

# Preparation, Characterization, Theoretical and Biological Studies of Mixed Ligands Complexes Derived from Heterocyclic Compound Against Different Types of Bacteria and Fungi

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## Abstract

New Mannich Base has been prepared from condensation reaction of 2-chloro-N-(5-mercapto-1,3,4-thiadiazole-2-yl) acetamide with piperidin(L) and drop of formaldehyde. The Resulting compound represents Mannich base (2-Chloro-N-(5-(piperidin-1-ylmethylthio)-1,3,4-thiadiazole-2-yl) acetamide (L). A series of mixed ligand complexes was prepared from (L) and 1,10-phenanthroline with the metal ion Co (II), Ni (II), Cu (II), Pd (II), Pt (IV) and Au (III). The compounds obtained were successfully characterized by different spectroscopic techniques such as C.H.N.S, FTIR, UV-Vis, <sup>1</sup>HNMR, <sup>13</sup>CNMR, magnetic sensitivity and molar conductivity. The ratio of M: L was measured by using molar ratio method in solution state. Experimental results showed that the mixed ligands coordinated as tri-dentate from Mannich base (L) and bi-dentate from (1,10-phenanthroline). The antibacterial and antifungal activity of ligand and complexes was studied against two types of bacteria and one type of fungi at 0.02M. The standard heat of formation and binding energy of the ligands and all prepared complexes were calculated using the Hyperchem 8.0.7 program, the study proved that the complexes are more stable than the ligands. The vibrational frequencies of the ligands were calculated, and the practical and theoretical results were compared, in addition to calculating the error ratio between the two methods. Keywords: Transition Metal Complexes, Mannich Base, Mixed ligands, 1, 10-Phenanthroline, Antibacterial and Antifungal activity

## 1. Introduction

Thiadiazol ring (C<sub>2</sub>H<sub>2</sub>SN<sub>2</sub>) is a heterocyclic aromatic penta cyclic compound containing three atoms in contrast to two nitrogen atoms and one sulfur atom in addition to two carbon and hydrogen atoms [1]. At present, there was a lot of interest on 1,3,4-thiadiazoles as a very important category of heterocyclic nitrogen-containing compounds for their diverse and presence of a portion of the N-C-S toxophoric [2]. Thiadiazol have different biological activity such as antitumor [3], antibacterial [4], anti-inflammatory [5]. Antifungal [6], antimicrobial [7] and analgesic [8]. The Mannich reaction is one of organic reactions [9], which includes the production of organic compounds that include a primary or secondary reaction of an amine, except for ammonia, with a formaldehyde compound and another third substance that contains an acid proton [10].

Mannich base have many practical applications such as in leathers, paper also in the production of industrial polymers, material additives used by the petroleum industry, as products used in water treatment, analytical reagents, cosmetics, dyes, etc. [11]. However, the most important application of the Mannich reaction lies in the field of medicinal chemistry. Mannich bases can offer present interesting biological activities. The amino methylation of drugs can be used to improve their delivery to the human body. One of the properties

of the amino methyl group is that it is hydrophilic and by introducing a polar function in its structure [12]. In addition, Mannich bases are among these new classes of antibacterial compounds that have drawn attention. Lately, researchers in this field [13].

Mannich bases are known to possess potent activities such as anti-inflammatory [14], anticancer [15] antibacterial, antifungal, [16] antispasmodic [17], anti-HIV, anti-tuberculosis [18], antimalarial [19], antiviral [20] [20] analgesic with biological activities, Mannich bases, and their derivatives are intermediates nitrogen [21].

The research aims to prepare a series of complexes with mixed ligands, Mannich bases with 1, 10-phenanthroline and study the prepared compounds in liquid and solid states, in addition to studying them biologically and theoretically.

## 2. Experimental Methods

In this paper, High purity chemicals were used in this research. CHNS elemental data were measured using an Eager300 elemental analyzer. Metal contents were carried out by using shimadzu atomic absorption 670 Flam spectrophotometer. Conductivity data were acquired at 10–3 M in DMF solution of the complexes using a WTW conductance meter at 25 °C. FT-IR spectra were measured with a Shimadzu and Perkin Elmer FT infrared spectrophotometer using KBr (4000-400) and CsI (4000-200) disk. Absorption in the UV-visible region

was recorded in ethanol solution using UV-Vis. Shimadzu spectrophotometer of 1800 pieces. Magnetic susceptibility measurement of the complexes was made using the Faraday method and the magnetic correction factor (D) was calculated using the Pascal constants of the atoms that make up the prepared complexes and using a Bruker Magent BM6 device.  $^1\text{H}$ ,  $^{13}\text{C}$  NMR for the compounds at 25  $^{\circ}\text{C}$ . The points of all prepared compounds were measured by Gallen kamp MF. B-60.

Preparation of starting material 2-amino 5-mercapto 1,3,4 thiadiazole (S1)

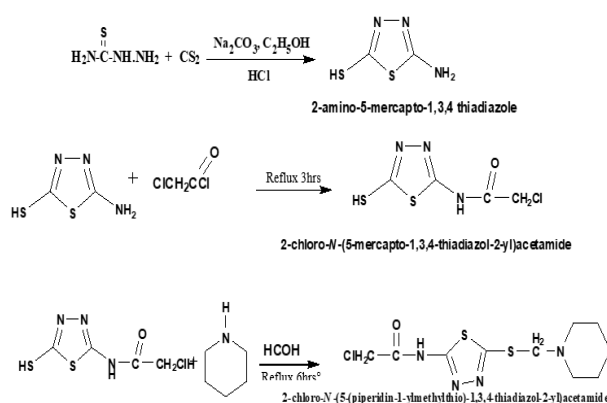
In a round bottom flask (2gm,0.02mol) of thiosimcarbazine was dissolved in (25ml) absolute ethanol and (0.016gm,0.0002mol) of anhydrous sodium carbonate and (4.712 gm,0.062mol) of ( $\text{CS}_2$ ) were added with stirring and heating at (40 $^{\circ}\text{C}$ ) for an hour. Then, the mixture was raised for 7hours, after which the solvent was evaporated, (50ml) distilled water and drops of concentrated hydrochloric acid were added. A greenish-yellow precipitate. The sediment was washed, and the precipitate was filtered with a quantity of distilled water to get rid of the excess acid it was recrystallized with absolute ethanol. The color of the precipitate (was yellowish white, with a melting point of (229-231)  $^{\circ}\text{C}$  and molecular formula ( $\text{C}_2\text{H}_3\text{N}_3\text{S}_2$ ) [19].

Preparation of 5-(piperidin-1-yl)-1,3,4-thiadiazol-2-amine (S2)

In a round flask, dissolve (0.1gm, 0.01m) of a substance 2-amino 5-mercapto 1,3,4 thiadiazole (S1) in (10ml) absolute ethanol, added with stirring (0.1 gm, 0.02M) of chloroacetyl chloride) in an ice bath, then the mixture was raised on reflux and heat for 3 hours, leave to dry. The precipitate has been washed with a quantity of distilled water to get rid of the excess acid and then recrystallized using ethanol. The precipitate has a yellowish-white color and has a molecular formula  $\text{C}_4\text{H}_4\text{N}_3\text{S}_2\text{OCl}$  and a melting point of (250-252)  $^{\circ}\text{C}$ .

Synthesis of 2- Chloro -N-5-( Piperidin-1-ylmethylthio)-1,3,4- thiadiazole, ligand (Mannich ligand) (L)

In a round bottom flask, dissolve (0.145 gm, 0.04m) of 5-(piperidin-1-yl)-1,3,4-thiadiazol-2-amine(S2) in(10ml) absolute ethanol, added with stirring and cooling (8ml) from formaldehyde, (0.08gm,0.03m) piperidin than the mixture was put on reflux and heat for six hours. The reaction mixture was kept overnight in the refrigerator. The precipitate was washed in distilled water. The precipitate has brown color, has a molecular fomula  $\text{C}_{10}\text{H}_{15}\text{ClN}_4\text{OS}_2$  and a melting point of over 300  $^{\circ}\text{C}$ .



Scheme (1) Synthesis of Mannich Base, 2chloro-N-5-(Piperidin-1-ylmethylthio)-1,3,4-Thiadiazole (L).

### Synthesis of mixed ligands complexes

Absolute ethanol is used as a solvent, a series of complexes have been prepared from the reaction (1mmol) of  $\text{CoCl}_2 \cdot 6\text{H}_2\text{O}$ ,  $\text{NiCl}_2 \cdot 6\text{H}_2\text{O}$ ,  $\text{CuCl}_2 \cdot 2\text{H}_2\text{O}$ ,  $\text{PdCl}_2$ ,  $\text{H}_2\text{PtCl}_6 \cdot 6\text{H}_2\text{O}$  and  $\text{HAuCl}_4 \cdot \text{H}_2\text{O}$  with, (1mmol) of ligand (L) and (1mmol) of 1,10-Phenanthroline in a molar ratio 1:1:1. Then they were refluxed and heating for three hours. The precipitates, which were colored and then were filtered, were washed using hot ethanol and finally dried using desiccators.

Table (1): The physical properties of color and melting point in addition to the values of C.H.N.S and the percentage of all prepared compounds

Comp.	color	m.p / $^{\circ}\text{C}$	Yield %	Atomic Abs.% Cal. (Found)	Elemental analysis Calc. (found)			
					C	H	N	S
1,10Phenotheroline	White	292-294	----	.....	79.90 (80.11)	4.43 (3.76)	15.53 (16.17)	0
Mannich(L)	brown	Over 300	76	....	39.10 (38.66)	4.88 (3.98)	18.25 (19.01)	20.85 (21.34)
CoL(1,10phen.)	Light Blue	190-192	87	9.02 (8.77)	40.43 (39.79)	4.13 (3.78)	12.86 (11.89)	9.80 (8.83)
NiL(1,10phen.)	Green	182-185	73	8.99 (8.02)	40.46 (39.56)	4.13 (5.22)	12.87 (12.00)	9.80 (10.45)
CuL(1,10phen.)	Dark Blue	180-182	69	9.85 (10.76)	41.27 (40.33)	3.90 (4.91)	13.13 (14.08)	10.00 (9.77)
PdL(1,10phen.)	Dark Yellow	170-172	71	15.59 (14.62)	38.68 (39.11)	3.66 (4.01)	12.30 (11.58)	9.37 (10.10)
PtL(1,10phen.)	Yellow	298-300	81	23.16 (24.01)	31.34 (30.54)	2.96 (3.98)	9.97 (10.11)	7.59 (6.65)
AuL(1,10phen.)	Brown	286-288	85	24.06 (23.77)	35.10 (34.99)	3.78 (4.60)	10.26 (9.77)	7.81 (8.30)

Hyperchem program is a sophisticated molecular

modeling environment that is known for its quality, flexibility, and ease of use. The standard heat of

formation and binding energy of the ligands and all prepared complexes were calculated using PM3 and ZINDO, AMBER methods, in addition to calculating the vibrational frequencies and calculating the error ratio between the practical and theoretical results of the ligands.

### Antibacterial and Antifungal activity

1-40 g of culture medium for bacteria and fungi was dissolved in a liter of distilled water, as the culture medium used for bacteria (Agar Mueller Hinton) and for fungi (Sabroid Dextroes Agar).

2- After dissolving by heating, the culture medium was placed in the sterilizer for 15 minutes, then poured into sterilized plastic dishes and left to solidify.

3-A hole is made using a cork drill with a diameter of 8 mm to add the material that inhibits the growth of bacteria and fungi.

4-The prepared ligands and complexes dissolved in DMSO at a concentration of 0.02M were injected into the pits of the culture medium.

5-The dishes were placed in the incubator at 37 °C for 24 hours for antibacterial activity and 72 hours for antifungal activity, then the inhibition diameters were measured using a ruler in mm for each of the prepared compounds.

### 3. Results and Discussion

The prepared complexes were obtained in the form of colored precipitates. The analytical data for the ligand(L) and their mixed ligands metal complexes together with some physical properties are summarized in (Table1). All complexes were soluble in organic solvents DMF & DMSO. Analytical data suggest a ratio of (1:1:1) for the mixed ligand complexes. The ligands and their metal complexes were characterization depended on the results of the element analysis, infrared spectra (FT-IR), (UV-vis) spectra, carbon and proton nuclear magnetic resonance spectra (<sup>1</sup>HNMR and <sup>13</sup>CNMR, magnetic susceptibility and conductivity for prepared complexes.

Fourier transforms spectroscopy (FT-IR) of Mannich ligand (L), 1,10phenatheroline and mixed ligands metal complexes

The infrared spectra are very important in determining the type of correlation in the case of complexes. The infrared spectra of Mannich ligand L and 1,10 phenatheroline their metal complexes appeared the number of the active site appeared at [ $\nu$  CO ( $\nu$ , CS),  $\nu$ (C S C)  $\nu$ (, CH<sub>2</sub>N )] which due to 1701, 720, 1161, 2943, 2854) cm<sup>-1</sup> sequentially [22]. When bonding to the nitrogen atom, according to the frequency's cobalt, nickel, copper, palladium, platinum and gold complexes, the band of  $\nu$ C=Nring of 1,3,4 thiazole and  $\nu$ C=N of 1,10 phenatheroline of all prepared complexes is shifted to higher and lower frequency (1610, 1606, 1602, 1631, 1643, 1601) and (1640, 1651, 1647, 1647, 1687, 1639) cm<sup>-1</sup> respectively. Other band bonding from oxygen of carbonyl group has been shifted according to the frequencies (1685, 1721, 1739, 1720, 1743, 1690) cm<sup>-1</sup>, in all prepared complexes. We also notice a shift in the sulfur band in each of the c-s, csc groups from the ligand band for each of the copper, nickel and platinum complexes, which indicates the occurrence of coordination through them. We conclude from this that the complexes of nickel, copper and platinum are linked from  $\nu$ C = N, carbonyl group carbon and sulfur in Mannich's base and from  $\nu$ C = N of ligand 1,10 phenothroline. [23]. As for the complexes of copper, palladium and gold, they are bound by  $\nu$ C=N and carbonyl of the Mannich base and through C=N of the ligand 1,10 phenothroline. Further appearance of medium bands at (543–578) and (567–586) cm<sup>-1</sup> which could be attributed to  $\nu$ M–N,  $\nu$ M–O,  $\nu$ M–S and  $\nu$ M–Cl for complexes with mixed ligands [13]. Other bands can be showed in Table (2). Also, other bands belonging to the  $\nu$ NH group, and the  $\nu$ CH<sub>2</sub>-N group appeared that did not have a displacement when the coordination occurred, which indicates non coordination through them [24].

Table (2): The main absorption bands of the infrared spectrum of ligand (L), 1,10 Phenath roline and its metal complexes (cm<sup>-1</sup>).

COMP	$\nu$ C=O	$\nu$ CH <sub>2</sub> -N	$\nu$ C=N 1,3,4thio.	$\nu$ C=N 1,10pheno.	$\nu$ CSC	$\nu$ CS	$\nu$ M-O	$\nu$ M-N	$\nu$ M-S	$\nu$ M-Cl
L	1701	2943 2854	1620	1618	1161	702	-----	-----	-----	-----
CoL (1,10phen.)	1721	2943 2854	1610	1640	1164	702	590	482	-----	-----
NiL(1,10phen.)	1739	2943	1606	1651	1192	719	563	470	416	312
CuL(1,10phen.)	1690	2943 2854	1602	1647	1195	736	590	536	470	320
PdL(1,10phen.)	1720	2857	1631	1647	1163	709	486	435	-----	---
PtL(1,10phen.)	1743	2940 Broad	1643	1687	1222	775	505	447	408	345
AuL(1,10phen.)	1685	2944 2854	1601	1639	1161	705	547	455	-----	-----

### Uv-vis Spectra, Magnetic susceptibility and molar conductivity

The Uv-vis spectra of the ligands and their metal

complexes were determined in DMSO at 25°C. The electronic spectra data of all prepared compounds are shown in Table (3). In Mannich ligand the band in the region (25773) cm<sup>-1</sup> is attributed to  $n \rightarrow \pi^*$

transition of non-bonding electrons presents on S, N in ligand. Another transition appeared in the region (33112 and 37314 cm<sup>-1</sup>) is attributed to  $\pi \rightarrow \pi^*$  transition [24]. In 1,10 phenathroline, two bands appeared, the first returning to  $n \rightarrow \pi^*$  transition and the second returning to  $\pi \rightarrow \pi^*$  transition.

In transitions sequentially and (26381, 38598) cm<sup>-1</sup> is due to transition and IL  $\rightarrow$  CoCT, which indicate tetrahedral geometry of Co (II). Magnetic moment, (3.52) B.M, showed higher orbital contribution. Conductivity measurement in DMF (79  $\mu$ S.cm<sup>-1</sup>) appeared that the complex was ionic. Light blue complex to be paramagnetic and high spin tetrahedral. The electronic spectrum of this complex can be seen in Table (3) [25].

In Ni complex spectrum bands are observed at (10737, 23640 cm<sup>-1</sup>) is assigned to  $3A_{2g} \rightarrow 3T_{2g}$ ,  $3A_{2g} \rightarrow 3T_{1g}$  (p) transitions sequentially and 13659 is assigned forbidden to  $3A_{2g} \rightarrow 1E_g$  which indicate octahedral geometry of Ni. Magnetic moment, (3.15) B.M showed higher orbital contribution [26]. Conductivity measurement in DMF (66  $\mu$ S.cm<sup>-1</sup>) appeared that the complex was ionic [27]. Green complex to be paramagnetic and high spin octahedral. The electronic spectrum of this complex can be seen in Table (3).

In Cu complex bands are observed at (18083 cm<sup>-1</sup>) is assigned to  $2E_g \rightarrow 2T_{2g}$ , and (25839 and 40983) cm<sup>-1</sup> is due to IL  $\rightarrow$  CuCT which indicate octahedral geometry of Cu (II) [28]. Magnetic moment, (1.85) B.M, showed a higher orbital contribution [29].

Conductivity measurement in DMF (69  $\mu$ S.cm<sup>-1</sup>) appeared that the complex was ionic. Dark blue complex to be paramagnetic and high spin octahedral. The electronic spectrum of this complex can be seen in Table (3).

In palladium complex bands are observed at (23923, 28571 cm<sup>-1</sup>) is assigned to  $1A_{1g} \rightarrow 1B_{1g}$ ,  $1A_{1g} \rightarrow 1E_g$  transitions sequentially and (44642) cm<sup>-1</sup> is due to IL  $\rightarrow$  PdCT, which indicate square planer geometry of Pd (II) [30]. Magnetic moment (0) B.M [31]. Conductivity measurement (73  $\mu$ S.cm<sup>-1</sup>) appeared that the complex was ionic. Yellow complex to be paramagnetic and low spin square planer. The electronic spectrum of this complex can be seen in Table (3).

Absorption bands are observed in the palladium complex spectrum at (108551 forbidden is assigned to  $1A_{1g} \rightarrow 3T_{2g}$ , (23138, 39677 cm<sup>-1</sup>) is assigned to  $1A_{1g} \rightarrow 1T_{1g}$ ,  $1A_{1g} \rightarrow 1T_{2g}$ , transitions sequentially, which indicate octahedral geometry of Pt (II). Magnetic moment, (0) B.M [32]. Conductivity measurement in ethanol (88) appeared that the complex was ionic [33].

Cobalt complex appeared bands at (3498, 16640 cm<sup>-1</sup>) is assigned to  $4A_2 \rightarrow 4T_2$ ,  $4A_2 \rightarrow 4T_1$

In the spectrum of Au complex bands appeared at (25575, 27624 cm<sup>-1</sup>) is assigned to  $1A_{1g} \rightarrow 1T_{1g}$ ,  $1A_{1g} \rightarrow 1E_g$  transitions sequentially which indicate square planer geometry Au (III). Magnetic moment (0) B.M [34]. Conductivity measurement in appeared that the complex was ionic [35].

Table (3): The electronic spectra,  $\mu_{\text{eff}}$  of complexes, conductivity in DMF and suggested geometry for ligands and its mixed ligands metal complexes.

Comp.	Absorption Cm <sup>-1</sup>	Assignments	$\mu_{\text{eff}}$ B.M.	Conductivity $\mu$ S.cm <sup>-1</sup>	Suggested geometry
L	25773 33112 37314	$n \rightarrow \pi^*$ $\pi \rightarrow \pi^*$ $\pi \rightarrow \pi^*$	.....	....	.....
(1,10 phenathroline)	30487 37593	$n \rightarrow \pi^*$ $\pi \rightarrow \pi^*$	---	----	----
CoL(1,10pheno.)	34980 16640 26381 38598	$^4A_2$ $^4T_2$ $^4A_2$ $^4T_1$ IL CoCT IL CoCT	3.52 (3.87)	79	Tetrahedral
NiL(1,10pheno.)	10737 13659 23640	$^3A_{2g}$ $^3T_{2g}$ $^3A_{2g}$ $^1E_g$ $^3A_{2g}$ $^3T_{1g}$ (p)	3.15 (2.82)	66	Octahedral
CuL(1,10pheno.)	18083 25839 40983	$^2E_g$ $^2T_{2g}$ IL Cu CT IL Cu CT	1.85 (1.73)	69	Octahedral
PdL(1,10pheno.)	23923 28571 44642	$^1A_{1g}$ $^1B_{1g}$ $^1A_{1g}$ $^1E_g$ IL Pd CT	0.00	73	Square planer
PtL(1,10pheno.)	108551 23138 39677	$^1A_{1g}$ $^3T_{2g}$ $^1A_{1g}$ $^1T_{1g}$ $^1A_{1g}$ $^1T_{2g}$	0.00	88	Octahedral
AuL(1,10pheno.)	25575 27624	$^1A_{1g}$ $^1T_{1g}$ $^1A_{1g}$ $^1E_g$	0.00	90	Square planer

The 1H-NMR and 13CNMR spectra of 2-Chloro -N-5-( Piperidin-1-Ylmethylthio)-1,3,4- Thiadiazole, Ligand(L),1,10phenotheroline and PtL

The 1H-NMR 13CNMR spectra of the L,1,10 phenatherolin and PtL (1,10phen.) complex measured in DMSO-d<sub>6</sub> showed the following chemical shifts, Table (4).

Table (4) <sup>1</sup> H and <sup>13</sup> C nuclear magnetic resonance spectra of Mannich base ligand (L), 1,10Phenanthroline and PtL	
<sup>1</sup> HNMR	<sup>13</sup> CNMR
<sup>1</sup> HNMR (DMSO- d <sub>6</sub> ) δ ppm:2.42,2.43,2.45 (d,2H, CH <sub>2</sub> of piperidin) 1.64 and 1.54 (d,2H, CH <sub>2</sub> of piperidin),12.39(S, H, NH) of amide,3.97,4.49(S, H,CH <sub>2</sub> alphatic of CH <sub>2</sub> -N and CH <sub>2</sub> -Cl respectively.	Mannich (L): <sup>13</sup> CNMR(DMSO-d <sub>6</sub> ) δppm:43.7 (CH <sub>2</sub> -Cl), 23.1,24.4 (CH <sub>2</sub> of piperidin), 53.1 (CH <sub>2</sub> -N of piperidin ) ,54.1 (CH <sub>2</sub> -N) of methylene group, 163.2 (S-C of 1,3,4 thiaziazole group ,168.4 (C=O group).
<sup>1</sup> HNMR (DMSO- d <sub>6</sub> ) δ ppm 7.67-8.53(m,H-Ar,phenyl ring) of 1,10 Phenothroline ,9.12,9.14(S,HC=N),2.5 of DMSO solvent	1,10 phenanthroline: <sup>13</sup> CNMR(DMSO-d <sub>6</sub> ) δppm:124.26,126.66,133.26,136.21,140.42 (C-of aromatic ring),151.41(HC=N group)
<sup>1</sup> HNMR (DMSO- d <sub>6</sub> ) δppm:2.42,2.43,2.45 (d,2H, CH <sub>2</sub> of pepriden) 1.64 and 1.54 (d,2H, CH <sub>2</sub> of pepriden),12.30(S, H, NH) of ,6.68-7.94(m,H-Ar,phenyl ring) of 1,10 Phenothroline,4.94,4.48(S,H,CH <sub>2</sub> alphatic of CH <sub>2</sub> -N and CH <sub>2</sub> -Cl respectively..	PtL(1,10phen.): <sup>13</sup> CNMR(DMSO-d <sub>6</sub> ) δppm ,22.9 ,25.0 (CH <sub>2</sub> of piperidin), 44.5 (CH <sub>2</sub> -N of piperidin), 55.4 (CH <sub>2</sub> -N) of methylene group, 52.3 (CH <sub>2</sub> -Cl),110.8-127.6, (C-Ar) of 1,10 phenothroline,162.58(S-C of 1,3,4 thiaziazole group, 167.8 (C=O of carbonyl).

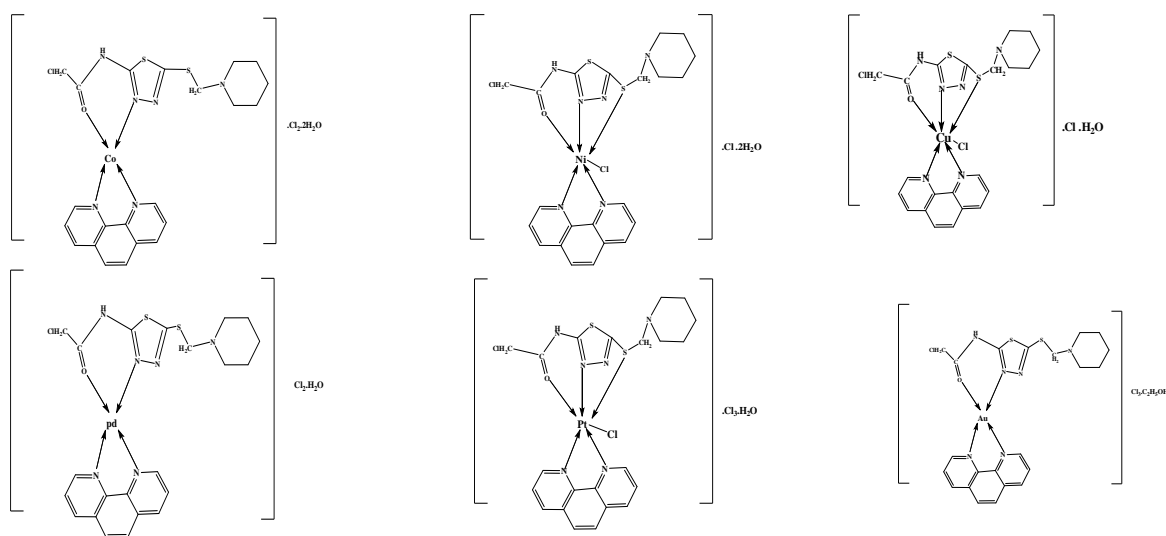


Figure 1: The proposed geometry of the prepared complexes

### Molar ratio method

The ratio of metal to ligand in solution state can be calculated using the method of molar ratios and at

the maximum wavelength and at concentration  $1 \times 10^{-3}$  of all the prepared complexes. The results proved that the ratio of metal to ligands is (1:1:1).

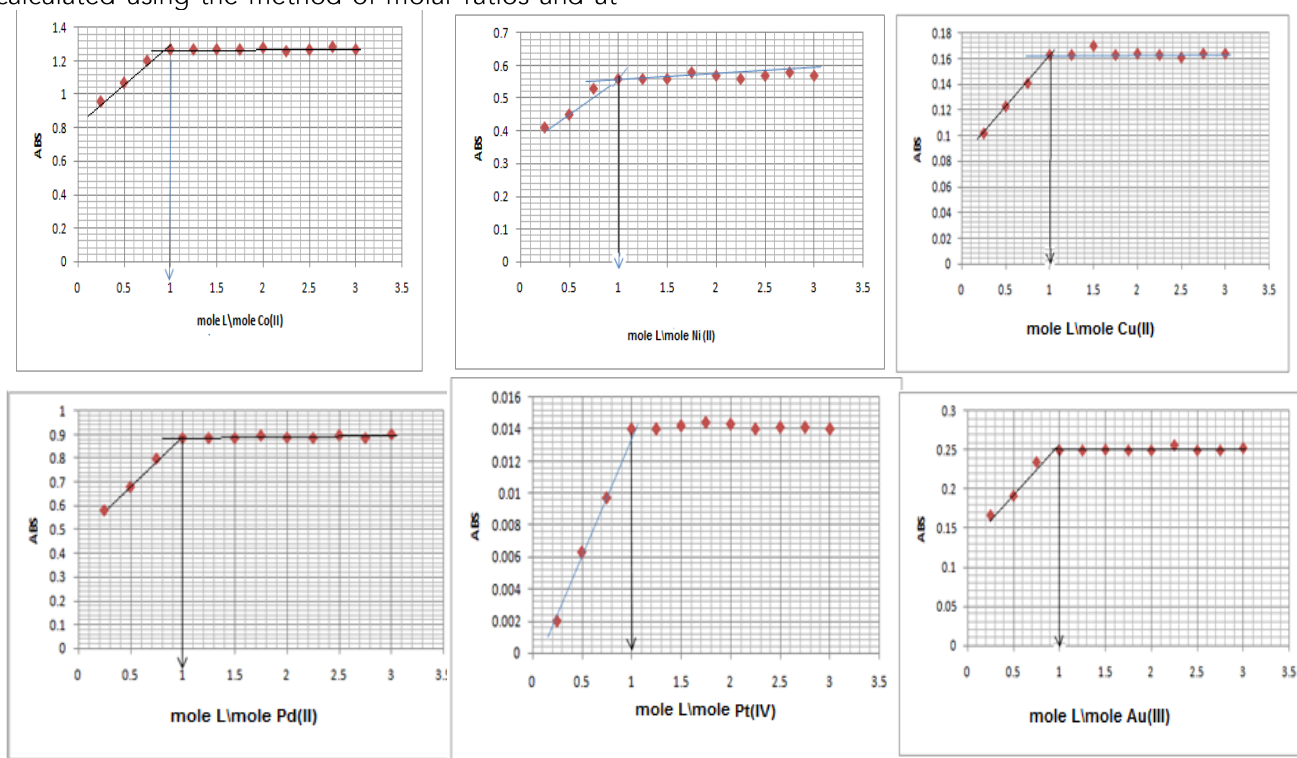


Figure 2: Molar ratio plot of L metal complexes

### Antibacterial and antifungal Activity

The results obtained for antibacterial and antifungal of the Mannich ligand base, 1,10 phenathroline and its new complexes are presented in the Table (5). The diameter of the zone of inhibition (mm) including the diameter of the disc was measured for each treatment. The antibacterial biological activity of the compounds prepared was measured against

selected gram-positive and gram-negative bacteria (Staph, bacillus Ecoli, klebsiella) at concentration 0.02M by using amoxicillin and metronidazole as standard drug for bacteria and fungi respectively. The cobalt and nickel complexes showed the higher activity against all types of bacteria and fungi [15] used more than the ligands and drug used. These increases in the activity of complexes are due to the chelating process [36].

Table (5) Antibacterial activity of L and its metal complexes at 0.02 M						
Compounds		Inhibition Zone (mm.)				
		Gram Positive		Gram negative		Fungi
		<i>staph</i>	<i>Bacillus</i>	<i>E.coli</i>	<i>klebsiella</i>	<i>Candida</i>
1	CoL (1,10pheno.)	30	40	27	40	27
2	NiL (1,10pheno.)	40	33	32	33	32
3	CuL (1,10pheno.)	20	30	23	27	23
4	PdL(1,10pheno.)	18	25	20	21	20
5	PtL(1,10pheno.)	16	13	18	15	18
6	AuL(1,10pheno.)	25	13	18	13	18
7	DMSO	-ve	-ve	-ve	-ve	-ve
8	L	28	25	25	21	25
9	1,10phenotheroline	11	17	18	11	18
10	Amoxicillin	12	12	13	11	---
11	Metronidazole					13

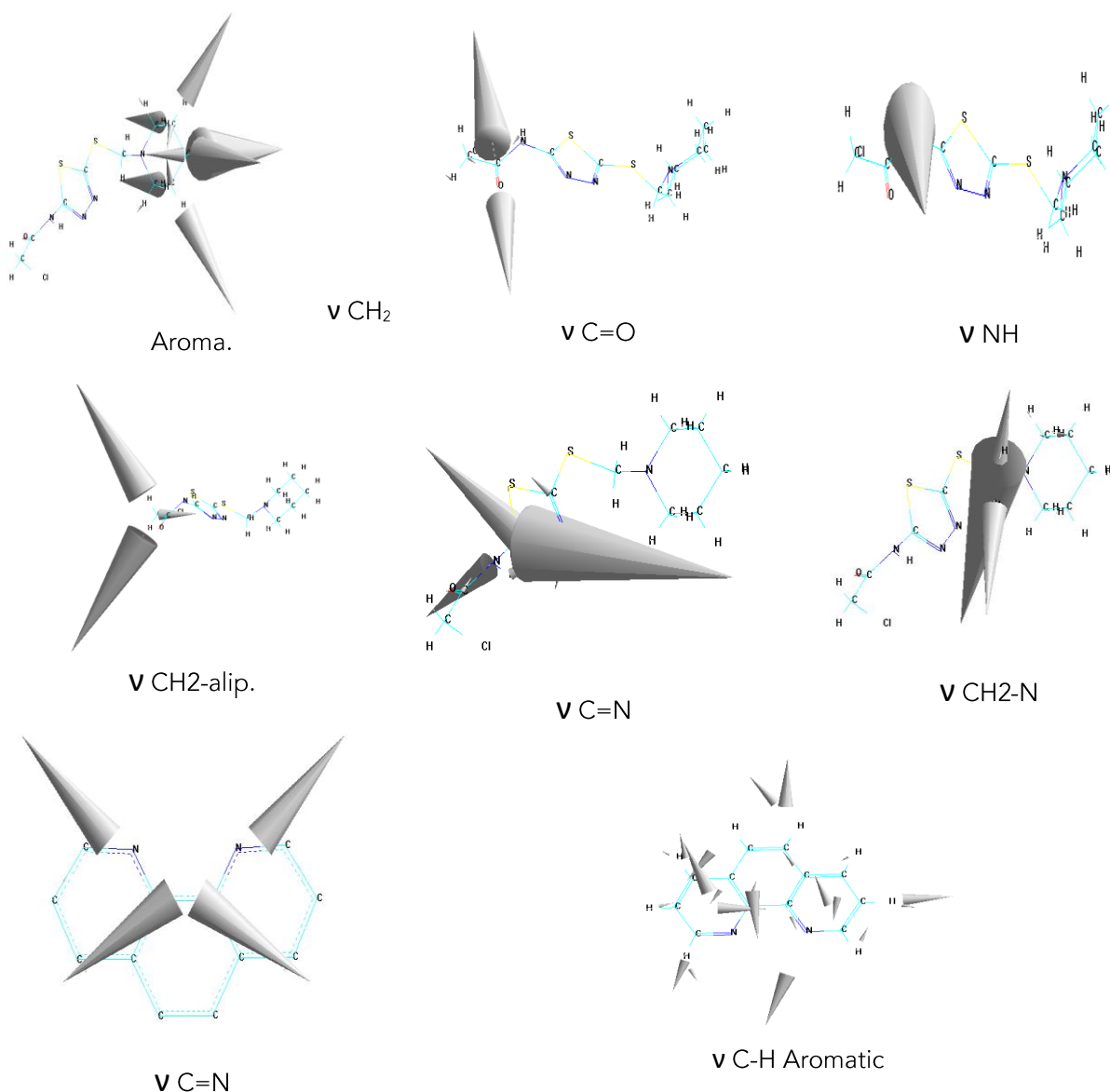
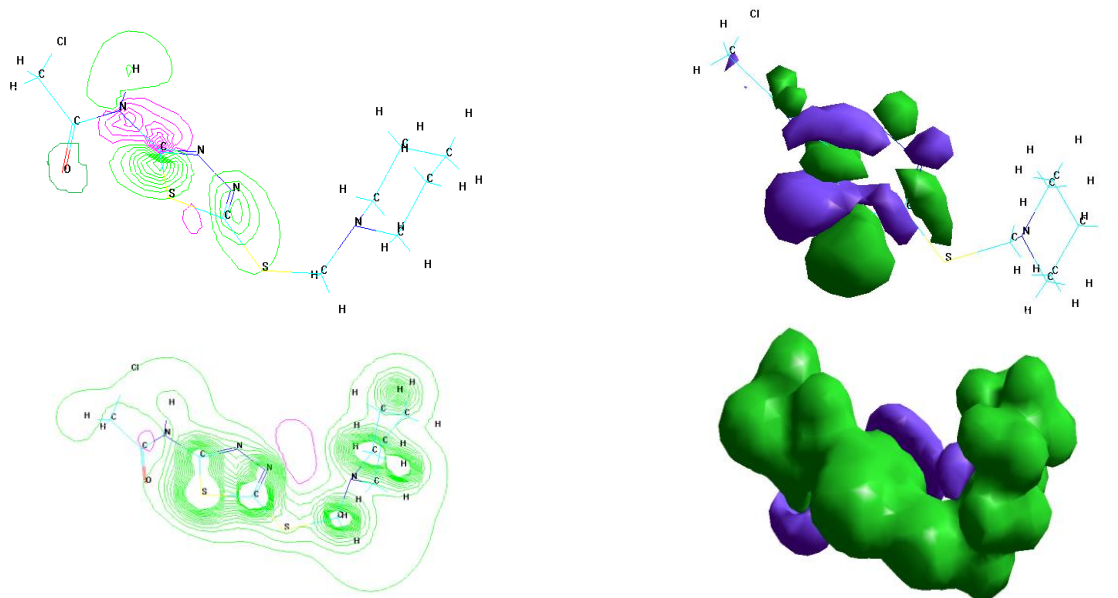


Figure 3: Vibration spectra of Mannich base(L) and 1,10 Phenotheroline

**Table (6): The vibrational frequencies of L and (1,10Phenotheroline) using Hyper Chem-8.0.7 program**

Symb.	$\nu(\text{C=N})$ ring	$\nu(\text{C=N})$ 1,10 phen.	$\nu\text{C=O}$	$\nu\text{CSC}$	$\nu\text{CH}_2\text{-N}$	$\nu\text{CS}$
Experimental	1620	1618	1701	1161	2854 2943	702
Theoretical	*1623	*1602	1768*	*1190	2*281 2998*	*739
Percentage of error	(0.18)	(-0.99)	(3.78)	(2.43)	(-1.49) (1.83)	(5.00)

**Table (7): Heat of formation, binding energy (in KJ.mol<sup>-1</sup>) and dipole moment (in Debye) for ligand (L), (1,10Phen.) and its metal complexes using HyperChem-8.0.7 program**

Comp.	PM3			ZINDO/1			AMBER	
	$\Delta H^{\circ}_f$	$\Delta E_b$	$\mu$	$\Delta H^{\circ}_f$	$\Delta E_b$	$\mu$	$\Delta E_b = \Delta H^{\circ}_f$	$\mu$
L	17.09737	-3146.68162	1.73	-8705.7206	-12205.5026	3.23		
(1,10Phen.)	70.20530	2623.2906-	2.99	-5301.0082	-7994.5042	3.93		
CoL(1,10Phen.)	-130.35220	2961.05255-	3.79	-993.82148	15511.5311-	9.57		
NiL(1,10Phen.)	-382.61862	7673.94128-	6.10	-673.90112	-382.2244	6.30		
CuL(1,10Phen.)	-275.42771	-5712.41219	2.19	-2972.71292	33600.4777 -	5.17		
PdL(1,10Phen.)	-----	-----	-----	-----	-----	-----	819.212	1.30
PtL(1,10Phen.)	-----	-----	-----	-----	-----	-----	236.701	2.09
AuL(1,10Phen.)							812.6213	1.20

## 4. Conclusions

A New mixed ligands complexes, Mannich base and 1,10 phenanthroline have been successfully synthesized using the conventional method. Synthesis of six proposed complexes was successfully performed by the procedures as described previously. The results obtained from this investigation were obtained according to the data shown by physical and chemical analysis. The results showed that the prepared complexes have an octahedral geometry for each of cobalt, nickel, copper and platinum complexes, and square planar geometry for each of palladium and gold complexes. Ni and Co complexes showed good activity against positive and negative antibacterial and antifungal. All the complexes and ligand (L) showed higher activity results compared to Amoxicillin. The theoretical study, using the hyperchem-8.0.7 program and calculating the standard heat of

formation and binding energy, proved that the prepared complexes are more stable than the ligands.

## References

- [1] A. K. Jain, S. Sharma, A. Vaidya, V. Ravichandran, and R. K. Agrawal, "1,3,4-Thiadiazole and its Derivatives: A Review on Recent Progress in Biological Activities," *Chemical Biology & Drug Design*, vol. 81, no. 5, pp. 557–576, May 2013, doi: 10.1111/cbdd.12125.
- [2] C. Ainsworth, "The Condensation of Aryl Carboxylic Acid Hydrazides with Orthoesters," *J Am Chem Soc*, vol. 77, no. 5, pp. 1148–1150, Mar. 1955, doi: 10.1021/ja01610a019.
- [3] S. Sahu, T. Sahu, G. Kalyani, and B. Gidwani, "Synthesis and Evaluation of Antimicrobial Activity of 1, 3, 4-Thiadiazole Analogues for Potential Scaffold," *Journal of Pharmacopuncture*, vol. 24, no. 1, pp. 32–40, Mar. 2021, doi: 10.3831/KPI.2021.24.1.32.

- [4] T. Glomb and P. Świątek, "Antimicrobial Activity of 1,3,4-Oxadiazole Derivatives," *International Journal of Molecular Sciences*, vol. 22, no. 13, p. 6979, Jun. 2021, doi: 10.3390/ijms22136979.
- [5] G. de Andrade Danin Barbosa and A. Palermo de Aguiar, "Synthesis of 1,3,4-Thiadiazole Derivatives and Microbiological Activities: A Review," *Revista Virtual de Química*, vol. 11, no. 3, pp. 806–848, 2019, doi: 10.21577/1984-6835.20190058.
- [6] T. Zvenihorodska, A. Hotsulia, S. Kravchenko, S. Fedotov, and B. Kyrychko, "Synthesis and antimicrobial action of 1,2,4-triazole derivatives containing theophylline and 1,3,4-thiadiazole fragments in their structure," *African Journal of Biomedical Research*, vol. 24, no. 1, pp. 159–163, 2021.
- [7] A. Irfan et al., "Synthetic Transformations and Medicinal Significance of 1,2,3-Thiadiazoles Derivatives: An Update," *Applied Sciences*, vol. 11, no. 12, p. 5742, Jun. 2021, doi: 10.3390/app11125742.
- [8] C. T. Keerthi Kumar, J. Keshavayya, T. N. Rajesh, S. K. Peethambar, and A. R. Shoukat Ali, "Synthesis, Characterization, and Biological Activity of 5-Phenyl-1,3,4-thiadiazole-2-amine Incorporated Azo Dye Derivatives," *Organic Chemistry International*, vol. 2013, pp. 1–7, Aug. 2013, doi: 10.1155/2013/370626.
- [9] S. G. Pyne and M. Tang, "The Boronic Acid Mannich Reaction," in *Organic Reactions*, Hoboken, NJ, USA: John Wiley & Sons, Inc., 2013, pp. 211–498. doi: 10.1002/0471264180.or083.02.
- [10] A. O. Ayeni, G. M. Watkins, and E. C. Hosten, "Synthesis, characterization and crystal structures of two new phenolic mannich bases," *Bull Chem Soc Ethiop*, vol. 33, no. 2, p. 341, Jul. 2019, doi: 10.4314/bcse.v33i2.14.
- [11] Maurilio Tramontini and Luigi Angiolini, *Mannich bases: chemistry and uses*. Boca Raton: CRC Press, 1994.
- [12] W. SIEDEL, A. SODER, and F. LINDNER, "[Amino methylation of tetracyclines; chemistry of reverin].," *Munchener medizinische Wochenschrift* (1950), vol. 100, no. 17, pp. 661–3, Apr. 1958.
- [13] K. M. Huttunen and J. Rautio, "Prodrugs - an efficient way to breach delivery and targeting barriers.," *Curr Top Med Chem*, vol. 11, no. 18, pp. 2265–87, 2011, doi: 10.2174/156802611797183230.
- [14] J. R. Dimmock et al., "Cytotoxic activities of Mannich bases of chalcones and related compounds.," *J Med Chem*, vol. 41, no. 7, pp. 1014–26, Mar. 1998, doi: 10.1021/jm970432t.
- [15] Y. Ivanova, G. Momekov, O. Petrov, M. Karaivanova, and V. Kalcheva, "Cytotoxic Mannich bases of 6-(3-aryl-2-propenoyl)-2(3H)-benzoxazolones," *European Journal of Medicinal Chemistry*, vol. 42, no. 11–12, pp. 1382–1387, Nov. 2007, doi: 10.1016/j.ejmech.2007.02.019.
- [16] B. N. Singh, S. K. Shukla, and M. Singh, "Synthesis and Biological Activity of Sulphadiazine Schiff's Bases of Isatin and their N-Mannich Bases," *asian Journal of chemistry*, vol. 19, no. 7, p. 5013, 2007.
- [17] S. C. Vashishtha et al., "Cytotoxic and anticonvulsant aryloxyaryl Mannich bases and related compounds," *European Journal of Medicinal Chemistry*, vol. 39, no. 1, pp. 27–35, Jan. 2004, doi: 10.1016/j.ejmech.2003.09.011.
- [18] D. Sriram, D. Banerjee, and P. Yogeewari, "Efavirenz Mannich bases: Synthesis, anti-HIV and antitubercular activities," *Journal of Enzyme Inhibition and Medicinal Chemistry*, vol. 24, no. 1, pp. 1–5, Feb. 2009, doi: 10.1080/14756360701404159.
- [19] G. B. Barlin and C. Jiravinyu, "Potential antimalarials. X. Di-Mannich Bases of 4-(7'-Trifluoromethyl-1', 5'-naphthyridin-4'-ylamino) phenol and N-(4'-Diethylamino-1'-methylbutyl)-7-trifluoromethyl-1, 5-naphthyridin-4-amine," *australian Journal of chemistry*, vol. 43, no. 7, pp. 1175–1181, 1990.
- [20] M. L. Edwards, H. W. Ritter, D. M. Stemerick, and K. T. Stewart, "Mannich bases of 4-phenyl-3-buten-2-one. A new class of antiherpes agent," *Journal of Medicinal Chemistry*, vol. 26, no. 3, pp. 431–436, Mar. 1983, doi: 10.1021/jm00357a020.
- [21] M. Arend, B. Westermann, and N. Risch, "Modern variants of the Mannich reaction," *Angewandte Chemie International Edition*, vol. 37, no. 8, pp. 1044–1070, 1998.
- [22] D. Karcz et al., "Structural Features of 1,3,4-Thiadiazole-Derived Ligands and Their Zn(II) and Cu(II) Complexes Which Demonstrate Synergistic Antibacterial Effects with Kanamycin," *International Journal of Molecular Sciences*, vol. 21, no. 16, p. 5735, Aug. 2020, doi: 10.3390/ijms21165735.
- [23] S. Lotfi and J. Brgoch, "Predicting pressure-stabilized alkali metal iridides: A–Ir (A=Rb, Cs)," *Computational Materials Science*, vol. 158, pp. 124–129, Feb. 2019, doi: 10.1016/j.commatsci.2018.11.018.
- [24] J. Guo, J. Zhou, Guorui Fu, Y. He, W. Li, and X. Lü, "Two efficient near-infrared (NIR) luminescent [Ir(C<sup>^</sup>N)<sub>2</sub>(N<sup>^</sup>O)]-characteristic complexes with 8-hydroxyquinoline (8-Hq) as the ancillary ligand," *Inorganic Chemistry Communications*, vol. 101, pp. 69–73, Mar. 2019, doi: 10.1016/j.inoche.2019.01.019.
- [25] I. H. Ibraheem, A. S. Sadiq, M. Al-Tameemi, and M. F. Alias, "Synthesis, Spectral Identification, Antibacterial Evaluation and Theoretical Study of Co, Fe, Rh and Pd Complexes for 2-benzoylthiobenzimidazol," *Baghdad Science Journal*, pp. 1326–1334, Jun. 2022, doi: 10.21123/bsj.2022.6704.
- [26] R. R. Leads et al., "Transcriptomic responses and apoptosis in larval red drum (*Sciaenops ocellatus*) co-exposed to crude oil and ultraviolet (UV) radiation," *Marine Pollution Bulletin*, vol. 179, p. 113684, Jun. 2022, doi: 10.1016/j.marpolbul.2022.113684.
- [27] D. Schweinfurth et al., "Electronic Structures of Octahedral Ni(II) Complexes with 'Click' Derived Triazole Ligands: A Combined Structural, Magnetometric, Spectroscopic, and Theoretical Study," *Inorganic Chemistry*, vol. 52, no. 12, pp. 6880–6892, Jun. 2013, doi: 10.1021/ic3026123.
- [28] W. A. R. Mahmood, A. K. A. Aldabbagh, and M. A. Mahmoud, "Synthesis and Characterization of New Benzothiazole-derived Schiff Bases Metal Complexes," *Baghdad Science Journal*, vol. 19, no. 2, Apr. 2022, doi: 10.21123/bsj.2022.19.2.0378.

[29] S. R. Baqer, S. S. Hassan, N. M. Hassan, and A. M. Saleh, "Biological Evaluation and Theoretical Study of Bi-dentate Ligand for Amoxicillin Derivative with Some Metal Ions," *Baghdad Science Journal*, vol. 18, no. 4, Dec. 2021, doi: 10.21123/bsj.2021.18.4.1269.

[30] M. Gülfen and A. Özdemir, "Monitoring Cu (II)-insulin and Mn(II)-insulin complexes using potentiometric, chromatographic, UV-vis absorption and fluorescence emission spectroscopic techniques," *Journal of Molecular Structure*, vol. 1259, p. 132763, Jul. 2022, doi: 10.1016/j.molstruc.2022.132763.

[31] M. F. Alias, J. H. Murtadha, and I. H. Abdul ALrazzaq, "Study of Cytotoxic Effect of Aqueous Extract Fenugreek(*Trigonella Foenum Graecum* L.S) Seeds and The New Complexes of Rh (II) and Pd (II) on Cancer Cell Lines," *Baghdad Science Journal*, vol. 9, no. 2, pp. 289–295, Dec. 2018.

[32] S. Z. Mortazavi, P. Parvin, A. Reyhani, A. N. Golikand, and S. Mirershadi, "Effect of Laser Wavelength at IR (1064 nm) and UV (193 nm) on the Structural Formation of Palladium Nanoparticles in Deionized Water," *The Journal of Physical Chemistry C*, vol. 115, no. 12, pp. 5049–5057, Mar. 2011, doi: 10.1021/jp1091224.

[33] T. Lopez, M. Villa, and R. Gomez, "UV-visible diffuse reflectance spectroscopic study of platinum, palladium, and ruthenium catalysts supported on silica," *The Journal of Physical Chemistry*, vol. 95, no. 4, pp. 1690–1693, Feb. 1991, doi: 10.1021/j100157a038.

[34] Y.-E. Kwon, K.-J. Whang, Y.-J. Park, and K. H. Kim, "Synthesis, Characterization and Antitumor Activity of Novel Octahedral Pt(IV) Complexes," *Bioorganic & Medicinal Chemistry*, vol. 11, no. 8, pp. 1669–1676, Apr. 2003, doi: 10.1016/S0968-0896(03)00044-0.

[35] J. P. Phillips et al., "Dispersion of Gold Nanoparticles in UV-Cured, Thiol–Ene Films by Precomplexation of Gold–Thiol," *Chemistry of Materials*, vol. 20, no. 16, pp. 5240–5245, Aug. 2008, doi: 10.1021/cm8007842.

[36] Y. Sun, Y. Lu, M. Bian, Z. Yang, X. Ma, and W. Liu, "Pt(II) and Au(III) complexes containing Schiff-base ligands: A promising source for antitumor treatment," *European Journal of Medicinal Chemistry*, vol. 211, p. 113098, Feb. 2021, doi: 10.1016/j.ejmech.2020.113098.

[37] R. A. M. Al-Hasani, "MANNICH BASE DERIVED FROM 1,3,4-THIADIAZOLE AS CHELATING LIGAND FOR SOME TRANSITION METAL COMPLEXES," *ANJS*, vol. 11, no. 2, pp. 42–56, Aug. 2008.