



# STUDIES ON BIOLOGICAL ACTIVITY OF NICKEL METAL COMPLEXES DERIVED FROM NOVEL HYDRAZONE DERIVATIVES

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## ABSTRACT

Some new nickel (II) metal complexes were prepared by treating nickel sulphate with different hydrazone derivative ligands which was obtained by condensation of 2-hydroxy benzoyl hydrazide with various aldehydes viz. benzaldehyde, p-methylbenzaldehyde,  $\alpha$ -naphthaldehyde, p-methoxybenzaldehyde and p-bromobenzaldehyde. The hydrazone derivatives and their nickel (II) metal complexes thus formed were characterized by elemental analysis and various physicochemical techniques such as IR, electronic absorption, molar conductance, magnetic susceptibility and TG-DTA analysis. The hydrazone derivatives and its nickel(II) metal complexes were investigated for their possible in vitro antimicrobial activities by paper disc diffusion method against *Bacillus*, *E.coli*, *Klebsiella*, *S.aureus* bacterial strain and *Aspergillus*, *Candida* and *Penicillium* fungal strain.

## KEYWORDS

Nickel sulphate; 2-hydroxy benzoyl hydrazide; Aldehydes; characterization; biological activity.

## INTRODUCTION

Hydrazones are an important class of ligand in co-ordination chemistry. Hydrazones form stable metal complexes with transition metal ions due to complexing ability of ligand through keto-enol tautomerism<sup>1-5</sup> and availability of other donor sites in the ligand i.e. due to presence of functional group, usually hydroxyl, azomethine, sufficiently near the site of co-ordination in the hydrazone ligands. Hydrazones and their metal complexes are biologically active. The coordination chemistry of nickel especially in high oxidation states is of considerable interest due to its importance not only in inorganic chemistry but also in other areas of chemistry and biology<sup>6</sup>. The synthesis of transition metal complexes with hydrazone derivatives of nitrogen and oxygen donor has stimulated interest due to their vast variety of biological activities ranging from pharmacological, antitumor, fungicide, bactericide, anti-inflammatory, antiviral activities and their uses in analytical chemistry as metal extracting agents<sup>7-11</sup>. The present investigation deals with the biological activity of Ni (II) metal complexes with various hydrazone derivatives.

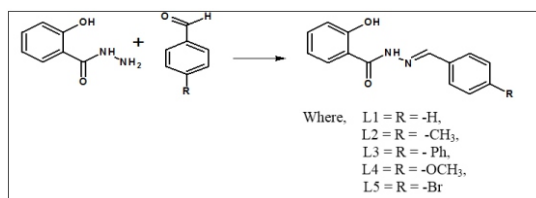
## EXPERIMENTAL

### Materials:

All the chemicals used were of the analytical grade (AR) and of highest purity. The 2-hydroxy benzoyl hydrazide was prepared by the method reported in the Vogel<sup>12</sup>. The ester like methyl salicylate and hydrazine hydrate was obtained from HIMEDIA while aldehydes such as benzaldehyde, p-methylbenzaldehyde,  $\alpha$ -naphthaldehyde, p-methoxybenzaldehyde, p-bromobenzaldehyde and nickel sulphate were obtained from THOMAS BAKER. Solvents like ethanol whenever used were distilled and purified according<sup>12</sup> to standard procedures.

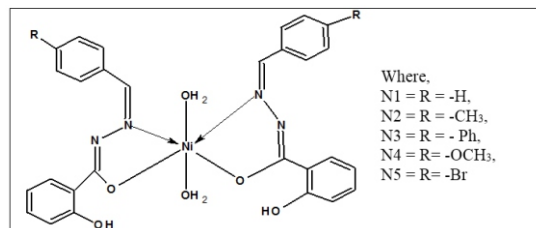
### Methods:

**Synthesis of hydrazones with various aldehydes:** The solution (0.01 M) of 2-hydroxy benzoyl hydrazide in ethanol was taken in a two neck round bottom flask fitted with water condenser. Stirred for 10 min and heated gently on heating mantle till to get clear solution. The solution of substituted aromatic aldehyde (0.01 M) in ethanol was added slowly to this stirred solution. This reaction mixture was further reflux on water bath for 3hrs. When this solution was cooled to room temperature, precipitate formed was separated by filtration and purified by recrystallisation from ethanol (yield 80%).



**Synthesis of nickel complexes:** To a hot suspension of ligand (0.01M) in ethanol, an ethanolic solution (0.01M) of the metal salt nickel sulphate was added drop wise with constant stirring with the help of rotameter and refluxed for 3hrs. The resulting reaction mixture was cooled to room temperature and maintains pH 7.8 to 7.9 by aq. NH<sub>3</sub>, then refluxed it further for 30min. The resultant product was filtered, repeatedly washed with ethanol and dried at room temperature.

The hydrazone derivatives and nickel metal complexes thus formed were characterized by elemental analysis and various physicochemical techniques<sup>13,14</sup>.



**Fig: Proposed structure of the nickel metal complexes**

### Biological studies:

The in vitro antimicrobial screening effects of the synthesized compounds were tested against four bacterial strains namely *Bacillus*, *E.coli*, *Klebsiella* and *S.aureus* and three fungal strains namely *Aspergillus*, *Candida* and *Penicillium* by paper disc diffusion method using nutrient agar medium for antibacterial activity and Sabouraud's dextrose agar for antifungal activity.

**Paper Disc Diffusion Method for antimicrobial activity:** The antimicrobial activity of the hydrazone ligands and their nickel (II) metal complexes was studied using this method against *Bacillus*, *E.coli*, *Klebsiella* and *S.aureus* pathogenic bacteria. The 0.1 ml of inoculum of the test organism was spread uniformly on the

surface of the agar medium in a petri plate by using a spreader. The sterile Whatmann filter paper discs of 5mm diameter were dipped into the 1% solution of hydrazone ligands and metal complexes in DMSO. Discs were placed on the surface of the agar in each plate.

The plates were incubated at 37°C for 24 hours. During incubation, the hydrazone ligands and metal complexes diffuse from the filter paper into agar. The activity of the hydrazone ligands and metal complexes was assessed by measuring the diameter of the inhibited zone in millimeter (mm). The control (Tetracycline) was screened simultaneously along with the hydrazone ligands. The results of all the hydrazone ligands and metal complexes are shown in table-1. DMSO solvent used as blank was also run to know its activity.

**Paper Disc Diffusion Method for antifungal activity:** The antifungal activity of the hydrazone ligands and their nickel (II) metal complexes was studied using this method against *Aspergillus*, *Candida* and *Penicillium* pathogenic bacteria. The 0.1 ml of inoculums of the test organism was spread uniformly on the surface of the agar medium in a petri plate by using a spreader. The sterile Whatmann filter paper discs of 5mm diameter were dipped into the 1% solution of hydrazone ligands and metal complexes in DMSO. Discs were placed on the surface of the agar in each plate.

The plates were incubated at 37°C for 24 hours. During incubation, the hydrazone ligands and metal complexes diffuse from the filter paper into agar. The activity of the hydrazone ligands and metal complexes was assessed by measuring the diameter of the inhibited zone in millimeter (mm). The control (Amphotericin) was screened simultaneously along with the hydrazone ligands and the results of all the hydrazone ligands and metal complexes are shown in table-1. DMSO solvent used as blank was also run to know its activity.

RESULT AND DISCUSSIONS

Table-1: Biological activity of hydrazone derivatives and their Nickel metal complexes

Compound	Antibacterial activity (Zone of inhibition in mm)				Antifungal activity (Zone of inhibition in mm)		
	<i>Bacillus</i>	<i>E.coli</i>	<i>Klebsiella</i>	<i>S.aureus</i>	<i>Aspergillus</i>	<i>Candida</i>	<i>Penicillium</i>
L1	-	-	6	-	-	-	-
L2	-	-	-	-	-	-	-
L3	-	8	8	-	-	7	-
L4	-	-	-	-	-	7	-
L5	-	10	-	-	-	10	-
N1	11	12	-	-	-	12	-
N2	11	14	-	11	-	12	-
N3	13	11	-	12	-	12	-
N4	15	11	-	12	-	13	-
N5	12	14	13	-	-	12	-
Tetracycline	18	18	20	30	-	-	-
Amphotericin	-	-	-	-	14	20	15

The *in vitro* antimicrobial screening results are given in table-1. The antimicrobial activity of all the complexes is less than that of standard tetracycline and amphotericin. On the basis of observed zone of inhibition, it was found that nickel (II) metal complexes are more active than their respective hydrazone ligands. Hydrazone ligand L1 exhibit antibacterial activity against *Klebsiella* sp. Ligand L3 exhibit antibacterial activity against *E.coli* sp and *Klebsiella* sp. and antifungal activity against *Candida* sp. Ligand L4 exhibit antifungal activity against *Candida* sp. and L5 exhibit antibacterial activity against *E.coli* and antifungal activity against *Candida* sp. All nickel complexes exhibit good antibacterial activity against *Bacillus* sp and *E.coli* sp, antifungal activity against *Candida* sp. The compounds do not show activity against *Aspergillus* and *Penicillium* fungal strains.

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