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# Spectroscopic Studies of Mixed-ligand Complexes of Cu(II), Co(II), Mn(II) and Zn(II) with Sulpha Drug and Heterocyclic Compound

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## ABSTRACT

*In view of the great biological, industrial and manifold applications of sulfamethoxazole and imidazole complexes, there is a need for an understanding of the coordination possibilities of sulfamethoxazole and imidazole. In this work, Cu(II), Co(II), Mn(II)and Zn(II) mixed-ligand complexes of sulpha drug (Sulfamethoxazole, $L_1$) and imidazole ($L_2$) in form of ($L_1$: M: $L_2$) (1:1:2), have been prepared and their infrared and UV-Vis spectra have been investigated. The infrared spectra of the samples were recorded in the range 4000-400 $cm^{-1}$ and their fundamental vibrational wave numbers were obtained. The electronic spectra of all the synthesized complexes were recorded on Spectro-UV-Vis double beam PC scanning spectrophotometer UVD 2960. In all the complexes, SMX behaves as a Tridentate ligand binding through two Ar-N atoms and sulfonic oxygen while imidazole behaves as a monodentate with N donor atom. UV-Visible spectra suggest probable octahedral geometry for the complexes.*

**Keywords:** Complex, Imidazole, IR, Ligand, Sulfamethoxazole, UV-visible

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## INTRODUCTION

Metal binding substances, many of which function by chelation, form a class of substances which have furnished many useful drugs and other substances of value in selective toxicity [1].

Many chemotherapeutically important sulpha drugs like sulphadiazine, sulphamethoxazole, sulphathiazole, sulphamerazine and so forth, possess $SO_2NH$ moiety which is an important toxophoric function [2]. The heterocyclic compounds with both sulphur and nitrogen atoms in the ring system have also been used in the synthesis of biologically active complexes. Complex formation between metal ions and sulfa drugs has been extensively investigated to establish metal-drug interactions [3]. The results suggest that the different behavior of the ligand depends on its deprotonation and/or the metal ion, and it is difficult to generalize metal-sulfonamide structures.

Numerous metal complexes of sulfonamides have been studied as simple models for metal–protein interactions and ligands containing a sulfonamide group have been investigated as reagents for the separation, concentration and selective determination of many first-row transition metal cations [4].

Sulphamethoxazole [4-amino-*N*-(5-methyl-3-isoxazolyl)-benzene sulphonamide] is widely used in the prevention and cure of bacterial infections, it a well-known antibacterial sulfa drug, contains several groups with donor atoms that are able to interact with metal ions: Ar–$NH_2$, NH sulfonamide, $SO_2$–R and N and O heterocyclic atoms [5]. It can act as monodentate or a bidentate ligand. Sulphamethoxazole (SMZ) has wide applications in pharmaceutical industry.

Heterocyclic compounds comprise the major family of organic compounds. These are enormously essential with wide range of synthetic, pharmaceutical and industrial applications and are famous for their biological activities. There is an extensive spectrum of biological activities shown by many compounds containing five membered heterocyclic rings in their structure. The high therapeutic properties of these heterocycles have encouraged the medicinal chemists to synthesize a large number of novel chemotherapeutic agents. These heterocyclic compounds have broadened scope in remedying various dispositions in clinical medicines [6]. Imidazole plays an important role as a ligand in bioinorganic chemistry [7,8]. Complexes of imidazole derivatives with transition metal ions have attracted much attention because of their biological and pharmacological activities, such as antiviral and antimicrobial, antifungal and anti-mycotic, antihistaminic and anti-allergic, anthelminthic, antitumoral and antimetastatic properties [9]. A variety of coordination compounds with imidazole ligands have been synthesized and characterized in order to elucidate the structure and function of such biologically active metal compounds.

This present work represents continuation of our physico-chemical studies on mixed-ligand complexes of sulfamethoxazole and imidazole. In this paper, Infrared and Electronic spectra on mixed-ligand complexes of sulfamethoxazole ($L_1$) and imidazole ($L_2$) with divalent metals (M) in ($L_1$:M: $L_2$) (1:1:2) are reported (Table 1).

## MATERIALS AND METHODS

### Reagents and solvents

The reagents and solvents used include ethanol, methanol, manganese acetate tetrahydrate, copper acetate monohydrate, zinc acetate dihydrate, cobalt acetate tetrahydrate, zinc sulphate heptahydrate, sodium hydroxide, solochrome black indicator, dimethylsulphoxide, dioxan, solochrome T, dichloromethane, tetrahydrofuran, dioxan, chloroform, distilled water, perchloric acid, ammonia, ammonia chloride, murexide indicator and imidazole. The ligand (sulphametoxazole) was obtained from Drug field Pharmaceutical Ltd, Sango Ota, Ogun State. All reagents and chemicals were of analytical grade and were used without further purification.

### Preparation of Cu(SMX) (Imi)

The complex was prepared by mixing 1.226 g (0.005 mol) of sulphamethoxazole in 20 ml of hot ethanol, 0.999 g (0.005 mol) of copper acetate in 20 ml of water and 0.680 g (0.01 mol) of imidazole in 10 ml of water at ratio 1:1:2. To this mixture a few drops of 0.002 M NaOH was added to adjust the pH of the mixture to 5.5 and the reaction mixture was heated and continuously stirred for about 3-4 h. The product was isolated after reduction of volume by evaporation. It was then filtered, washed and dried in vacuum over silica gel. The same procedure was used in the preparation of the other complexes involving zinc acetate, cobalt acetate, manganese acetate, and zinc sulphate.

### Metal analysis

Percentage metal composition in the complex was determined by complex metric titration using Ethylenediaminetetraacetic Acid (EDTA) solution, murexide indicator and ammonia/ammonium chloride buffer.

### Infrared spectra

The infrared spectra of the all complexes synthesized and those of ligands were recorded using Perkin Elmer FT−IR Spectrophotometer equipped with KBr disc. The infrared region is between 4000-400 $cm^{-1}$.

### Electronic spectra

The electronic absorption spectra in the UV-Visible range were recorded on UVD-2960 Double Beam PC Scanning spectrophotometer between 190- 400 nm (UV) and 400-900 nm (visible) for the compounds using Dimethyl Sulfoxide (DMSO) as the solvent for almost all the compounds except in Co(II) complexes where THF was used as the solvent.

**Table 1: Physical analytical data for the complexes**

| Complex | Colour | Formula weight (g) | Yield | % M observed | %M expected |
|---|---|---|---|---|---|
| $Cu(SMX)(Imi)_2\ H_2O$ | Deep green | 452.98 | 55.72 | 14.03 | 14.54 |
| $Zn(SMX)(Imi)_2\ H_2O$ | White | 472.85 | 48.21 | 13.83 | 14.15 |
| $Mn(SMX)(Imi)_2\ H_2O$ | White | 462.84 | 37.89 | 11.87 | 12.06 |
| $Co(SMX)(Imi)_2\ H_2O$ | Pale pink | 466.37 | 68.83 | 12.64 | 13.21 |
| $Zn(SMX)(Imi)_2\ SO_4$ | White | 550.85 | 41.75 | 11.88 | 11.49 |

## RESULTS AND DISCUSSION

### Solubility

All the synthesized metal complexes were generally insoluble in water and chloroform but showed different degree of solubility in other solvents with exception to DMSO and THF in which all the complexes were freely soluble (Table 2).

**Table 2: Solubility data of the compounds**

| Compounds | EtOH | MeOH | $CHCl_3$ | $CH_2Cl_2$ | DMSO | THF | $H_2O$ | Dioxan | $CH_3NO$ |
|---|---|---|---|---|---|---|---|---|---|
| $Cu(SMX)(imidazole)_2\ H_2O$ | SH | S | I | I | S | S | I | S | SS |
| $Zn(SMX)(imidazole)_2\ H_2O$ | S | SH | I | I | S | S | I | SS | S |
| $Co(SMX)(imidazole)_2\ H_2O$ | SS | SH | I | I | S | S | I | SS | I |
| $Mn(SMX)(imidazole)_2\ H_2O$ | SS | SS | I | I | S | S | I | S | SS |
| $Zn(SMX)(imidazole)_2\ SO_4$ | SH | S | I | I | S | S | I | SS | SH |

### Infrared spectra

The bonding of the ligands to metals was investigated by comparing the FT-IR spectra of the complexes with those of the free ligands in order to determine the coordination sites that may be involved in chelation. In the infrared spectra of sulphamethoxazole, two sharp bands observed at 3462 and 3383 $cm^{-1}$ are assigned to the asymmetric and symmetric stretching vibrations of aniline $NH_2$ group respectively [10]. While bands at 1615 s, 928 w and 3297 are assigned to υC=N, υS–N and υN–H stretching vibrations respectively. And in the free imidazole, bands at 1646 m, 1150 w and 3222 m are assigned to υC=N, υC–N and υN–H stretching vibrations respectively [11]. The v$NH_2$ bands shifted to lower frequencies in all the complexes which indicate coordination via the aniline group [12]. Vibrations were also observed at 1370 and 1310 $cm^{-1}$ which were assigned to asymmetric and symmetric stretches of sulphonyl oxygen of sulphamethoxazole and were shifted to lower frequencies in all the complexes indicating coordination via the sulphonyl oxygen [1]. A sharp band at 1615 $cm^{-1}$ and 1646 $cm^{-1}$ due to v (>C=N) frequency of the azomethine and imine in the free ligands (SMX and IMI). The shift of vC=N to lower wave number by 30-40 $cm^{-1}$ in the complexes indicates that these groups are involved in complexation [13].

The bands for vM–O mode [14] appeared in the range of 560-580 cm$^{-1}$ in both the complexes. The presence of sharp band in the region 680-690 cm$^{-1}$ in the spectra of the complexes assigned to vM–N mode [15], further support the involvement of nitrogen atom in coordination (Table 3).

**Table 3: Infra-red bands (cm-$^{1}$) for the mixed ligands metal complexes**

| Complexes/ Ligands | υNH$_2$, asym, sym | υC=N | υS=O asym, sym | υC─N | υS – N | υN─H | M−N | υM−O |
|---|---|---|---|---|---|---|---|---|
| Sulphamethoxazole | 3462 w, 3383 w | 1615 s | 1370 m, 1310 m | ─ | 928 w | 3297 w | ─ | ─ |
| Imidazole | ─ | 1646 m | ─ | 1150 w | ─ | 3222 m | ─ | ─ |
| Cu(SMX)(Imi)$_2$ H$_2$O | 3453 s, 3368 s | 1612 s | 1413 m, 1319 s | 1150 s | 944 s | 3240 w | 689 m | 564 m |
| Mn(SMX)(Imi)$_2$ (H$_2$O) | 3451 m, 3360 m | 1601 s | 140 m, 1313 s | 1150 s | 934 m | 3245 m | 686 w | 563 s |
| Co(SMX)(Imi)$_2$ H$_2$O | 3422 br ─ | 1615 s | 142 s, 1316 m | 1133 w | 942 w | 3228 w | 680 m | 569 m |
| Zn(SMX)(Imi)$_2$ H$_2$O | 3449 s, 3360 w | 1603 s | 1404 w, 1312 s | 1148 s | 935 m | 3240 w | 680 w | 563 s |
| Zn(SMX)(Imi)$_2$ SO$_4$ | 3451 m, 3361 m | 1601 s | 1407 w, 1312 s | 1144 s | 937 s | 3240 w | 681 m | 561 s |

## Electronic spectra

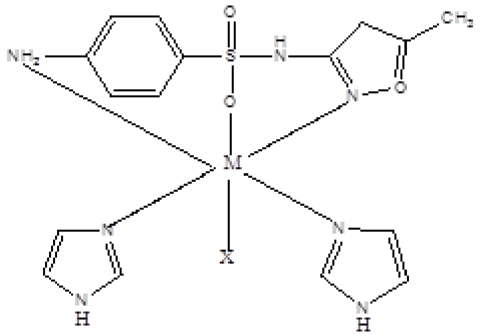
There are two bands and one band in the spectra of sulphamethoxazole imidazole ligands respectively. The band which appeared at 32680 cm$^{-1}$ sulphamethoxazole is ascribed to n⟶π* transition. While, at band 32895 cm$^{-1}$ in imidazole is ascribed to n⟶π* transition. In CuSMX(IMI)$_2$, a prominent band is observed in the region 23923 cm$^{-1}$ and is assigned to $^{2}E_{g} \rightarrow {}^{2}T_{2g}$ transition in octahedral geometry Raman et al. The electronic spectra of Manganese complex in MnSMX(IMI)$_2$ system display weak absorption band in visible region at 23923 cm$^{-1}$, which is assigned to metal to ligand charge transfer respectively typical of octahedral geometry. The electronic spectra of zinc complex in ZnSMX(IMI)$_2$ showed band in visible region at 24630 cm$^{-1}$ while in Zn SMX(IMI)$_2$ SO4, band observed at 23202 cm$^{-1}$ which are all probably due to metal to ligand charge transfer in an octahedral geometry. In SMX(IMI)$_2$, three bands were also observed, bands at 21367 cm$^{-1}$, 17953 cm$^{-1}$ and 14662 cm$^{-1}$, and are assigned to $^{4}$T1g⟶ $^{4}T_{1g}$ (P), $^{4}T_{1g}$⟶ $^{4}A_{2g}$ and $^{4}T_{1g}$⟶4T$_{2g.}$ which are in agreement with octahedral geometry (Table 4).

**Table 4: Electronic spectra of the ligands and the mixed-ligand complexes**

| Complex/Ligand | Energy (cm$^{-1}$) | Tentative assignment | Probable geometry |
|---|---|---|---|
| Sulphamethoxazole | 42194<br>32680 | π⟶π*<br>n⟶π* | - |
| Imidazole | 32895 | n⟶π* | - |
| Cu(SMX)(Imi)$_2$ H$_2$O | 23923 | $^{2}E_{g} \rightarrow {}^{2}T_{2}g$ | Octahedral |
| Mn(SMX)(Imi)$_2$ H$_2$O | 23753 | MLCT | Octahedral |
| Co(SMX)(Imi)$_2$ H$_2$O | 21367<br>17953<br>14662 | $^{4}$T1g→$^{4}T_{1}$g(P)<br>$^{4}$T1g→$^{4}A_{2}$g<br>$^{4}$T1g → $^{4}T_{2}$g | Octahedral |
| Zn(SMX)(Imi)$_2$ OAc | 24630 | MLCT | Octahedral |
| Zn(SMX)(Imi)$_2$ SO$_4$ | 23202 | MLCT | Octahedral |

## CONCLUSION

The study of coordination chemistry of the complexes is very necessary to establish their structures. All the synthesized metal complexes were generally insoluble in water and chloroform but showed different degree of solubility in other solvents. From the IR spectral data, it can be concluded that the Sulfamethoxazole and imidazole ligands behave as tridentate and monodentate respectively. And with the evidences from UV-Vis spectra, synthesized complexes are formed with following probable structure (Scheme 1).



M=Cu, Co, Mn and Zn, X=H$_2$O

**Scheme 1: Synthesized complexes**

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