

## Metal complexes of 3-{[(1Z)-1-phenylethylidene]amino}-2-thioxoimidazolidin-4-one, Synthesis, Characterization and cytotoxic activity

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**Abstract :** A series complexes of Co(II), Ni(II), Cu(II), Pd(II), Pt(IV) and Cd(II) were synthesized with new heterocyclic ligand 3-{[(1Z)-1-phenylethylidene]amino}-2-thioxoimidazolidin-4-one. This ligand was characterized by C.H.N.S analysis, FTIR, UV-Vis, <sup>1</sup>HNMR, <sup>13</sup>CNMR and Mass spectral analysis, the synthesized complexes were identified and their geometrical were suggested in solid state by using (FT-IR) and (UV-Vis) spectroscopy, elemental analysis (C.H.N.S), flame atomic absorption technique, in addition to magnetic susceptibility and conductivity measurements. The anticancer activity of the ligand and their metal complexes have been extensively studied on HeLa cancer cell line.

**Key words :** Schiff base, 2-thioxoimidazolidin-4-one, 2-thioxoimidazolidin-4-one complexes, spectral data, anticancer activity, MTT assay.

### Introduction

Thioxoimidazolidin is a five membered heterocyclic ring with two nitrogen atoms and contain two groups, thion (C=S) and carbonyl (C=O) at position, 2 and 4, respectively<sup>1-3</sup>. It has a wide range of biological and pharmacological properties, such as antimicrobial activity (antifungal, antibacterial)<sup>4</sup>, antitumor<sup>5</sup>, antiinflammatory<sup>6</sup>, anti HIV<sup>7</sup>, Anticonvulsant<sup>8</sup> and hypoglycemic<sup>9</sup> effects. The coordination properties of 2-thioxoimidazolidin-4-one could produce promising biologically active substances<sup>10,11</sup>. This gave us motives to synthesize new metal complexes of a new Schiff base [3-{[(1Z)-1-phenylethylidene]amino}-2-thioxoimidazolidin-4-one] [L] to investigate the coordination behavior of the new ligand toward some transition metal ions, then compare the cytotoxicity of ligand with its metal complexes.

### Experimental

#### 1. Instrumentation

Melting points were recorded on a Gallenkamp MF B600 melting point apparatus. Elemental analyses (C.H.N.S) were obtained using EA-034.mth. for ligand and their metal complexes. Metal contents of complexes were estimated Spectrophotometrically using Flame atomic absorption Shimadzu-670 AA Spectrophotometer. Infrared spectra were recorded using FT-IR-8300 Shimadzu in the range of (4000-350)cm<sup>-1</sup>, samples were measured as (CsI) disc. Magnetic susceptibilities of samples in the solid state were measured by using Magnetic Susceptibility Balance of Sherwood Scietifi. The molar conductivity was measured by using Electrolytic Conductivity Measuring set Model MC-1-Mark V by using platinum electrode (EDC 304) with cell constant

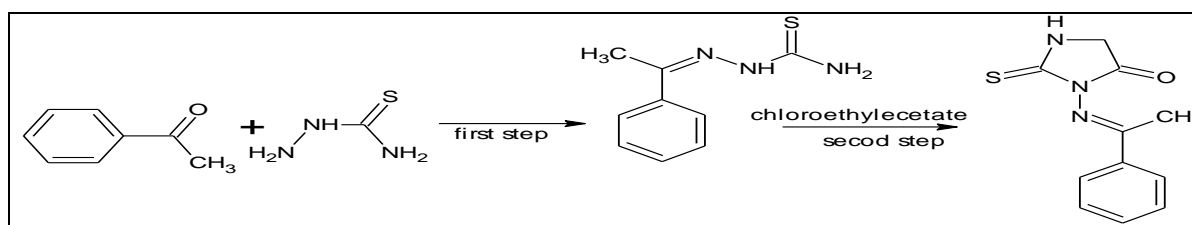
( $1\text{cm}^{-1}$ ), concentration ( $10^{-3}$  M) in dimethylformamide as a solvent at room temperature. Electronic spectra were obtained using UV-1650PC-Shimadzu Spectrophotometer at room temperature, the measurement were recorded using a concentration of ( $10^{-3}$ M) of the ligand and its metal complexes.

## 2 .Materials and Methods

All chemical were of highest purity and were used as received.

### Synthesis of ligand (L)

(0.025mole,3.0g ) acetophenone was dissolved in 30mL absolute ethanole,and then (0.025 mole,2.27g ) thiosemicarbazide was added. The reaction mixture was refluxed for 4 hrs. ,then the resulting mixture was poured into crushed ice and stirred for 15 min. from the product (0.01mole) and chloroethylacetate (0.01 mole,1.225g) were dissolved in 30ml ethanol<sup>12</sup>. The mixture was stirred for a few minutes, and then added (0.02mole,1.64g)sodium acetate was added to the mixture. The mixture was refluxed for 6hr. after cooling the precipitate was filtered off and recrystallization from ethanol. Scheme (1)



**Scheme (1): Synthesis of Ligand (L)**

### Synthesis of metal complexes (S<sub>1</sub>-S<sub>6</sub>)

An Ethanolic solution of each of the following metal ions salts(0.05 mmol)

[ CoCl<sub>2</sub>.6H<sub>2</sub>O, NiCl<sub>2</sub>.6H<sub>2</sub>O, CuCl<sub>2</sub>.2H<sub>2</sub>O, H<sub>2</sub>PtCl<sub>6</sub>.6H<sub>2</sub>O, PdCl<sub>2</sub>, and CdCl<sub>2</sub>.4H<sub>2</sub>O]was added to an ethanolic solution (0.233 g, 1 mmol) of (L). The reaction mixture was heated under reflux for (2-3) hours, during this time a precipitate was formed. The product was filtered off, washed with hot ethanol, followed by cold water and then dried under vacuum. All complexes were identified by elemental analysis (C.H.N.S),flame atomic absorption, FT-IR and Uv-Vis spectrophotometers, magnetic and conductivity measurements.

### Cytotoxic study

This research was done in laboratories of Iraqi center for cancer and medical genetic researches (ICCMGR). All cell culture procedures were carried out in a vertical laminar flow bench, which was previously sterilized by exposing it to ultraviolet light and swabbing of 70% ethanol. All equipment that was used was either bought sterile, autoclaved or filtered with 0.22  $\mu\text{m}$  Nalgene filter or syringe filter or swabbed or with 70% ethanol. The *in vitro* method was used to investigate the effect of pure cimetidine and sodium valproate of tumor cell lines (HeLa) in different concentrations and at different exposure times by MTT assay<sup>13</sup>.

#### a)HeLa cell line (NCI-DCTD, USA)

This human cervical cancer cell line was primarily established by George Gey at Johns Hopkins medical school in 1951 from a 31 years old mother of four, named ‘Henrietta Lacks[5,13]. It was supplemented from ICCMGR, Passages 18-25 of HeLa cell line were used throughout this study and the cell were maintained in MEM with 10% FCS.

#### b)Cell culture and MTT assay

HeLa (human cervical cancer cells), cell lines were obtained from Iraqi center for cancer and medical genetic researches (ICCMGR). Cells were cultured in RPMI-1640 medium supplemented with 10% FBS, 100 U/mL penicillin and 50 µg/mL amphotericin at 37°C with 5% CO<sub>2</sub>. The negative control for all the assays was represented by the untreated medium containing DMSO (0.1%). The cytotoxicity of the ligands and some its metal complexes was determined using the MTT assay, Briefly, cells were treated with four different concentrations (10, 25, 50 and 100 µg/mL) of the ligand and its metal complexes in 96-well plates and incubated for 72 h. After the incubation time, MTT dye (20 µL, 5 mg/mL) was added to the cells for 4h. followed by incubation with DMSO for 10 min. The colorimetric assay was measured at the absorbance of 570 nm using a micro plate reader<sup>5,13</sup>.

## Results and Discussion

### 1. Elemental Analyses

The physical and analytical data of the (L) ligand and (S<sub>1</sub>-S<sub>6</sub>) metal complexes are given in Table (1). The results obtained from elemental analysis are in satisfactory agreement with the calculated value. The suggested molecular formula was also supported by spectral measurement as well as magnetic moment. The new (S<sub>1</sub>-S<sub>6</sub>) complexes colored crystalline solid were soluble in (CH<sub>2</sub>Cl<sub>2</sub>, CHCl<sub>3</sub>, DMF and DMSO). They are thermally stable and unaffected by atmospheric oxygen and moisture.

**Table (2): Some Physical properties and elemental analysis of ligand and its metal complexes (S<sub>1</sub>-S<sub>6</sub>)**

Comp. Symbol	General formula	Mwt g.mol <sup>-1</sup>	Color	M.P (°C)	Elemental analysis(%)				
					Found(calc.)				
					C	H	N	S	M
L	C <sub>11</sub> H <sub>11</sub> N <sub>3</sub> OS	233	White	162-164	56.69 (56.65)	4.79 (4.72)	18.34 (18.02)	12.72 (13.73)	-----
S <sub>1</sub>	[Co(L <sub>3</sub> ) <sub>2</sub> Cl <sub>2</sub> ]	595.93	Orange	250-252	44.16 (44.30)	3.54 (3.69)	14.71 (14.09)	10.39 (10.74)	10.22 (9.89)
S <sub>2</sub>	[Ni(L <sub>1</sub> ) <sub>2</sub> Cl <sub>2</sub> ]	545.69	Orange	273dec	35.25 (35.67)	2.93 (3.11)	20.52 (21.03)	11.93 (12.08)	10.76 (10.94)
S <sub>3</sub>	[Cu(L <sub>1</sub> )]Cl <sub>2</sub> .H <sub>2</sub> O	600.54	Dark green	256-258	44.13 (43.96)	4.02 (3.66)	14.30 (13.99)	11.13 (10.66)	11.16 (10.58)
S <sub>4</sub>	[Pt(L <sub>3</sub> ) <sub>2</sub> Cl <sub>2</sub> ]Cl <sub>2</sub> .H <sub>2</sub> O	821.07	brown	170-172	32.22 (32.15)	3.04 (2.68)	10.39 (10.23)	7.66 (7.79)	24.10 (23.76)
S <sub>5</sub>	[Pd(L <sub>3</sub> ) <sub>2</sub> ]Cl <sub>2</sub>	643.42	Yellow ish brown	321-323	41.86 (41.03)	3.91 (3.42)	13.89 (13.06)	10.15 (9.95)	17.08 (16.54)
S <sub>6</sub>	[Cd(L <sub>3</sub> ) <sub>2</sub> ]Cl <sub>2</sub>	649.41	Off white	232-234	40.39 (40.65)	3.45 (3.39)	13.22 (12.93)	9.80 (9.86)	17.57 (17.31)

### 2. Mass spectrum of Ligand(L)

The mass spectrum of ligand (L) figure (1), showed the mother ion peak at (*m/z*=264), as a base peak, which is corresponds to (M<sup>+</sup>). The others fragments and their relative abundances and fragmentation pathways are shown in scheme (2):



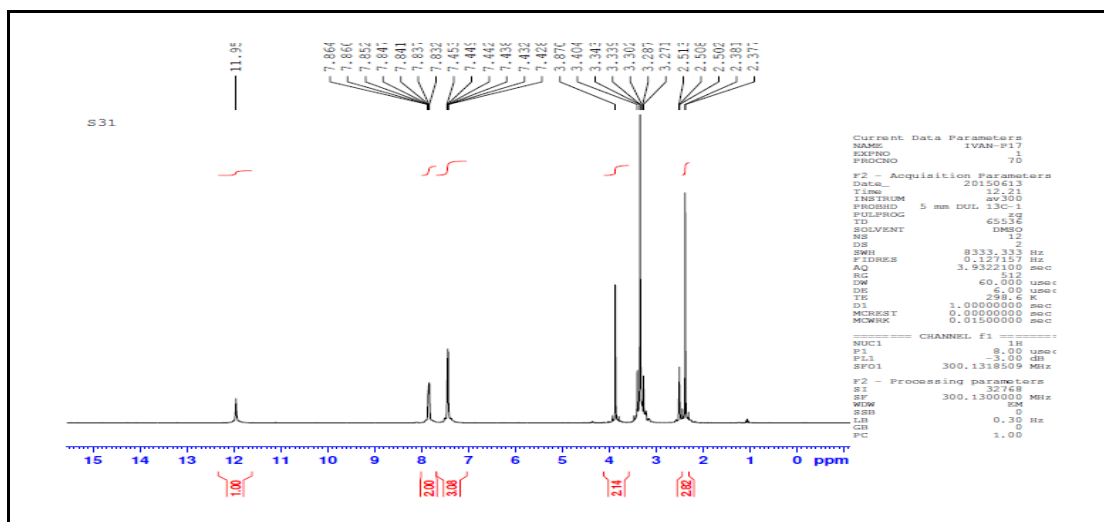


Figure (2):  $^1\text{H}$ -NMR spectrum of (L) in  $\text{DMSO-d}_6$

#### 4. $^{13}\text{C}$ -NMR spectrum of ligand

$^{13}\text{C}$ -NMR spectrum of ligand, figure (3), in  $\text{DMSO-d}_6$  exhibited chemical shifts, at (175.48, 160.03, 137.75 and 32.7 ppm and 14.54 ppm) assigned to carbonyl carbon atom, carbon of (C=S) group of imidazolidine ring, carbon atom of (C=N) group of azomethane ring, carbon atom of ( $\text{CH}_2$ ) group and carbon atom of methyl group respectively, chemical shifts at (148.18, 140.70, 129.70, 124.03) attributed to carbon atoms of aromatic ring<sup>14,15</sup>.

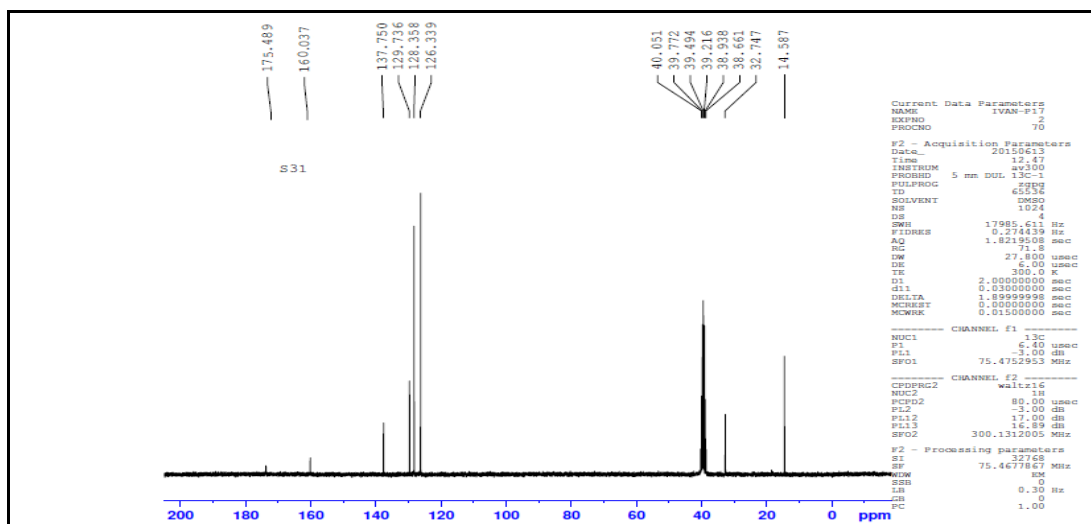


Figure (3):  $^{13}\text{C}$ -NMR spectrum of (L) in  $\text{DMSO-d}_6$

#### 5. FTIR Spectra of ligand (L) and their metal complexes ( $\text{R}_1\text{-R}_6$ )

FTIR spectra of the ligand and its complexes and important vibration modes are listed in Table (2), Fig. (4).

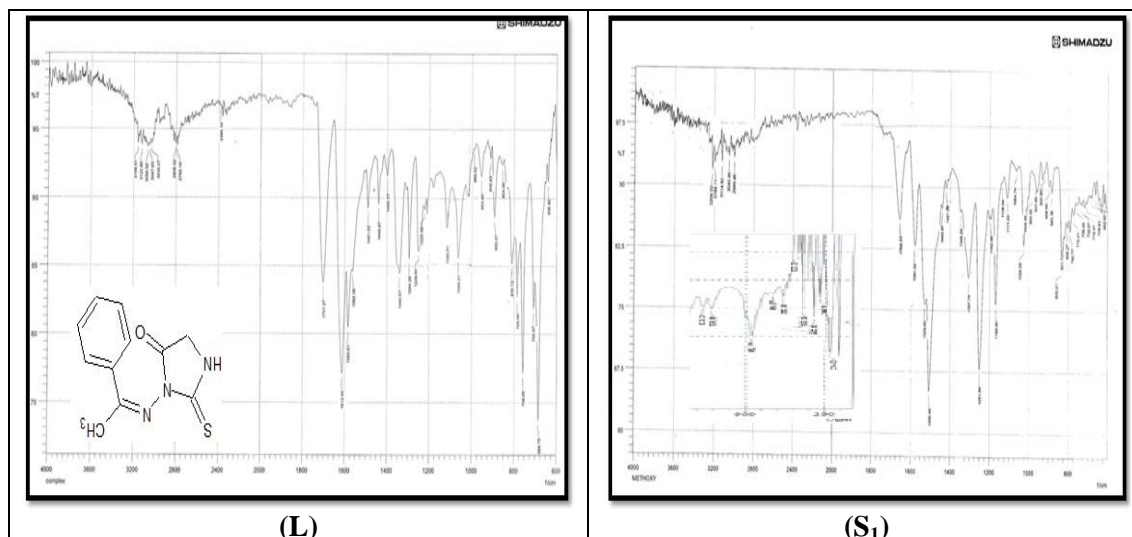
FTIR spectrum of the ligand showed bands at ( $3159\text{ cm}^{-1}$ ) due to  $\nu(\text{N-H})$  vibration of thioxoimidazolidine ring, also observed at complexes spectra, this mean that this group does not participates in coordination, spectrum of the ligand showed band at ( $1701\text{ cm}^{-1}$ ) attributed to  $\nu(\text{C=O})$  vibration [14], This band not change in all complexes of ligand. Various changes have occurred at frequencies of  $\nu(\text{C=N})$  vibrations of Schiff base and thione group, were the first observed at ( $1612\text{ cm}^{-1}$ ) in the spectrum of free ligand shifted by ( $13\text{-}25\text{ cm}^{-1}$ ) to a lower frequencies in the spectra of complexes as shown in table (2), The  $\nu(\text{C=S})$  vibration which observed at ( $1090\text{ cm}^{-1}$ ) in free ligand shifted by ( $3\text{-}39\text{ cm}^{-1}$ ) to a lower frequencies, These two different

behaviors indicated the involvement of (C=N) group of Schiff and thion group in the coordination with metal ions. The frequencies of  $\nu(\text{M-N})$  and  $\nu(\text{M-S})$  in the spectra of complexes were observed at (538-530  $\text{cm}^{-1}$ ) and (460-445)  $\text{cm}^{-1}$ , respectively<sup>16</sup>.

**Table (2): FTIR spectral data ( $\text{cm}^{-1}$ ) of ligand and its metal complexes**

Comp.	L	S <sub>1</sub>	S <sub>2</sub>	S <sub>3</sub>	S <sub>4</sub>	S <sub>5</sub>	S <sub>6</sub>
$\nu(\text{N-H})$ Imidazolidine	3159(w)	3174(w)	3170(w)	3242(w)	3164(w)	3156(w)	3160(w)
$\nu(\text{C=O})$	1701(s)	1702(m)	1701(m)	1701(m)	1701(m)	1703(m)	1703(m)
$\nu(\text{C=N})$	1612(s)	1593(s)	1597(s)	1597(s)	1591(s)	1587(s)	1599(s)
$\nu(\text{C=S})$	1095(m)	1076(s)	1072(w)	1051(m)	1087(m)	1064(m)	1064(m)
$\nu(\text{M-N})$	-----	530(w)	533(w)	530(w)	538(w)	530(w)	533(w)
$\nu(\text{M-S})$	-----	445(w)	452(w)	462(w)	458(w)	455(w)	450(w)
$\nu(\text{M-Cl})$	-----	361(w)	365(w)	-----	359(w)	-----	-----

Where : S=strong, W=weak, M=medium



**Figure (4): FT-IR spectra of (L) and (S<sub>1</sub>)Complex**

## 6. Electronic absorption spectra, Magnetic susceptibility, and Conductivity measurements

The (U.V-Vis) spectrum of ligand, in absolute ethanol exhibited three absorption bands at (230 nm, 43478 $\text{cm}^{-1}$ ), (260 nm, 38461 $\text{cm}^{-1}$ ) were assigned to ( $\pi \rightarrow \pi^*$ ) transitions, and band at (305 nm, 32786 $\text{cm}^{-1}$ ) assigned to ( $n \rightarrow \pi^*$ ) transitions<sup>14</sup>. Complexation of (L) with metal ions appearance a new bands in the visible and UV. These bands were attributed to M-L charge transfer and to ligand field transitions. Table (3), Fig.(5) describes bands of maximum absorption of (R<sub>1</sub>-R<sub>6</sub>) complexes in chloroform with their assignments

The electronic spectrum of the (S<sub>1</sub>) complex showed two transitions at (655nm, 15267 $\text{cm}^{-1}$ ) and (530nm, 18867 $\text{cm}^{-1}$ ), which might be assigned to the transition  ${}^4\text{T}_{1g} \rightarrow {}^4\text{A}_{2g}(\text{F})$  ( $\nu_2$ ) and  ${}^4\text{T}_{1g} \rightarrow {}^4\text{T}_{1g}(\text{P})$  ( $\nu_3$ ) respectively<sup>17,18</sup>, these indicate an octahedral geometry. On the basis of these assignment it was possible to calculate ( $\nu_1$ ) for  $d^7$  of (Tanaba- Sugano) diagram, the calculated value of ( $\nu_1$ ) to be (7917) $\text{cm}^{-1}$  due to the transition  ${}^4\text{T}_{1g} \rightarrow {}^4\text{T}_{2g}(\text{F})$ . The magnetic susceptibility and molar conductivity measurement indicated that the complex to be a paramagnetic (4.3 B.M) and non conducting.

The electronic spectrum of (S<sub>2</sub>) complex, shows two bands, (495nm, 20202 $\text{cm}^{-1}$ ) and (430nm, 23255 $\text{cm}^{-1}$ ) assigned to  ${}^1\text{A}_{1g} \rightarrow {}^1\text{A}_{2g}(\text{F})$ , and  ${}^1\text{A}_{1g} \rightarrow \text{E}_g(\text{P})$  ( $\nu_3$ ) transitions respectively<sup>19</sup>. These bands indicate a square planer

geometry around Ni (II)ion, the calculated values of magnetic moment were (0.08 B.M). This confirm the diamagnetic character of complex and non conducting behavior<sup>20,21</sup>.

The electronic spectrum of (S<sub>3</sub>) complex shows one broad band at (680nm,14705 cm<sup>-1</sup>) which corresponds to <sup>2</sup>B<sub>1g</sub>→<sup>2</sup>E<sub>g</sub> transition, and a shoulder band at (425nm,23529cm<sup>-1</sup>) which assigned to <sup>2</sup>B<sub>1g</sub>→<sup>2</sup>A<sub>1g</sub> transition<sup>22</sup>. The position of these bands is in a good agreement with a square planer configuration. The value of magnetic moment at room temperature was found to be (2.05B.M), which agree well with distorted octahedral geometry around Cu (II) complex<sup>18,22,23</sup>. Conductivity measurement in DMF showed that the complex has electrolytic nature.

The electronic spectrum of (S<sub>4</sub>) complex, shows bands, (506nm,19762cm<sup>-1</sup>), (433nm,23094cm<sup>-1</sup>) and (361nm,27700cm<sup>-1</sup>) assigned to <sup>1</sup>A<sub>1g</sub>→<sup>3</sup>T<sub>1g</sub>, <sup>1</sup>A<sub>1g</sub>→<sup>3</sup>T<sub>2g</sub> and (M→L<sub>CT</sub>) respectively[19,21,23],fig.(5). The complexes may have an octahedral coordination of the central metal ion by the surrounding ligands. The magnetic value (1.16 B.M) for Pt(IV) is observed, this agree with octahedral geometry around Pt(IV)ion[22-24]. The conductance measurements indicate the ionic behavior of this complex.

The electronic spectrum of (S<sub>5</sub>) complex, shows two bands, (480nm,20833cm<sup>-1</sup>) and (433nm,23094cm<sup>-1</sup>) assigned to <sup>1</sup>A<sub>1g</sub>→<sup>1</sup>B<sub>1g</sub> and <sup>1</sup>A<sub>1g</sub>→<sup>1</sup>E<sub>g</sub> transitions respectively<sup>18,22,24</sup>. The complex may have a square-planar coordination of the central metal ion by the surrounding ligands. The magnetic moment data of Pd(II) complexes indicate that this complex is diamagnetic .This agree with square-planar geometry around Pd(II) ion<sup>18,23,25</sup>. The conductance measurements indicate the ionic behavior of this complex.

According to the electronic spectrum of (S<sub>6</sub>) complex, no **d-d** transition is located as it belongs to **d<sup>10</sup>**. The prepared complexes are off white in color with the diamagnetic being expected, The U.V-Vis spectrum of (R<sub>6</sub>), in CHCl<sub>3</sub>, displayed three bands at (239 nm, 41841 cm<sup>-1</sup>), (288nm, 34722 cm<sup>-1</sup>) and (343 nm, 29154 cm<sup>-1</sup>), respectively, assigned to (π→π\*), (n→π\*) and (M→L<sub>CT</sub>)transitions<sup>18,22,23,26</sup>. The conductivity measurements indicate ionic conducting behavior of the complex.

**Table (3): Electronic spectra, Magnetic moment (B.M) and Conductance in (DMF) for (R<sub>1</sub>-R<sub>6</sub>) complexes**

No.	Maximum absorption ν <sub>max</sub> (cm <sup>-1</sup> )	Band assignment	B`	β	10Dq	Molar Cond. S.cm <sup>2</sup> .mol <sup>-1</sup>	μ <sub>eff</sub> . B.M	Suggested geometry
(S <sub>1</sub> )	15267 18867 7917	<sup>4</sup> T <sub>1g</sub> → <sup>4</sup> A <sub>2g</sub> (F) <sup>4</sup> T <sub>1g</sub> → <sup>4</sup> T <sub>1g</sub> (P) <sup>4</sup> T <sub>1g</sub> → <sup>4</sup> T <sub>2g</sub> (F) (calc.)	380.6	0.48	78608	13.93	4.3	O.h
(S <sub>2</sub> )	20202 23255	<sup>1</sup> A <sub>1g</sub> → <sup>1</sup> A <sub>2g</sub> <sup>1</sup> A <sub>1g</sub> → <sup>3</sup> E <sub>g</sub>				167-99	Dia	S. P
(S <sub>3</sub> )	23529 14705	<sup>2</sup> B <sub>1g</sub> → <sup>2</sup> A <sub>1g</sub> <sup>2</sup> B <sub>1g</sub> → <sup>2</sup> E <sub>g</sub>	----	-----	-----	171.43	2.05	S.P
(S <sub>4</sub> )	19762 23094 27700	<sup>1</sup> A <sub>1g</sub> → <sup>3</sup> T <sub>1g</sub> <sup>1</sup> A <sub>1g</sub> → <sup>3</sup> T <sub>2g</sub> LMCT	-----	-----	-----	167.9	1.16	O.h
(S <sub>5</sub> )	20833 23094	<sup>1</sup> A <sub>1g</sub> → <sup>1</sup> B <sub>1g</sub> <sup>1</sup> A <sub>1g</sub> → <sup>1</sup> E <sub>g</sub>	-	-	-	172.43	Dia	S. P
(S <sub>6</sub> )	41841 34722 29154	π→π* n→π* MLCT	----	----	---	167.43	Dia	T.h

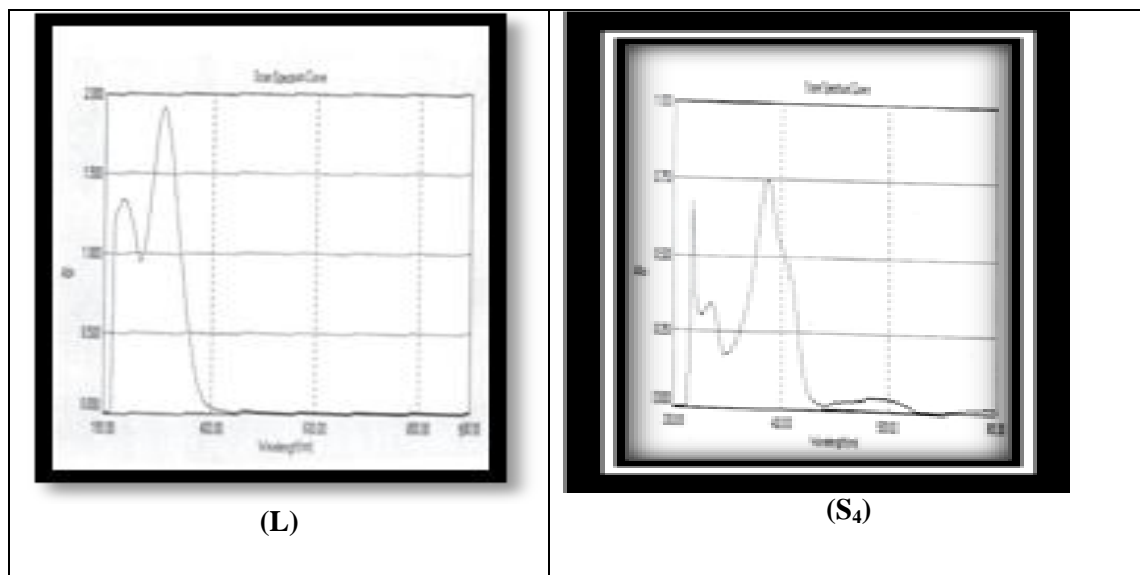
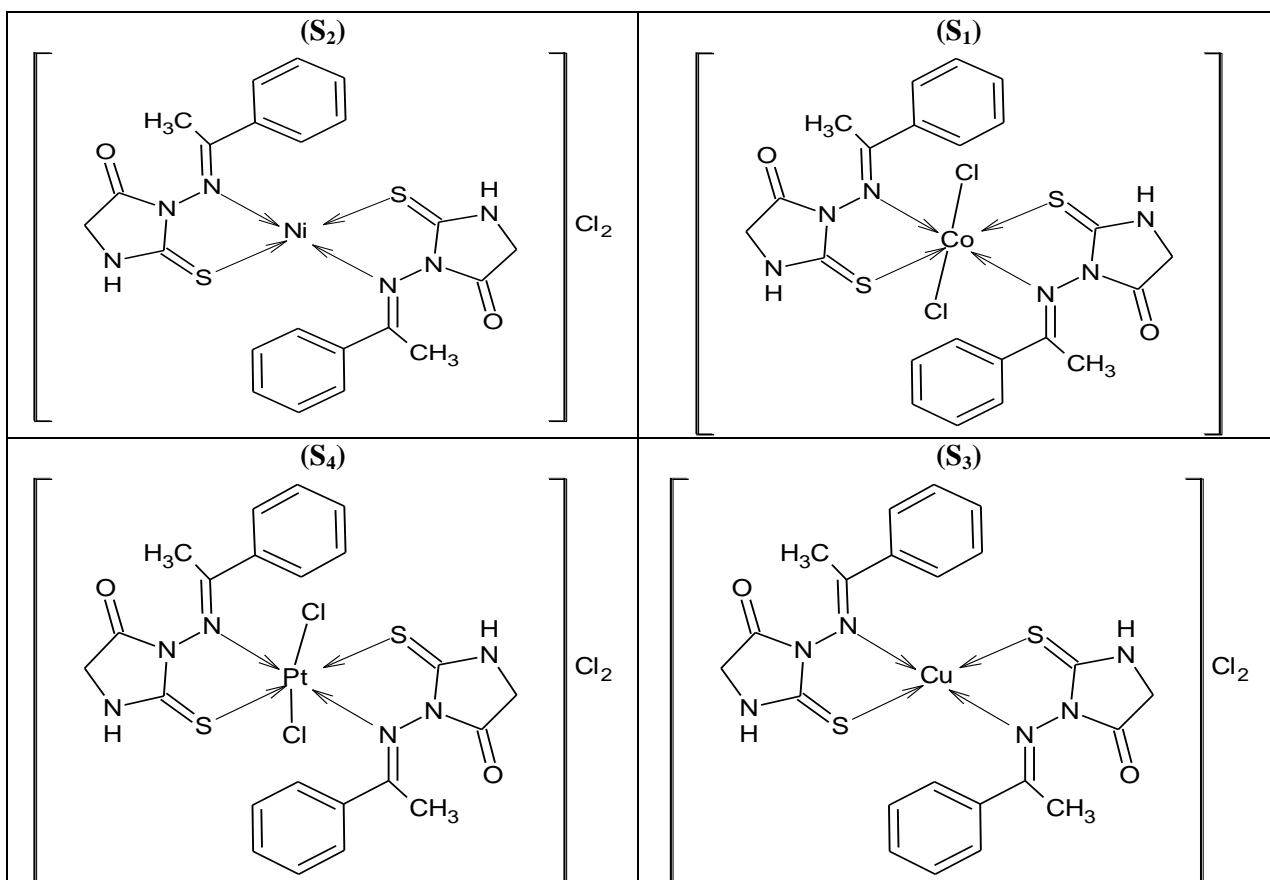


Figure (5): UV-Vis spectra of (L) and (S<sub>4</sub>)Complex

**Suggested Chemistry Structure of Metal complexes (S<sub>1</sub>-S<sub>6</sub>)**

According to the results obtained from elemental and spectral analysis as well as magnetic moment and conductivity measurements, the structure of the above mentioned compounds can be illustrated as follows, figure(6).





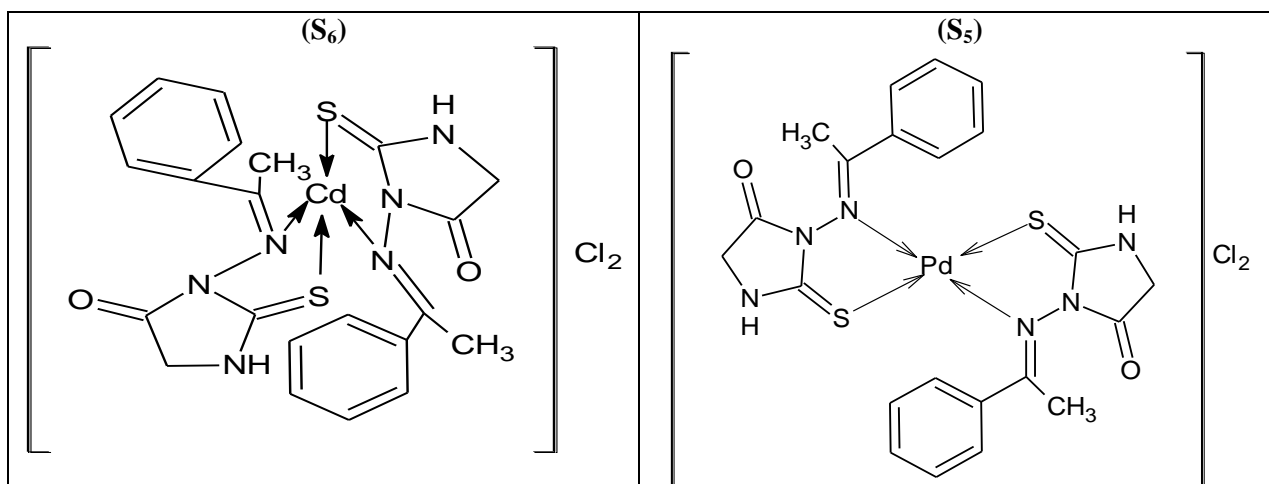


Figure (6): Suggested Chemistry Structure of Metal complexes ( $R_1$ - $R_6$ )

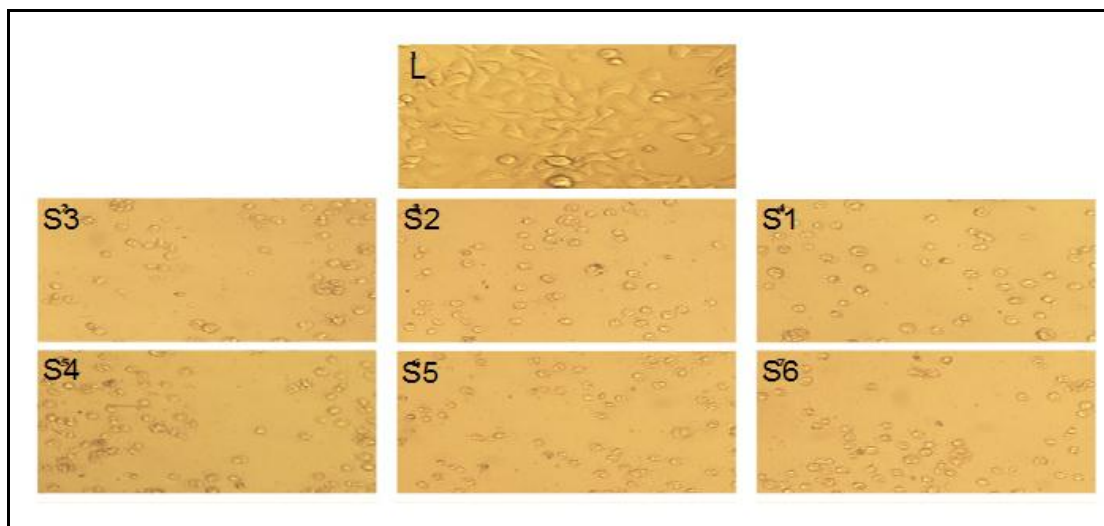
### 7.cytotoxic activity Studies

The cytotoxic effects of ligands and some of its metal complexes were studied against HeLa cancer cell line. This cell line was exposed to concentrations of these ligands and some of its metal complexes ranged from (10 to 100  $\mu\text{g/ml}$ ) for 72 hrs only. The optical density was measured under wavelength 570 nm with ELISA reader after their staining with MTT stain. The results showed that these ligands and some of its metal complexes led to decrease the growth of HeLa cancer cell significantly as compared to untreated control cells as estimated by comparison of the optical density of the treated and control cell lines. The results showed that the inhibition rate at **10 $\mu\text{g/ml}$**  that L has the lowest percentage of inhibition while the complex  $S_{15}$  has highest inhibition percentage and the other ligands and complexes have different inhibition percentage in order  $S_3 > S_6 > S_4 > S_5 > S_1 > S_2 > L$ , as shown in Table (4) , fig(7).

When the concentration of ligand L and its metal complexes ( $S_1$ .  $S_6$ ) increased to **25 $\mu\text{g/ml}$** , the inhibition rates for these concentrations increase and the  $S_3$  stay at greatest inhibition percentage and which include the following order,  $S_3 = S_6 > S_4 > S_5 > S_1 = S_2 > L$ , table (4) , fig(7). At **50 $\mu\text{g/ml}$**  the complexes  $S_3$  and  $S_4$  record highest inhibition activity against HeLa cancer cell line compare with other complexes and ligand L while complex  $S_1$  was the lowest inhibition activity against same cell line, the order of ligand and its metal complexes was  $S_4 > S_3 > S_6 > S_2 > S_5 > S_1 > L$  . While at **100 $\mu\text{g/ml}$**  the complexes  $S_3$  and  $S_4$  were remained at the highest rate of inhibition, while other complexes showed varying in the percentage of inhibition, the percentage of inhibition arranged as follows:  $S_3 > S_4 > S_6 > S_2 > S_1 > S_5 > L$ . This study demonstrated that ligand (L) and its metal complexes ( $S_1$ - $S_6$ ) have significant cytotoxic effect and its inhibition effect was concentration manner as shown in Table (4) , fig (7). This may be due to its activity as potent inhibitor of  $\text{Na}^+/\text{H}^+$  antiporter[27,28] this ubiquitous transport system participates in many important cellular functions, such as regulation of intracellular pH, trans cellular movement of acid and base equivalents, cell growth and proliferation, and regulation of cell volume . The HeLa cell line is a non polarized epithelial cell which is known to express  $\text{Na}^+/\text{H}^+$  exchanger activity [27,29] The inhibition caused by ligands and its metal complexes on HeLa is mediated not through their receptors but through direct interaction with the  $\text{Na}^+/\text{H}^+$  exchanger and bonded to nucleic acids in DNA [27-29] Interaction of complexes and nucleic acids cause conformational changes of DNA and then lead to cell damage. Determination of the interactions between ligands or metal complexes and DNA should be elucidated to help explain the mechanisms of apoptotic events and drug potential of these compounds [27,30]

**Table(4): Evaluation of cytotoxicity of ligands and some of its metal complexes against HeLa cell line**

Sample conc.µg/ml	Inhibition rate (%)						
	L	S <sub>1</sub>	S <sub>2</sub>	S <sub>3</sub>	S <sub>4</sub>	S <sub>5</sub>	S <sub>6</sub>
10	4.75	5.83	5.35	10.91	8.24	6.98	8.38
25	8.32	14.08	14.08	18.52	16.99	15.22	18.52
50	20.64	22.60	28.89	39.25	40	25.65	38.79
100	31.27	39.10	40.53	49.44	48.96	37.50	48.12

**Fig(7): HeLa cancer cell line after treatment with 100 µg/ml of ligand (L) and its metal complexes (S<sub>1</sub>-S<sub>6</sub>) for 72 hr**

## Conclusions

The new 3-[[1Z]-1-phenylethylidene]amino}-2-thioxoimidazolidin-4-one (L) ligand and its metal complexes (S<sub>1</sub>-S<sub>6</sub>) were successfully synthesized and characterized. The free ligand and its metal complexes show significant cytotoxic activity against HeLa cancer cell line.

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