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## Study of multidentate biologically active legends with some heavy metazoans

**Sandeep Sudhanshu**

### Abstract

Due to the wide range of medicinal properties of hydrazones and their ability to form chelates with the metal ions. Due to the wide range of medicinal properties of hydrazones and their ability to form chelates with the metal ions, we undertook the synthesis and characterization, and biological activities of some new metal complexes of Morpholine-N-Thiohydrazida and its derivatives along with mixed ligands. A study and comparison of the infra-red spectra of free ligand and their Fe(III), Co(II), Ni(II) and Cu(II) complexes imply that the possible donor and azomethine nitrogen.

**Keywords:** Multidentate biologically

### Introduction

An important class of compounds containing sulphur as an essential constituents, obtained by the action of hydrazine hydrate on carboxy methyl dithoate are known as acylthiohydrazides, Thiohydrazide consists of CSNHNH<sub>2</sub> group attached to an aromatic or heterocyclic nucleus. These compounds exist in two tautomeric forms.



where R=Phenyl P-anisidyl, furfuryl, thiophenyl, pyridinyl and o-hydroxy phenyl etc. Along with the donor capability<sup>[1]</sup> of sulphur it has been shown that its presence in the compounds increases their therapeutic value. Further, the inclusion of a mercapto group (-SH) in a number of compounds has been found to increases the therapeutic value. The first compound to be examined for biological activity, 2-formyl Pyridine thiosemicarbazone, was shown to possess mild antileukemic activity against L-1210 tumour in mice at levels of drug which produced significantly toxicity<sup>[2,3]</sup>. The biological activity of such type of compounds is associated with chelation and direct correlation between antitumour activity and chelating ability of such compounds was shown by many workers<sup>[4]</sup>. Also the increasing commercial value of transition metal complexes with sulphur donor ligands has created much interest in the field of chemistry. A large number of hydrazides and hydrazones<sup>[5,6]</sup> have shown significant amoebicidal activates. Thus there has been considerable interest in the chemistry of acid hydrazides and hydrozones because of their use in biological system<sup>[7]</sup>. The increased biological significance of sulphur compounds<sup>[8]</sup> as well as of hydrazides prompted us to study the coordination capability of acyl thiohydrazides as chelation with metal ions has been suggested one of the important mechanism for drug action<sup>[9,10]</sup>.

### Material and Method

**Preparation of Ligands:** Various hydrazones are prepared by the condensation of morpholine-N- Thiohydrazide with p-chloro benzaldehyde; P-ethoxy benzaldehyde; 3, 4-diethoxy benzaldehyde benzophenone, cyclohexanone, benzyl acetone p-diethyl amino benzaldehyde; p-diethyl amino cinnamaldehyde; 3-ethoxy-4-hydroxy-benzaldehyde; 4-methyl salicylaldehyde and thiophene aldehyde. The purity of synthesized compounds was checked by thin layer chromatography, and the molecular weight and molecular formulae were

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confirmed by chemical analysis infrared absorption spectroscopy and nuclear magnetic resonance  $H^1$ -NMR-

studies. After that their biological activities were determined by cup plate diffusion method. (Table 1)

**Table 1:** Antibacterial activity of Morpholine-N-Thiohydrazide(mth) and its various derivatives against gram positive and gram negative organisms

Compound	Gram Positive Organisms		Gram Negative Organisms		
	S. Aureus	B. Subtilis	B. Pumilis	K. Pneumoniae	E. Coil
	Diameter of zone of Inhibition (mm)	Diameter of zone of Inhibition (mm)	Diameter of zone of Inhibition (mm)	Diameter of zone of Inhibition (mm)	Diameter of zone of Inhibition (mm)
(C <sub>5</sub> H <sub>11</sub> N <sub>3</sub> OS)	9.6	13.6	10.7	10.1	17.2
(C <sub>12</sub> H <sub>14</sub> N <sub>3</sub> OSCl)	9.2	9.3	9.4	11.0	9.5
(C <sub>14</sub> H <sub>19</sub> N <sub>3</sub> O <sub>2</sub> S)	10.1	13.4	10.2	9.2	9.8
(C <sub>16</sub> H <sub>23</sub> N <sub>3</sub> O <sub>3</sub> S)	11.5	9.2	13.0	9.3	9.6
(C <sub>18</sub> H <sub>19</sub> N <sub>3</sub> OS)	24.5	8.4	12.5	9.5	8.4
(C <sub>11</sub> H <sub>19</sub> N <sub>3</sub> OS)	10.4	8.7	11.2	8.5	7.5
(C <sub>15</sub> H <sub>21</sub> N <sub>3</sub> OS)	12.0	9.6	13.6	7.6	8.2
(C <sub>16</sub> H <sub>24</sub> N <sub>4</sub> OS)	11.2	10.2	11.6	8.1	9.1
(C <sub>16</sub> H <sub>26</sub> N <sub>4</sub> OS)	10.4	9.6	11.6	7.4	8.6
(C <sub>14</sub> H <sub>19</sub> N <sub>3</sub> O <sub>3</sub> S)	17.3	18.5	16.0	13.0	21.6
(C <sub>13</sub> H <sub>17</sub> N <sub>3</sub> O <sub>2</sub> S)	11.7	15.7	13.0	9.2	16.8
(C <sub>10</sub> H <sub>13</sub> N <sub>3</sub> OS <sub>2</sub> )	11.2	9.8	13.3	8.2	7.4

Zone of inhibition (mm) are the mean of the three experimental observation

**Preparation of Complexes:** The methanolic solutions of aldehydic/ketonic hydrazone of mth and of metal salt were slowly mixed by following the stoichiometry, M:L = 1:2 and refluxed in a quick fit assembly for nearly two/three hours. The reacted mixture was concentrated, cooled and the solid

material was filtered, washed with methanol, benzene and solvent ether. The end product was recrystallized from ethanol (95%) and completely dried under vacuum over fused calcium chloride, after that their biological activities were determined by cup plate diffusion method. (Table 2)

**Table 2:** Antibacterial activity of Iron (III) complexes with various Hydrazones of Morpholine-N-Thiohydrazide(mth) against gram positive and gram negative organisms

Compounds	Gram Positive Organisms		Gram Negative Organisms		
	S. Aureus	B. Subtilis	B. Pumilis	K. Pneumoniae	E. Coil
	Diameter of zone of Inhibition (mm)	Diameter of zone of Inhibition (mm)	Diameter of zone of Inhibition (mm)	Diameter of zone of Inhibition (mm)	Diameter of zone of Inhibition (mm)
[Fe(C <sub>12</sub> H <sub>14</sub> N <sub>3</sub> OSCl) <sub>2</sub> Cl <sub>2</sub> ]Cl	12.5	11.6	9.4	12.6	13
[Fe(C <sub>14</sub> H <sub>19</sub> N <sub>3</sub> O <sub>2</sub> S) <sub>2</sub> Cl <sub>2</sub> ]Cl	9.8	9.6	10.6	10.0	10.5
[Fe(C <sub>16</sub> H <sub>23</sub> N <sub>3</sub> O <sub>3</sub> S) <sub>2</sub> Cl <sub>2</sub> ]Cl	13.2	11.2	10.5	12.2	12.5
[Fe(C <sub>18</sub> H <sub>19</sub> N <sub>3</sub> OS) <sub>2</sub> Cl <sub>2</sub> ]Cl	13.6	13.2	11.2	11.3	9.8
[Fe(C <sub>11</sub> H <sub>19</sub> N <sub>3</sub> OS) <sub>2</sub> Cl <sub>2</sub> ]Cl	11.2	10.7	11.6	10.6	9.8
[Fe(C <sub>15</sub> H <sub>21</sub> N <sub>3</sub> OS) <sub>2</sub> Cl <sub>2</sub> ]Cl	14.0	11.7	10.2	11.0	12.7
[Fe(C <sub>16</sub> H <sub>24</sub> N <sub>4</sub> OS) <sub>2</sub> Cl <sub>2</sub> ]Cl	14.2	11.6	12.4	10.2	9.6
[Fe(C <sub>18</sub> H <sub>26</sub> N <sub>4</sub> OS) <sub>2</sub> Cl <sub>2</sub> ]Cl	13.5	11.2	12.6	10.6	9.3
[Fe(C <sub>14</sub> H <sub>19</sub> N <sub>3</sub> O <sub>3</sub> S) <sub>2</sub> Cl <sub>2</sub> ]Cl	11.7	10.2	10.3	11.4	11.5
[Fe(C <sub>13</sub> H <sub>16</sub> N <sub>3</sub> O <sub>2</sub> S) <sub>2</sub> Cl <sub>2</sub> ]Cl	13.3	11.5	10.0	12.3	13.0
[Fe(C <sub>10</sub> H <sub>13</sub> N <sub>3</sub> OS <sub>2</sub> ) <sub>2</sub> Cl <sub>2</sub> ]Cl	13.0	10.6	9.7	12.0	12.7

Zone of inhibition (mm) are the mean of the three experimental observations

## Result and Discussion

All the thiohydrazones were found significantly active against *S. aureus* and *B. pumilus* [11-15]. The activity of the compounds against *K. pneumoniae* was not very significant [16-20]. All the iron(III) complexes under investigation showed antitubercular activity, minimum inhibitory concentration (mic) being about 5µg/ml. However complexes with Morpholine-N-Thiohydrazimido-pethoxy benzaldimines, Morpoline -N- Thihydrazimido-p-diethyl amino benzaldinine and Morpholine-N- thiohydrazimido-3 ethoxy-4- hydroxyl benzaldehydimine had mic about 1 µg/ml.

## Conclusion

The infrared spectral studies from mixed ligands complexes, using morpholin-N- Thiohydrazide (mth) as primary ligand, the involvement of both cyclic and exocyclic nitrogen atom with same metal atom is not observed. Of the two, involvement of exocyclic primary amino-nitrogen only in co-ordination noticed, with the formation of five member ring with lesser ring strain, as compared to that in the four membered ring. Hence elemental, magnetic, electronic spectral and infra-red spectral studies of mixer ligands complexes revealed tetragonal distorted high spin octahedral stereo chemistry in the mixer ligands complexes.

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