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# ANTIMICROBIAL ACTIVITIES OF SOME MIXED LIGANDS ADDUCTS OF BENZOYLACETONE AND SALICYLALDEHYDE

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***ABSTRACT***
***A series of four mixed ligand complexes synthesized by reacting benzoylacetone and salicylaldehyde with different metal chlorides in ethanolic medium, were tested for their antimicrobial studies and indicated that the compounds are active against microorganisms used (Escherichia coli, Staphylococcus aureus, and Candida albicans) when compared with the activity of the reference or standard drugs (Erythromycin and Suptrin).***
***Keywords: Antimicrobial, Synthesis, Ligands, Complexes,***

## INTRODUCTION

The chemistry of antimicrobial studies with mixed ligand complexes has received interest in recent decades due to the wide applications of coordination compounds in various fields. Mixed ligand complexes appeared to be relevant in biological fluids, create specific structures and manifest themselves as enzyme-metal ion-substrate complexes (Reddy *et al.,* 2005).

N-Anilinoacetohydrazobenzoylacetone ($H_2L$) and their manganese(II), cobalt(II), nickel(II), copper(II) and zinc(II) complexes have been synthesized and characterized by IR, electronic spectra, molar conductivities, thermal analyses and magnetic susceptibilities. Binuclear complexes with molar ratios of (M:L) = 2:1 are formed. The IR spectra of these compounds shows that the ligand ($H_2L$) coordinates to the metal ions in a tetradentate manner with $O_2N_2$ as donor sites in Mn(II), Co(II), Ni(II) and Zn(II) complexes while in the Cu(II) complexes the ligand coordinates as bidentate via N and O donor atoms. The copper(II) complexes, also, shows higher antibacterial activity towards gram positive (G+) bacteria (*Bacillus subtilis* ) than the ligand and other complexes while Mn(II) complex shows higher antifungal activity than the free ligand (Kashar, 2014).

Dinuclear complexes from salicylaldehyde and 2-aminophenol with Cu(II), Ni(II) and Co(II) were synthesized and characterized by IR, UV-visible and elemental analysis. The mass spectral data obtained was in good agreement with the result obtained from plates were incubated at $37^0$C for one day. The zone of inhibition was measured and recorded (Mistchen *et. al.,* 2012)

the thermogravimetric analysis (TGA) in accordance with its fragmentation pattern (VD Bhatt, SR Ram 2012). The magnetic properties of these complexes were studied and the probable mechanism for the formation of the complexes was proposed. The complexes also shows very high antimicrobial activity.

## MATERIALS AND METHODS

**Materials :** Mueller Hinton Agar (MHA), Sabourad Destrose Agar (SDA) Erythromycin, Septrin, Benzoylacetone(Aldrich), Salicylaldehyde(Aldrich), Manganese (II) Chloride, Iron (III)Chloride (lobachem), Nickel (II) chloride, copper(II) chloride, ethanol (Glanson chemicals ltd), chloroform (cartvalues ltd), solvents were AnalaR and were used as supplied.

**Antimicrobial Screening (method)**

The *in-vitro* antibacterial activities of the compounds were tested using Mueller hinton agar (disk method) against gram positive (*Staphylococcus aureus)* and gram negative bacteria *Escherichia coli.* The bacterial strains grow on nutrient agar at 37ºC for 18 hours and then suspended in a saline solution using sterile inoculation well loop. The bacterial colony was picked from the test isolate and streaked on the labelled Petri dish containing nutrient agar. Four disks containing the concentrated metal complex and two disks containing the control were picked and placed on the labeled Petri dishes using sterilized forces. The procedure was repeated for the remaining Petri dishes respectively. Each column was separately streaked in a radical pattern. The inoculated

The *in-vitro* antifungal activity of the compounds was tested using the same method of (Mistchen *et. al.*, 2012) , Sabourad destrose agar (SDA) was used and *Candida albicans* was the fungi used

**RESULTS AND DISCUSSION**

Mixed ligand complexes of Cu(II), Fe(III), Mn(II), Ni(II) used in this study were prepared by the reaction of manganese (II) chloride tetrahydrate , ferrous (III) chloride hexahydrate, nickel(II) chloride, zinc(II) chloride with the ligands Salicylaldehyde and Benzoylacetone in 1:1:1 ratio.

The complexes of copper (II), Iron (III), Manganese (II) and Nickel (II) gives decomposition temperatures of 235$^{o}$C, 220$^{o}$C, 239$^{o}$C and 239$^{o}$C respectively. These high decomposition temperatures revealed that the complexes are thermally stable. However, the complexes appeared to have dark brown, reddish, light orange and pale green colours in their respective order.

DMSO being it a polar aprotic solvent, has the ability to dissolve a wide range of solutes, and also has a high di-electric constant. Therefore, it was the solvent used in the antimicrobial analysis.

The results of conductivity measurements showed that the Mn(II), Fe(III), Ni(II) and Cu(II) complexes, have values in the range 49–90.6 $\Omega^{-1}$ mol$^{-1}$ cm$^{2}$. This indicates that they are non-electrolyte, the slight increase in the conductance values observed, may be due to some solvolysis or dissociation (El-Qisairi *et al*., 2007). Moreover, it is reported that, in a complex, the positive charge of the metal is partially shared with the donor atoms present in the ligand, and there may be π-electron delocalisation over the whole complex (Sanap *et al.,* 2013). This increases the lipophilic character of the complex and favors its permeation through the lipoid layer of the bacterial membranes, consequently increasing it antibacterial activity.

The antimicrobial activities of the complexes Cu(II), Fe(III), Mn(II) and Ni(II) was carried out using two bacterial and one fungal species. For the antibacterial evaluation, the gram positive (*Staphylococcus aureus)* and the gram negative (*Escherichia coli)* were used, while the antifungal studies was carried out using *Candida albicans.* The complexes were evaluated by disc diffusion methods. The result of the *in-vitro* antimicrobial activities of the metal complexes was shown in (Table 3a and b). The study was made using serial dilution at $10^{-1}$, $10^{-2}$, $10^{-3}$, $10^{-4}$, and $10^{-5}$ mgmL$^{-1}$. Inhibition zones were measured and the results indicate that the test compounds are active against gram +ve and gram –ve bacterial isolates. This corresponds to the report of (Malathy *et al*., 2014). Moreover, the Gram -ve bacteria strain displayed more resistance to the complexes than the gram +ve . On the other hand, the compounds also displayed high activity against the fungal strain (*Candida albicans)* used for antifungal study (Table 3b)

The activity of the compounds can be attributed to many other factors such as solubility, conductivity and bond length between the metal and the ligand. In addition, a marked decreased in the microbial activity was noted at decreased concentration of the compounds. However, Ni(II) complex shows higher activity towards the gram positive (*E. coli*) and gram negative (*S. aureus*) bacterial strains when compared with the other complexes.

Table 1: Physical measurements.

| S/N | Compound | Empirical Formula | Mwt. | M.P ($^{O}$C) | Cond. Λ, Ω-1 mol-1 cm2 | %C found | %H found | %Cl found | %O found | % M. found | Color |
|---|---|---|---|---|---|---|---|---|---|---|---|
| **1** | Mn(II) complex | $[MnC_{17}H_{15}ClO_4]$ | 373.00 | 239 | 52.9 | 54.64 | 4.05 | 9.49 | 17.13 | 14.74 | Light Orange |
| **2** | Fe(III) Complex | $[FeC_{22}H_{15}Cl_3O_5]$ | 408.97 | 220 | 90.6 | 49.79 | 3.69 | 17.29 | 15.61 | 13.62 | Reddish Brown |
| **3** | Ni(II) complex | $[NiC_{17}H_{15}ClO_4]$ | 377.44 | 239 | 51.2 | 54.10 | 4.01 | 9.39 | 16.96 | 15.55 | Pale green |
| **4** | Cu(II) complex | $[CuC_{17}H_{15}ClO_4]$ | 382.30 | 235 | 49.6 | 53.42 | 3.95 | 9.27 | 16.74 | 16.62 | Dark brown |

**Key;**
Mwt : Molecular weight, Cond : Conductance

Table 2. Solubility of the complexes.

| **Solvents** | **Cu(II) complex** | **Fe(III) complex** | **Mn (II)complex** | **Ni (II)complex** |
|---|---|---|---|---|
| Distilled water | S | IS | S | SS |
| Ethanol | IS | SS | S | S |
| Methanol | S | SS | S | S |
| Acetone | S | S | S | SS |
| Chloroform | S | SS | S | SS |
| N-hexane | S | SS | S | S |
| Dimethylsulfoxide | S | S | S | S |

S= Soluble, SS= slightly soluble, IS=Insoluble

Table 3. Antimicrobial activity of the complexes

| **Clinical isolates** | **Complexes** | **Zone of inhibition (mm) Concentration of complexes (mg/ml)** | | | | |
|---|---|---|---|---|---|---|
| | | **$10^{-1}$** | **$10^{-2}$** | **$10^{-3}$** | **$10^{-4}$** | **$10^{-5}$** |
| | $[Cu(L^2)]$ | 11.4 | 8.5 | 8.3 | <5 | NA |
| *E. coli* | $[Fe(L^2)]$ | 8.6 | 9.0 | <5 | <5 | NA |
| | $[Mn(L^2)]$ | 7.0 | 5.4 | 6.0 | NA | NA |
| | $[Ni(L^2)]$ | 13.2 | 12.0 | 8.0 | 8.2 | 6.5 |
| | $[Cu(L^2)]$ | 11.0 | 9.0 | 9.1 | 6.6 | <5 |
| *S. aureus* | $[Fe(L^2)]$ | 9.0 | 5.1 | <5 | <5 | NA |
| | $[Mn(L^2)]$ | 6.0 | 6.0 | <5 | NA | NA |
| | $[Ni(L^2)]$ | 12.8 | 12.0 | 11.6 | 8.0 | <5 |

**Standard**: *Erythromycin*, zone of inhibition (mm) = 20 (+ve control)
DMSO, zone of inhibition (mm) = 6 (-ve control)
**Key**; NA= No Activity.

Table 3b. Antifungal activities

| **Clinical isolates** | **Complexes** | **Zone of inhibition (mm) Concentration of complexes (mg/ml)** | | | | |
|---|---|---|---|---|---|---|
| | | **$10^{-1}$** | **$10^{-2}$** | **$10^{-3}$** | **$10^{-4}$** | **$10^{-5}$** |
| | $[Cu(L^2)]$ | 9.3 | 9.0 | 8.2 | 6.6 | 7.2 |
| ***Candida albican*** | $[Fe(L^2)]$ | 10.1 | 8.4 | 8.0 | 5.1 | 5.4 |
| | $[Mn(L^2)]$ | 13.0 | 10.0 | 9.9 | 9.3 | <5 |
| | $[Ni(L^2)]$ | 13.4 | 11.2 | 8.0 | 6.0 | 6.2 |

**Standard:** *Suptrin*, zone of inhibition (mm) = 12mm (+ve control)
DMSO, zone of inhibition (mm) = NA (-ve control)
**Key**; NA= No Activity.

**CONCLUSION**

In this paper, we have reported the antimicrobial activity of a series of four mixed ligand complexes synthesized by the reaction of benzoylacetone and salicylaldehyde with suitable metal chlorides in ethanolic medium. The complexes showed high thermal stability and are active against the micro-organisms used.

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