Journal of Science and Technology vol. 14
ISSN 1858-6805
ESSN 1858-6813
Natural and Medical Sciences (NMs No.2)
mena@sustech.edu

SUST
Journal of natural and Medical Sciences

Journal homepage: http://journals.sustech.edu/

# Synthesis, characterization and biological activity of N- thioureidophthalimic acid and its divalent transition metal complexes.

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## ABSTRACT

The thiosemicarbazide derivative, N-thioureidophthalimic acid and its complexes with Zn(II), Cu(II), Co(II), Ni(II) and Pd(II) ions have been prepared and characterized by elemental analysis, molar conductivity, thermal analysis, spectroscopy (I.R, U.V. VIS., $^1$H NMR, mass spectrometry) and magnetic susceptibility measurements. The thiosemicarbazide derivative coordinates to the metal ions as a mononegative tridentate ligand or a mononegative bidentate ligand. The free ligand and its metal complexes have been tested *in vitro* against a number of microorganisms, to assess their antimicrobial properties. Antimicrobial screening of the ligand and its complexes against A*spergillus*, *flavus* and *Candida albicans* (fungi); *Esherichia Coli* ($G^-$) and *Staphilococcus aureus* ($G^+$) (bacteria). The ligand and its complexes exhibit higher activity against bacteria than fungi. The experimental results show that nearly all complexes exhibit antibacterial activity higher than the free ligand but less than the standard. In general the studied compounds are thermally stable. The TGA of the complexes revealed loss of water of hydration molecules in the first step followed by decomposition of the ligand in subsequent steps.

**Keywords**: Antimicrobial, $^1$H NMR, diffusion method, PDA.

**المستخلص:**

أجريت هذه الدراسة لتحضير وتشخيص حمض *Thioureidophthalimic* كأحد مشتقات *Thiosemicarbazide* ولتحضير وتشخيص معقداته مع أيونات الخارصين والنحاس والنيكل والبلاديوم الثنائية وقد تم إستخدام طرق وأجهزة مختلفة مثل تحليل العناصر، التوصيل الكهربي المولاري، التحليل الحراري الوزني، المطيافية المرئية وفوق البنفسجية، تحت الحمراء، الرنين المغنطيسي النووي للبروتون، وطيف الكتلة. كما تم تحديد العزم المغنطيسي عن طريق قياس القابلية المغنطيسية. وقد أثبتت الدراسة أن الحمض يرتبط الى الفلزات إما كمترابطة أحاديةالشحنة السالبة ثلاثية السن أو كمترابطة أحاديةالشحنة السالبة ثنائية السن. وقد تم إختيار النشاطية المضادة لعدد من البكتريا والفطريات بالنسبة للمترابطة الحرة غير المرتبطة ومعقداتها لتقييم خواصها كمضادات للأجسام الميكروبية مثل *Aspergillus flavus* و *Candida albicans* والبكتيريا مثل *Escherichia coli*($G^-$) و *Staphilococcus aureus*($G^+$) وقد إتضح من الدراسة أن المترابطة ومعقداتها أبدت نشاطية ضد البكتريا أعلى من نشاطيتها ضد الفطريات وأن جميع

Journal of Science and Technology vol. 14
ISSN 1858-6805
ESSN 1858-6813
Natural and Medical Sciences (NMs No.2)
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المعقدات تقريباً أكثر نشاطية ضد البكتريا مقارنة بالمترابطة الحرة ولكنها أقل نشاطية مقارنة بالمضاد الحيوي. كما أثبتت الدراسة أن المركبات المحضرة ثابتة ضد التحلل الحراري بصفة عامة كما أثبت التحلل الحراري الوزني أن المركبات تتحلل بفقد ماء التبلور كخطوة اولى يليها تحلل المترابطة في خطوات لاحقة.

## INTRODUCTION:

It has been shown that thiosemicarbazide may either behave as a monodentate ligand bonding only through the sulfur atom or as a bidentate ligand coordinating through the terminal nitrogen and the sulfur atoms. If the chelating ability of the thiosemicarbazide moiety is increased by inserting a suitable organic molecule possessing a further donor atom in the proximity of the N,S, thiosemicarbazide may act as a tridentate ligand forming a polymeric compound in some cases [1, 2]. The reaction of $CuCl_2.2H_2O$ with 1-(2-carboxybenzoyl) thiosemicarbazide ($H_3L$) and imidazole (Hlm) in NaOH gave a Cu(II) complex, which was crystallized from (py) to give the polynuclear complex $[Cu_3L_2(Py)_6(Hlm)]$ $(H_2O)_2$. The complex molecule contains a linear Cu array in which the central Cu atom has an octahedral environment and the other two Cu atoms are square pyramidal, each bridged to the central Cu atom via the ligand group with the atoms O and N chelating to one of the Cu atoms, and the atoms S and O to the other Cu atom. The carboxylate groups coordinate to the metal atoms in a unidentate fashion [3]. The crystal structure of bis(N(3)-methylthiosemicarbazide) copper(II) Chloride and bis[hexamythyleneiminylthiosemicarbazide) copper(II) chloride were reported. Both Cu(II) complexes are coordinated by the hydrazinic nitrogen and the thione sulfur of the thiosemicarbazide in a cis arrangement[4]. Thiosemicarbazides, thiosemicarbazones and their complexes are of considerable interest because of their antimicrobial activity especially as virus growth inhibitors [5]. They possess antifungal [6,7], antibacterial [8 9,10,11], antitumor [12,13,14,15] and antiamoebic [16,17,18,19] activities. It has been assumed that the microbial activity of thiosemicarbazones is due to their ability to chelate traces of metal ions, and the metal complexes themselves being the active ingredients. This hypothesis has been substantiated some what by the fact that selenosemicarbazones in which the sulfur atom is replaced by selenium, are more active against fungi than the corresponding thiosemicarbazones which in turn are more active than semicarbazones. The difference in activity is attributed to the formation of metal complexes which occur more readily in the case of selenosemicarbazone [20]. There is considerable experimental evidence to support the view that formation of a toxic metal- organo complex is a possible mechanism of fungicidal action. It has been shown that 8-hydroxy- quinoline is relatively non-toxic in triply distilled water, but the addition of a trace of an iron salt makes it effective [20]. Cymerman – Craig et al., [21] showed conclusively that the high specific activity of isonicotinic hydrazide against bacteria is due to the formation of a metal complex. It is also of interest to note that activity is lost completely when the terminal – $NH_2$ group of p-acetamidobenzaldehyde thiomsemicarbazone is replaced by a $CH_3$ group. The most likely explanation being that the latter group

Journal of Science and Technology vol. 14
ISSN 1858-6805
ESSN 1858-6813
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would prevent chelation [20]. A series of indole-3-carboxaldehydethiosemicarbazones (TSC) and their Pd(II) complexes of the type [Pd (TSC) $CL_2$] were synthesized. Among all compounds evaluated for antiamoebic activity using a strain of Entamoeba histolytica, all Pd(II) complexes were found to be more active than the respective ligands [18]. The synthesis, characterization and in vitro antiamoebic activity of 5-nitrothiophene-2-carboxaldhydethiosemicarbazones and their bidentate complexes with Ru(II) were investigated against Entamoeba histolytica and the concentration causing 50% cell growth inhibition ($IC_{50}$) was calculated in the micro molar range. Screening results indicated that the potencies of the compounds increased by the incorporation of Ru(II) in the thiosemicarbazones [19]. The objective of this study is to synthesize N-thioureidophthalimic acid and its chelates with some metal ions. Different physicochemical techniques are used to characterize the compounds. The biological activity of the ligand and complexes is reported.

## MATERALS and METHODS

Unless otherwise stated all metal chlorides are of analytical (AR) grade and used without further purification. All chemicals, reagents and solvents were of the analytical grade (AR). Thiosemicarbzide 98% (Pareac, EU), phthalic acid anhydride 98% (pareac). $PdCl_2$ provided by Johnson and Matthey chemicals limited; $HgCl_2$ provided by CDH, extrapure. Magnetic susceptibility measurements on powder samples were carried out on a Johnson Mathey magnetic susceptibility balance. Elemental analysis were carried in the micro analytical unit Cairo university, using chemical analyzer Carlo – Erba model 1106. Uv-Vis. spectra were carried out using Shimadzu models 3101 PC and 1800 spectrophotometers. Infrared spectra of solid samples were recorded on a Perkin-Elmer and Shimadzu model FT-IR 8400 S, spectrophotometers. Thermal analyses were recorded by Shimadzu thermal analyzer model TGA-50H and DTA-50H. Mass spectra were obtained by Shimadzu model Q-P-2010 plus, spectrometer. $^1H$ NMR spectra were measured using an NMR spectrometer model VX-300.

### Preparation of the ligand

The ligand N-thioureidophthalamic acid ($H_3L$) was prepared by adding 1.82 g (0.02 mol) of thiosemicarbazide (dissolved in 25 ml glacial acetic acid), in portions with instant stirring to 2.96 g (0.02 mol) phthalic acid anhydride (dissolved in 15 ml of hot glacial acetic acid).

The white crystals were collected by filtration, washed with 100 ml $H_2O$ and about 50 ml ether and left to dry in air.

### Preparation of the metals complexes

The metal complexes were all prepared by the same procedure. To a stirred solution containing 0.5 g (0.002 mol) of N-thioureidophthalimic acid (dissolved in 40 ml of hot absolute ethanol), a solution containing the appropriate weight of the metal chloride equivalent to (0.0014 mol) in 40 ml hot absolute ethanol was added while stirring. The mixture was refluxed for 1 hour followed by addition of few drops of ethanolic solution of ammonia. The solid precipitate was collected by filtration, washed with ethanol and left to dry in air.

**Biological Activity:**

Antifungal activity of the synthesized ligand $H_3L$ and its complexes in term of their inhibition to the linear growth of Aspergillus *flavus*, and Candida *albicans* was investigated. Potato-dextrose agar (PDA) was used to evaluate the effect of the compounds under investigation on the mycelia linear growth of the two tested fungi. Fifty milliliters of the medium were poured into 150 ml conical flasks and autoclaved at 121° C for 20 minutes. Three drops of 25% lactic acid were added to prevent bacterial contamination. Dilutions of each of the tested compounds were carried out (v/v) by dissolving appropriate amounts of each compound in 10 ml DMSO. Equal volumes of DMSO containing diluted compounds were added to sterile molten (40° C) PDA to get a series of different concentrations for each compound in PDA. A zero concentration treatment was prepared for each fungus which contains equivalent volume of DMSO only and used as control. Compounds amended PDA was dispensed aseptically into 9 centimeter Petri dishes. Plugs of mycelium were cut from the margins of actively growthing cultures of the fungi and placed in the center of compound-amended and unamended PDA plates with four replicate plates for each fungus. All plates were incubated at 25° C. Colony diameter in (mm) was measured after three days and the inhibition zone was calculated for each compound. The growth inhibition percentage diameter of the fungal colony using the equation (C-T) x 100/C, where C is the diameter of the fungus colony in the control plate after three days and T is the diameter of the fungus colony in the tested plates after the same period of time. The antibacterial activity of the ligand and its complexes were tested using diffusion method against Staphylococcus *aureus* as gram positive bacteria and Esherichia *coli* as gram negative bacteria. Nutrient agar (NA) medium was used. The test compounds were dissolved in DMSO. 25 ml of nutrient agar (NA) were placed in Petri plates. After solidification, the test bacteria was spread over the medium using a spreader. Discs of What-mann no. 1 filter paper saturated with the test compounds were placed at four equidistant places from the center in the inculated Petri plates. Filter paper discs treated with DMSO served as control and Tetracycline was used as standard drug. The Petri dishes were kept in a refrigerator for 24 hours for prediffusion and then incubated for 72 hours at 38 °C and the inhibition zone around each disc was measured. The zone of inhibition was carefully calculated in millimeters.

**RESULTS and DISCUSSION**

The analytical data of the ligand and complexes are in agreement with the empirical formulae shown in Table1. The results obtained indicate the formation of one type namely the 1:1 metal: ligand species. The molar conductivities ( in micro semen) in carbon tetrachloride (Table 1) at room temperature showed them to be non-electrolytes. Figure 1 shows the postulated structure of the thiosemicarbazone ligand.

Journal of Science and Technology vol. 14
ISSN 1858-6805
ESSN 1858-6813
Natural and Medical Sciences (NMs No.2)
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Table 1: Analytical data of $H_3L$ and its metal complexes.

| Formulae | m.p °C | color | Elemental analysis found (calculated)% | | | | $\Lambda_m$ * | Formula mass found (calculated) |
|---|---|---|---|---|---|---|---|---|
| | | | C | N | S | H | | |
| $C_9H_9N_3O_3S$ ($H_3L$) | 204 | white | 44.90 (45.1) | 16.00 (17.oo) | 13.94 (13.39) | 3.00 (3.00) | - | 240 (239) |
| $[Co(C_9H_7N_3O_3S)NH_3].2H_2O$ | | Grey | 32.81 (31.03) | 15.80 (16.09) | 9.67 (9.19) | 3.22 (4.02) | Nil | - |
| $[Ni(C_9H_7N_3O_3S)(H_2O)_2NH_3].2H_2O$ | | Brown | 28.19 (28.13) | 14.74 (14.84) | | 3.65 (3.90) | Nil | - |
| $[Cu(C_9H_8N_3O_3S)Cl]_2.2H_2O$ | | Dark brown | 32.55 (31.00) | 13.8 (12.00) | 8.72 (9.00) | 2.22 (2.82) | Nil | - |
| $[Zn(C_9H_7N_3O_3S)(H_2O)]$ | | White | 34.05 (33.75) | 12.49 (13.13) | | 4.57 (2.81) | - | - |
| $[Pd(C_9H_7N_3O_3S)(H_2O)(NH_3)]H_2O$ | | Orange | 25.80 (27.27) | 14.83 (14.14) | 8.35 (8.80) | 3.59 (3.54) | Nil | - |

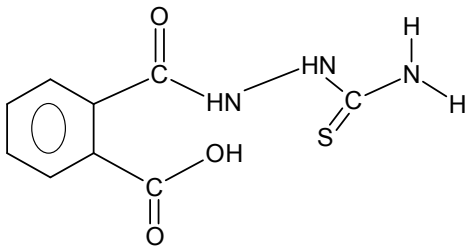


Fig.1 N-thiouredophthalamic acid

Journal of Science and Technology vol. 14
ISSN 1858-6805
ESSN 1858-6813
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**$^1$H NMR spectra**

For the free ligand ($H_3L$), the aromatic protons appear at δ 7.94 ppm. The OH (COOH), NH (CONH), NH (NHCS), $NH_2$ ($CSNH_2$) protons appear as singlets at δ 10.32, δ 8.17, δ 9.39, δ 7.4 ppm, respectively. In the Zn(II) complex, the disappearance of the peak at 10.32 ppm assigned to OH (COOH) suggests that the carboxylate group is involved in coordination to the Zn(II) ion through a deprotonated OH. The two proton signals at δ 8.17 ppm a[illegible] 7.4 ppm assigned to NH (CONH, [illegible] NH ($CSNH_2$) protons, respectively in the free ligand $H_3L$ almost remain unchanged in the complex indicating that neither of these two nitrogen atoms is deprotonated. The single proton signal at δ 9.39 ppm assigned to NH (NHCS) in the free ligand is missing in the Zn(II) complex indicating the coordination of the ligand through a deprotonated thiolate sulfur atom as a result of enolization of NHCS moiety . The proton signal at δ 6.00 ppm assigned to OH ($H_2O$) indicating a Zn-$OH_2$ bond in the complex. The $^1$H NMR spectral data is summarized in Table 2.



**Vibration Spectra:**

The I.R spectral data of the ligand $H_3L$ and its complexes are shown in Table (3).

Table(2): $^1$H NMR spectral data (ppm) of the ligand ($H_3L$) and its Zn(II) complex

| | Compound | OHδ(COOH) | NH δ(CONH) | NH δ (NHCS) | $NH_2$ δ($CSNH_2$) | δ(Ar) |
|---|---|---|---|---|---|---|
| 1 | $C_9H_9N_3O_3S$ | 10.32 | 8.17 | 9.39 | 7.4 | 7.94 - 6.7 |
| 2 | $[Zn(C_9H_7N_3O_3S).H_2O]$ | - | 8.17 | - | 7.21 | - |

**Table (3):** IR spectral data (4000-400cm$^{-1}$) of the ligand $H_3L$ and its complexes

| Compound | ν(OH) | ν (NH) (CONH) | ν($NH_2$) | ν(NH) (NHCS) | ν(COOH) | ν(CONH) | ν(CN) | ν(CS) |
|---|---|---|---|---|---|---|---|---|
| $H_3L^1$ | 3382 | 3263 | 3190 | 3028 | 1682 | 1655 | 1226 | 763 |
| $[Cu(C_9H_8N_3O_3S)Cl]_2 2H_2O$ | 3413 | 3308 | 3204 | - | 1705 | 1624 | 1186 | 736 |
| $[Ni(C_9H_7N_3O_3S)(H_2O)_2NH_3]2H_2O$ | 3564 | 3200 | 3167 | - | 1620 | 1519 | 1180 | 740 |
| $[Co(C_9H_7N_3O_3S)NH_3]2H_2O$ | - | 3301 | 3182 | - | 1680 | 1655 | 1182 | 733 |
| $[Pd(C_9H_7N_3O_3S)(H_2O).NH_3]H_2O$ | - | 3289 | 3167 | - | 1615 | 1547 | 1151 | 733 |
| $Zn(C_9H_7N_3O_3S)H_2O]$ | 3422 | 3312 | 3194 | - | 1614 | 1558 | 1188 | 738 |

Journal of Science and Technology vol. 14
ISSN 1858-6805
ESSN 1858-6813
Natural and Medical Sciences (NMs No.2)
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The intense band assigned to υ (C=S) which is observed at 763 $cm^{-1}$ in the free ligand is shifted to lower wave numbers in the Zn(II) , Ni(II), Co(II) and Pd(II) complexes indicating the coordination of the ligand through the sulfur atom. However, the band assigned to (NH) of the thioamide (NHCS) observed at 3082 $cm^{-1}$ in the free ligand is missing in the Zn(II) , Ni(II) , and Pd(II) complexes confirming the thiolate form of the coordinated ligand. The negative shift of υ (COOH) from 1682 $cm^{-1}$ in the free ligand to lower wave numbers in the three complexes indicates involvement of the deprotonated OH group of the COOH moiety in complexation to the metal ions. The band observed at 1655 $cm^{-1}$ assigned to υ (C=O) of the amido – carbonyl (CONH) group in the free ligand is shifted to lower wave numbers in the Zn(II), Ni(II) and Pd(II) complexes. Furthermore, the shift of the band υ (C-N) observed at 1226 $cm^{-1}$ in the free ligand to lower wave numbers supports the suggestion that the ligand is coordinated to the metal ions through the hydrazinic nitrogen atom. In the three complexes the ligand is therefore acting as dibasic tridentate coordinating through deprotonated OH, C-S and C-N. The I.R band observed at 3422 $cm^{-1}$ in the spectrum of Zn(II) complex is assigned to coordinated water molecule. The intense band due to the υ (C=O) carbonyl stretching frequency observed at 1682 $cm^{-1}$ in the free ligand is observed at 1705 $cm^{-1}$ in the Cu(II) complex, suggesting the non-involvement of this group in complexation. The intense band observed at 1655 $cm^{-1}$ assigned to υ (CO) of the (CONH) group in the free ligand is shifted to lower wave numbers suggesting complexation via the nitrogen atom of the admidocarbonyl group to the Cu(II) ion . The band at 736 $cm^{-1}$ assigned to υ (C=S) in the free ligand is shifted to lower wave numbers in the Cu(II) complex suggesting coordination through the thiolate sulfur atom, a fact confirmed by the absence of the band observed at 3028 $cm^{-1}$ assigned to υ (NH) in the free ligand. The new bands at 496 $cm^{-1}$ and 471 $cm^{-1}$ which are not observed in the free ligand are assigned to υ (Cu-N) and υ (Cu-S) [3].

**Electronic spectra:**

The reflectance spectrum of the Cu(II) chelate exhibited a shoulder at 573 nm (17452 $cm^{-1}$) and bands at 371 nm (26954 $cm^{-1}$) and 320 nm (31250 $cm^{-1}$) corresponding to the transition $^2T_2g \rightarrow {}^2Eg$. The observed magnetic moment of 1.98-2.02 BM falls within the range normally observed for Cu (II) octahedral complexes [22]. However, the color of the complex and position of the band suggests a square planar geometry. The band observed at 371 nm (26950 $cm^{-1}$) may be due to ligand to metal charge transfer. The peaks at 320 nm (31250 $cm^{-1}$) are assigned to intraligand transitions. The reflectance spectrum of the Co(II)($d^7$) complex exhibited bands at 237 nm (42194 $cm^{-1}$ ) and 259 nm (38610 $cm^{-1}$ ) assignable to excitations within the organic ligand. The bands at 557 nm (17953 $cm^{-1}$ ) and 534 nm (18727 $cm^{-1}$) are due to d-d transitions within the metal ion; the band at 326 nm (30675 $cm^{-1}$) is assignable to a charge transfer transition. The observed magnetic moment of 2.01 BM is suggestive of a square planar geometry. The Ni(II)($d^8$) complex displays bands at 596 nm(16776 $cm^{-1}$) $A_2g \rightarrow T_2g$, 473 nm (21142 $cm^{-1}$) $A_2g \rightarrow T_1g(F)$ and 344 nm (29069 $cm^{-1}$) $A_2g \rightarrow T_1g(P)$ transitions. The room temperature magnetic moment of 2.86 B.M. falls

within the range observed for octahedral Ni(II) complexes [22]. The Pd(II) complex exhibits three bands at 225 nm (44444 $cm^{-1}$), 357 nm (28090 $cm^{-1}$) and 677 nm (14782 $cm^{-1}$). The observed magnetic moment zero suggests a five coordinate trigonal bipyramidal structure.

**Thermal studies:**

The thermogravimetric analysis of the metal complexes along with the % mass loss at different temperature ranges measured at heating rate of 10°C $min^{-1}$ are shown in Table(4). The thermograms show three decomposition steps for the Co(II) and Zn(II) complexes, four decomposition steps for Cu(II), Ni(II) and Pd(II) complexes. All complexes show both endothermic and exothermic peaks within the temperature ranges of decomposition.

*Table (4): Thermoanalytical results (TGA and DTA) of the complexes of the ligand $H_3L$*

| Complex | TG range (°C) | DTA (°C) | No. of steps | Mass loss (%) | Total mass loss (%) | Assignment | Metallic residue |
|---|---|---|---|---|---|---|---|
| $[Co(C_9H_7N_3O_3S)NH_3]2H_2O$ | 30-120<br>120-434<br>434-1000 | 70 (+),400 (-)<br>700(-),750(-)<br>100 (-),800(+)<br>850(+) | 1<br>2 | 10.345 (10.36)<br>66.85 (60.92)<br>13.67 (12.068) | 90.88<br>(83.33) | Loss of $2H_2O$<br>Loss of $NH_3$ and lignd | Co |
| $[Cu(C_9H_8N_3O_3S)Cl]_2 2H_2O$ | 30-120<br>120-250<br>250-400<br>400-1000 | 196(+), 500(+)<br>390(+),540(+)<br>600(-),800(-) | 1<br>3 | 5.082(5.085)<br>32.6(29.4)<br>26.9(25.00)<br>15.8(18.22) | 80.5<br>(77.7) | Loss of $H_2O$<br>Loss of 2HCl<br>and 2ligands | CuO |
| $[Pd(C_9H_7N_3O_3S)H_2ONH_3]H_2O$ | 30- 120<br>120-240<br>240-350<br>350-1000 | 70(+),500(-)<br>800(+),850(+)<br>900(-) | 1<br>3 | 3.812(4.55)<br>34.165(30.56)<br>14.558(15.15)<br>22.32(22.47) | 74.855<br>(72.73) | Loss of $H_2O$<br>Loss of $NH_3$ and one ligand | Pd |
| $[Ni(C_9H_7N_3O_3S)(H2O)_2NH_3]2H_2O$ | 30-120<br>120-200<br>200-460<br>460-1000 | 600(+), 620(+)<br>700(+),800(-)<br>890(-) | 1<br>3 | 12.895(9.34)<br>5.383(5.2)<br>52.658(54.4)<br>8.7(10.68) | 79.64<br>(79.96) | Loss of $H_2O$<br>Loss of $NH_3$ loss of ligand | NiO |
| $[Zn(C_9H_7N_3O_3S)H_2O]$ | 30-285<br>285-430<br>430-700 | 300(+),586<br>(-),859(-) | 3 | 27.09 (26.25)<br>28.2 (30%)<br>28.4 (26.88) | 83.8<br>(82.92) | Loss of ligand | ZnO |

+ = endothermic - = exothermic

Journal of Science and Technology vol. 14
ISSN 1858-6805
ESSN 1858-6813
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**Results of the microbial studies**

The antimicrobial screening data for the ligand and its complexes are shown in Tables (5) and (6). The results show no antibacterial activity towards Escherichia *coli* (G- Negative) Asperigilus *flavus* and Candida *albicans* (fungus) for Pd (II) complex. The complexes of Cu(II) , and Zn(II) show zero antifungal activity toward Asperigilus *flavus*. The Pd(II) complex is inactive toward the two fungi under study . The Ni(II) complex although inactive toward Asperigilus f*lavus*, shows antifungal activity equal to that of the standard against candida *albicans*. The ligand and its complexes exhibit higher activity against bacteria than fungi. The experimental results show that nearly all complexes exhibit antibacterial activity higher than the free ligand, but less than the standard. This fact can be understood in terms of the chelation theory which states that upon complexation the polarity of the metal ion is reduced which increase the lipophilicity of the metal complex enabling them to cross the cell membrane easily [(22)].

Table (5): Antifungal screening data of the ligand ($H_3L$) and its complexes

| | | Inhibition zone diameter (mm/mg sample) | | % of inhibition | |
|---|---|---|---|---|---|
| | Sample | Aspergillus *flavus* (Fungus) | Candida *albicans* (Fungus) | Aspergillus *flavus* (fungus) | Candida *albicans* (Fungus) |
| | Control; DMSO | - | - | - | - |
| | Amphotericia B (Antifungal agent) | 18 | 19 | - | - |
| | Ligand $H_3L^1$ | 11 | 12 | 61 | 63.2 |
| 1 | $[Cu(C_9H_8N_3O_3S)Cl]_2 2H_2O$ | 00.0 | 12 | - | 63.2 |
| 2 | $[Ni(C_9H_7N_3O_3S)(H_2O)_2NH_3]2H_2O$ | 0.0 | 19 | - | 100.00 |
| 3 | $[Co(C_9H_7N_3O_3S)NH_3]2H_2O$ | 13 | 14 | 72 | 74 |
| 4 | $[Pd(C_9H_7N_3O_3S)(H_2O)NH_3]H_2O$ | 0.0 | 0.0 | - | - |
| 5 | $[Zn(C_9H_7N_3O_3S)H_2O]$ | 0.0 | 13 | - | 68.4 |

Table 6: Antiacterial activity of the ligand ($H_3L$) and its complexes and the standard antibacterial (Tetracycline) on the tested $G^-$ and $G^+$ bacteria.

| | | Inhibition zone diameter (mm/mg sample) | | % of inhibition | |
|---|---|---|---|---|---|
| NO. | Sample | Esherichia *coli* ($G^-$) | Staphylococcus *aureus* ($G^+$) | Esherichia *coli* ($G^-$) | Staphylococcus *aureus* ($G^+$) |
| | Control DMSO | 0.0 | 0.0 | - | - |
| | Standard Tetracycline | 33 | 30 | - | - |
| | Ligand ($H_3L^1$) | 12 | 12 | 36.4 | 40.0 |
| 1 | $[Cu(C_9H_8N_3O_3S)Cl]_2H_2O$ | 16 | 15 | 48.5 | 50.0 |
| 2 | $[Ni(C_9H_7N_3O_3S)(H_2O)_2NH_3]2H_2O$ | 14 | 21 | 42.4 | 70.0 |
| 3 | $[Co(C_9H_7N_3O_3S)NH_3]2H_2O$ | 13 | 13 | 39.4 | 43.3 |
| 4 | $[Pd(C_9H_7N_3O_3S)(H_2O)NH_3]H_2O$ | 0.0 | 10 | - | 33.3 |
| 5 | $[Zn(C_9H_7N_3O_3S)\ H_2O]$ | 13 | 13 | 39.4 | 43.3 |

## REFERENCES

1- Padhye S. and Kauffman G.B. (1985).Transition metal complexes of semicarbazone and thiosemicarbazones. *Coordination Chemistry Reviews*, **63**:127-160.

2- Casas J. S., Garcia M.S and Sordo J (2000), main group metal complexes of semicarbazones and thiosemicarbazones. *Coordination Chemistry Reviews*, **209:**197-261.

3- Xu Shen, Daxu Wu, and Beisheng Kang (1997). Copper complexes derived from 1-(2-carboxybenzoyl thiosemicarbazide ($H_3L$): Synthesis, characterization and crystal structure of $[Cu_3L_2(Py)_6]$ ($H_1m$) ($H_2O$). *Polyhedron Vol*.**16**:1477-1482,.

4- Castineirasa.A, Bermejoa E and West D.X (2000). Structural studyof two N(3)-substitued thiosemicarbazide copper (II) complexes. *Journal of Molecular Structure*, **522**:271-278.

5-Genova P., Varadinova T. and Souza P. (2004). Toxic effects of bis(thiosemicarbacone compounds and its Pd(II) complexes on herps simplex virus growth. *Toxicology and Applied Pharmacology* **197**:107-112.

6- Kannan S., Sivagamasundari M. and Yu Liu (2008), Ruthenium (II) carbonyl complexes of dehydroacetic acid thiosemicarbazone; Synthesis, structure light emission and biological activity. *Journal of Organometallic Chemistry* **693**:2251-2257.

7- Kumar U. and Sulekh Chandra S (2011).Synthesis spectroscopic characterization of some Schiff base complexes derived from 2-methylcyclohexanone and their activity against some fungi, *Journal of Soudi Chemical Society* **15:**19-24.

8- Domagk K G, Behnisch R. nd Schimidt H(1946). Uber eine neue, gegen Tuberkelbazillen in vitro wirksame Verbindungsklasse. *Naturwissenschaften* **33**: 315.

9- Khan S.A and Yusuf M. (2008). Synthesis, spectral studies and in vitro antibacterial activity of steroidal thiosemicarbazone and thierPd(II) complexes. *Eur. J. Med. Chem.* **06:** 1-5.

10- Poyras M., Sari M. and Buyukgungor O. (2008). Synthesis, crystal structure and biological activity of 1(1H-benzoimidazol-2-yl)-ethanone thiosemicarbazone and its cobalt complex. *Polyhedron* **27:**2091-2096.

11- Prabhakaran R., Penukadevi S,V., Huang R. and Natarajan K(2008). tructural and biological studies of mononuclear Pd(II) complexes containing N-substituted thiosemicarbazones. *Eur. J. of Med Chem* **43**: 268-273.

12- Ferrari M.B., Bisceglie F., Albertini R. and Pinelli S. (2002), Synthesis, characterization and biological activity of two new polymeric copper (II) complexes with α-ketoglutaric acid thiosemicarbazone. *Journal of Inorganic Biochemistry* **89**:36-44.

13- Demetzi D.K., Alexandratos A. and Demertizis M.A (2008). Synthesis, characterization, crystal structures, in vitro entitumepr activity of Pd(II) and Zn(II) complexes with 2-formyl and 2-acetylpyridine N(4)-1-(2-pyridyl)-piperazinyl thiosemicarbazone. *Polyhedran* **27**: 2731-2738.

14- da Silva A.P., Martini M.V., da Silva C. (2010). Antitumor activity of alpha-bisabolol based thiosemicarbazo-nes against human tumor cell lines *Eur. J. of Med Chem* **45**:2987-2993.

15- Karina O.F., Solange M.S., and Beraldo H. (2009). Copper ( complexes with 2-pyridineformamide-derived thiosemicarbazones: Spectral studies and toxicity against artemia salina. *Spectrochimica Acta part A* **73**:140-145.

16- Singh S., Bharti N. and Azam A. (2004), Synthesis, characterization and in vitro antiamoebic activity of 5-nitrothiophene2-carboxaldehyde thiosemicarbazones and their Pd(II) and Ru(II) complexes. *Eur.J of Med.Chem* **39**:459-465.

17- Hussain K., Abid M. and Azam A. (2007). Synthesis, characterization and antiamoebic activity of new indole-3-carboxaldehyde thiosemicarbazones and their Pd(II) complexes. *Eur. J. of Med. Chem*. **42**:1300-1308.

18- Singh S., Athar F. and Azam A. (2005), Synthesis, spectral studies and in vitro assessement for antiamoebic of new cyclooctadiene ruthenium (II) complexes with 5-nitrothiophene 2-carboxaldehyde thiosemicarbazones. *Bioorganic and Medicinal chemistry letters* **15:**5424-5428.

19- Hussain K., Bhar A. and Azam A. (2008). New Pd(II) complexes of the synthesized 1-N-substituted thiosemicarbazones of 3-indole carboxaldehyde: Characterization and antiamoebic assessment against E.histolytica *European Journal of Medicinal chemistry* **43**:2016-2028.

20- Gingras B.A., Hornal R.W and Bayley C.H. (1960). The preparation of some thiosemicarbazones and their copper complexes. *Can.J.Chem.* **38**: part1.

21- Cymerman J., Willis D.C. and Edgar J. (1955). Mode of action of iso nicotinic hydrazide. *Nature* **176**:34-35.

22- Mohamed G., Ibrahim N.A. and Attia H.A. (2009). Synthesis and antifungicidal activity of some transition metal complexes with benzimidazole dithiocarbamate ligand. Spectrochimica *Actra part A* **72**:610-615.