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Evaluation of the antifungal and anti-hyperthyroidism efficacy of copper(II), nickel(II), cobalt(II) and zinc(II) complexes with thiourea derivatives.

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Abstract

Anew ligand N-((3,5-dichloropyridin-2-yl)carbamothioyl) pivalamide (L^2) was synthesized by reaction of benzoyl isothiocyanate with 2-Amino-3,5-dichloropyridine by using acetonitrile as a solvent , The ligand was characterized by elemental analysis apparatus , FT-IR , ^{13}C,^{1}H-NMR spectra , UV-Visible, , some transition metals complexes(Co , Ni , Cu , Zn) of this ligand was prepared and characterized by FT-IR , UV-Visible spectra , conductivity measurements , magnetic susceptibility ,From results the proposed molecular structure for these complexes as obtained , the following formula where M^{+2} = Co , Cu , Ni , Zn [M :L^2] [1 :1] Tetrahedral and [M:L^2] [1:2] Octahedral . The biological activity of the prepared compounds was measured and tested as antifungals against (Candida albicans, Aspergillus Niger) and using DMSO as a control solution The results showed that the prepared compounds possess antifungal activity at different concentrations, The effectiveness of the prepared ligands and their complexes with Zn(ll) ions were studied as anti-elevation of T3 and T4 thyroid hormones induced by thyroxine, and the results showed a decrease in T3 and T4 hormones after (20) days of taking these compounds.

Introduction

Thiourea is the class of the organic compound having sulphur with general formula $(R_1R_2N)(R_3R_4N)C=S$. These have structural resemblance to urea , except that the oxygen atom of urea is replaced by a sulfur atom , the chemical properties of urea and thiourea are quite different from each other . [(1)]

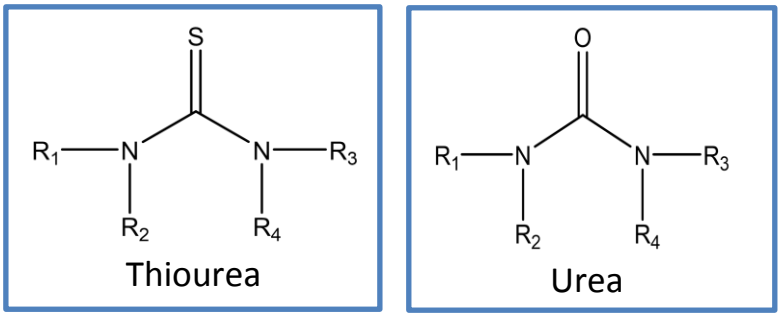


Figure 1: The chemical formula for Urea and Thiourea

Thiourea Complexes multi-linked ligands that have the ability to bond and coordinate with the central metal ion as ligands anionic mono and dual ligands , The causation is attributed to the presence of the tow nitrogen atoms and the sulfur atom that allows thiourea to bond with more than one possibility to form stable complexes , and thiourea has important resonance structures that allow it to bond with other molecules[(2)(3)]

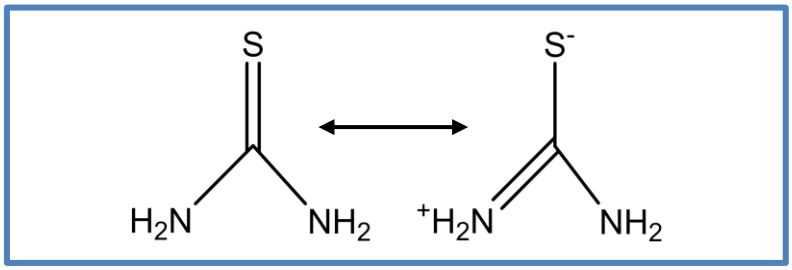


Figure 2: Resonance structures of thiourea

Applications of complexes of thiourea derivatives have a great to act as ligand especially co-ordination chemistry of benzoyl thiourea satisfactorily explained . These form more stable complexes having six membered ring . These thiourea have capability to act as chelating because of the presence of C=S and C=O functional groups . That is why novel thiourea have attention researchers due to their property to act as ligand[(4)]. thiourea derivatives are effective as antifungals[(5)] and they are effective as anti-hyperthyroidism. Thyroid gland hyperplasia results in swelling in the neck area and this inflation occurs as a result of excessive secretion of thyroid hormones. These cases are treated using (antithyroid drugs) and thiourea derivatives are used to treat hyperthyroidism thyroid[(6)]

2-Experimental

2.1- Synthesis of N-((3,5-dichloropyridin-2-yl)carbamothioyl)pivalamide (L)

Dissolve (0.201 g, 0.00207 mole) of potassium thiocyanate (KSCN) in 2 ml of acetonitrile (meCN) in a circular flask and add to it (0.250 g, 0.00207 mole) of Tri methyl acetyl chloride ($(CH_3)_3COCl$) dissolved in 2 ml of acetonitrile. Return distillation of the mixture was carried out for three hours at a room temperature of (25°C) , an orange-colored solution was formed . (0.337g,0.00207 mole) 3,5-dichloropyridin-2-amine dissolved in 2ml of acetonitrile. The mixture was refluxed for three hours at room temperature, during which a white-yellow precipitate was formed. The solution was filtered and the precipitate was purified by washing with the solvent several times. Compound L^2 was obtained.[7]

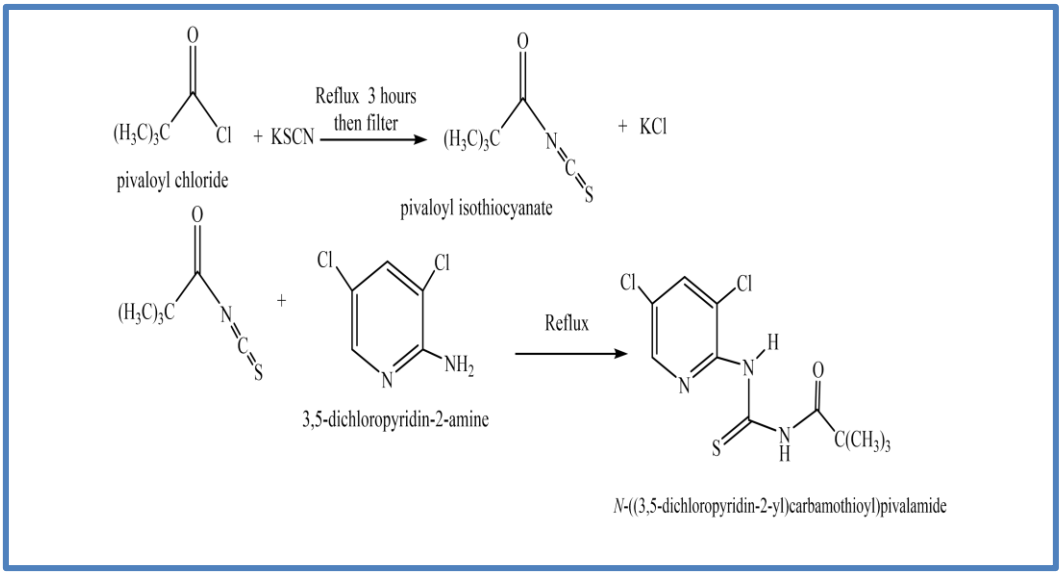


Figure 3: Synthesis of [N-((3,5-dichloropyridin-2-yl) carbamothioyl)pivalamide] (L)

2.2 . Synthesis of complexes[8]

2.2.1. Synthesis of [L Cu Cl] in the ratio of (1:1)

The salt of $CuCl_2.2H_2O$(0.166 g) dissolved in 20 ml ethanol and added to (0.3g) of L dissolved in 40ml ethanol. The mixture was stirrer at room temperature for (30 sec) . Light green precipitate was formed and filtered washing with 2 ml of ethanol to remove unreacted ligand and dried under vacuum . light green crystals were grown at room temperature by the diffusion of ethanol solution .

2.2.2. Synthesis of [L Ni Cl] in the ratio of (1:1)

The salt of $NiCl_2.6H_2O$(0.232 g) dissolved in 20 ml ethanol and added to (0.3g) of L dissolved in 40ml ethanol. The mixture was stirrer at room temperature for (30 sec) . Green precipitate was formed and filtered washing with 2ml of ethanol to remove unreacted ligand and dried under vacuum . Green crystals were grown at room temperature by the diffusion of ethanol solution .

2.2.3. Synthesis of [L Zn Cl] in the ratio of (1:1)

The salt (0.133 g) of $ZnCl_2.1H_2O$ (0.133 g) dissolved in (20 ml) ethanol and added to (0.3g) of L dissolved in 40ml ethanol . The mixture was stirrer at room temperature for (30 sec) . palt Yellow precipitate was formed and filtered washing with 2ml of ethanol to remove unreacted ligand and dried under vaccum . palt Yellow crystals were grown at room temperature by the diffusion of ethanol solution .

2.2.4. Synthesis of [LCOCl] in the ratio of (1:1)

The salt of $COCl_2.6H_2O$(0.233 g) dissolved in 20 ml ethanol and added to (0.3g) of L dissolved in 40ml ethanol . The mixture was stirrer at room temperature for (30 sec) . Pink precipitate was formed and filtered washing with 2ml of ethanol to remove unreacted ligand and dried under vaccum . Pink crystals were grown at room temperature by the diffusion of ethanol solution .

2.2.5. Synthesis of [$(L)_2$ Cu AC] in the ratio of (2:1)

The salt of $Cu(CH_3COO)_2.H_2O$ (0.097 g) dissolved in 20 ml ethanol and added to (0.3g) of L dissolved in 40ml ethanol . The mixture was stirrer at room temperature for (30 sec) . Dark green precipitate was formed and filtered washing with 2ml of ethanol to remove unreacted ligand and dried under vaccum . Dark green crystals were grown at room temperature by the diffusion of ethanol solution .

2.2.6. Synthesis of [$(L)_2$ Ni AC] in the ratio of (2:1)

The salt of $Ni(CH_3COO)_2.4H_2O$ (0.121 g) dissolved in 20 ml ethanol and added to (0.3g) of L dissolved in 40ml ethanol . The mixture was stirrer at room temperature for (30 sec) . Mustard precipitate was formed and filtered washing with 2ml of ethanol to remove unreacted ligand and dried under vaccum . Mustard crystals were grown at room temperature by the diffusion of ethanol solution .

2.2.7. Synthesis of [$(L)_2$ Zn AC] in the ratio of (2:1)

The salt of $Zn(CH_3COO)_2.2H_2O$ (0.107 g) dissolved in 20 ml ethanol and added to (0.3g) of L dissolved in (4oml) ethanol . The mixture was stirrer at room

temperature for (30 sec) . Greenish white precipitate was formed and filtered washing with 2ml of ethanol to remove unreacted ligand and dried under vaccum . Greenish white crystals were grown at room temperature by the diffusion of ethanol solution .

2.2.8. Synthesis of [$(L)_2$ CO AC] in the ratio of (2:1)

The salt of $CO(CH_3 COO)_2.4H_2O$ (0.25 g) dissolved in 20 ml ethanol and added to (0.3g) of L dissolved in 40ml ethanol . The mixture was stirrer at room temperature for (30 sec) . Green precipitate was formed and filtered washing with 2ml of ethanol to remove unreacted ligand and dried under vaccum . Green crystals were grown at room temperature by the diffusion of ethanol solution .

2.3- Characterization of L and complexes

The various available spectroscopies and techniques were used to characterize and confirm the formula of the free ligand and its element compounds. HNMR, ^{13}CNMR, IR, UV-vis, , CHNS, solubility investigation, , conductance values and magnetic effective moment were dedicated to confirm their structural characterization.

2.4- Test of antifungals activity

The antifungal activity of 108 samples of ligand and complexes was assayed through screening of the *Aspergillus niger* and *Candida albicans* fungi, by the diffusion technique on PDA growth medium . The fungal suspension was standardized to 10^6 conidia/mL in sterile saline solution (0.85%) and 100 μL of each fungal suspension was spread onto the surface of the Petri dishes. After 10 min of rest, 6-mm-diameter holes were punched and filled with 100 μL of the previously prepared ligand and complexes samples in concentrations(50mg/ml, 25mg/ml, 12.5mg/ml, 6.25mg/ml, 3.12mg/ml, 1.56mg/ml). DMSO,As control samples for each experiment, Subsequently, the plates were incubated at (28 ± 2) °C. Each extract form was evaluated with 3 repetitions, and the assessment was conducted after 72 h by measuring the diameter of the inhibition of the fungi mycelial growth (clear zone of inhibition formed around were considered indicative of antifungal activity). [9 ,10]

2.5 - Experimental animals

In this study, 24 male domestic rabbits (Lupus domestics rabbit) with weights ranging from (1000-1200) gm. and eight months old were used. These rabbits were placed in iron cages and left for a week in order to acclimatize

2.5.1- Induced of thyroid hormones

Hyperthyroidism was induced by giving rabbits Thyroxin at a dose of (0.3mg/kg) dissolved in 1ml of distilled water and the dose was given orally by a medical syringe for (14) days. Blood samples were drawn and placed in tubes using to determine how high thyroid hormones are. [11]

2.5.2- Study the effect of thiourea ligand and complexes with zinc as anti - Hyperthyroidism

The effect of ligand, L and its complexes with zinc, L, LZnCl, $(L)_2$ZnAC) on the rise of thyroid hormones was studied by giving these compounds to rabbits with elevated T3 and T4 thyroid hormones. The rabbits were divided into (5) groups, (3) Groups were given the ligand, L and its complexes with zinc at a dose of (25mg/kg) dissolved in DMSO, one group was given Carbimazole treatment at a dose of (5 mg) as a standard group, the last group was given (0.5ml) of DMSO and considered as a control group. The treatment process lasted for (20) days. Blood samples were collected(0.10.20) days after the start of the dosing process. Blood samples were placed in glass tubes containing a gel for blood clotting. The process of separating the blood serum was carried out by centrifugation (centrifuge), and kept the blood serum at a temperature of (4 $^{\circ}$C) until the determination of thyroid hormones . The level of T3and T4 Harmon was measured by[12] By alias as dpend in level of T4 Harmon measure by[13]

3. Result Discussion

3.1- Characterization of Land complexes CHNS Element analysis CHNS technique and the data shows matching between theoretical calculation and experimental , Table 1 show CHNS of complexes .

Table 1:The results of the analysis of the microelements of the L and complexes

Sample Name	Calculated				Obtained			
	C%	H%	N%	S%	C%	H%	N%	S%
L	43.15	4.28	13.72	10.47	42.93	4.15	13.61	10.57
LNiCl	30.32	3.01	9.64	7.36	30.24	2.97	9.56	7.28
$(L)_2$NiAC	39.57	4.09	7.44	8.12	39.28	4.01	7.65	8.32
LCuCl	29.98	2.97	9.54	7.28	29.58	2.87	9.42	7.15
$(L)_2$CuAC	39.33	4.06	10.58	8.58	39.98	4.46	10.19	8.18
LCoCl	30.30	3.01	9.64	7.35	30.19	3.95	9.48	7.27
$(L)_2$CoAC	39.56	4.09	10.65	8.12	39.33	3.97	10.49	8.22
LZnCl	29.86	2.96	9.50	7.25	29.72	2.92	9.39	7.16
$(L)_2$ZnAC	39.24	4.05	10.56	8.06	39.39	3.87	10.43	8.11

3. 2- FT-IR Spectra

The L and complexes was characterized by FTIR technique (KBr dick, cm^{-1}) in the region (400- 4000cm^{-1}) . The ligand was given the following packages υC=S (1234)cm^{-1} , υC=O (1690) cm^{-1} , υC=N (1624) cm^{-1} , υC=C (1516) , υNH (3452) , υC-Cl (771) cm^{-1} . complexes υC=S(1211 - 1231) , υ(C=O) cm^{-1} (1608-1689) cm^{-1}, υC=N (1516-1546) cm^{-1}, υNH (3450-3151) cm^{-1}, υM-S (459-474) cm^{-1} , υM-N(557-517) cm^{-1}.Tabale 2 show FTIR spectrum to L and its complexes.[14-19]

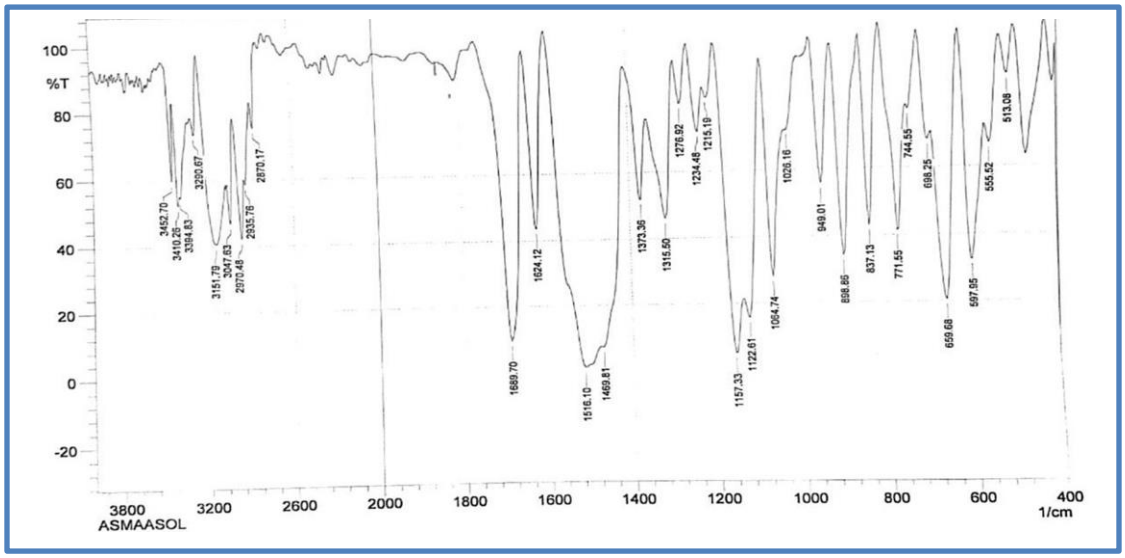


Figure 4: FT-IR spectral ligand L

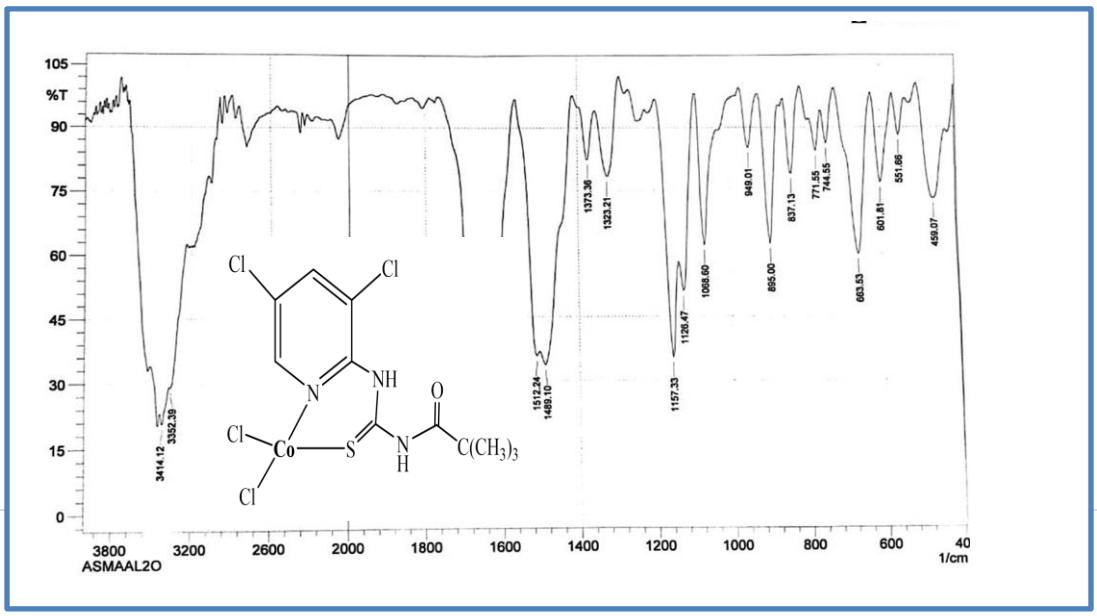


Figure 5: FT-IR spectral LCoCl

Tabale 2: FT-IR spectral assignments (cm^{-1}) of L and complexes

Compounds	υ(N-H)	υ(C- H) Aliphatic	υ(C-Cl)	υ(C=O)	υ(C=N)	υ(C=S)	υ(M-N)	υ(M-S)
L	3452	2970	771	1690	1624	1234	--------	--------
LNiCl	3414	2970	772	1689	1620	1215	555	474
$(L)_2$NiAC	3394	2870	787	1687	1516	1211	555	475
LCuCl	3429	2950	744	1651	1616	1219	557	459
$(L)_2$CuAC	3159	2970	671	1689	1640	1230	517	474
LCoCl	3450	2974	748	1608	1547	1231	552	459
$(L)_2$CoAC	3151	2974	694	1680	1570	1230	555	474
LZnCl	3414	2935	745	1685	1620	1231	551	459
$(L)_2$ZnAC	3390	2963	745	1689	1639	1232	551	474

3. 3-Magnetic Suscepility:

The magnetic moment of a complexes was calculated and found to be equal μeff 2.76 to (LNiCl) , μeff 2.84 to (($L)_2$NiAC), μeff 1.67 to (LCuCl), μeff 1.68 to (($L)_2$CuAC), μeff 3.46 to (LCoCl) μeff 3.94 to (($L)_2$CoAC). Where they are magnetic sensitivity calculations proved that tetrahedral(1:1)(M:L) Octahedral(1:2)(M:L) and cobalt oxidative stress(+2) , Table 3 that show the molecular weight , magnetic moment coefficient , oxidahion state and the geometry of the complexes .[20][21]

Table 3 :The observed magnetic moments of the Copper(II), Cobalt(II) and Nickel(II) compounds of the L, AC= (CH_3COO^-) X_D= Correction factor, X_g= Gravimetric magnetic susceptibility, X_M= Molar magnetic susceptibility and X_A= Atomic susceptibility.

Comp.	$\chi D*10^{-6}$ $emumol^{-1}$	Xg*10 -5	X_M	XA	μeff B.M	Type of hybridisation	Shape	Of unpaired electron	Oxidation state
LNiCl	**-178.93**	**0.7**	**0.003**	**0.0032**	**2.76**	**SP^3**	**Tetrahedral**	**2**	**+2**
$(L)_2$NiAC	**-239.22**	**0.4**	**0.0031**	**0.0033**	**2.84**	**SP^3d^2**	**Octahedral**	**2**	**+2**
LCuCl	**-177093**	**0.23**	**0.001**	**0.0011**	**1.67**	**SP^3**	**Tetrahedral**	**1**	**+2**
$(L)_2$CuAC	**-138.93**	**0.12**	**0.0009**	**0.001**	**1.68**	**SP^3d^2**	**Octahedral**	**1**	**+2**
LCoCl	**-178.93**	**1.05**	**0.004**	**0.005**	**3.46**	**SP^3**	**Tetrahedral**	**3**	**+2**

$(L)_2CoAC$	-239.22	0.8	0.006	0.0065	3.94	SP^3d^2	Octahedral	3	+2

3. 4- UV-Visible Spectra:

The L and its complexes was characterized by UV-Visible as shown in Table 4, revealed three transitions 240-212 nm can be assigned to $\pi - \pi *$ and 374- 245$n - \pi *$ 559 , 690nm is assigned to d-d transitions.[22-24]

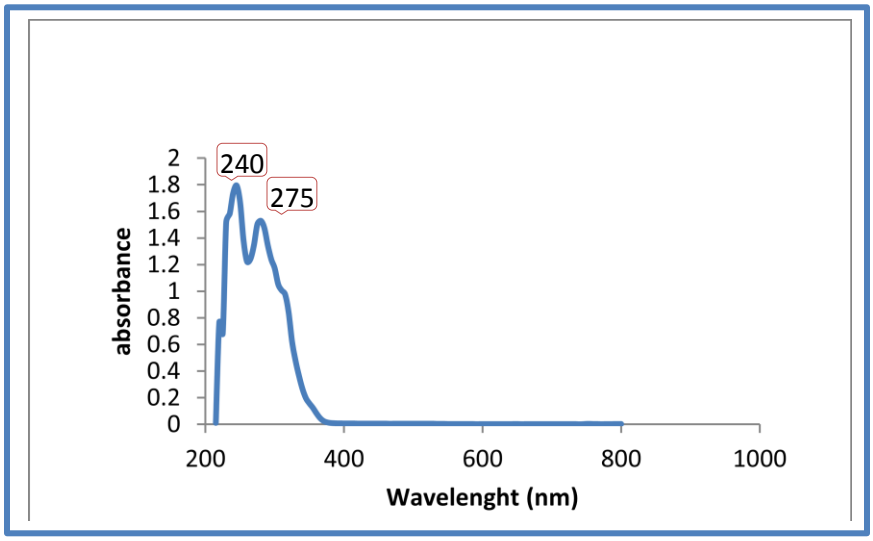


Figure 6 : Ultra-Violet-Visible spectra of ligand (L)

Table 4:UV-Visible spectral data λ_{max}(nm), (ε, M^{-1} cm^{-1}) of the Copper(II), Cobalt(II), Nickel(II) and Zinc(II) compounds of the L^2in DMSO solution. AC = (CH_3COO^-).

Compound	λ(nm)	Type of transition
L	240	$\pi - \pi *$
	275	$n - \pi *$
LNiCl	234	$\pi - \pi *$
	274	$n - \pi *$
	570	d-d
	612	
$(L)_2NiAC$	241	$\pi - \pi *$
	267	$n - \pi *$
	559	d-d
	628	
LCuCl	210	$\pi - \pi *$
	245	$n - \pi *$
	646	d-d

	682	
$(L)_2CuAC$	214	$\pi - \pi *$
	257	$n - \pi *$
	602	d-d
	690	
LZnCl	240	$\pi - \pi *$
	268	$n - \pi *$
	306	LMCT
$(L)_2ZnAC$	245	$\pi - \pi *$
	272	$n - \pi *$
	301	LMCT
LCoCl	239	$\pi - \pi *$
	273	$n - \pi *$
	549	d-d
	614	
$(L)_2CoAC$	212	$\pi - \pi *$
	268	$n - \pi *$
	670	d-d

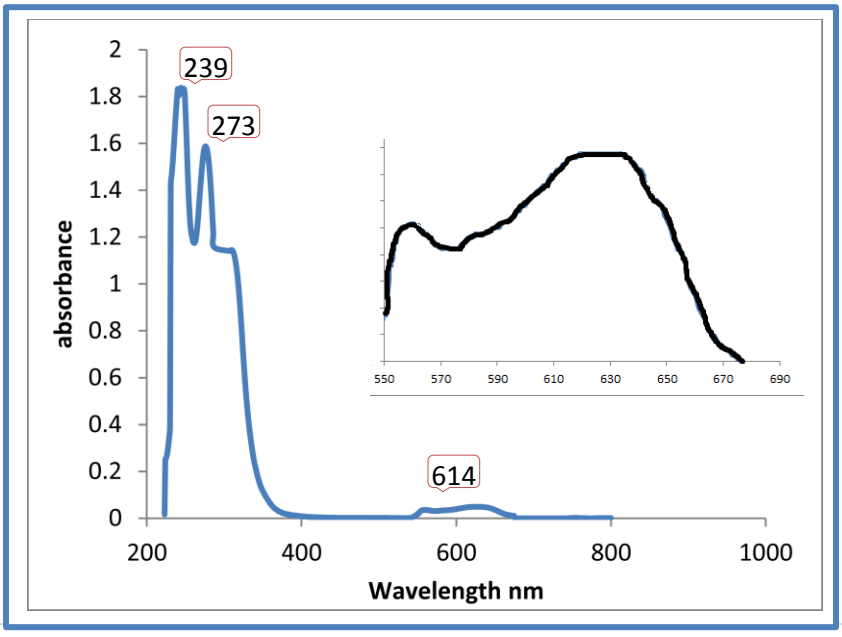


Figure 7: Ultra-Violet-Visible spectra of LCoCl

3.5- Molar Conductivity Measurements

The higher the concentration of the solution, the higher the conductivity. This characteristic is due to increasing of the number of ions that are settled in the solution, this rising of conductivity perhaps is due to the change in the concentration of the electrolyte or the change in the degree of dissociation for these reasons , molar conductance should be used to investigate the difference of the chemical conductivity with concentration. The molar conductance of (L, LNiCl, $(L)_2$NiAC , LCuCl, $(L)_2$CuAC, LCoCl, $(L)_2$CoAC , LZnCl, $(L)_2$ZnAC) were investigated in dimethyl sulfoxide (DMSO) as solvent and concentration of these complexes were at 25 $^{\circ}$C .[25]- [28]

Table 5: Molar conductance values at 1 x 10^{-4} M (Λ_m), for Cu(II), Co(II), Ni(II) and Zn(II) compounds of the L.

No	Compound	Λ_m (ohm^{-1} cm^2 mole^{-1})	Λ_0 (ohm^{-1} cm^2 mole^{-1})
1	LNiCl	19	49
2	$(L)_2$NiAC	25	54
3	LCuCl	26	56
4	$(L)_2$CuAC	24	57
5	LCoCl	20	52
6	$(L)_2$CoAC	23	60
7	LZnCl	28	56
8	$(L)_2$ZnAC	27	55

3.6- NMR spectral Analysis

The 1HNMR and ^{13}CNMR spectra of ligand L and complexes were obtained using DMSO solvent at room temperature[29-36]

Table 6: Characteristic bands in the 1HNMR spectrum of the L ligand and its complexes

NO	Compound	Chemical Formula	Chemicalshift(ppm)

1	L	$C_{11}H_{13}Cl_2N_3OS$	H_A :11 46 H_B :12.41 H_C :8.29 H_S :7.92 H_F :1.26
2	LZnCl	$C_{11}H_{13}Cl_4N_3OSZn$	$H_{(NHCO)}$:11 .25 $H_{(NHCS)}$:12.67 $H_{(CHarm)}$:8.40 $H_{(CHalph)}$:1.26
3	$(L)_2ZnAC$	$C_{26}H_{32}Cl_4N_6O_6S$	$H_{(NHCO)}$:6 .1 $H_{(NHCS)}$:12.85 $H_{(CHarm)}$:7.92 $H_{(AC)}$:2.5 $H_{(CHalph)}$:0.47

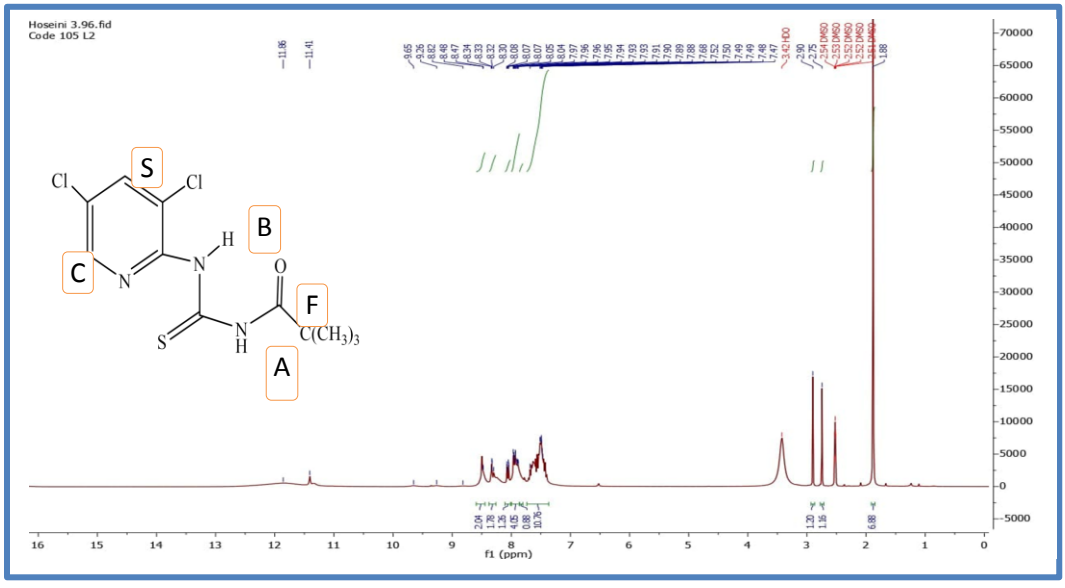


Figure 8: 1HNMR spectrum of L

Table 7:Characteristic bands in the ^{13}CNMR spectrum of the L ligand and its complexes

NO	Compound	Chemical Formula	Chemicalshift(ppm)
1	L	$C_{11}H_{13}Cl_2N_3OS$	C_X:179 C_V:30 C_G:39C C_T:159 C_L:162 C_J:120
2	LZnCl	$C_{11}H_{13}Cl_4N_3OSZn$	$C_{C=S)}$:190 $C_{(CH3)}$:27 $C_{(C(CH3)3}$:39 $C_{(CNH)}$:159 $C_{CHarm)}$:140 $C_{(c-cl)}$:122
3	$(L)_2ZnAC$	$C_{26}H_{32}Cl_4N_6O_6S_2Zn$	$C_{(C=S)}$:181 $C_{(CH3)}$:23 $C_{(CNH)}$::145 $C_{CHarm)}$:140 $C_{(c-cl)}$::124

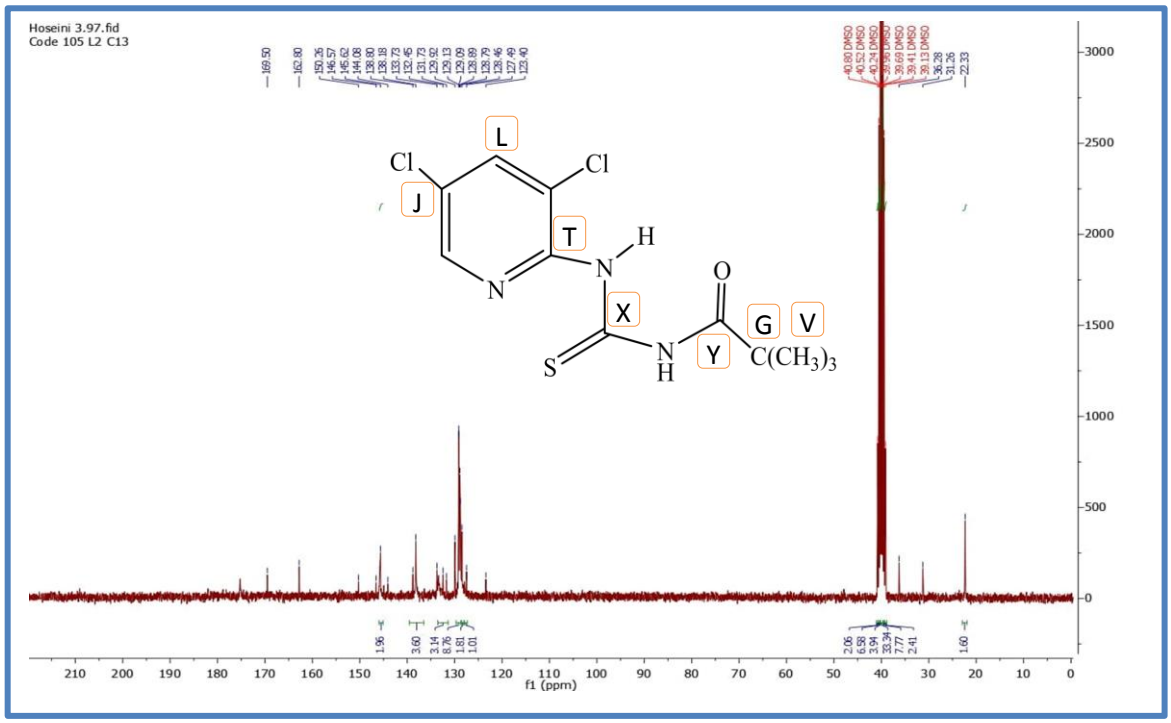


Figure 9: ^{13}CNMR spectrum of L

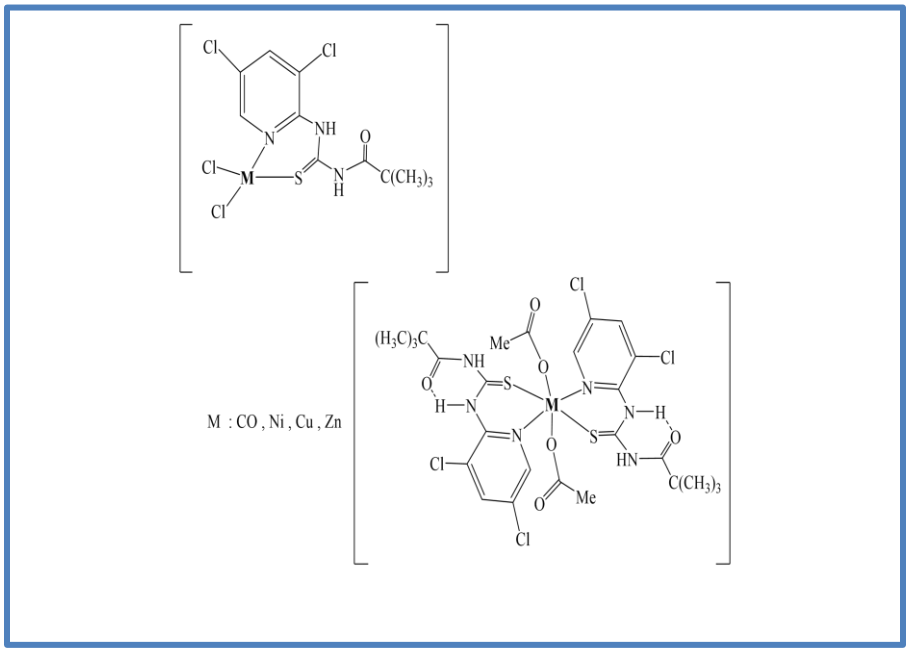


Figure 10: Thiourea complexes with ligand L

3.7- Anti- fungal activity

The biological activity was measured in vitro of the compounds prepared against and by using DMSO as a control solution. The results showed that the prepared compounds possessed anti-fungal activity at different concentrations. The reason for the antifungal activity of these compounds is due to the presence of halogen (Cl) in the composition of the prepared compounds, which enhanced the solubility of fats, and the presence of (CSNH) (CONH) groups possessing important anti-fungal pharmacological properties.[37-42]

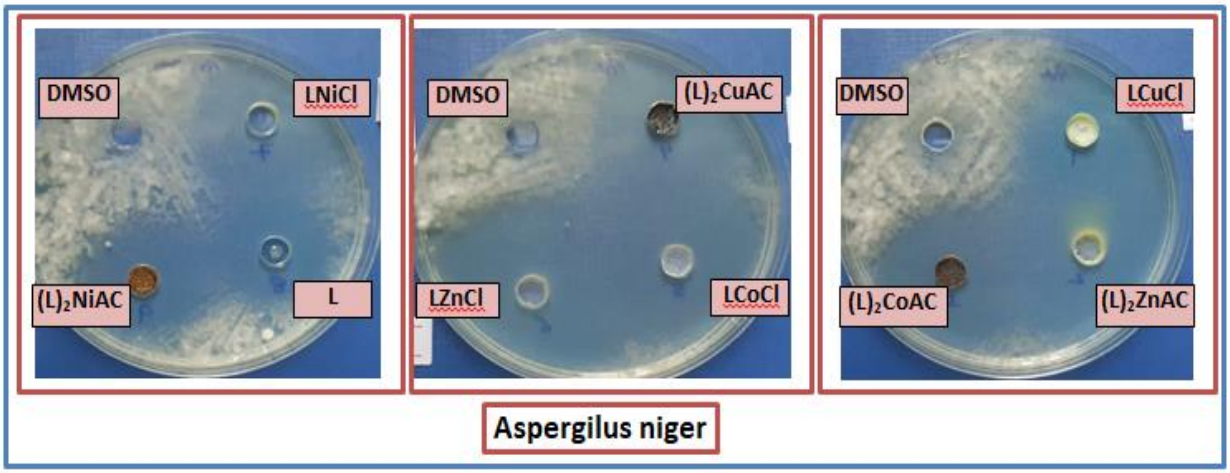
Table 8: Anti- fungal activity of ligand L and complexes *Candida*

Comp.	*Candida* (Diameter of Inhibition Zone (mm)				
	25mg/ml	12.5mg/ml	6.25mg/ml	3.12mg/ml	1.56mg/ml
L	32	28	27	-----	-----
L NiCl	32	26	24	13	-----
$(L)_2$ NiAC	24	22	15	-----	-----
L CuCl	19	17	16	11	------
$(L)_2$CuAC	36	30	30	14	10
L CoCl	34	33	16	-----	-----
$(L)_2$ CoAC	32	28	20	9	-----

L ZnCl	31	30	25	14	-----
$(L)_2$ ZnAC	40	32	30	12	-----

Table 9: Anti- fungal activity of ligand L and complexes *Aspergillus*

Comp.	***Aspergillus* (Diameter of Inhibition Zone (mm)**				
	25mg/ml	**12.5mg/ml**	**6.25mg/ml**	**3.12mg/ml**	**1.56mg/ml**
L	17	15	13	-----	-----
L NiCl	34	-----	-----	-----	-----
$(L)_2$ NiAC	15	-----	-----	-----	-----
L CuCl	17	-----	-----	-----	-----
$(L)_2$CuAC	24	-----	-----	-----	-----
L CoCl	12	-----	-----	-----	-----
$(L)_2$ CoAC	26	12	7	-----	-----
L ZnCl	14	-----	-----	-----	-----
$(L)_2$ ZnAC	35	-----	-----	-----	-----



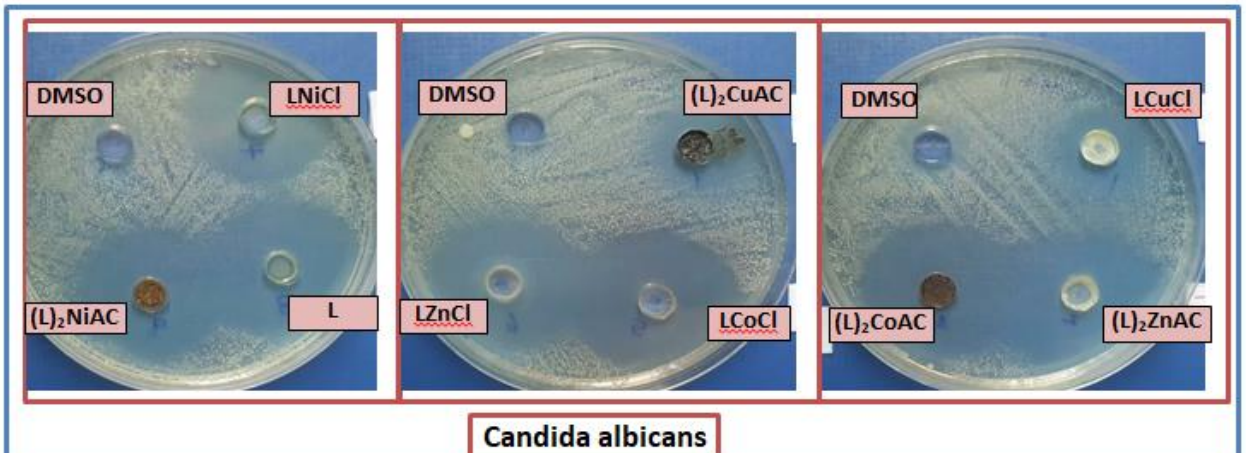


Figure 11 : Antifungal activity of L and its complexes (50mg/ml)

3.8- Effect of L and complexes with zinc on the thyroid hormone

The results of the study showed the effectiveness of ligand L and its complexes with zinc as anti-elevation of thyroid hormones, and these results showed a decrease in the level of T3 thyroid hormones. After 10 days of taking these compounds, the decrease was not significant compared to the control group. The results showed a significant decrease ($P \leq 0.05$) in the level of T3 hormone after (20 days) of taking the compounds, as shown in the table [43,44].

Table 10: Effect of L ligand and their complexes with zinc on Tri-iodothyrionine T3 hormone

Time / Group	NO.	0 day	10 days	20 days
Control	6	2.82 ± 0.30	2.64 ± 0.46	2.39 ± 0.42
Carbimiazol	6	2.84 ± 0.30	1.85 ± 0.37	1.49 ± 0.25
P – value		0.919	0.008	0.001
L	6	2.73 ± 0.27	2.19 ± 0.41	1.79 ± 0.41
p-value		0.584	0.107	0.036
LZnCl	6	2.83 ± 0.80	2.17 ± 0.34	1.72 ± 0.43
p-value		0.982	0.075	0.024
$(L)_2ZnAC$	6	2.77 ± 0.41	2.20 ± 0.31	1.77 ± 0.20
p-value		0.834	0.086	0.015

P≤0.05 vs. control

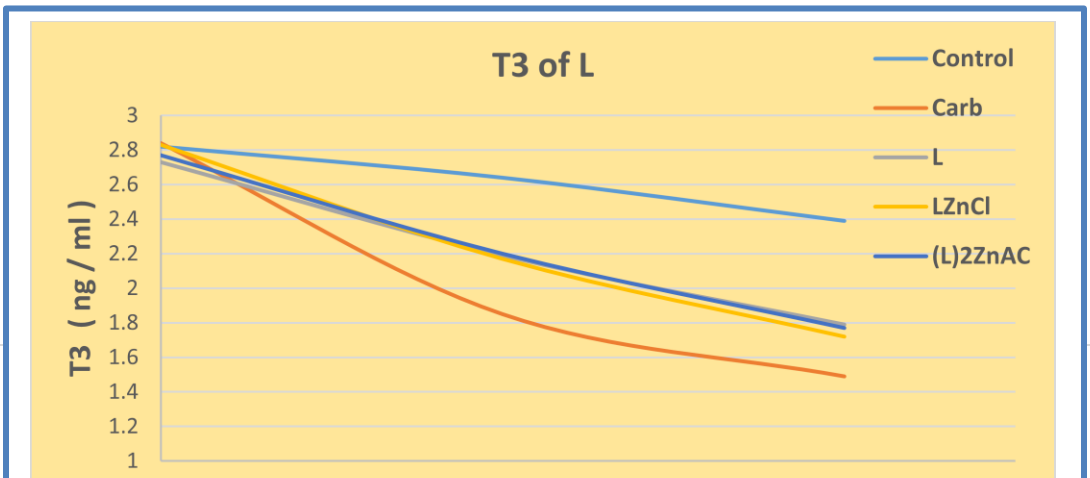


Figure 12: Effect of L ligand and their complexes with zinc on Tri-iodothyrionine T3 hormone

The results of the study showed the effectiveness of ligand L and its complexes with zinc as anti-elevation of thyroid hormones, and these results showed a decrease in the level of T4 thyroid hormones. After 10 days of taking these compounds, the effect was significant for the compound (L)2ZnAC compared to the control group. The results showed a significant decrease ($P \leq 0.05$) for the compound (L)2ZnAC in the level of T4 hormone after (20 days) and a significant effect for the L ligand, and no significant effect was observed for the rest of the compounds from taking the compounds[45].

Table 11: Effect of L ligand and their complexes with zinc on thyroxine (T4) hormone

Time / Group	NO.	0 day	10 days	20 days
Control	6	11.25± 1.26	10.27± 0.81	8.23 ± 0.75
Carbimiazol	6	10.48± 1.90	7.81 ± 0.51	5.50 ± 1.88
P – value		0.430	0.001	0.001
L	6	10.33± 2.87	9.16 ± 1.70	6.37 ± 1.59
p-value		0.489	0.178	0.027
LZnCl	6	10.51± 2.15	9.31 ± 0.80	6.25 ± 0.55
p-value		0.485	0.066	0.001
$(L)_2ZnAC$	6	11.14± 1.69	9.29 ± 0.48	6.28 ± 0.64
p-value		0.902	0.030	0.001

P≤0.05 vs. control

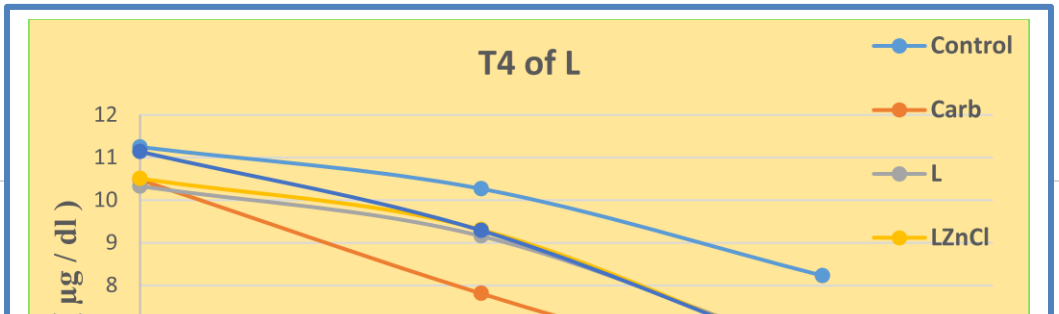


Figure 13: Effect of L ligand and their complexes with zinc on thyroxine (T4) hormone

Conclusion

A new derivative of thiourea was prepared and complexes with ions of transition elements (Copper(II), Cobalt(II) and Nickel(II) Zink(II). A ligand was diagnosed with its complexes with the technique of (The ligand was characterized by elemental analysis apparatus , FT-IR , ^{13}C,1H-NMR spectra , UV-Visible,) and through the results obtained and the results of low conductivity it was proved that the non-ionic complexes are tetrahedral (1:1)(M:L) and octahedral (1:2))(M:L) and ligand and its complexes have effective Anti-fungal and anti-hyperthyroidism efficacy for ligand and its zinc complexes

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