

# Synthesis, Characterization and Antibacterial Activity of some New Metal Complexes Containing Semicarbazide

Eman Ahmed Kadhim<sup>1</sup>, Nasry Jassim Hussien<sup>2</sup>, Siti Fairus M. Yusoff<sup>3</sup>

<sup>1,2</sup>Department of Chemistry, College of Education for Pure Science (CoEIPS),

University of Diyala (UoD), Diyala, Iraq

<sup>3</sup>School of Chemical Science and Food Technology, Faculty of Science and Technology, University Kebangsaan Malaysia, 43600 UKM Bangi, Selangor, Malaysia

## Article Information

### Article history:

Received: 25, 04, 2024

Revised: 30, 05, 2024

Accepted: 15, 06, 2024

Published: 30, 06, 2024

### Keywords:

Antibacterial  
activity  
metal complexes  
Synthesis  
Semicarbazide

## Abstract

The research includes the preparation and characterization of the new N-cyclohexyl-2-((dimethylcarbamoyl) carbamothioyl) hydrazine-1-carboxamide (L). Metal ions  $\text{Co}^{+2}$ ,  $\text{Ni}^{+2}$  and  $\text{Cu}^{+2}$  were combined with the ligand (L) to form three transition metal complexes. The chemical formulas are the following  $[\text{LCoCl}_2 \cdot \text{H}_2\text{O}]$ ,  $[\text{LNiCl}_2 \cdot \text{H}_2\text{O}]$ ,  $[\text{LCuCl}_2 \cdot \text{H}_2\text{O}]$ . The reaction was performed by mixing metal ligand in a [1:1] mole ratio using (MeOH) acting as a solvent. The entity of the expected structure of the ligand and its metal complexes were illustrated through a range of physicochemical techniques. These include: FT-IR, electronic spectra, ( $^1\text{H}$  and  $^{13}\text{C}$ -NMR) spectra, elemental analysis(CHNS), chloride content, metal content, melting point, molar conductivity, and magnetic susceptibility of three-coordinate complexes with deformed octahedral geometry around the center atom was determined by the spectral and analytical for the  $\text{Co}^{+2}$ ,  $\text{Ni}^{+2}$  and  $\text{Cu}^{+2}$  atoms. The biological activity (antibacterial) ( $\text{G}^+$ ) and ( $\text{G}^-$ ) bacterial was explored

This is an open-access article under the [CC BY-SA](https://creativecommons.org/licenses/by-sa/4.0/) license.



## Corresponding Author:

**Nasry Jassim Hussien**

Department of Chemistry Science, College of Education for Pure Science

Diyala University

Baqubah City, Diyala Governorate, Iraq

Email: nasry.hussien@uodiyala.edu.iq



## 1. INTRODUCTION

coordination chemistry, an academic field, focuses on metal complexes, which are groups of ions or particles that coexist but prefer to be linked in a specific configuration. Critical to current inorganic research is the proof of the compounds' heterogeneity, reactivity, analytical uses, and catalytic effects. [1] The intriguing biological actions of heteroleptic complexes have recently heightened interest in their coordination chemistry. Using semicarbazone derivatives for metal coordination has become more important for pharmaceutical and bioinorganic chemists [2]. Semicarbazone-derived ligands demonstrate many bioactivities, such as antiviral effects [3], antioxidant properties, antifungal and antibacterial activities [4], and even antiparasitic effects [5]. Condensation of semicarbazides with appropriate aldehydes or ketones yields significant chemicals such as semicarbazones and thiosemicarbazones. A sulfur-containing derivative of semicarbazone, thiosemicarbazone is an alternative to semicarbazone that contains oxygen. Typically, semicarbazones and thiosemicarbazones act as chelating ligands and combine with the cations of metals to form complexes. Important pharmacological features make the production of transition metal complexes with thiosemicarbazone and semicarbazone ligands an important topic of research [6].

The probable biological properties of these species have prompted extensive research on them and their metal complexes [7]. Semicarbazides are commonly used nitrogen or oxygen compounds that have several biological applications, various structural choices, and a variety of binding processes.[8-10] interacting with transitory elements as chelating agents, these chemicals become even more important. [11] The ion coordination modes seen by semicarbazides are sensitive to a variety of factors, including reaction circumstances, carbonyl substituent type, presence of metal salts, and counter-ion nature.[12] It is believed that semicarbazides possess a diverse array of structural characteristics and that the physiological activity of their metal complexes surpasses that of free ligands.[13, 14] Semicarbazone transition metal complexes' coordination and analytical uses have prompted substantial research into these compounds [15]. This work represents the synthesis and spectral characterization of a new ligand namely, the N-cyclohexyl-2-((dimethylcarbamoyl)carbamothioyl) hydrazine-1-carboxamide (L) reaction with  $M^{+2}$  ions ( $Co^{+2}$ ,  $Ni^{+2}$ , and  $Cu^{+2}$ ). The antibacterial properties of the ligand and its metal complexes are also investigated.

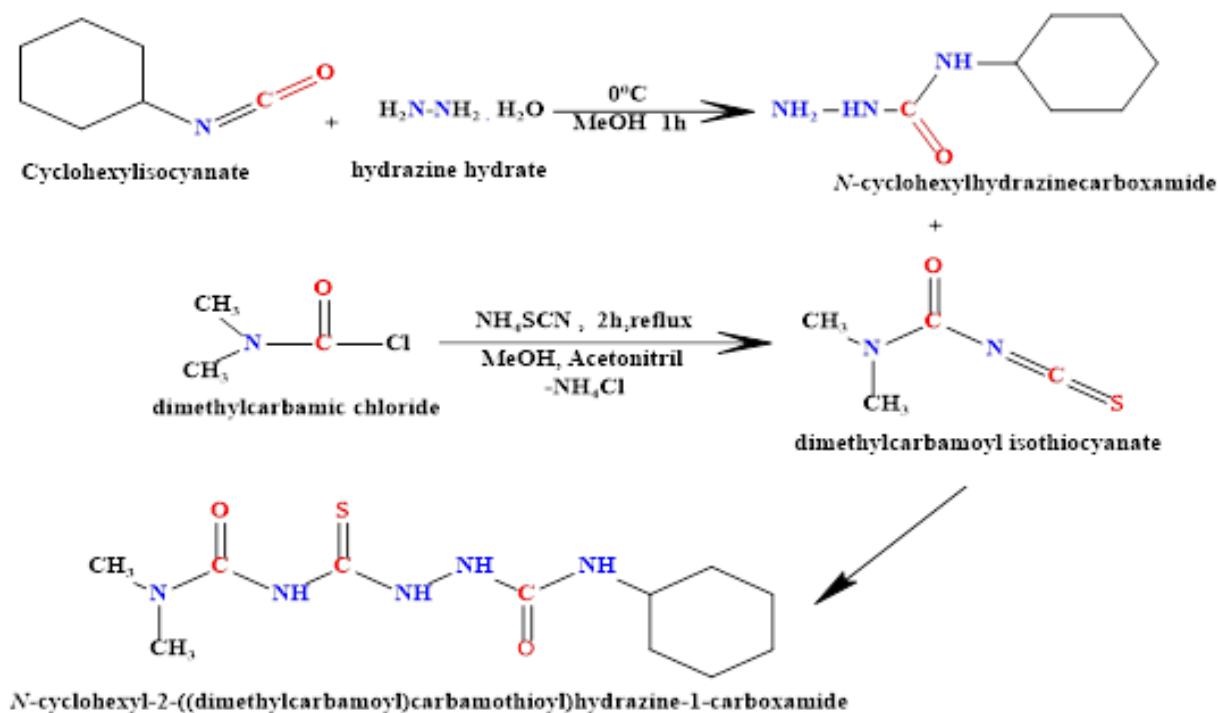
### Materials and methods

Reagents that were purchased from Aldrich were used as received. Solvents were dried using standard protocols before their use in the preparation.

## 2. METHOD

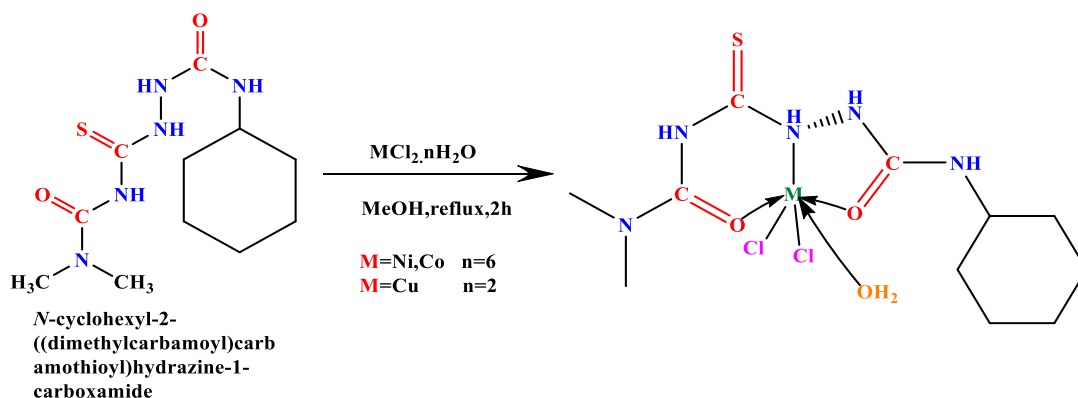
### Synthesis of the N-cyclohexyl-2-((dimethylcarbamoyl) carbamothioyl) hydrazine-1-carboxamide (L)

The ligand was prepared according to the method reported in [16] and it was synthesized in two steps. The first step included the preparation of N-cyclohexylhydrazinecarboxamide, which was achieved from the reaction of cyclohexyl isocyanate 0.625g, 5mmol, and 0.250 g, 5 mmol of hydrazine hydrate using methanol. Below the freezing point, the reaction occurred. In the second step, a solution containing (1.35g, 5 mmol) of dimethyl carbamoyl chloride and (0.76g, 5mmol) of ammonium thiocyanate in 40 mL of acetonitrile and methanol was heated under reflux for 1 hour. To filter off the reaction mixture, it was cooled to room temperature. N-cyclohexylhydrazinecarboxamide (1.02g, 5 mmol) in acetonitrile 10 mL was added to the filtrate, and the mixture was refluxed for 2 hours. A white solid appeared upon cooling. it was collected via filtration, washed with 10 mL of acetonitrile, and desiccated over anhydrous silica gel in a desiccator. to give the title compound, Scheme 1:



### Synthesis of complexes

In 100 mL of a round-bottomed flask was mixed N-cyclohexyl-2-((dimethylcarbamoyl) carbamothioyl) hydrazine-1-carboxamide (L) (0.5g, 2mmole). The resulting mixture was refluxed for 1hours and then a methanolic solution (10mL) of metal ions  $[MCl_2 \cdot nH_2O]$  (2 mmol) ( $M^{+2} = Co, Ni$  or  $Cu$ ) was added dropwise. The resulting colored solution was allowed to reflux for 2h and then cooled to room temperature. The metal complexes were collected by filtration and air-drying (Scheme 2).



Scheme 2. Synthetic route of complexes

## 3. RESULTS AND DISCUSSION

### 3.1. FT-IR spectrum of (L)

Solid state infrared of the prepared ligand Figure (1) was recorded in the range of  $4000-400\text{ cm}^{-1}$ . The main FTIR bands of the ligand are presented in Table 1. The FTIR spectra of ligand (L) show bands around  $(3302-3039), 1666, 1558\text{ cm}^{-1}$  assigned to  $\nu$  (N-H),  $\nu$  (C=O)<sub>carbamoyl</sub> and  $\nu$  (C=O)<sub>semicarbazide</sub>, respectively. Bands detect at  $(1149)$  and  $(1080)$  were attributed to  $\nu$  (C-N) and  $\nu$  (N-N), respectively. the  $\nu$  (C=S) of the appeared at  $763\text{ cm}^{-1}$  [17].

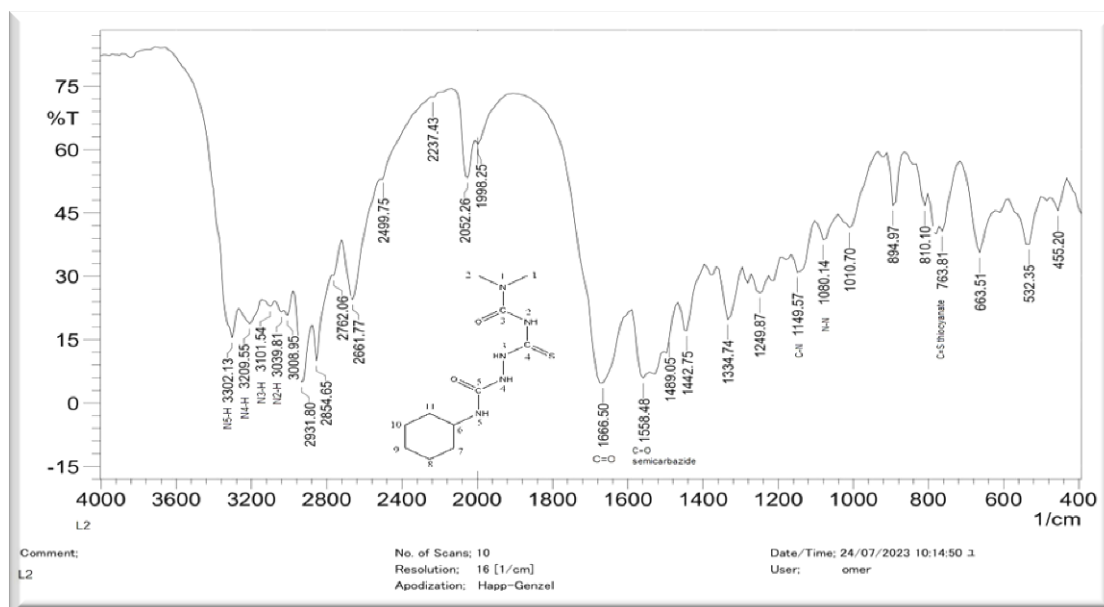


Figure 1. FTIR spectrum of N-cyclohexyl-2- (dimethyl carbamoyl) carbamothioyl) hydrazine-1-carboxamide (L)

### Diagnostics of the complexes

#### FT-IR spectra of the prepared complexes

Figures 2 and 3 show the FT-IR spectra of complexes C<sub>1</sub>, C<sub>2</sub>, and C<sub>3</sub>, while Table 1 includes the assignment of the distinct bands. The FT-IR spectra in the complexes (Co<sup>+2</sup>, Ni<sup>+2</sup>, and Cu<sup>+2</sup>) showed peaks related to  $\nu(\text{O-H})$  stretches around (3502-3700) cm<sup>-1</sup>. These peaks were assigned to the OH of the aqua molecule [18-20]. The spectra exhibited distinct bands ranging from (3332 to 3062) cm<sup>-1</sup>, which were classified as  $\nu(\text{N-H})$  [21] Table 1. A band was found in the free ligand at 1666 cm<sup>-1</sup>, which was connected to the  $\nu(\text{C=O})$  carbonyl. Figure 1 shows this association. Within the complexes C<sub>1</sub>-C<sub>3</sub>, the band was observed at the lower shift, which occurred within the region of (1651-1620) cm<sup>-1</sup>. There is a connection between the involvement of these moieties in the coordination to the metal center and the carbonyl bands [22].

Table 1. The most important characteristic bands of the (L) and their complexes in the FT-IR spectrum

ON	$\nu(\text{O-H})$	$\nu(\text{N}_5\text{-H})$	$\nu(\text{N}_4\text{-H})$	$\nu(\text{N}_3\text{-H})$	$\nu(\text{N}_2\text{-H})$	$\nu(\text{C=O})$ carbonyl	$\nu(\text{C=O})$ semicarbazide	$\nu(\text{C-N})$	$\nu(\text{N-N})$	$\nu(\text{c=s})$ thiocyanate	$\nu(\text{O-H})$	$\nu(\text{M-O})$	$\nu(\text{M-O})$	$\nu(\text{M-N})$	$\nu(\text{M-Cl})$
L	-----	3302	3209	3101	3008	1666	1558	1149	1080	763	-----	---	--	---	--
C <sub>1</sub>	3502	3332	3225	3132	3062	1651	1535	1134	1062	763	995	540	478	385	293
C <sub>2</sub>	3502	3387	3232	3155	3086	1651	1527	1134	1026	763	989	507	462	385	262
C <sub>3</sub>	3700	3317	3248	3163	3093	1620	1527	1126	1049	762	933	532	470	378	277

FT-IR spectra of complexes C<sub>1</sub>, C<sub>2</sub>, and C<sub>3</sub> revealed bands that fall in the range of (1535-1527)cm<sup>-1</sup> that attributed to  $\nu(\text{C=O})$  semicarbazide group. These bands were shifted to a lower wavenumber when compared to that observed at 1558 cm<sup>-1</sup> in the infrared spectrum of ligand (L) confirming the involvement of this  $\nu(\text{C=O})$  semicarbazide group upon coordination [23-25]. The spectra of metal complexes showed the presence of extra peaks between 600-200cm<sup>-1</sup> whose presence was not demonstrated in the spectra of the ligand. Peaks correlated to  $\nu(\text{Co-O})$ ,  $\nu(\text{Ni-O})$ , and  $\nu(\text{Cu-O})$  were detected at (540,478) cm<sup>-1</sup>, (507,462) cm<sup>-1</sup>, and (532,470) cm<sup>-1</sup>, respectively [26, 27]. Bands detected at 385,385 and 378 cm<sup>-1</sup> were assigned to  $\nu(\text{Co-N})$ ,  $\nu(\text{Ni-N})$ , and  $\nu(\text{Cu-N})$ , respectively. Peaks detected at 293,262 and 277cm<sup>-1</sup> were correlated to  $\nu(\text{Co-Cl})$ ,  $\nu(\text{Ni-Cl})$ , and  $\nu(\text{Cu-Cl})$ , respectively [27-29].

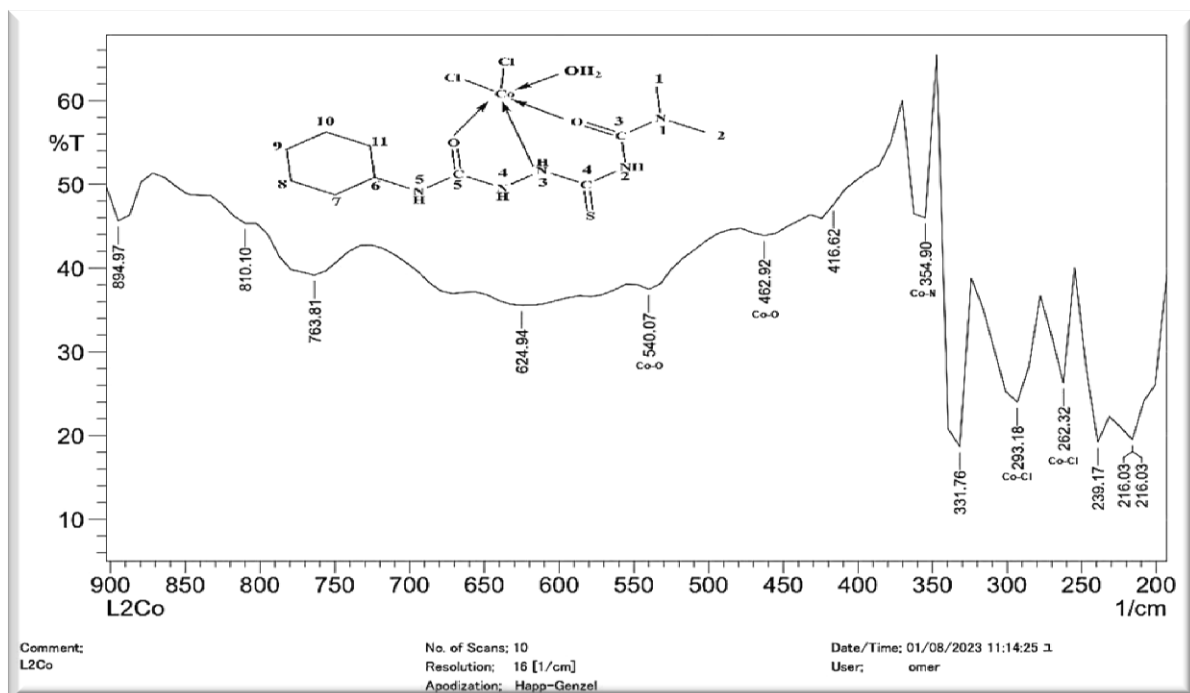
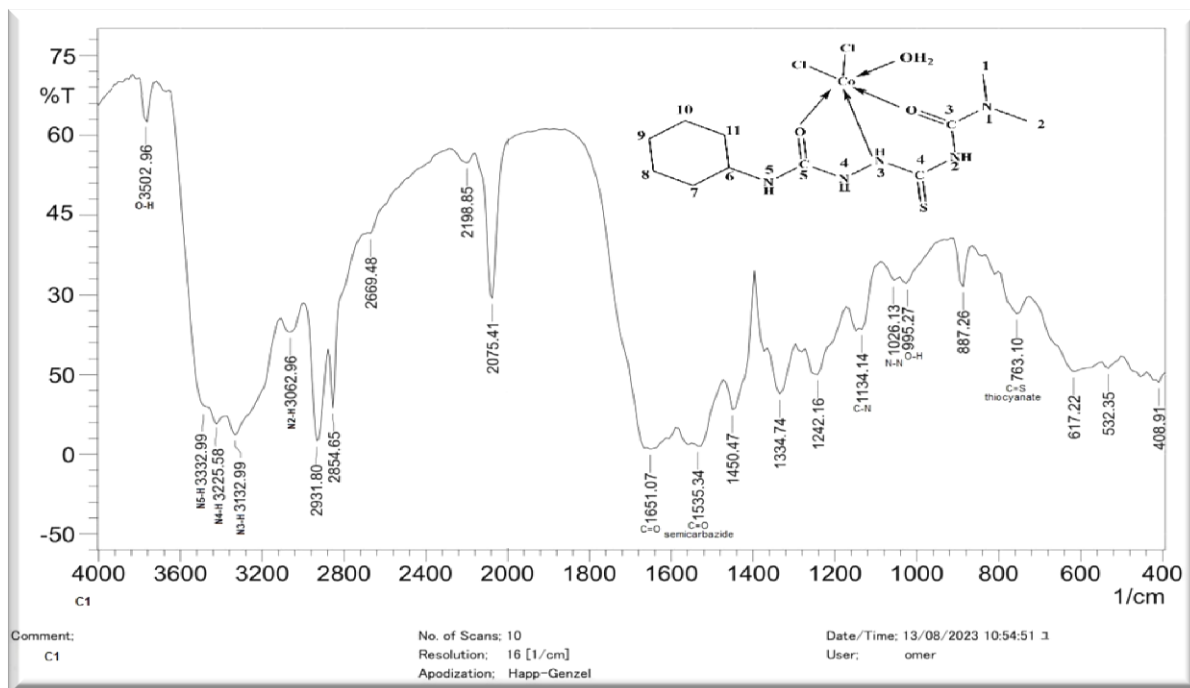


Figure 2. The Infrared spectrum of  $[LCoCl_2H_2O](C_1)$

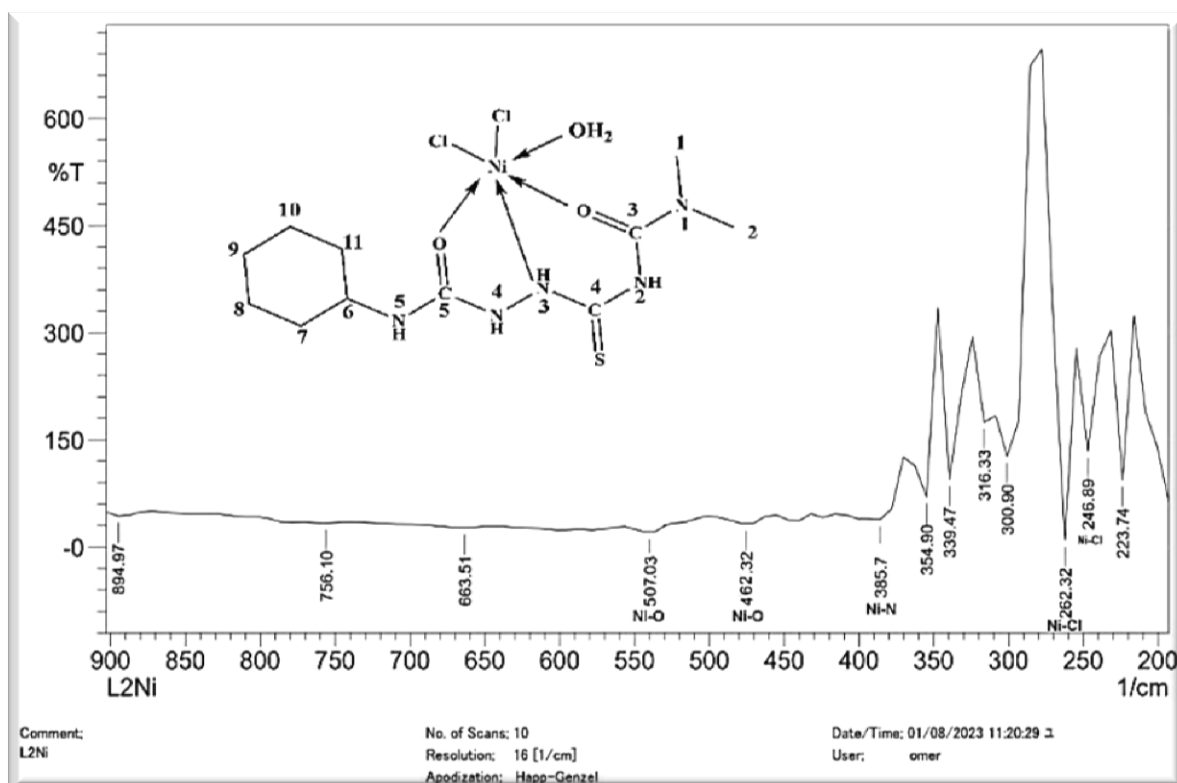
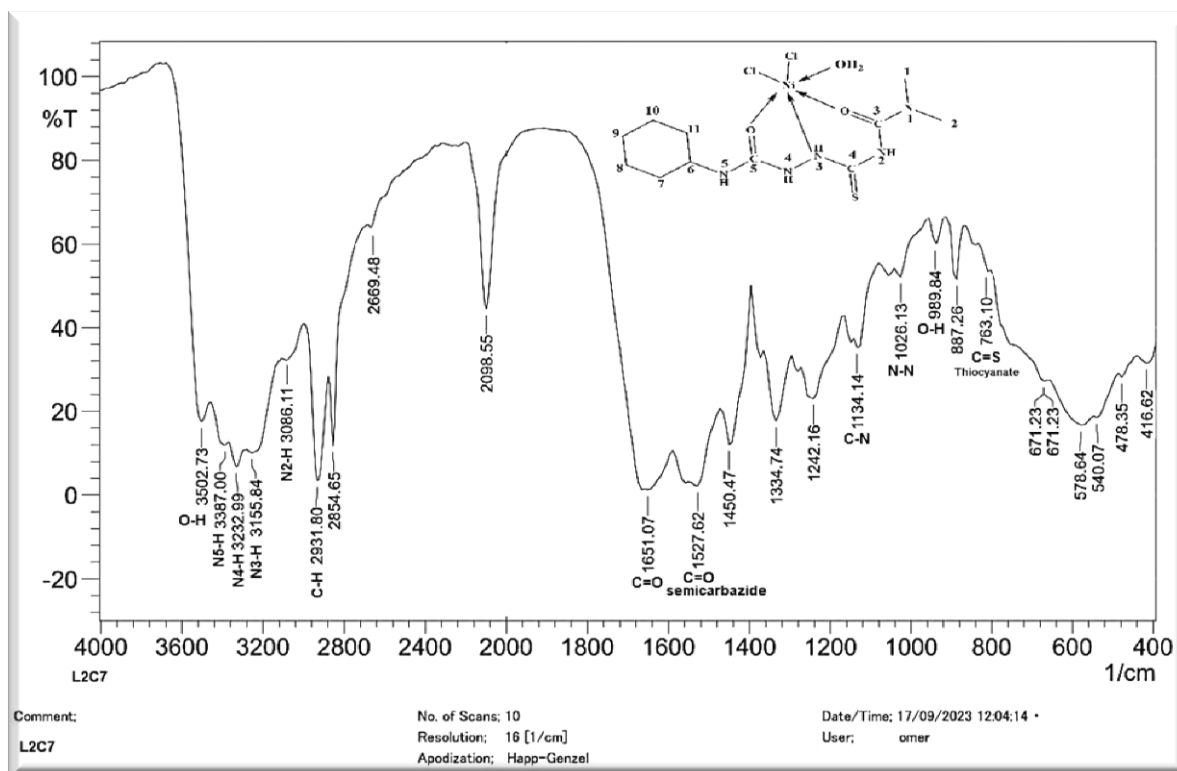


Figure 3. The Infrared spectrum of  $[LNiCl_2H_2O](C_2)$

### 3.2. U.v.-Vis Spectrum of Ligand

The UV spectrum for N-cyclohexyl-2-(dimethyl carbamoyl) carbamothioyl hydrazine-1-carboxamide (L) Figure 4, shows a high-intensity absorption peak at 259 nm and 293nm and were ascribed to the  $n \rightarrow \pi^*$  and  $\pi \rightarrow \pi^*$  electron transitions, sequentially [30].

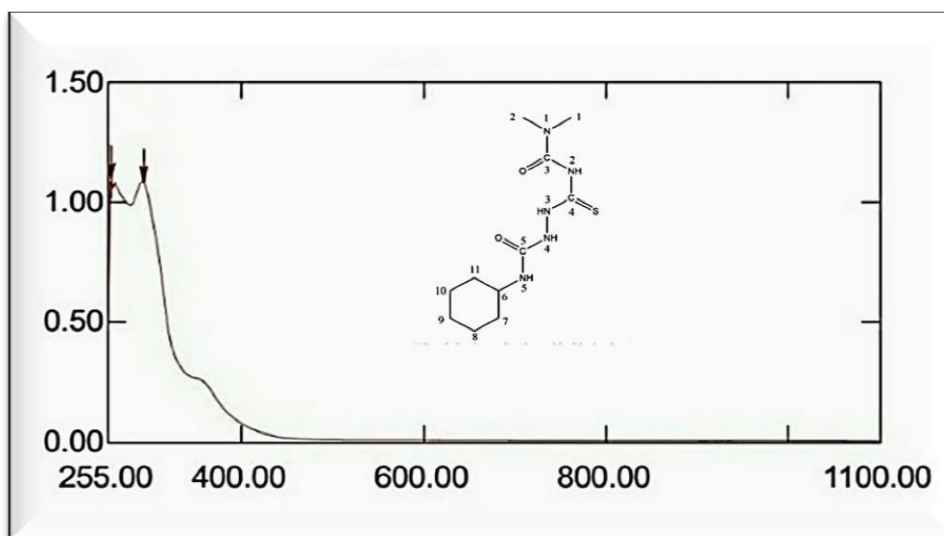


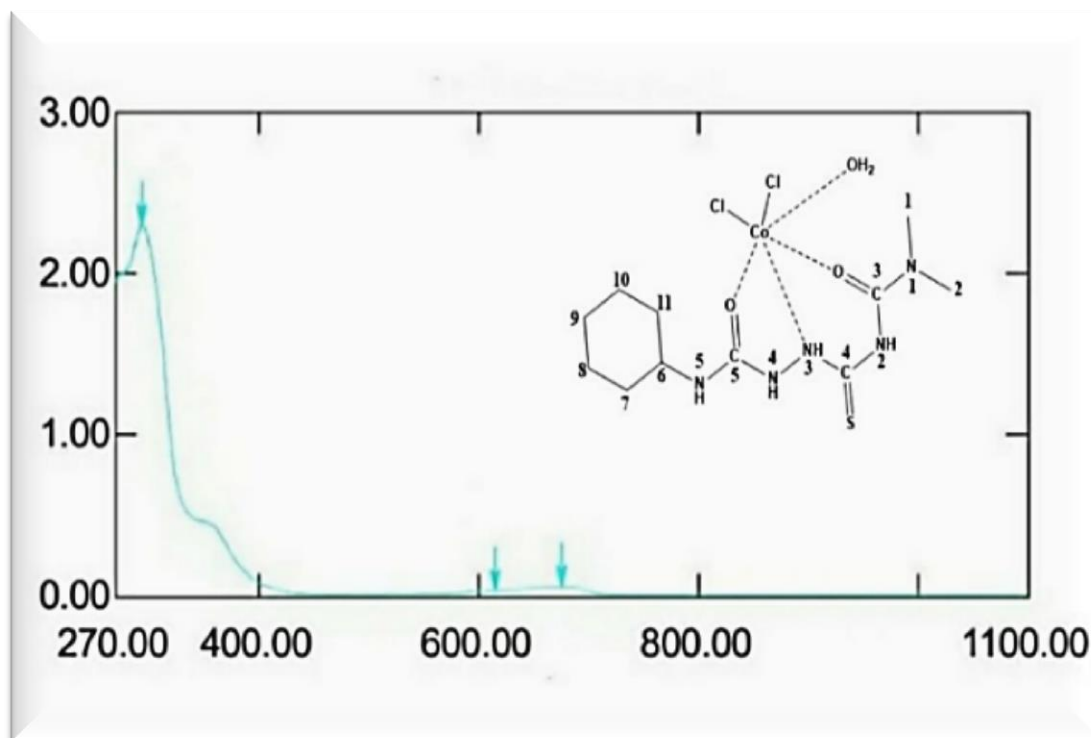
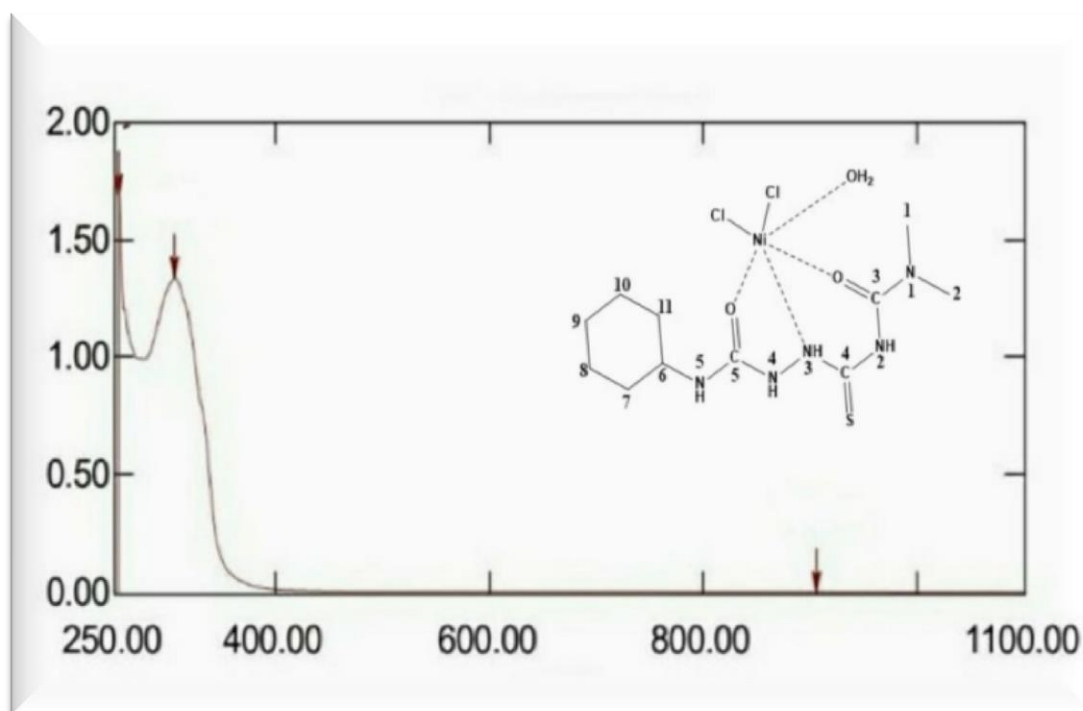
Figure 4. Electronic spectrum of Ligand (L)

### U.v.-Vis Spectra of the complexes

In the range of (200-1100) nanometers, the electronic spectra of the metal complexes that were prepared were recorded with DMSO (con. =  $1 \times 10^{-3}$  M) as the solvent. The electronic data, which are presented in Table 2 and illustrated in Figures (5) and (6). illustrate absorption peaks in the (254) and (306-293) nm range that are associated with  $\pi \rightarrow \pi^*$  and  $n \rightarrow \pi^*$  (ligand field transitions) [31-33]. Within the d-d area of the C<sub>1</sub> complex's structure, the band at (615 and 676 nm), sub  ${}^4T_{1g} \rightarrow {}^4T_{1g}(P)$ , and  ${}^4T_{1g} \rightarrow {}^4A_{2g}$  provided evidence of a deformed octahedral geometry about the metal center [34]. In the C<sub>2</sub> complex peak at 906 nm, it is attributed to  ${}^3A_{2g} \rightarrow {}^1E_g$  the metal center is surrounded by a deformed distorted octahedral shape [35].

Table 2. UV-visible spectrum of ligand and complexes

Complex	nmλ	cm <sup>-1</sup> λ	ΣMax (dm <sup>3</sup> mo <sup>-1</sup> cm <sup>-1</sup> )	Assignment	Suggested geometry
L	259 293	38610 34129	1850 1099	$\pi \rightarrow \pi^*$ $n \rightarrow \pi^*$	
C <sub>1</sub> [LCo]	293 615 676	34129 16260 14792	1304 32 47	$n \rightarrow \pi^*$ ${}^4T_{1g} \rightarrow {}^4T_{1g}(P)$ ${}^4T_{1g} \rightarrow {}^4A_{2g}$	<b>Distorted Octahedral</b>
C <sub>2</sub> [LNi]	254 306 906	39370 22679 11037	1688 1335 3	$\pi \rightarrow \pi^*$ $n \rightarrow \pi^*$ ${}^3A_{2g} \rightarrow {}^1E_g$	<b>Distorted Octahedral</b>

Figure 5. Electronic spectrum of  $[LCoCl_2.H_2O]Cl_1$ Figure 6. Electronic spectrum of  $[LNiCl_2.H_2O]Cl_2$



### 3.3. Nuclear Magnetic Resonance (NMR) spectra of Ligand

The  $^1\text{H-NMR}$  spectrum of **N-cyclohexyl-2-((dimethyl carbamoyl) carbamothioyl) hydrazine-1-carboxamide (L)** in  $\text{DMSO-d}_6$  solvent is presented in Figure 7. The singlet peak when (9.54 ppm) is equal to a single the proton as a result of [1H, N(2)H,s]. The singlet peak at (9.03 ppm) equivalent to the proton is due to [1H, N(3)H,s] [38]. A singlet peak at (5.02ppm) which is equal to a proton is due to [1H, N(4)H,s] [39]. The singlet peak when ( 4.52 ppm) is equal to the proton is due to [1H, N(5)H,s]. The chemical shift due to the  $\text{H-}_{\text{aliphatic}}$  was detected as a multiplet when ( 3.22-2.59) ppm which is due to [11H,  $\text{C}_{(6,11)}\text{-H}_{\text{aliphatic,m}}$ ] and the chemical shift at ( 1.10 ppm) which is due to a single peak of [6H,  $\text{C}_{(1,2)}\text{-H}_{\text{aliphatic, s}}$ ].

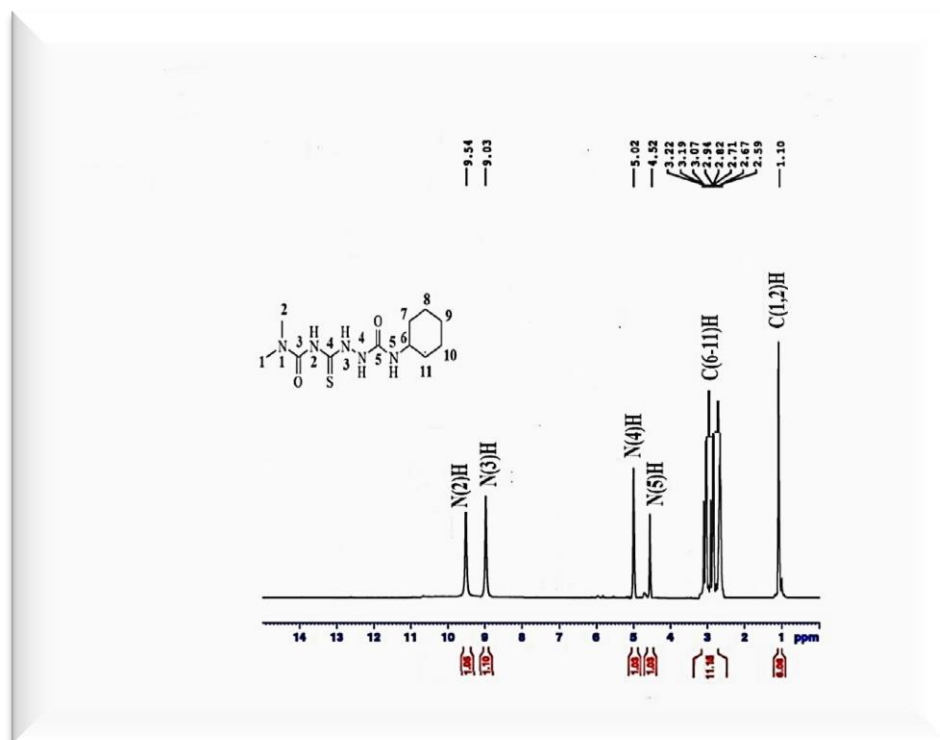


Figure 7.  $^1\text{H-NMR}$  of N-cyclohexyl-2-((dimethyl carbamoyl) carbamothioyl) hydrazine-1-carboxamide (L)

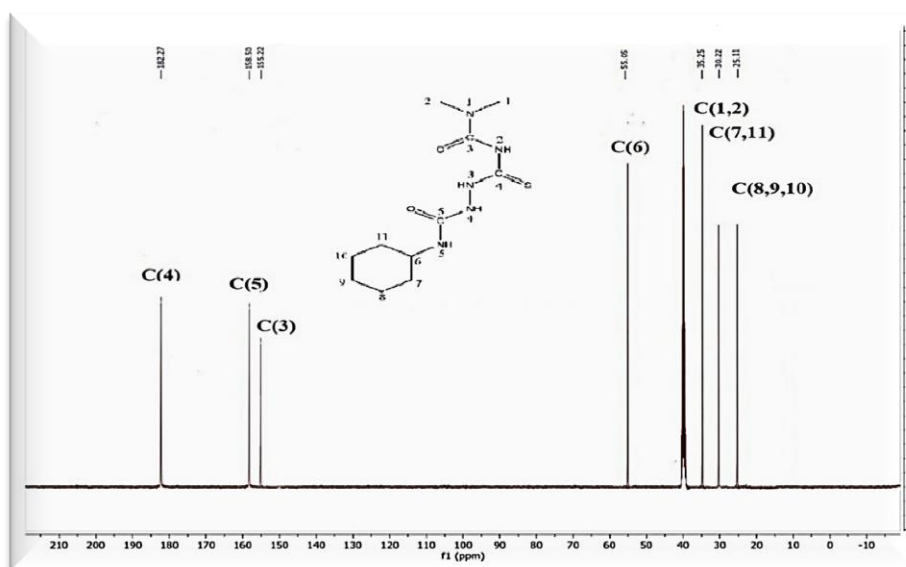


Figure 8.  $^{13}\text{C-NMR}$  spectrum of N-cyclohexyl-2-((dimethyl carbamoyl) carbamothioyl) hydrazine-1-carboxamide (L)

Figure 8 illustrates the  $^{13}\text{C}$  NMR spectrum of the ligand in  $\text{DMSO-d}_6$ . The ligand spectrum shows downfield shifts at 158 and 155 ppm assigned to carbonyl carbon ( $\text{C}=\text{O}$ ) for semicarbazide and carbonyl, respectively. The slight differences in the chemical shifts of these peaks in the spectrum of ligands are probably due to different environments around them ( $\text{C}=\text{O}$ ). The spectrum showed an indicated ( $\text{C}=\text{S}$ ) signal at 182 ppm, attributed to the thiocyanate group. The aliphatic carbon signals of the ( $\text{C}_6$ ), ( $\text{C}_{1,2}$ ), ( $\text{C}_{7,11}$ ), and ( $\text{C}_{8,9,10}$ ) appeared as expected in the range of 55-25 ppm, respectively. All  $^{13}\text{C}$ -NMR chemical shift positions of the ligand (L) are in agreement with values reported by other semicarbazide ligands [40].

### 3.4. Mass Spectrum of of Ligand (L)

The electrospray (+) mass spectroscopy of L figure (9) shows the molecular ion peak at  $m/z = (287.14)$  amu (22%) this peak is related to (L) + calculated (287.38) amu for ( $\text{C}_{11}\text{H}_{21}\text{N}_5\text{O}_2\text{S}$ )

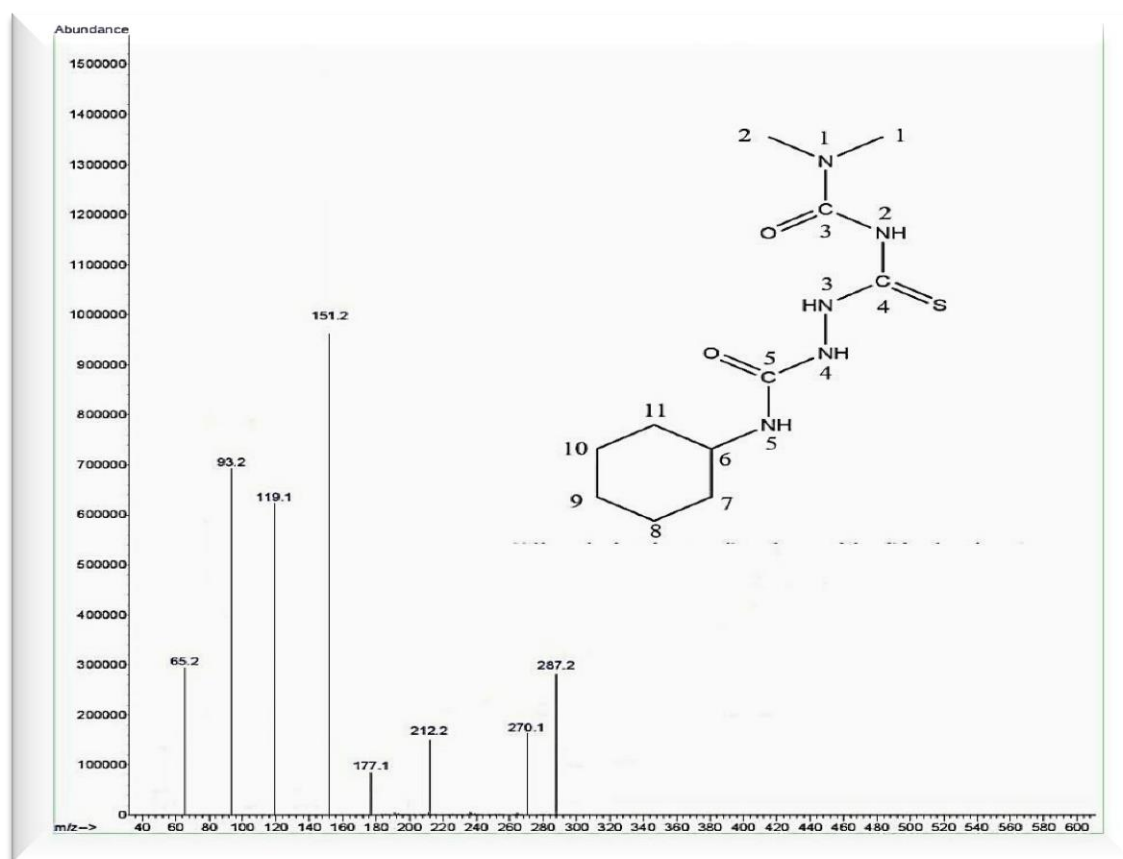


Figure 9. The mass spectrum of (L)

### Biological Activity

Determine the antibacterial activity of the ligand and its metal complexes, a dye-negative bacteria strain and a specific strain of Gram-positive bacteria isolate (*Staphylococcus aureus*) and (*Escherichia coli*) were used as test organisms. To determine whether or not ligand and its complexes possessed antibacterial properties, the disc diffusion method was utilized. The *in vitro* antibacterial studies were conducted at a range of concentrations of 50mg/ml, 25mg/ml, and 12. mg/ml against pathogenic bacterial strains. Levofloxacin ( $10 \mu\text{g}/\text{disc}$ ), was used as a positive control, and (CFU  $10 \mu\text{g}$ ) a negative control. The nutrient agar solution was poured into the sterilized petri plates to create the agar medium. Following an incubation period of twenty-four hours at 37 degrees Celsius in the nutrient broth, all of the bacteria were cultivated and then distributed throughout the nutritional agar's surface. Whatman No. 1 filter paper was cut into 5 mm diameter discs, which were then autoclaved for 15 minutes at 15 psi in an aseptic environment. The chemicals diffuse from a filter paper disc onto agar when it is impregnated with the chemical and placed on the agar. The chemical in the

agar will only be distributed across the disc by diffusion. If the disc is chemically sensitive, the extent of the chemical infiltration around it will depend on the chemical's solubility and molecular size. The "zone of inhibition" is the region that does not expand. To create a consistent suspension, a loopful of the test organism's overnight slant culture was injected with 5 $\mu$ L of sterile physiological saline. To create a homogeneous grass culture, this suspension culture was surface distributed over a nutrient agar plate using a sterile cotton swab. Using sterile forceps, the discs containing the test samples that were prepared as previously indicated were put on the plates' swabbed surfaces (five discs per plate). After an incubation time of twenty-four hours at 37 degrees Celsius, the plates were examined to look for zones of inhibition surrounding the discs. Regarding the biological activity of *Escherichia coli*, the L in the third and second concentrations 50,25 showed stronger activity, while the complexes C<sub>6</sub>, and C<sub>7</sub>, in all concentrations, gave medium activity against this bacteria strain. The examined chemicals' biological action against *Staphylococcus aureus* indicated that the L in the third concentration 50 showed a stronger activity against this type of bacteria. C<sub>1</sub>, in the second and third concentrations 25,50 showed a stronger activity against this type of bacteria. activity in the third, first, and second concentrations C<sub>2</sub> showed medium activity, but did not give activity against this type of bacteria.

Table 3. Antibacterial activity values of some prepared compounds against isolates of pathogenic bacteria

Compound	Concentration (μg/ml)	Staphylococcus aureus (G+)	Escherichia Coli (G-)
L	50	R	26
	25	27	32
	12	48	36
C <sub>1</sub>	50	R	11
	25	R	15
	12	30	25
C <sub>2</sub>	50	R	17
	25	R	18
	12	21	19
C <sub>3</sub>	50	R	11
	25	17	14
	12	21	18

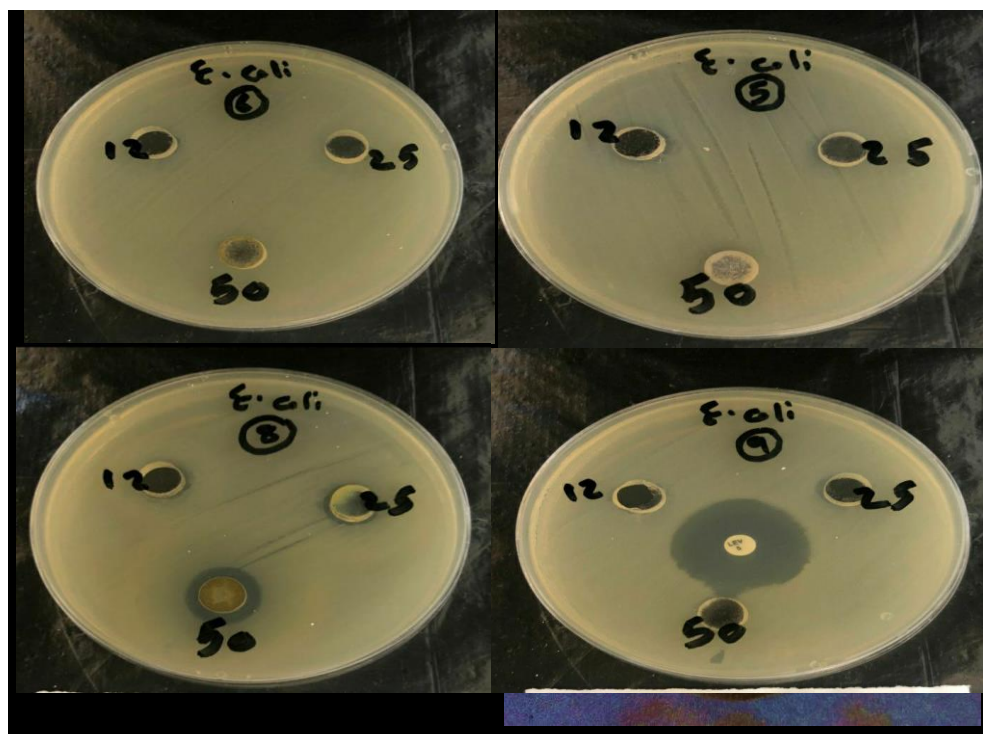


Figure 12. Antibacterial I activity of the compounds against *Escherichia aureus* of the L ligand and its complexes [C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>]



Figure 13. Antibacterial activity of the compounds against *Staphylococcus* *Escherichia coli* of the L ligand and its complexes [C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>]

#### 4. CONCLUSION

The synthesis of a new ligand N-cyclohexyl-2- ((dimethyl carbamoyl) carbamothioyl) hydrazine-1-carboxamide (L) and the new metal complexes are recorded. The monomeric complexes were formed by the interaction of the ligand with Co<sup>+2</sup>, Ni<sup>+2</sup>, and Cu<sup>+2</sup> metal ions in a 1:1 (ligand - metal) mole ratio. The chemical structure of compounds and the bonding behavior of complexes were confirmed using physicochemical methods. Six-coordinate monomeric complexes with the formula [LCoCl<sub>2</sub>H<sub>2</sub>O], [LNiCl<sub>2</sub>H<sub>2</sub>O], and [LCuCl<sub>2</sub>H<sub>2</sub>O] were isolated and confirmed through characterization. An assessment of the ligand and its complexes was conducted to determine their antibacterial activity against both Gram-positive and Gram-negative bacteria.

#### ACKNOWLEDGEMENTS

In recognition of the University of Diyala's ongoing assistance, the authors would express their gratitude.

#### REFERENCES
















- [1] Mir, I.A., QU.Ain, T.Qadir,A.Q.malik,Sjan,S.Shahverdi., A review of semicarbazone-derived metal complexes for application in biomedicine and related fields. *Journal of Molecular Structure*, 2023: p. 136216.
- [2] Pervaiz, M., R.Quratulain., AEjaz Thiosemicarbazides, 1, 3, 4 thiadiazole Schiff base derivatives of transition metal complexes as antimicrobial agents. *Inorganic Chemistry Communications*, 2024. 160: p. 111856.
- [3] Walczak-Nowicka, Ł.J., A.Szopa, M-Pituch., Newly synthesized derivatives with a thiosemicarbazide group reduce the viability of cancer cell lines. Acute toxicity assessment in Zebrafish (*Danio rerio*) early life stages. *Toxicology in Vitro*, 2024. 95: p. 105741.
- [4] Yu, W., et al., Effect of different preservation treatments on the formation of semicarbazide in *Litopenaeus vannamei* and the potential molecular mechanisms. *Journal of Food Composition and Analysis*, 2023. 124: p. 105664.
- [5] Alkhatib, F.M. and H.M. Alsulami, Synthesis, characterization, DFT calculations and biological activity of new Schiff base complexes. *Heliyon*, 2023. 9(8).
- [6] Sanaa, J.H., N.J. Hussein, and Z.A. Muneam, Synthesis, Spectral Characterization and Biological Activity of new niii, Cooi and Cuii Complexes with Thiosemicarbazide Ligand. *HIV Nursing*, 2022. 22(2): p. 2361–2367-2361–2367.

- [7] Zehra, S., S. Tabassum, and F. Arjmand, Biochemical pathways of copper complexes: Progress over the past 5 years. *Drug Discovery Today*, 2021. 26(4): p. 1086-1096.
- [8] Shukla, S.N., et al., Tailored synthesis of unsymmetrical tetradentate ONNO schiff base complexes of Fe (III), Co (II) and Ni (II): Spectroscopic characterization, DFT optimization, oxygen-binding study, antibacterial and anticorrosion activity. *Journal of Molecular Structure*, 2020. 1202: p. 127362.
- [9] Dawoud, S.M. Synthesis and DNA binding study of Co (II) and V (IV) complexes with O, N, O tridentate 3-methoxysalicylaldehyde-semicarbazide based ligand. in *Journal of Physics: Conference Series*. 2021. IOP Publishing.
- [10] Lobana, T.S., et al., Bonding and structure trends of thiosemicarbazone derivatives of metals—an overview. *Coordination Chemistry Reviews*, 2009. 253(7-8): p. 977-1055.
- [11] Belikov, M.Y. and A.G. Milovidova, Synthesis of heterocyclic compounds containing the 3, 3-dicyanoacrylamide fragment. *Chemistry of Heterocyclic Compounds*, 2021. 57: p. 1-6.
- [12] Salah, N., et al., Novel NO<sub>2</sub> semicarbazone ligand and its metal complexes as VEGFR-2 inhibitors: Synthesis, spectral characterization, density functional theory calculations, molecular docking, and antimicrobial and antitumor evaluation. *Applied Organometallic Chemistry*, 2022. 36(10): p. e6845.
- [13] Kavitha, P. and K.L. Reddy, Pd (II) complexes bearing chromone based Schiff bases: Synthesis, characterisation and biological activity studies. *Arabian Journal of Chemistry*, 2016. 9(5): p. 640-648.
- [14] Ammar, R.A., et al., Synthesis, spectroscopic, molecular structure, antioxidant, antimicrobial and antitumor behavior of Mn (II), Co (II), Ni (II), Cu (II) and Zn (II) complexes of O<sub>2</sub>N type tridentate chromone-2-carboxaldehyde Schiff's base ligand. *Journal of Molecular Structure*, 2017. 1141: p. 368-381.
- [15] Dawood, Z., S. Hussein, and M. Al-Shama'a, SOME COMPLEXES OF Ni (II) CONTAINING MIXES LIGANDS. *Sciences & Technology. A, exactes sciences*, 2004: p. 71-75.
- [16] Salam, M., et al., Synthesis, spectral characterization and crystal structure of a novel trinuclear di-n-butyltin (IV) complex with pyruvic acid-N (4)-cyclohexylthiosemicarbazone (H2PACT). *Journal of Organometallic Chemistry*, 2012. 696(26): p. 4202-4206.
- [17] Affan, M., et al., Synthesis and spectroscopic characterization of organotin (IV) complexes with 2-benzoylpyridine-N (4)-cyclohexylthiosemicarbazone (HBPCT): X-ray crystal structure of [PhSnCl<sub>2</sub> (BPCT)]. *Inorganica Chimica Acta*, 2011. 366(1): p. 227-232.
- [18] Hussain, S.A. and M.J. Al-Jeboori, New metal complexes derived from Mannich-base ligand; Synthesis, spectral characterisation and biological activity. *J. Global Pharma Tech*, 2019. 11(2): p. 548-560.
- [19] Kano, T., et al., Highly Diastereo- and Enantioselective Mannich Reactions of Synthetically Flexible Ketimines with Secondary Amine Organocatalysts. *Angewandte Chemie*, 2012. 124(5): p. 1217-1220.
- [20] González-García, C., et al., Synthesis and antimicrobial activity of tetradentate ligands bearing hydrazone and/or thiosemicarbazone motifs and their diorganotin (IV) complexes. *Journal of inorganic biochemistry*, 2016. 163: p. 118-130.
- [21] Boulechfar, C., et al., Synthesis, electrochemical, and quantum chemical studies of some metal complexes: Mn (II), Co (II), and Zn (II) with 2-furaldehyde semicarbazone. *Journal of Molecular Structure*, 2023. 1271: p. 134007.
- [22] Singh, H., J. Singh, and K. Sharma, Synthetic, structural, and antimicrobial studies of organotin (IV) complexes of semicarbazone, thiosemicarbazone derived from 4-hydroxy-3-methoxybenzaldehyde. *Research on chemical intermediates*, 2012. 38: p. 53-65.
- [23] Zayed, E.M., et al., Coordination behaviour and biological activity studies involving theoretical docking of bis-Schiff base ligand and some of its transition metal complexes. *Applied Organometallic Chemistry*, 2018. 32(12): p. e4603.
- [24] Ilhan, S. and H. Temel, Synthesis and spectral studies of macrocyclic Cu (II), Ni (II) and Co (II) complexes by template reaction of 1, 4-bis (3-aminopropoxy) butane with metal (II) nitrate and salicylaldehyde derivatives. *Journal of molecular structure*, 2008. 891(1-3): p. 157-166.
- [25] Zayed, E.M., M. Zayed, and A.M. Hindy, Thermal and spectroscopic investigation of novel Schiff base, its metal complexes, and their biological activities. *Journal of Thermal Analysis and Calorimetry*, 2014. 116: p. 391-400.
- [26] Pavia, D., et al., Introduction the Spectroscopy. USA: Cengage Learning, 2013.
- [27] Hasan, H.A., E.I. Yousif, and M.J. Al-Jeboori, Metal-assisted assembly of dinuclear metal (II) dithiocarbamate Schiff-base macrocyclic complexes: Synthesis and biological studies. *Global J. Inorg. Chem*, 2012. 3(10): p. 1-7.
- [28] Hussein, S.A. and E.I. Yousif, METAL COMPLEXES OF SEMICARBAZONE LIGAND DERIVED FROM MANNICH-β-AMINOCARBONYL: SYNTHESIS, STRUCTURAL CHARACTERISATION, THERMAL PROPERTIES, AND BIOLOGICAL ACTIVITY.
- [29] Al-Qazzaz, A.H. and M.J. Al-Jeboori, New metal complexes derived from mannich ligands: Synthesis, spectral investigation and biological activity. *Biochem. Cell. Arch*, 2020. 20: p. 4207-4216.
- [30] Chandra, S. and L.K. Gupta, EPR, mass, IR, electronic, and magnetic studies on copper (II) complexes of semicarbazones and thiosemicarbazones. *Spectrochimica Acta Part A: Molecular and Biomolecular Spectroscopy*, 2005. 61(1-2): p. 269-275.
- [31] Ramachandran, E., et al., Synthesis, characterization and cytotoxic activity of novel copper (II) complexes with aroylhydrazone derivatives of 2-Oxo-1, 2-dihydrobenzo [h] quinoline-3-carbaldehyde. *Journal of inorganic biochemistry*, 2018. 182: p. 18-28.
- [32] Dong, X.-Y., et al., Structurally characterized solvent-induced homotrinary cobalt (II) N<sub>2</sub>O<sub>2</sub>-donor bisoxime-type complexes. *Crystals*, 2018. 8(3): p. 139.
- [33] Mahross, M.H., et al., Synthesis, characterization and corrosion inhibition of N'-phenylbenzohydrazide derivative metal complexes: Experimental and quantum chemical studies. *Zeitschrift für Physikalische Chemie*, 2019. 233(7): p. 949-972.
- [34] Al-Jeboori, M.J., A.H. Al-Dujaili, and A.E. Al-Janabi, Coordination of carbonyl oxygen in the complexes of polymeric N-crotonyl-2-hydroxyphenylazomethine. *Transition metal chemistry*, 2009. 34: p. 109-113.
- [35] Al-Qazzaz, A.H. and M.J. Al-Jeboori, NEW METAL COMPLEXES DERIVED FROM MANNICH LIGANDS: SYNTHESIS, SPECTRAL INVESTIGATION AND BIOLOGICAL ACTIVITY. *Biochemical & Cellular Archives*, 2020. 20.
- [36] Hassaan, A.M., M.A. Khalifa, and A.K. Shehata, COMPLEXES OF SOME METAL IONS WITH A SCHIFF BASE LIGAND DERIVED FROM ISATIN AND O-AMINOPHENOL. *Bulletin des Sociétés Chimiques Belges*, 1995. 104(3): p. 121-124.
- [37] Chandra, S. and A. Gautam, Spectroscopic and biological approach in the characterization of Cr (III), Mn (II) and Co (II) complexes with a novel hexaazamacrocyclic ligand derived from semicarbazide. *Journal of the Serbian Chemical Society*, 2009. 74(12): p. 1413-1422.



- [38] Suresh, M. and V. Prakash, Preparation and characterization of Cr (III), Mn (II), Co (III), Ni (II), Cu (II), Zn (II) and Cd (II) chelates of Schiff's base derived from vanillin and 4-aminoantipyrine. Int. Phys. Sci, 2010. 5(14): p. 2203-2211.
- [39] El-Sayed, B., et al., Synthesis and structural study of the ligand o-OH acetophenone azine and its Cu (II), Ni (II), Co (II) and Zn (II) complexes. Vibrational spectroscopy, 2002. 30(1): p. 93-100.
- [40] Banerjee, A., D. Prasad, and S. Roy, METAL-COMPLEXES AS LIGANDS-BINUCLEAR ALKALI-METAL COMPLEXES WITH COPPER (II)-SALICYLADIMINES AND NICKEL (II)-SALICYLALDIMINES. JOURNAL OF THE INDIAN CHEMICAL SOCIETY, 1982. 59(11-1): p. 1303-1305.

### BIOGRAPHIES OF AUTHORS

	<p><b>Eman Ahmed Kadhim</b> is a Master's student at the College of Education for Pure Sciences at the University of Diyala. she obtained a bachelor's degree in chemistry from College of Education for Pure Sciences at the University of Diyala. 2016 and she is a teacher at Al-Iraqiya Girls Secondary School . She can be contacted at email: <a href="mailto:eman.a.khadim.msc23@uodiyala.edu.iq">eman.a.khadim.msc23@uodiyala.edu.iq</a></p>
<p>Scopus®    </p>	
	<p><b>Dr. Nasry Jassim Hussien</b> is an associate professor at the College of Education for Pure Sciences at the University of Diyala. He obtained a bachelor's degree in chemistry from Al-Mustansiriya University and a master's degree from the University of Technology, Department of Applied Sciences. He obtained a doctorate from the Malaysian University UKM, College of Science and Technology, FST, in the specialty of inorganic chemistry. His areas of research are: Chemistry includes organic and inorganic aspects and includes the diagnosis of complexes and their applications. He has published several scientific papers in national, and international conferences and journals. He can be contacted at email: <a href="mailto:nasry.hussien@uodiyala.edu.iq">nasry.hussien@uodiyala.edu.iq</a></p>
<p>Scopus®    </p>	
	<p><b>Dr. Siti Fairus M. Yusoff</b> received a Bachelor of Science (Pure Chemistry) from Universiti Teknologi Malaysia (2007) and a Doctor of Philosophy in the same field from the University of Bristol in the United Kingdom (2011). Currently, she is a senior lecturer at the Faculty of Science and Technology, Universiti Kebangsaan Malaysia. Her research focuses on the development of polymer and inorganic materials for different applications, such as wastewater treatment, agriculture, and biomedicine has published several scientific papers in national, and international conferences and journals. She can be contacted at email: <a href="mailto:sitifairus@ukm.edu.my">sitifairus@ukm.edu.my</a></p>
<p>Scopus®    </p>	