

## STUDIES ON BIOLOGICAL ACTIVITIES OF METAL COMPLEXES DERIVED FROM 2-HYDROXY-4,5-DIMETHYL ISONITROSO ACETOPHENONE

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### ABSTRACT

A series of ternary metal complexes of the type  $[M(\text{HDMINAP})_2(\text{H}_2\text{O})_2]$  were prepared with sodium salt of 2-Hydroxy-4,5-dimethyl isonitroso acetophenone as ligand with metal salts like  $\text{CoSO}_4 \cdot 7\text{H}_2\text{O}$ ,  $\text{NiSO}_4 \cdot 7\text{H}_2\text{O}$ ,  $\text{CuSO}_4 \cdot 5\text{H}_2\text{O}$  and  $\text{ZnSO}_4 \cdot 7\text{H}_2\text{O}$ . The complexes were characterized by elemental analysis and various physicochemical techniques. The antibacterial and antifungal activities of the complexes were studied by paper disc diffusion method and Tube dilution method respectively against some pathogenic bacteria like *E. coli* and *S. aureus* and some pathogenic fungi like *C. albicans*.

**KEYWORDS:** Oxime ligand, Antibacterial and antifungal activity, Metal complexes, Inhibition

### INTRODUCTION

The synthesis and study of coordination compounds containing biologically important ligands have been paid much attention in recent years because of their wide applicability in biological, environmental and other system<sup>1</sup>.

The vast majority of compounds are used for substitution of essential metal ions and for maintaining their appropriate concentration<sup>2</sup>. Many of the inorganic medicinal compounds are mixed ligand complexes<sup>3</sup>. Cobalt is present in vitamin B12, a co-enzyme that plays significant roles in some biochemical processes<sup>4</sup>. A new Schiff base ligand and its metal complexes  $[M(\text{HDMIAP})_2(\text{H}_2\text{O})_2]$  have been synthesized using 2-Hydroxy-4,5-dimethyl isonitroso acetophenone, a bifunctional ligands with two kinds of dative sites.

Some gold complexes have been used as injections to reduce the pain and swelling of rheumatoid arthritis and tuberculosis<sup>6</sup>. Oxime ligands are well known of their biological importance as structure units that their common use in nutritional supplements, fertilizers and food technology<sup>7-9</sup>.

## EXPERIMENTAL

### Materials:

The A.R. grade chemicals were used as such without further purification. The sodium salt of 2-Hydroxy-4,5-dimethyl isonitroso acetophenone was prepared<sup>10</sup> by using the reported method. Cobalt(II) sulphate heptahydrate, Nickel(II) sulphate heptahydrate, Copper(II) sulphate pentahydrate and Zinc(II) sulphate heptahydrate are the various metal salts used for the synthesis of oxime metal complexes and which brought from THOMAS BAKER. All the solvents to be used were distilled and purified according to standard procedures<sup>11</sup>.

### Methods:

#### 1) Preparation of Complexes:

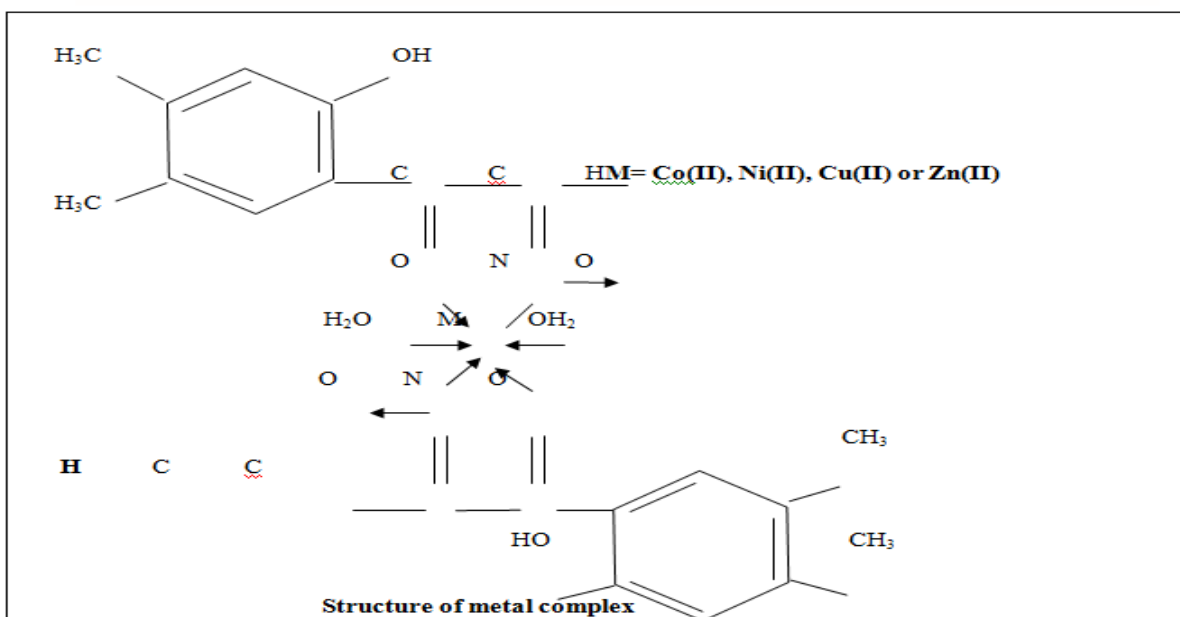
The aqueous solutions (1mmol) each of metal(II) sulphate heptahydrate and sodium salt of 2-Hydroxy-4,5-dimethylisonitrosoacetophenone mixed with constant stirring and then kept in a boiling water bath for three hours. The mixture was cooled. Solid complexes were filtered off, washed first with ice-cold water followed by 1:1 ethanol:water. Complexes were dried under vacuum.

Synthesis of present complexes may be represented by following equation:



Where Na-HDMINAP: Na salt of 2-Hydroxy-4,5-dimethylisonitrosoacetophenone,

The complexes thus formed were characterised by elemental analysis and various physicochemical techniques<sup>12</sup>.





## 2) Biological Studies:

**Broth Dilution Method:** Using this method the Minimum Inhibition Concentration (MIC) of complexes was found<sup>13-14</sup>. The nutrient media used for antibacterial activity was Muller Hinton Broth and Sabouraud Broth used for antifungal activity. Firstly the 500ppm concentration individual stock solution of each complex in DMSO was prepared. Further required dilutions were made by using respective Broth medium. The 500ppm, 250ppm, 125 ppm and 62.5ppm concentrations

of the complexes taken for each microbial species.

**Paper Disc Diffusion Method:** The antibacterial activity of the complexes against E.coli and S.aureus pathogenic bacteria was tested using Paper Disc Diffusion Method. The 0.1mL inoculum of the test organism was spread uniformly on the surface of the agar medium in a petri plate by using a spreader. The 5 mm diameter sterilized Whatmann filter paper discs were sterilized, dipped into the 400ppm solution of the complexes in DMSO and were placed on the surface of the agar in each plate. The plates were placed in incubator at 37°C for 24 hours. The complex diffuses from the filter paper into agar during incubation. INDIAN JOURNAL OF APPLIED RESEARCH X 331 RESEARCH PAPER Volume : 5 | Issue : 12 | December 2015 | ISSN - 2249-555X REFERENCE 1. Adkhis, O. Benali Baitich, M.A. Khan, G. Bouet, Synthesis Reaction Inorganic Metal-Organic Chemistry, 30(10), 1849, 2000. 2. Zoltán Nagy,

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tion.

The diameter of the inhibited zone was measured in millimeters (mm). This will be used to assess the activity of the complexes. The results of all the complexes were compared against that of the control (tetracycline) which was screened simultaneously. Solvent DMSO, used as blank, was also run to know its activity.

**Tube Dilution Method:** Using this method antifungal activity of the complexes was obtained against C.albicans pathogenic fungi. For the preparation of fungus inoculum the selected fungus was inoculated into sterilized Sabouraud broth. 0.1 mg per mL of streptomycin was added to prevent bacterial

contamination. After sporulation the spores were harvested in the same media by gentle stirring using a magnetic stirrer and the spore suspension was poured into another sterile flask. 5mL of Sabouraud broth was taken in a 15 mL Corning test tube and 0.1mL of 300ppm solution of the complexes in DMSO was added to it. It was autoclaved at 15 lb pressure for 15 minutes. The tubes were then kept on a rotary shaker and incubated at room temperature for 24 hours. The optical density (OD) of the solution was determined using a spectrophotometer at 530 nm with inoculated Sabouraud broth as blank and on the basis of optical density the percentage

growth of the fungus was calculated. The growth of the fungus in the tube without an antifungal agent was assumed as 100%. The results were compared against those of the control (amphotericin), which was screened simultaneously.

### 3) Results and Discussions:

The antimicrobial activity of all the complexes is less than that of standard streptomycin. Primary ligand shows little antibacterial and

antifungal activity. The activity of metal sulphate and primary ligand is significantly enhanced on complexation. The MIC of present CML complexes at which the culture does not show bacterial and fungal growth were found to be 400ppm and 300ppm respectively. The antibacterial and antifungal activity data is shown in table.

**Table : Biological activity of the metal complexes and their salts**

Complexes, metal salts, streptomycin and solvent	Antibacterial activity in 62.5 mm (zone of inhibition in mm)		Antifungal activity in 300 mm (% Inhibition)
	E. coli	S. aureus	C. albicans
[Co(HDMINAP) <sub>2</sub> (H <sub>2</sub> O) <sub>2</sub> ]	6	6	12
[Ni(HDMINAP) <sub>2</sub> (H <sub>2</sub> O) <sub>2</sub> ]	5	6	17
[Cu(HDMINAP) <sub>2</sub> (H <sub>2</sub> O) <sub>2</sub> ]	8	8	23
[Zn(HDMINAP) <sub>2</sub> (H <sub>2</sub> O) <sub>2</sub> ]	4	5	11
CoSO <sub>4</sub> ·7H <sub>2</sub> O	9	8	22
NiSO <sub>4</sub> ·7H <sub>2</sub> O	8	10	22
CuSO <sub>4</sub> ·5H <sub>2</sub> O	12	14	25
ZnSO <sub>4</sub> ·7H <sub>2</sub> O	6	7	17
streptomycin	14	15	43
DMF solvent	5	7	16