H <sub>2</sub> O   | 1:02    | 46                       | 32                                 | 33.7                           |
| [CoLH <sub>2</sub> OCl]H <sub>2</sub> O                 | 1:01:01 | 60                       | 45                                 | 50                             |
| [CoL <sub>2</sub> L'H <sub>2</sub> OCl]H <sub>2</sub> O | 1:02:01 | 72                       | 60                                 | 54                             |
| L Sulfamethoxazole                                      |         | 24                       | 29                                 | 23                             |
| L' Urea                                                 |         | 8                        | 6                                  | 8                              |
| Control Benlote)                                        |         | 98                       | 100                                | 99                             |

#### 4. Discussion

Table 1 presents the color, % yield, and elemental analysis of zinc (II) complexes of SMX with urea as secondary ligands, and from their outcomes, the % yield was appreciable; complexes give white colors indicating that the ligands have no dominant effect on the colors of the zinc (II) complex; the melting point determination using melting point apparatus.

Mere looking at the cobalt (II) complexes as a primary ligand, it has an overall tendency of generating an effect on the metal, thereby changing from purple to pink, which cannot be possible while using mixed metal complexes; the melting point was very sharp, indicating pure metal complexes (Table 2).

The percentage yields were commendable (Table 2) compared to results reported by Ejelonu and Olagboye [14] (51.57-67.1 %), percentage yield in this study was below.

The solubility of the metal complexes of Zn (II) has revealed that they are slightly soluble in benzene, hexane, and toluene, insoluble in water, chloroform, and carbon tetrachloride but soluble in butanol, ethanol, acetone, and propan-2-ol as indicated in Table 3.

The results (Table 4) have shown that metal complexes were non-polar, while the solubility tests of cobalt complexes also facade that they were insoluble in water, chloroform, carbon tetrachloride but soluble in ethanol, propan-3-ol, acetone, and butanol, likewise the results show that cobalt (II) complexes were non-polar compounds.

According to Bamigboye *et al.* [15], the solubility of the metal complexes in the solvents indicated their low polarity to determine the suitable solvents to engage for spectroscopic measurements.

Tables 5 and 6 gives an account of UV-visible spectra of the ligands and their metal complexes showing the peaks, and cobalt (II) complexes showed a strong peak between 421-510 nm attached to 4T<sub>1g</sub> (the sign of octahedral configuration). Zinc (II) complexes display absorbance between 254-355 nm designated to  $\pi$  and MCLT (metal-ligand charge transfer) since they belong to d<sup>10</sup> configuration and they do not have d-d transition [16, 17].

Table 5 presents the prominent IR spectral of zinc (II) complexes, the presence of urea in the other complexes as a mixed ligand display a brilliant band at 1271.42cm<sup>-1</sup> attributed to C=O in urea (NH<sub>2</sub>CONH<sub>2</sub>) but with a shift to 1261.91 cm<sup>-1</sup> and 1309 cm<sup>-1</sup> in the mixed ligand metal complexes, indicating the involvement of C=O in the coordination. A pronounced band around 1470 and 1502 cm<sup>-1</sup> in the ligand (SMX) have shifted to lower frequency bands at 1404 and 1405 cm<sup>-1</sup>, showing the participation of sulphur oxygen atoms in coordination. Moreso, strong bands around 3144 and 3372 cm<sup>-1</sup> attributed to NH<sub>2</sub> in the parent ligand but with bathochromic shifts to 3394-3396cm<sup>-1</sup> in the metal complexes, suggesting the involvement of nitrogen atom in the coordination of metal complexes, therefore, predicting a bidentate coordinate dative bonding [18]. The presence of water was confirmed in the absorption bands around 754-755 cm<sup>-1</sup> then, in the ligand with prominent bands around 3754-3760 cm<sup>-1</sup> assigned to -OH group from the water of crystallization in the metal salt [19]. The broad bands around 1093 and 1146 cm<sup>-1</sup> in the metal complexes were absent in the ligand and could be attached to the presence of sulfate ions in the coordination [20]. The new bands in the spectra of zinc (II)

metal complexes at 559-560 and 682-684  $\text{cm}^{-1}$  could be assigned to M-L and M-O, suggesting the coordination between metal to ligand bonding [19].

Tables 5 and 6 also presents the data for the UV-Visible wavelength maxima and prominent IR spectra of both zinc and cobalt complexes. The IR spectra of the complexes indicate that the ligand behaves as bidentate and the metals coordinate via the nitrogen atom of the amine ( $\text{NH}_2$ ) and hard base donor atom, the oxygen atom of  $\text{O}=\text{S}=\text{O}$  in the parent/free ligand formed a strong absorptions/ bands around 1404-1405  $\text{cm}^{-1}$  which is assignable to NH vibration, but not visible in the ligand spectrum [21].

Moreso, a prominent band at 3372  $\text{cm}^{-1}$  formed in the parent ligand spectrum, then shifted to a lower frequency band at 3469-3394  $\text{cm}^{-1}$  in the complexes. The urea-mixed ligand absorbed at 3309  $\text{cm}^{-1}$  is traceable to  $\text{NH}_2$  with some similar features in all the spectra of the mixed ligand metal complexes without change.

This study indicated there was no coordination through the nitrogen atom while the oxygen atom of the  $\text{C}=\text{O}$  bond has its absorption at 1272  $\text{cm}^{-1}$  frequency showing the total disappearance at the band (1272  $\text{cm}^{-1}$ ) in the mixed ligand complexes at the cobalt (II) ion.

Also, the presence of coordinated water molecules in the inner sphere of the metal coordinated complexes occurs around 686-755  $\text{cm}^{-1}$ , and then the uncoordinated water molecule has a strong absorption band between 3754-3760  $\text{cm}^{-1}$ , unlike the free ligand spectra, which indicate the presence of the -OH group is due to the water of crystallization in the salts used [19]. There are prominent bands observable at 554-559  $\text{cm}^{-1}$  and 682-685  $\text{cm}^{-1}$  that can be attached to the M-L and M-O bonds, and these bands confirmed the coordination between the parent and mixed ligands to the (cobalt) metal site, which shows that the metal's coordination to the ligand is through the nitrogen atom [22].

Tables 7, 8, 9, and 10 presents the antimicrobial evaluation for the mixed ligand sulphamethoxazole complexes of zinc and cobalt in an aqueous medium against seven different bacteria pathogens such as *Xanthomonas*, *Bacillus aureus*, *Escherichia coli*, *Staphylococcus aureus*, *Pseudomonas syringiae*, *Bacillus subtilis*, *Pseudomonas aureus*.

Zinc (II) complexes and their mixed ligands have proven to be active against some bacteria pathogens (Table 7) but with little resistance from microorganisms like *Bacillus aureus*, *Xanthomonas spp.*, and *Pseudomonas aureus*. The resistance of these organisms could be attached to their versatile nutritional capability, adaptability to various hydrocarbon rings, and the possession of pump mechanisms that ejects metal complexes as soon as they enter the cell [23]. The *Bacillus aureus* resistance to complexes may be related to its ability to produce an extended-spectrum of beta-lactamases (ESBL) which inactivates the compounds; also, the presence of a thick peptidoglycan layer which is less permeable to the metal complexes [24, 25]. Cobalt (II) parent and mixed ligand complexes were tested against these bacteria: *Xanthomonas spp*, *Bacillus cereus*, *Escherichia coli*, *Staphylococcus aureus*, *Pseudomonas syringiae*, *Bacillus subtilis*, *Pseudomonas aureus* (Table 8). The metal complexes of cobalt (II) showed appreciable inhibition against the microorganisms using the minimum zone of inhibition being 0-5mm (+).

In this present study, the minimum inhibition zone observed for the metal complexes against the *Xanthomonas spp.* and *Escherichia coli* may be resulted from the resistance to solubilize center around lipophobic characters [26].

Zn (II) complexes of both the parent and mixed ligands showed the maximum zone inhibition at all levels against *S. rofsil*, *C. linder* and *C. capsicia*.

In addition, the inhibition zone observed on *S. rofsil* is in line with that examined by Kenssey *et al.* [27] on *E. floccosum* using isatin-3-thiosemicarbazone zinc complexes.

Table 8 reports the antibacterial zone of inhibition activities of cobalt (II) complexes against these bacteria *Xanthomonas spp*, *Bacillus cereus*, *Escherichia coli*, *Staphylococcus aureus*, *Pseudomonas syringiae*, *Bacillus subtilis*, *Pseudomonas aureus*, and the activity has proven it can withstand any forms of pathogens even at higher concentration. The findings in this study using cobalt (II) have also shown metal complexes' sensitivity to different modes of organisms due to the metal ions.

Table 9 presents the antifungal analysis of the zinc (II) sulphamethoxazole and mixed ligand complexes against three fungal (*S. rofsil*, *C. linder*, and *C. capsicia*) and the Zn (II) complexes with the parent and mixed ligands at different mole ratio concentrations have demonstrated a high level of inhibition against the pathogens under investigation.

It was evident from the result that the performances of the complexes have increased tremendously with concentration, and a significant maximum inhibition zone is lower than the one observed by Mitu et al. [22] but higher than that observed by Kenssey [27].

The antifungal properties of Cobalt (II) parent and mixed ligands complexes were also screened against three fungi pathogens to seizure their reactivity (Table 10) as well compared with standards, following outcomes have proven proactive against *Sclerotium rolfsii*, *Collettricum lindimutanium*, and *collettricum capsicia* than expected even at a lower concentration of ratio 1:1 of metal-ligand.

The antifungal toxicity properties of metal complexes increased with the increasing concentrations of the ligand (sulphamethoxazole), besides increase in the antifungal activity was not based on different concentrations, but due to an intricate blend of the solubility, melting point, and metal chelation effects of the medium [28, 29].

The maximum inhibition zone observed for *B. subtilis* is higher than that obtained by Oforka and Mkpennie [25] (5mm of zone inhibition against *S. aureus*, *E. coli*, *S. faecalis* by using isatin-3-thiosemicarbazone mercury complexes).

Conversely, metal (II) complexes and their mixed ligands were more effective than the metal-free ligands due to chelation which reduces the polarity of the metal atom mainly because of partial sharing of its positive charge with donor groups of the ligand and the  $\pi$ - electron delocalization over the aromatic rings [30].

## 5. Conclusion

Cobalt (II) and Zinc (II) complexes of sulphamethoxazole (SMX) and their mixed ligand complexes have been synthesized in a water-methanol medium and characterized.

This study shows that ligand (SMX) coordinates covalently and bidentate with cobalt (II) and Zinc (II) through the nitrogen atom (the free ligand), while the urea (secondary ligand) coordinated through the carbonyl C=O group.

Moreso, the biological activities of metal complexes were more proactive than the ligands (good antibacterial and antifungal agents), the Zn (II) complexes showing more affinity for microorganisms than Co (II) complexes due to the involvement of more lone pairs of d-electrons in Zn (II) complexation with sulphamethoxazole than the cobalt (II) complexes.

## Compliance with ethical standards

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### Disclosure of conflict of interest

I single-handed work on this manuscript, there is no conflict of interest.

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