

UDC 541.49+546.92+539.26

# SYNTHESIS, CHARACTERIZATION, STUDY OF MOLECULAR DOCKING AND BIOLOGICAL ACTIVITY OF MIXED LIGANDS PLATINUM (II) COMPLEXES WITH 2-((5-CHLOROQUINOLIN-8-YL)OXY) ACETOHYDRAZIDE AND TERTIARY DI PHOSPHINES

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Received 15.05.2024

Accepted 26.07.2024

**Abstract.** This study involves the preparation of various organic compounds. Ethyl 2-((5-chloroquinolin-8-yl)oxy)acetate compound ( $A_1$ ) was synthesized by adding Potassium carbonate to quinoline and ethyl chloroacetate. The 2-((5-Chloroquinolin-8-yl)oxy) acetohydrazide ( $A_2$ ) was prepared by reacting compound ( $A_1$ ) with hydrazide. Complex of ( $A_3$ ) were obtained by reacting equimolar amounts of compound ( $A_2$ ) with the Platinum salt solution of using ethanol as the solvent. Phosphinate complexes were prepared by reacting equal moles of the complex ( $A_3$ ) with the various phosphines used and using ethanol as a solvent. The synthesized compounds and complexes were characterized using various spectroscopic techniques, including Fourier-Transform Infrared (FT-IR) spectroscopy, Uv-Vis spectrum and Nuclear Magnetic Resonance ( $^{31}\text{P}$ ,  $^1\text{H}$ , and  $^{13}\text{C}$ -NMR) spectroscopy. Additionally, their melting points, purity, molar conductivity, and magnetic susceptibility were determined. The impact of some prepared compounds and complexes on the growth of two antibiotic-resistant bacterial strains, namely the Gram- positive *Staphylococcus* and the Gram- negative *Escherichia coli*, was studied. Ciprofloxacin was used as control antibiotics. Some of the synthesized compounds exhibited significant inhibitory activity against the tested bacterial strains.

**Keywords:** Chloroquinolin-8-ol, Ester, Tertiary diphosphines, Complexes, Biological Activity.

**DOI:** 10.32737/2221-8688-2024-4-525-539

## 1. Introduction

The interesting pharmacological properties of quinoline derivatives and complexes have been associated with these compounds showing great effectiveness against bacteria [1-4] and also against cancerous tumors [5-7], in addition, quinoline complexes with transition metals were of great importance in organometallic chemistry and coordinate chemistry [8-10]. The 2-((5-Chloroquinolin-8-yl) oxy) Aceto hydrazide derivative and its coordinate with platinum metal were rare. For this we studied in this research (Platinum (II) Complexes with 2-((5-Chloroquinolin-8-yl) oxy) Aceto hydrazide and diphosphines) where the quinolone derivative was bonded with

platinum through the atom of nitrogen and oxygen bidentate and the complex was in the form of a square planar and then we did this complex with a compound (tertiary phosphines)  $[\text{ph}_2\text{p}(\text{CH}_2)_n \text{pph}_2]$  ( $n = 1, 2, 3$ ) and its coordinated was a bidentate chelating. The reason we chose tertiary di phosphine is because it is easy to bind to platinum and forms a stable compound due to reverse donation [11] in addition to that (tertiary diphosphines) has efficacy against the growth of cancer cells [12]. The aim of this research is to provide a study that is useful in the field of chemistry and medicine.

## 2. Experimental part

**2.1. Materials Employed.** All chemicals utilized were procured from Fluka, and Aldrich Companies.

**2.2. Used Instruments.** Infrared spectra of the synthesized compounds were recorded at the Chemistry Department of the College of Sciences at the University of Tikrit using an FTIR-8400S instrument provided by SHIMADZU. The spectra were recorded in the range of 4000-400  $\text{cm}^{-1}$  using KBr pellets. ( $^1\text{H}$ ,  $^{13}\text{C}$ -NMR) Nuclear Magnetic Resonance spectra were acquired using a Bruker Spectrometer (500 MHz), respectively, in  $\text{d}^6$ -DMSO solvent at the University of Tehran in Iran. The measurements were conducted using an SMP10 Automatic Melting Point apparatus from the British company STUART. The Magnetic susceptibility measurements of certain solid metal complexes were carried out at the laboratory temperature using a Sherwood Scientific instrument in the Chemistry Department of the College of Sciences at the University of Tikrit. The Faraday method was employed for these measurements.

**2.3. Synthesis of ethyl nyl 2-((5-chloroquinolin-8-yl)oxy)acetate compound ( $\text{A}_1$ )** [13]. Potassium carbonate (0.01 mol, 1.38 g) was added to quinoline (0.01 mol, 1.79 g) dissolved in dimethylformamide (15 mL) and stirred for 15 minutes. Ethyl chloroacetate (0.01 mol, 1.07 mL) was then added to the mixture. The reaction mixture was stirred for 4 hours at a temperature range of 40-50  $^\circ\text{C}$ . After cooling the solution, distilled water (50 mL) was added with continuous stirring. The resulting precipitate was filtered, and the crystals were recrystallized using absolute ethanol. The obtained product was a white solid with a melting point ranging from 90 to 96  $^\circ\text{C}$ , and the yield was 89%.

**2.4. Synthesis of Compound 2-((5-Chloroquinolin-8-yl)oxy)acetohydrazide ( $\text{A}_2$ )** [14, 15]. Compound  $\text{A}_1$  (0.01 mol, 2.65 g) was dissolved in ethanol (20 mL), and hydrazine hydrate (0.02 mol, 1 mL) was added dropwise with stirring for 15 minutes. The reaction mixture was allowed to react for 4 hours at a temperature range of 70-80  $^\circ\text{C}$  and then left at room temperature 24 hours. The resulting precipitate was filtered, dried, and recrystallized using absolute ethanol. The reaction completion was confirmed by measuring through TLC (Thin-Layer Chromatography). The product obtained was a white solid with a melting point ranging from 212 to 214  $^\circ\text{C}$ , and the yield was 82%.

**2.5. Synthesis of (2-((5-Chloroquinolin-8-yl)oxy)acetohydrazide di chloro Platinum (II) ( $\text{A}_3$ )).** Compound  $\text{A}_2$  (0.002 mol) was dissolved in methanol (15 mL), and the  $\text{K}_2\text{PtCl}_4$  (0.002mol) soluble in water (10ml) was added. The mixture was stirred for 2 hours and then left at room temperature 24 hours. The precipitate was filtered, dried, and recrystallized using absolute ethanol. The progress of the reaction was confirmed by monitoring physical properties such as color and melting point. Table 1 displays the physical properties of the prepared complexes.

**2.6. Synthesis of Pt(II)complexes with tertiary di Phosphines ( $\text{A}_4$ - $\text{A}_6$ )**

A solution of tertiary phosphines (dppm, dppe, dppp) (0.002mol) dissolved in  $\text{CHCl}_3$  (15 ml) was added to a hot suspension of ( $\text{A}_3$ )(0.002mol) in  $\text{CHCl}_3$  (15 ml) with stirring and refluxed for 2 h. precipitate was filtered, dried. The progress of the reaction was confirmed by monitoring physical properties such as color and melting point (Table 1).

**Table 1.** Some physical properties, conductivity and magnetic measurements of complexes ( $\text{A}_3$ - $\text{A}_6$ )

No	Complex	Yield	M.P/ $^\circ\text{C}$	Color	Cond.Am ( $\Omega^{-1}.\text{cm}^2.\text{mol}^{-1}$ )	Magnetic moment $\mu_{\text{eff}}$ (B.M)
$\text{A}_3$	$[\text{PtA}_2\text{Cl}_2]$	90%	230-232	yellow	32.69	0.00000029
$\text{A}_4$	$[\text{PtA}_2\text{dppm}]$	84%	187-189	pale- orange	11.24	0
$\text{A}_5$	$[\text{PtA}_2\text{dppe}]$	87%	176-178	pale- yellow	14.07	0.00000025
$\text{A}_6$	$[\text{PtA}_2\text{dppp}]$	82%	180- 182	white-yellow	10.48	0

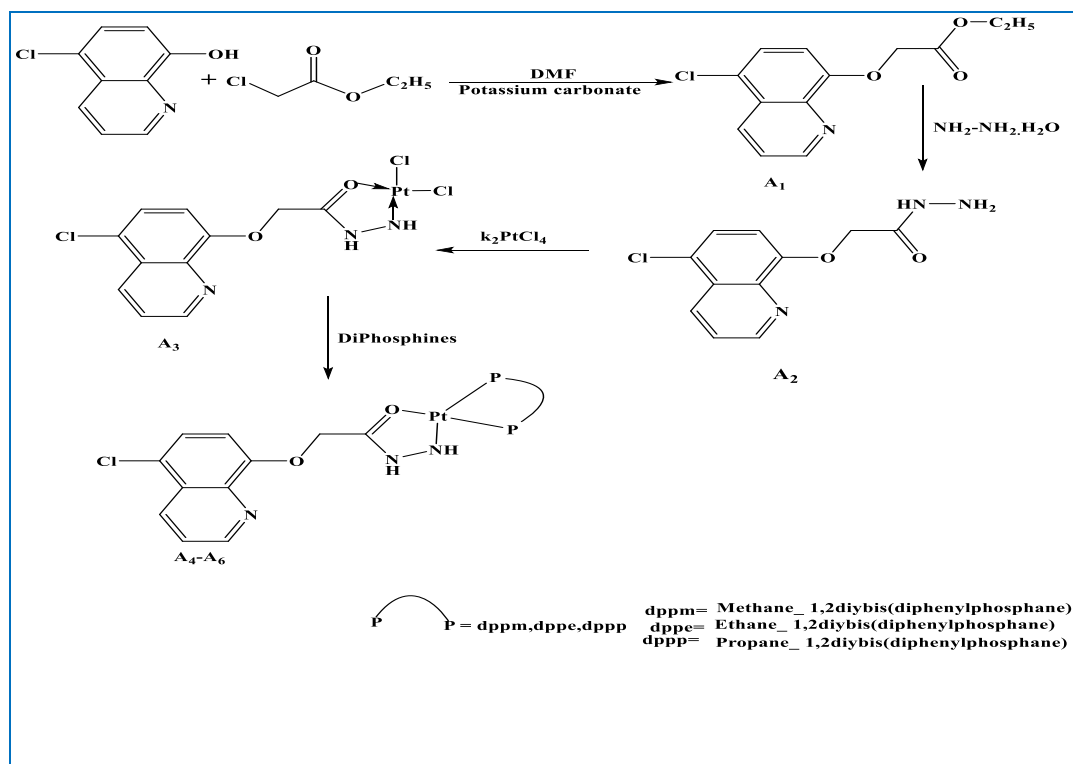
### 2.7. Measurement of Biological Activity [16-18]

Biological activity evaluation was performed through the Agar-well diffusion method. This involved inoculating the bacterial cultures across the entire growth medium using a cotton swab. Wells were then created in the agar medium employing a sterile puncture tool with a diameter of 6 mm. Subsequently, 100 microliters of each compound were placed within these wells on separate culture plates, each harboring a distinct bacterial strain. This

process was replicated across all prepared solutions, encompassing their respective concentrations and targeted bacterial strains under study. The antibacterial activity assessment was conducted on two distinct bacterial types: the gram-positive *Staphylococcus* and the gram-negative *Escherichia coli*. To ensure the effectiveness of the test, both bacterial species were initially re-cultivated and subsequently incubated in a controlled laboratory environment at 37°C for duration of 18-24 hours.

## 3. Results and discussion

In this study, many compounds and complexes were prepared, as shown in Scheme (1).



**Scheme 1.** Prepared compounds and complexes (A<sub>1</sub>-A<sub>6</sub>)

### 3.1. The electronic spectra of platinum complexes (A<sub>4</sub>-A<sub>6</sub>)

The low-spin platinum (II) complexes have a quadrilateral geometric arrangement and take the shape of a square planar. The low-spin

state is preferred with ligands containing donor atoms such as (S, O, and N). These complexes possess the properties of a magnetic dia, as they the electronic spectrum of these complexes shows three permitted transitions:

$$\begin{array}{ll}
 A_1g^1 \rightarrow B_1g^1 & (23255 - 27027) \text{ cm}^{-1} \\
 A_1g^1 \rightarrow A_1g^1 & (14694 - 16551) \text{ cm}^{-1} \\
 A_1g^1 \rightarrow {}^1Eu^* & (25641 - 31645) \text{ cm}^{-1}
 \end{array}$$

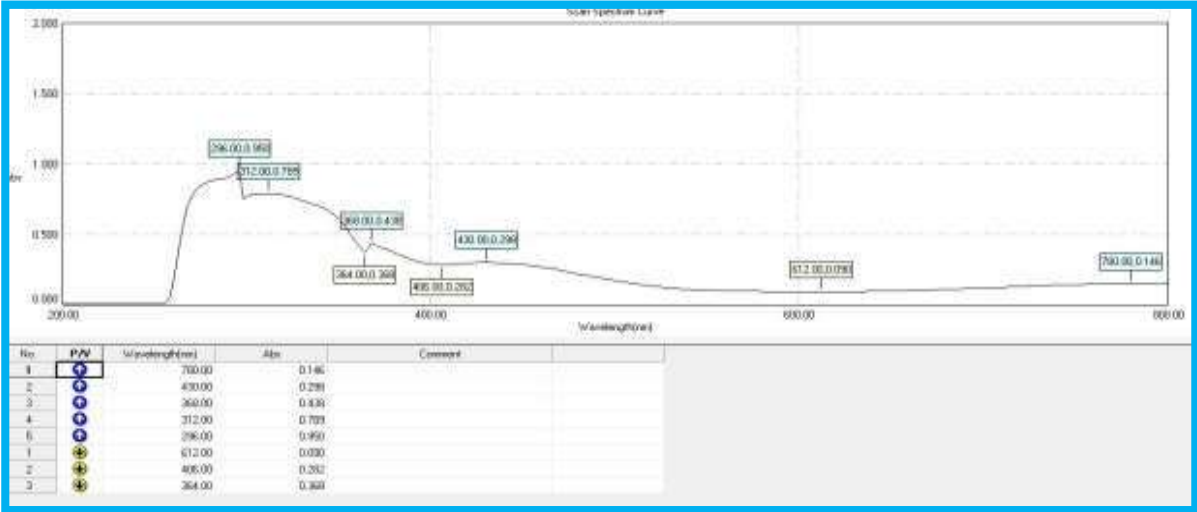
Electron spectrometry of the prepared platinum complexes (Figures 1-3) showed

absorption bands in the region enclosed between the highest peak and the lowest peak in the table that belongs to the transitions ( $A_1g^1 \rightarrow B_1g^1$ ) and that the location of these bands

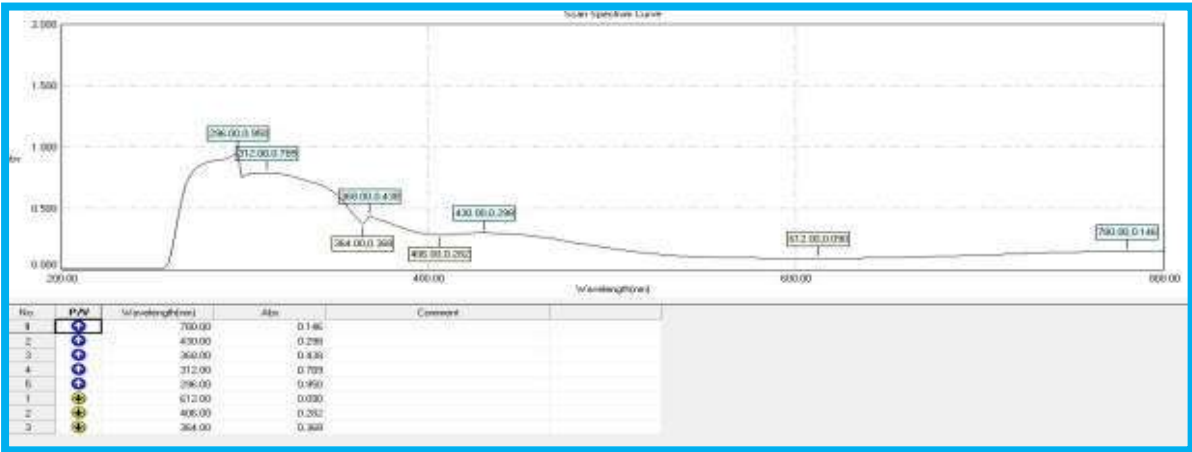
corresponds to the arrangement of the platinum (II) pt complexes and forms a square planar as shown in Table 2.

**Table 2.** The electronic spectra for the prepared complexes ( $cm^{-1}$ ) ( $A_4$ -  $A_6$ )

No	Compound	$\lambda_{max}(nm)$	Waveno. ( $cm^{-1}$ )	Transition Type	Geometric shape
A <sub>4</sub>	[PtA <sub>2</sub> dppm]	780	12820	$A_1g \rightarrow E_g$	square planar
		430	23255	$n \rightarrow \pi^*$	
		368	27173	$\pi \rightarrow \pi^*$	
		312	32051	$\pi \rightarrow \pi^*$	
A <sub>5</sub>	[PtA <sub>2</sub> dppe]	780	12820	$A_1g \rightarrow E_g$	square planar
		430	23255	$n \rightarrow \pi^*$	
		312	32051	$\pi \rightarrow \pi^*$	
		296	33783	$\pi \rightarrow \pi^*$	
A <sub>6</sub>	[PtA <sub>2</sub> dppp]	780	12820	$A_1g \rightarrow E_g$	square planar
		430	23255	$n \rightarrow \pi^*$	
		312	32051	$\pi \rightarrow \pi^*$	



**Fig. 1.** The electronic spectra of complex [Pt(A<sub>2</sub>)dppm]



**Fig. 2.** The electronic spectra of complex [Pt(A<sub>2</sub>)dppe]

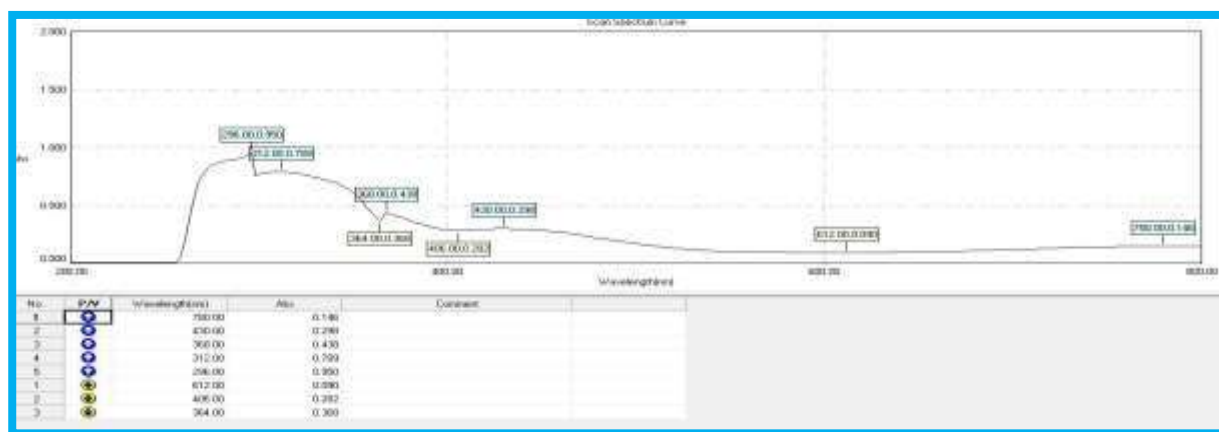


Fig. 3. The electronic spectra of complex  $[\text{Pt}(\text{A}_2)\text{dppp}]$

### 3.2. Characterization of Compounds ( $\text{A}_1$ - $\text{A}_6$ ) by FT-IR Spectroscopy

The infrared spectra of various compounds and complexes are presented in this study, shedding light on their structural characteristics and interactions. Infrared spectroscopy, a powerful analytical technique, provides valuable insights into the chemical composition of these substances by identifying the specific vibrational modes of their constituent functional groups. Compound  $\text{A}_1$  exhibits distinctive absorption bands in its infrared spectrum. A strong band at  $1766\text{ cm}^{-1}$  corresponds to the carbonyl group ( $\text{C}=\text{O}$ ), while two bands at  $1589$  and  $1504\text{ cm}^{-1}$  are attributed to the aromatic  $\text{C}=\text{C}$  bonds. Another band at  $1303$ - $1103\text{ cm}^{-1}$  is associated with the  $\text{C}-\text{O}-\text{C}$  sym, asym group, and a band at  $786\text{ cm}^{-1}$  arises from the  $\text{C}-\text{Cl}$  group. Compound  $\text{A}_2$  (Figure 4) reveals distinct bands in its infrared spectrum. Bands at  $3444$  and  $3321\text{ cm}^{-1}$  correspond to the  $\text{NH}_2$  group, while a band at  $3032\text{ cm}^{-1}$  indicates the presence of the  $\text{NH}$  group. The amide carbonyl group ( $\text{C}=\text{O}$ ) is marked by a band at  $1747\text{ cm}^{-1}$ , and bands at  $1589$  relate to aromatic  $\text{C}=\text{C}$  bonds. Additionally, a band at  $1303$ - $1103\text{ cm}^{-1}$  signifies the  $\text{C}-\text{O}-\text{C}$  sym, asym group, and a band at  $821\text{ cm}^{-1}$  suggests the presence of  $\text{C}-$

$\text{Cl}$  bonds. Complex  $\text{A}_3$  (Figure 5) displays changes in its infrared spectrum, reflecting interactions between the metal and specific functional groups. A decrease in frequency at  $(3321)\text{ cm}^{-1}$  is indicative of  $\text{NH}_2$  group-metal bonding, while a reduction in frequency at  $1800\text{ cm}^{-1}$  points to metal- $\text{C}=\text{O}$  amide bonding. Notably, a band at  $3600\text{ cm}^{-1}$  corresponds to water molecules coordinated with the metal, while other bands remain unchanged. New bands were noticed when examining the phosphonate complexes' infrared spectrum (Figures 6 and 7). Another band at a frequency of  $(1419$ - $1436)\text{ cm}^{-1}$  assigned to the  $(\text{P}-\text{Ph})$  bond, and a band at frequencies  $(3321)\text{ cm}^{-1}$  associated with the  $(\text{NH}_2)$  group. Additionally, a band at  $(3107)\text{ cm}^{-1}$  was identified as originating from the  $(\text{NH})$  group, a band at  $(1766$ - $1800)\text{ cm}^{-1}$  was linked to the  $(\text{C}=\text{O})$  bond, and a band at  $(1589$ - $1666)\text{ cm}^{-1}$  was attributed to the  $(\text{C}=\text{C})$  bond. Furthermore, a band at  $(1303$ - $1103)\text{ cm}^{-1}$  corresponded to the  $(\text{C}-\text{O}-\text{C})$  bond, and a band at  $(937$ - $941)\text{ cm}^{-1}$  was associated with the  $(\text{Pt}-\text{O})$  bond, while a band at  $(532$ - $505)\text{ cm}^{-1}$  corresponded to the  $(\text{Pt}-\text{N})$  bond and a band at  $(493$ - $478)\text{ cm}^{-1}$  corresponded to the  $(\text{Pt}-\text{P})$  bond.

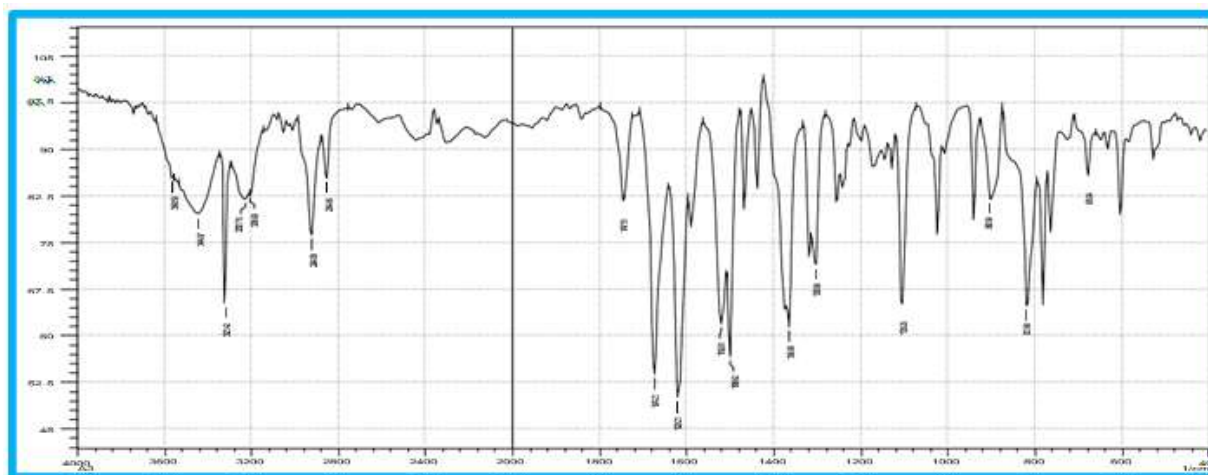
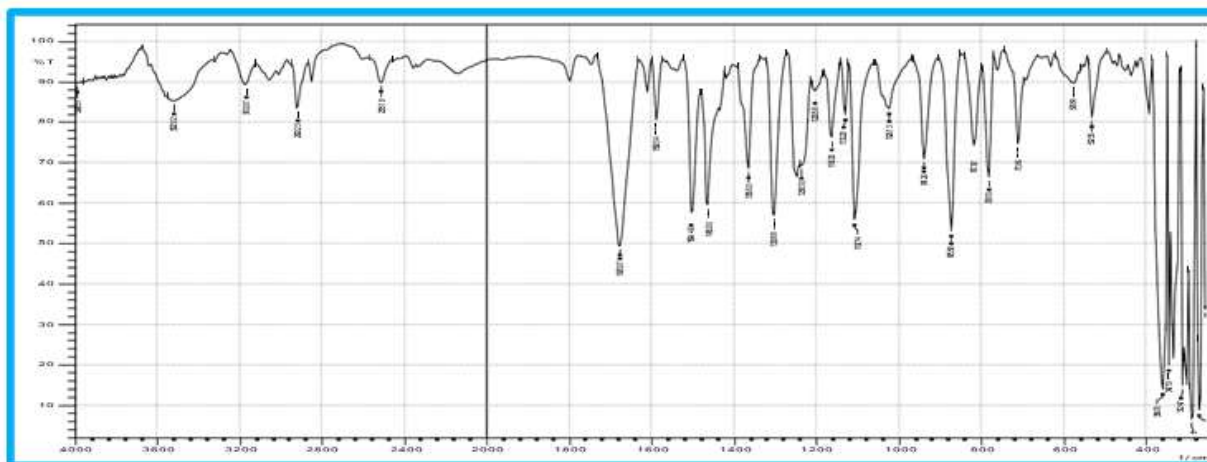
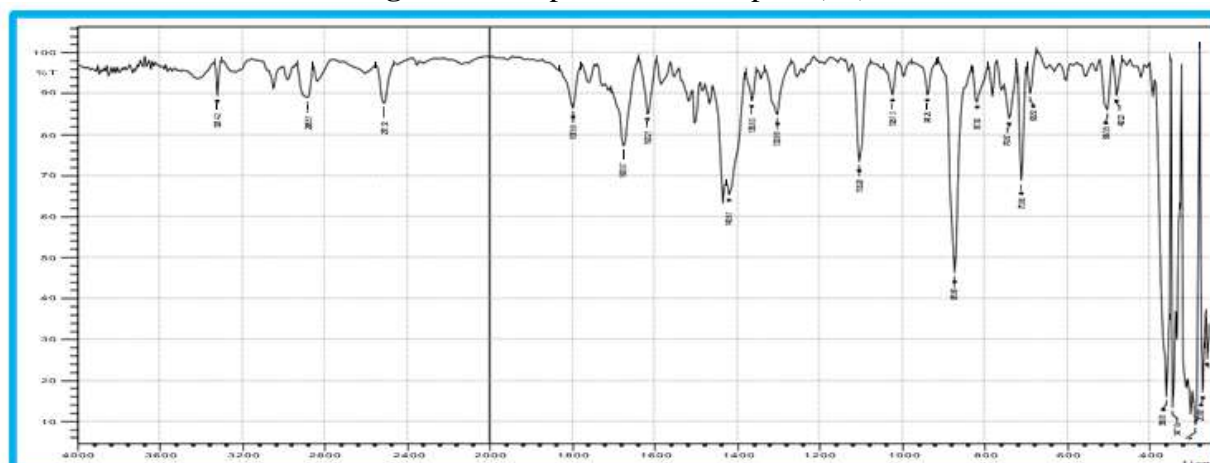
These data (Table 3) closely aligned with the literature findings.

Table 3. IR Absorption Results ( $\text{cm}^{-1}$ ) for compounds and complexes ( $\text{A}_1$ - $\text{A}_6$ )

No.	$\nu\text{NH}_2$	$\nu\text{NH}$	$\nu\text{C}=\text{O}$	$\nu\text{C}=\text{C}$ Arom.	$\nu\text{P}-\text{Ph}$	$\nu(\text{C}-\text{O}-\text{C})$ sym / asym	$\nu\text{Pt}-\text{O}$	$\nu\text{Pt}-\text{N}$	$\nu\text{Pt}-\text{P}$
A1	---	---	1766	1589	---	1303-1103	---	---	
A2	3444, 3321	3032	1747	1674	---	1303-1103	---	---	



<b>A3</b>	3322	3107	1800	1678	---	1303-1107	941	532	-
<b>A4</b>	3321	3107	1797	1678	1419	1303-1107	941	505	482
<b>A5</b>	3321	3199	1766	1666	1435	1303-1103	937	505	478
<b>A6</b>	3321	3086	1762	1674	1436	1307-1099	941	509	493

Fig. 4. FT-IR spectrum of compound ( $A_2$ )Fig. 5. FT-IR spectrum of complex ( $A_3$ )Fig. 6. FT-IR spectrum of complex ( $A_4$ )

### 3.3. Characterization $^1\text{H}$ - $^{13}\text{C}$ - NMR Spectroscopy and of ( $\text{A}_2$ ) and $^{31}\text{P}$ -NMR Spectroscopy of ( $\text{A}_5$ )

$^1\text{H}$ -NMR spectrum of ( $\text{A}_2$ ) confirm the suggested structure displays a singlet for two protons at  $\delta=4.39$  ppm assigned to the  $\text{NH}_2$  group labeled (Ha) (S, 2H). Another singlet showed at  $\delta=4.39$  ppm assigned to the methylene protons, which labeled as Hb (S, 2H). Moreover, the protons of the aromatic

rings display a doublet at  $\delta=7.23$  ppm attributed to Hd with a coupling constant of ( $^3J_{\text{H-H}}=8.40$  Hz). A multiple at  $\delta\text{H}$  (7.71) ppm with an integration value of two protons assigned to Hg and He respectively. The Hf proton showed as a doublet at  $\delta 8.54$  ppm with a coupling constant of ( $^3J_{\text{H-H}} = 8.90\text{Hz}$ ). The integration value of Hf is one proton. Another doublet showed at  $\delta=9.00$  ppm which represents Hh proton.

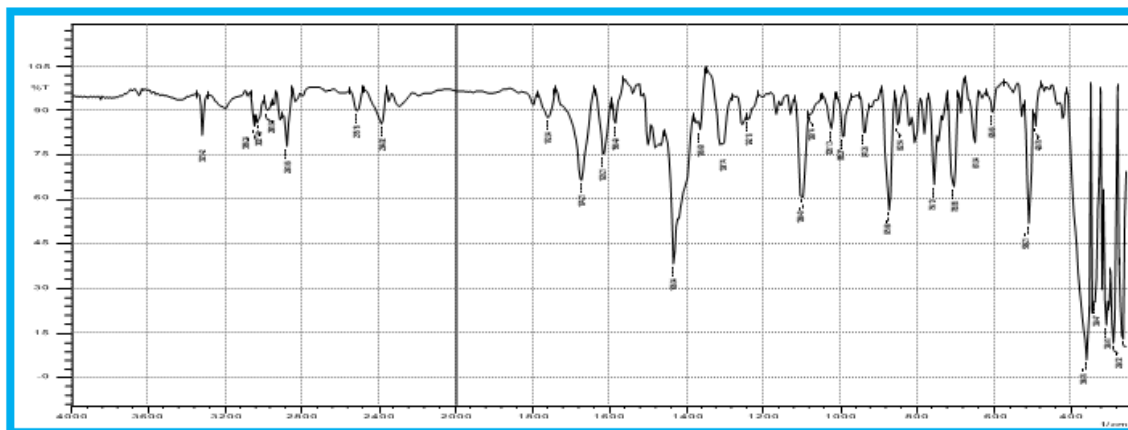


Fig. 7. FT-IR spectrum of complex ( $\text{A}_6$ )

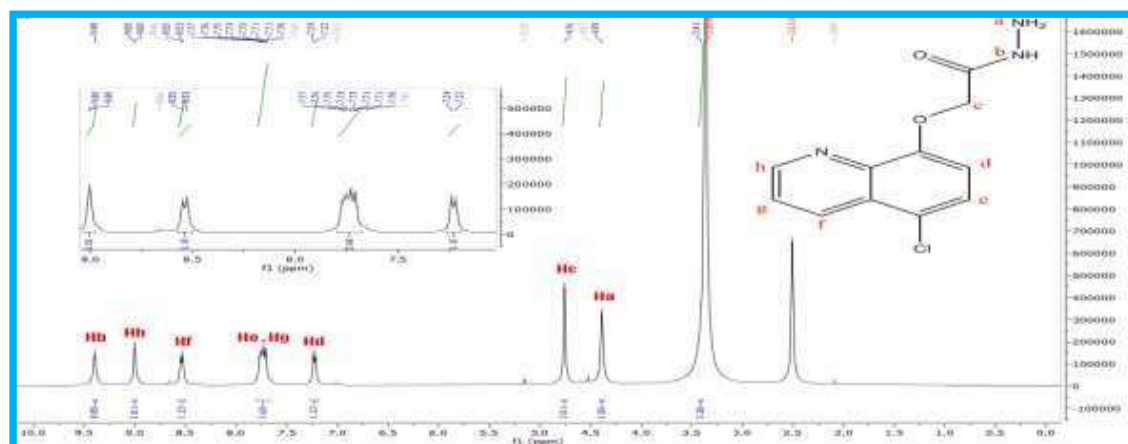


Fig. 8.  $^1\text{H}$ -NMR spectrum of ( $\text{A}_2$ )

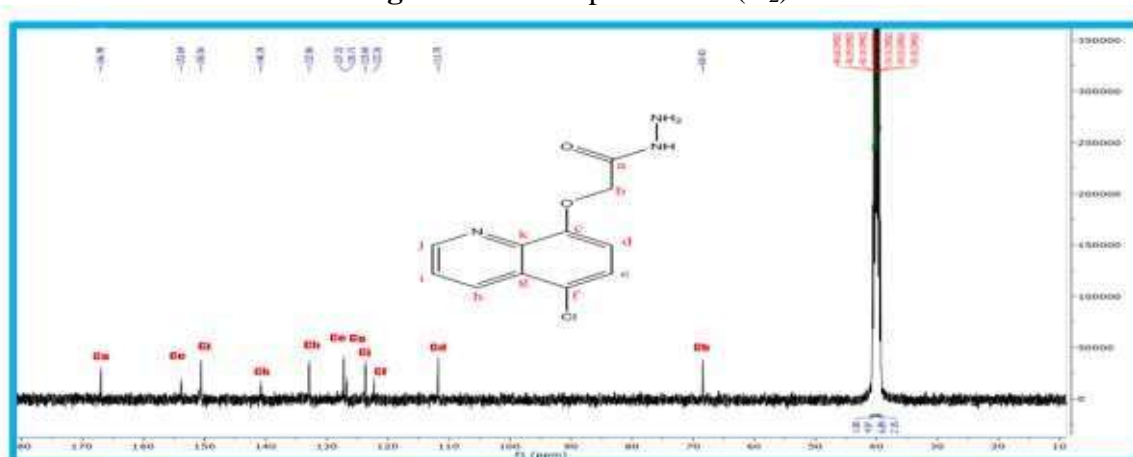
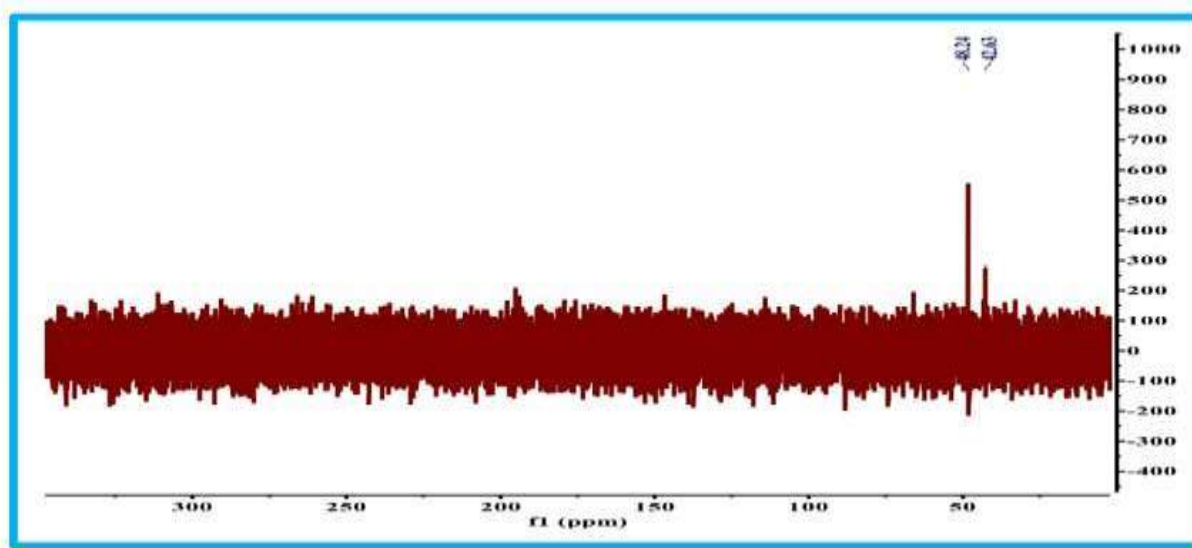


Fig. 9.  $^{13}\text{C}$ -NMR spectrum of ( $\text{A}_2$ )

$^{13}\text{C}$ -NMR spectrum of ( $\text{A}_2$ ) confirms the suggested structure. The spectrum showed the methylene carbon labeled Cb at  $\delta=68.43$  ppm. The carbons of the aromatic rings appear at  $\delta=$

(111.78- 153.84) ppm which attributed to Cd, Cf, Cj, Cg, Ce, Ch, Ck, Ci and Cc. Finally, the carbonyl carbon which is labeled as Ca display at  $\delta=166.98$  ppm, as shown in Figure 9.



**Fig. 10.**  $^{31}\text{P}\{-^1\text{H}\}$  NMR spectrum of ( $\text{A}_5$ )

The  $^{31}\text{P}$ -NMR spectrum of the complex ( $\text{A}_5$ ) [ $\text{PT}(\text{M-L}) \text{dppeK}_2$ ] confirms the proposed structure, as the spectrum showed a signal at  $\delta=(48.24, 42.63)$  ppm attributed to the phosphorus (dppe) present in the complex, as shown in Figure 10.

### 3.4. Magnetic Measurements of Prepared Complexes ( $\text{A}_3$ - $\text{A}_6$ )

The magnetic susceptibility of the prepared platinum complexes was calculated at a temperature of  $25^\circ\text{C}$ . The diamagnetic corrections (D) for the atoms in the organic molecules, metal ions, and non-organic radicals were applied using Pascal's constants for the constituent atoms of the prepared complexes. D (in  $\text{cm}^3\cdot\text{molecule}^{-1}$ ) is equal to the sum of the number of ions or atoms of the element multiplied by the Pascal's constant. The calculated values of the effective magnetic moment ( $\mu_{\text{eff}}$ ) for the prepared complexes were determined through magnetic measurements. The magnetic measurements of the prepared platinum (II) complexes ( $\text{A}_3$ - $\text{A}_5$ ) revealed values ranging from (0.00000029, 0.00000025,0) B.M. These results suggest that the metallic (II) ion exhibits tetra coordination with a high-spin square planar configuration.

### 3.5. Evaluation of the Biological Activity of Some Prepared Compounds ( $\text{A}_2$ - $\text{A}_5$ )

The study included the use of two types of bacteria that were purely isolated and correctly diagnosed. The bacteria (*Staphylococcus aureus* and *Escherichia coli*) were chosen because of their vital importance in the field of medicine, which in turn affects human health, causing many different diseases. The susceptibility test method was conducted using the simple diffusion method in the culture medium agar diffusion method. The results indicate that the prepared compounds could inhibit the growth of both Gram-positive and Gram-negative bacteria to varying degrees.

It was noted that the effectiveness of inhibition is directly proportional to the concentration of the inhibitor, that is, it increases with increasing inhibitor concentration, and that the concentration (mg/ml 100) is the best concentration to obtain the highest inhibition. The compound ( $\text{A}_5$ ) showed a high inhibition of 27 mm against staphylococcal bacteria, While compound ( $\text{A}_3$ ) showed a high inhibition of 26 mm against *Escherichia coli* bacteria, it is possible that the inhibition of the growth of the two types of bacteria used in this study can be attributed to the presence of active groups in the prepared compounds, as these groups interfere with the cell division mechanism and thus work to stop bacterial growth and that their effectiveness.



These aggregates differ in their effect on the cell wall membrane barrier (Table 4).

**Table 4.** Biological effectiveness of prepared compounds, complexes and control parameters (*in mm*)

Comp. No.	Staphylococcus Conc. (mg/ml)			Escherichia coli Conc. (mg/ml)		
	25	50	100	25	50	100
A <sub>2</sub>	10	12	13	11	13	15
A <sub>3</sub>	14	15	18	13	15	26
A <sub>4</sub>	16	17	24	12	15	22
A <sub>5</sub>	18	22	27	14	16	24
Ciprofloxacin	13	15	20	19	25	36
Blank disk	0	0	0	0	0	0

### 3.6. Study of Molecular Docking [19-21]

The molecular docking of some prepared compounds (A<sub>2</sub>, A<sub>3</sub>, A<sub>5</sub>,) on one line, which is *Pseudomonas aeruginosa* bacteria, was studied using MOE (2014) program, where the energy reduction process of the vehicles under study was completed in order to obtain the most stable vacuum form (least obstructive energy), then the composition of *Pseudomonas aeruginosa* bacteria was downloaded from the

World Bank Protein Bank website (6R3X receptor), and a personal calculator was used. The values of the binding energies of the compounds were calculated as in Table 5. The study of molecular fusion of prepared organic derivatives gave the number and types of bonds through which these prepared derivatives are connected with amino acid residues found in the active site by forming a number of bonds [22].

**Table 5.** Values of binding energy, hydrogen bond lengths and amino acid effect between prepared compounds and receptor (6R3X) One line of *Pseudomonas aeruginosa* bacteria *Pseudomonas aeruginosa*.

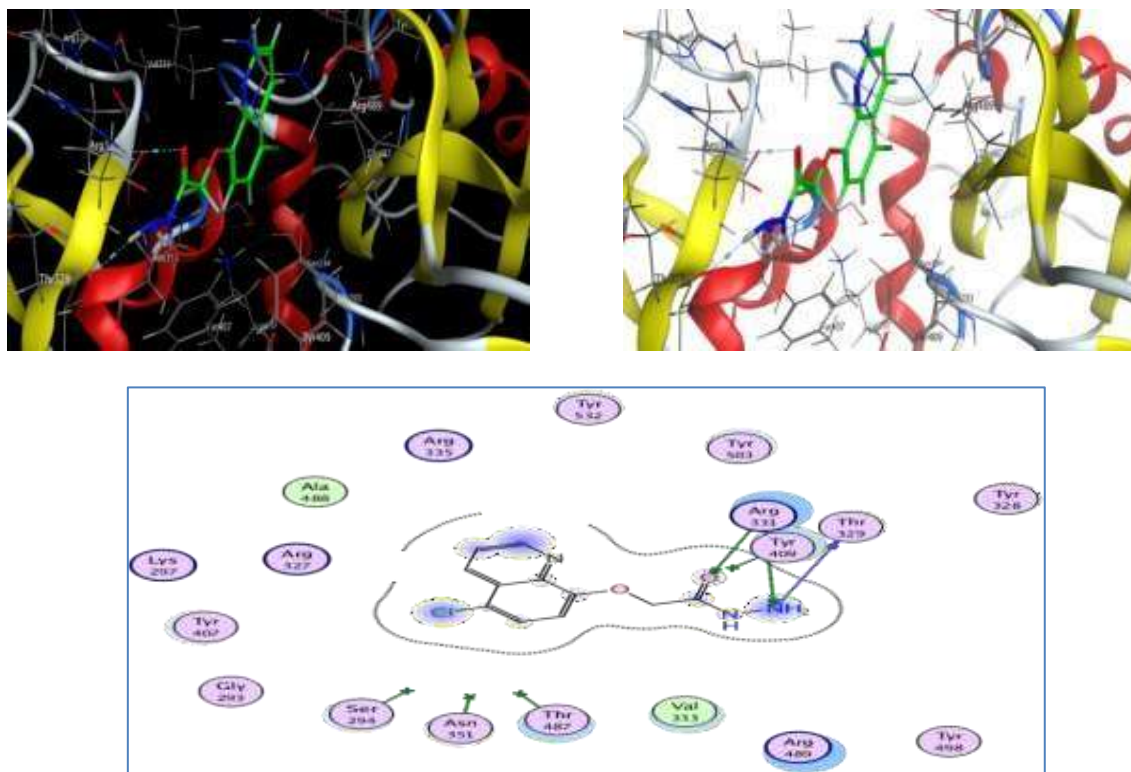
Compound	Correlation on Energy Docking Score	RMDS	Hydrogen bond			Other amino acids affected by van der Waals and other forces	Number of aminoacids affected
			Number of hydrogen bonds	Associated amino acids	Hydrogen bond length		
A <sub>2</sub>	-6.286	2.27	3	Arg.331 Thy.239 Tyr.409	2.35(A) 1.90(A) 2.04(A)	Val.333, Arg.329,489Ser.294, Lys.297 Ala.488,Asn.69 Gly.293, Asn.351 Thy.(326,498,503,532,407,487)	9
A <sub>3</sub>	-7.389	2.38	3	Tyr.223 Arg.331 Arg489	1.89(A) 2.08(A) 2.40(A)	Ser.249,Arg.489Val.333,Asn.351 Tyr(407, 487.409.328,498)	18
A <sub>5</sub>	-6.633	4.19	3	Arg.489 Arg.335 Arg.331	2.28(A) 2.04(A) 2.00(A)	Val.333,Glu.500Asn.(501,351) Thr.487,Ala.488Asp.332,Phe.533 Ser.294,Tyr.(532,409,407,503,487,)	14

The study showed that the compound (A<sub>2</sub>) reacts with the amino acid residues that reside in the active site by forming two types of bonds, namely three hydrogen bonds, the first linking the amino acid residues, Arg.331

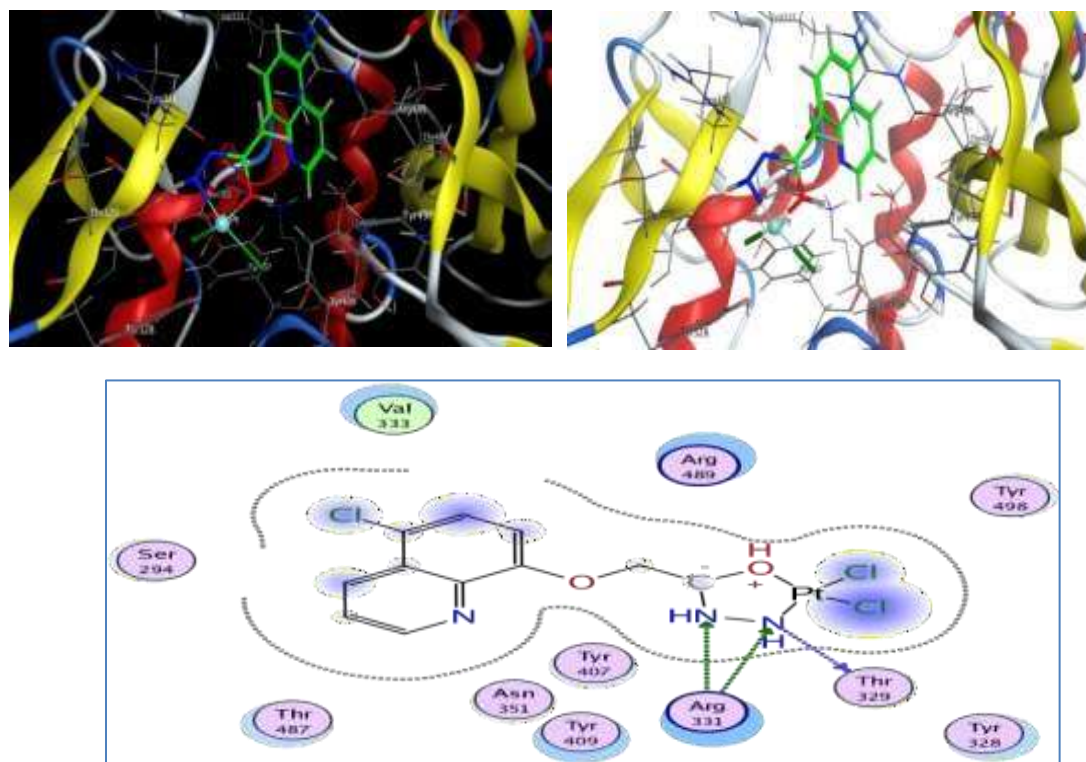
located in the active site with the electronic pair of the oxygen atom of the carbonyl group, and the second and third linking the amino acid residues Tyr.409 and Thy.239 located in the active site with the electronic pair of the

nitrogen atom hydrazide group. And a number of amino acids affected by van der Waals forces as in Table 5 above. Figure 11 shows the two-dimensional and three-dimensional

representation of the molecular anchoring results and the association between the prepared compound A<sub>2</sub> and the 6R3X receptor.



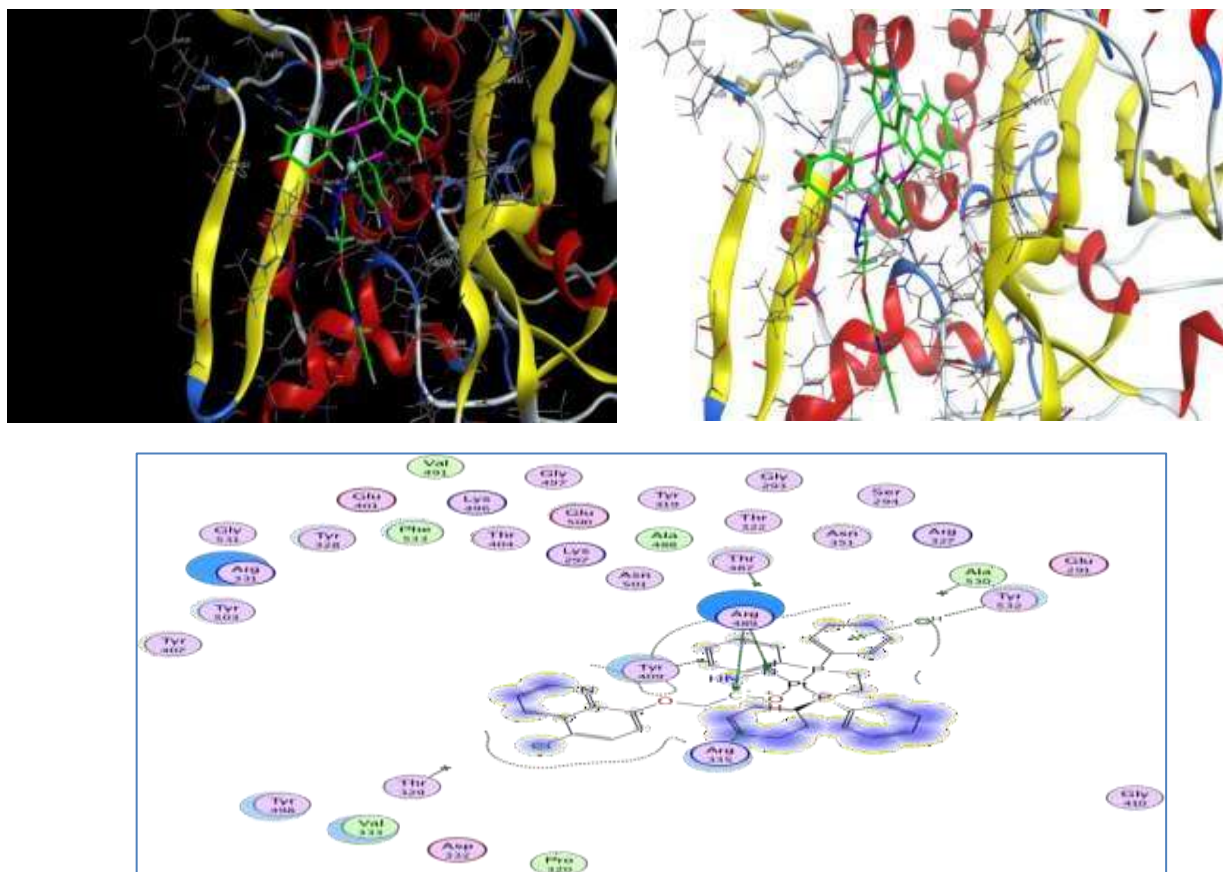
**Fig. 11.** Interactions of A<sub>2</sub> and receptor 6R3X



**Fig. 12.** Interactions of A<sub>3</sub> and receptor 6R3X

The study showed that the compound ( $A_3$ ) reacts with the amino acid residues that exist in the active site by forming two types of bonds, namely three hydrogen bonds, the first and the second linking the amino acid residue Arg.331 located in the active site with the electronic pair of the two nitrogen atoms of the hydrazide group associated with the metal, and the third links the residues of the amino acids Thr.329 located in the active site with the

electronic pair of the nitrogen atom associated with the metal, and a number of amino acids affected by the van der Waals forces of as in Table 5 above. Figure 12 shows the two-dimensional and three-dimensional representation of the molecular anchoring results and the association between the prepared compound ( $A_3$ ) and the receptor (R3X6)) one line of *Pseudomonas aeruginosa*.



**Fig. 13.** Interactions of  $A_5$  and receptor 6R3X

The study showed that the compound ( $A_5$ ) reacts with the amino acid residues that reside in the active site by forming two types of bonds, namely three hydrogen bonds, the first linking the amino acid residue Arg.489 located in the active site with the electron pair of the Arg.335 amino acid residue located in the active site with the electronic pair of the sulfamide group oxygen atom, and the third linking the amino acid residues. Arg.331 is located in the active position with the electron pair of an oxygen atom of the hydroxylic acid carboxylic acid

group, and a Pi-Alkyl type bond residue of the amino acid Val.333 which resides in active situ with the electron pairs of the furan aromatic ring, and a number of amino acids affected by van der Waals forces as in Table 5 above and Figure 13 shows the two-dimensional and three-dimensional representation of the molecular anchoring results and the association between the prepared compound ( $A_5$ ) and the receptor (6R3X) One line of *Pseudomonas aeruginosa*.



#### 4. Conclusions

Compound (A<sub>2</sub>) readily forms complexes, especially with platinum salt. The prepared compounds and complexes exhibited high stability and strength, maintaining their structure, color, and melting point even under varying laboratory temperatures between winter and summer. The biological study revealed that most of the prepared compounds and

complexes possess antibacterial activity and the ability to inhibit bacterial growth. These compounds exhibited higher biological efficacy compared to their parent compounds, which is of significant importance since the parent compounds are used as pharmaceuticals in the medical field.

#### References

1. Rbaa M., Jabli S., Lakhrissi Y. Synthesis, antibacterial properties and bioinformatics computational analyses of novel 8-hydroxyquinoline derivatives // *Heliyon*, 2019, V. 5(10), e02689. <https://doi.org/10.1016/j.heliyon.2019.e02689>
2. Althobiti H.A., Zabin S.A. New Schiff bases of 2-(quinolin-8-yloxy) acetohydrazide and their Cu (ii), and Zn (ii) metal complexes: there in vitro antimicrobial potentials and in silico physicochemical and pharmacokinetics properties // *Open Chemistry*, 2020, V. 18(1), p. 591-607. <https://doi.org/10.1515/chem-2020-0085>
3. Faydy M.E., Dahaief N., Rbaa M., Ounine Kh. Synthesis, Characterization and Biological Activity of Some Novel 5-((4-Alkyl piperazin-1-yl) methyl) quinolin-8-ol Derivatives // *J. Mater. Environ. Sci.*, 2016, V. 7 (1), p. 356-361.
4. Shehab A.S., Jawdat H. Synthesis Characterization and Biological Investigation of Some New Metal Complexes of Cu<sup>2+</sup>, Mn<sup>2+</sup>, Co<sup>2+</sup>, Zn<sup>2+</sup> and Ni<sup>2+</sup> ions with the Ligand of 2-[(8-hydroxy-1-quinolin-5-yl)-methyl]-1H-1,2-benzothiazole-3-(2H)-one-1,1-dioxide // *Kirkuk Journal of Science*, 2015, V. 10(3), p. 355-367.
5. Zhou S.-H., Liao W.-H., Yang Y. (8-Hydroxyquinoline) Gallium (III) Complex with High Antineoplastic Efficacy for Treating Colon Cancer via Multiple Mechanisms // *ACS Omega*, 2023, V. 8, p. 6945–695. <https://doi.org/10.1021/acsomega.2c07742>
6. Du L.-Q., Zhang T.-Y., Huang X.-M., Xu Y. Synthesis and anticancer mechanisms of zinc(II)-8-hydroxyquinoline complexes with 1,10-phenanthroline ancillary // *Dalton Trans.*, 2023, V. 52, p. 4737-4751. <https://doi.org/10.1039/D3DT00150D>
7. Ribeiro N., Bulut I., Posa V., Sergi B. Solution chemical properties and anticancer potential of 8-hydroxyquinoline hydrazones and their oxidovanadium (IV) complexes // *Journal of Inorganic Biochemistry*, 2022, V. 235, 111932. <https://doi.org/10.1016/j.jinorgbio.2022.111932>
8. Rbaa M., Benhiba F., Galai M., Abousalem A.S., Ouakki M., Lai C.-H., Lakhrissi B., Jama C., Warad I., Touhami M.E., Zarrouk A. Synthesis and characterization of novel Cu (II) and Zn (II) complexes of 5-[(2-Hydroxyethyl) sulfanyl] methyl}-8-hydroxyquinoline as effective acid corrosion inhibitor by experimental and computational testing's // *Chemical Physics Letters*, 2020, V. 754, 137771. <https://doi.org/10.1016/j.cplett.2020.137771>
9. El-Saied F.A., Shakdofa M.M., Al-Hakimi A.N., Shakdofa A.M. Transition metal complexes derived from N'-(4-fluorobenzylidene)-2-(quinolin-2-yloxy) acetohydrazide: Synthesis, structural characterization, and biocidal evaluation // *Applied Organometallic Chemistry*, 2020, V. 34(11), e5898. <https://doi.org/10.1002/aoc.5898>
10. Hamama W.S., Ibrahim M.E., Gooda A.A., Zoorob H.H. Recent advances in the chemistry of 2-chloroquinoline-3-carbaldehyde and related analogs // *Journal RSC Adv.*, 2018, V. 8, p. 8484–8515. <https://doi.org/10.1039/C7RA11537G>
11. Al-Jibori S.A., Al-Zaubai A.S.S., Modher Y.

- M., Al-Allaf T.A.K. Mixed ligand palladium (II) and platinum(II) complexes of tertiary diphosphines and benz-1,3-imidazoline-2-thione, benz-1,3-oxazoline-2-thione or benz-1,3-thiazoline-2-thione // *Transition Metal Chemistry*, 2007, V. 32, p. 281–286. <https://doi.org/10.1007/s11243-006-0108-z>
12. Yilmaz V., Icel C., Turgut O.R., M. Aygun, Erkisa M., Turkdemir M.H., Ulukaya E. Synthesis, structures and anticancer potentials of platinum (II) saccharinate complexes of tertiary phosphines with phenyl and cyclohexyl groups targeting mitochondria and DNA // *European Journal of Medicinal Chemistry*, 2018, V. 155, p. 609–622. <https://doi.org/10.1016/j.ejmech.2018.06.035>
13. Ahmed M., Sharma R., Nagda D.P. Synthesis and antimicrobial activity of succinimido (2 - aryl - 4 - oxo - 3 - {[quinoline - 8 - yloxy] acetyl} amino) - 1, 3 - thiazolidin-5-yl)acetates // *Arkivoc*, 2006, No. 11, p. 66–75.
- 14 Parveen S., Naseem H.A., Ahmad K., Shah H.U.R., Aziz T., Ashfaq M., Rauf A. Design, synthesis and spectroscopic characterizations of medicinal hydrazide derivatives and metal complexes of malonic ester // *Current Bioactive Compounds*, 2023, V. 19(4), p. 31–46. <https://doi.org/10.2174/1573407218666211222124947>
- 15 Wang Y., Zhang F.-L., Liu Z.-J., Yao Z.-J. Half-Sandwich Iridium Complexes with Hydrazone Ligands: Synthesis and Catalytic Activity in N -Alkylation of Anilines or Nitroarenes with Alcohols via Hydrogen Autotransfer // *Inorg. Chem.*, 2022, V. 61(27), p. 10310–10320, <https://doi.org/10.1021/acs.inorgchem.2c00703>
16. Patel A.K., Jadeja R.N., Roy H., Patel R.N., Patel S.K. Pseudo-tetrahedral copper (II) complex derived from N'-[(2E, 3Z)-4-hydroxy-4-phenylbut-3-en-2-ylidene] acetohydrazide: Synthesis, molecular structure, quantum chemical investigations, antioxidant and antiproliferative properties // *Journal of Molecular Structure*, 2019, V. 1185, p. 341–350. <https://doi.org/10.1016/j.molstruc.2019.03.004>
17. Pivarsik T., Pósa V., Kovács H., May N.V., Spengler G., Pósa S.P., Tóth S., Nezafat Yazdi Z., Özvegy-Laczka C., Ugrai I., Szatmári I., Szakács G., Enyedy É.A. Metal Complexes of a 5-Nitro-8-Hydroxyquinoline-Proline Hybrid with Enhanced Water Solubility Targeting Multidrug Resistant Cancer Cells // *Int J Mol Sci.*, 2022, V. 24(1), p. 593. doi: 10.3390/ijms24010593.
18. Abdalrazaq S.M., Shihab A.S., Hamad I.S. Preparation, Characterization and Study of the Biological Activity of 5-Chloroquinoline-8-ol Derivatives and its Coordination with the Nickle (II) and Di Phosphines // *Chemical Problems*, 2024, V. 22(2), p. 157–167.
19. Hashem H.E., Nath A., Kumer A. Synthesis, molecular docking, molecular dynamic, quantum calculation, and antibacterial activity of new Schiff base-metal complexes // *Journal of Molecular Structure*, 2022, V. 1250, 131915. <https://doi.org/10.1016/j.molstruc.2021.131915>
20. Mashood Ahamed F.M., Shakya B., Shakya S. Synthesis and characterization of a novel Mannich base benzimidazole derivative to explore interaction with human serum albumin and antimicrobial property: experimental and theoretical approach // *Journal of Biomolecular Structure and Dynamics*, 2022, V. 41(18), p. 8701–8714. <https://doi.org/10.1080/07391102.2022.2136757>
21. Shihab A.S. Synthesis, Diagnosis, Evaluation of Biological Activity and Study of Molecular Docking for Furosemide Derivative and Its Coordination with Some Metals // *Chemical Problems*, 2024, V. 22 (3), p. 312–322.
22. Kogut M.M., Marcisz M., Samsonov S.A. Modeling glycosaminoglycan–protein complexes // *Current Opinion in Structural Biology*, 2022, V. 73, 102332. <https://doi.org/10.1016/j.sbi.2022.102332>



**PLATİNİN (II) QARIŞIQ LIQANDLI KOMPLEKSLERİNİN 2-((5-XLOROKINOLİN-8-İL) OKSİ) ASETOHİDRAZİD VƏ ÜÇLÜ DİFOSFİNLƏRLƏ SİNTEZİ, XARAKTERİSTİKASI, MOLEKULYAR DOKİNGİ VƏ BİOLOJİ AKTİVLİYİNİN ÖYRƏNİLMƏSİ**

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**Xülasə:** Bu tədqiqat müxtəlif üzvi birləşmələrin hazırlanmasına həsr olunmuşdur. Etilnil 2-((5-xlorokinolin-8-il)oksi)asetat birləşməsi ( $A_1$ ) kalium karbonatın xinolin və etilxloroasetata əlavə edilməsi ilə sintez edilmişdir. 2-((5-Xlorokinolin-8-il)oksi) asetohidrazid ( $A_2$ ) birləşməsi isə ( $A_1$ ) hidrazidlə reaksiya nəticəsində alınmışdır. Həllədiçi kimi etanoldan istifadə etməklə ekvimolyar miqdarda ( $A_2$ ) birləşməsinin platin duzunun məhlulu ilə reaksiya nəticəsində ( $A_3$ ) kompleksi əldə edilmişdir. Fosfin kompleksləri, ( $A_3$ ) kompleksinin müxtəlif fosfinlərlə reaksiyandan və həllədiçi kimi etanoldan istifadə etməklə hazırlanmışdır. Sintez edilmiş birləşmələr və komplekslər Furiye-İnfraqırmızı (FT-IR) spektroskopiyası, UV-Visual spektri və Nüvə Maqnit Rezonansı ( $^{31}\text{P}$ ,  $^1\text{H}$  və  $^{13}\text{C}$ -NMR) spektroskopik üsullardan istifadə etməklə xarakterizə edilmişdir. Bundan əlavə, onların ərimə nöqtələri, təmizliyi, molyar keçiriciliyi və maqnit həssaslığı müəyyənləşdirilmişdir. Sintez edilmiş bəzi birləşmələrin və komplekslərin antibiotiklərə qarşı davamlı iki bakteriya ştamının, yəni qram-müsbət *Stafilokok* və qram-mənfi *Escherichia coli*-nin böyüməsinə təsiri öyrənilmişdir. *Tsiprofloksasin* nəzarət antibiotiki kimi istifadə edilmişdir. Sintez edilmiş birləşmələrin bəziləri sınaqdan keçirilmiş bakteriya ştammlarına qarşı əhəmiyyətli inhibitor təsiri göstərmişdir.

**Açar sözlər:** Xlorokinolin-8-ol, efir, üçlü difosfinlər, komplekslər, bioloji aktivlik.

**СИНТЕЗ, ХАРАКТЕРИСТИКА, ИЗУЧЕНИЕ МОЛЕКУЛЯРНОГО ДОКИНГА И БИОЛОГИЧЕСКОЙ АКТИВНОСТИ СМЕШАННЫХ ЛИГАНДОВ КОМПЛЕКСОВ ПЛАТИНЫ (II) С 2-((5-ХЛОРХИНОЛИН-8-ИЛ) ОКСИ) АЦЕТОГИДРАЗИДОМ И ТРЕТИЧНЫМИ ДИФОСФИНАМИ**

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**Резюме:** Это исследование включает в себя получение различных органических соединений. Соединение этилнил 2-((5-хлорхинолин-8-ил)окси)ацетата ( $A_1$ ) было синтезировано путем добавления карбоната калия к хинолину и этилхлорацетату. 2-((5-хлорхинолин-8-ил)окси)ацетогидразид ( $A_2$ ) был получен путем взаимодействия соединения ( $A_1$ ) с гидразидом. Комплекс ( $A_3$ ) был получен путем взаимодействия эквимольных количеств соединения ( $A_2$ ) с раствором соли платины с использованием этанола в качестве растворителя. Фосфинатные комплексы были получены путем взаимодействия равных молей комплекса ( $A_3$ ) с различными используемыми фосфинами и использованием этанола в качестве растворителя. Синтезированные соединения и комплексы были охарактеризованы с использованием различных спектроскопических методов, включая Фурье-ИК-спектроскопию (FT-IR), УФ-видимый спектр и ядерный магнитный резонанс ( $^{31}\text{P}$ ,  $^1\text{H}$  и  $^{13}\text{C}$ -ЯМР). Кроме того, были определены их температуры плавления, чистота, молярная

проводимость и магнитная восприимчивость. Было изучено влияние некоторых полученных соединений и комплексов на рост двух устойчивых к антибиотикам бактериальных штаммов, а именно грамположительного *Staphylococcus* и грамотрицательного *Escherichia coli*. Ципрофлоксацин использовался в качестве контрольного антибиотика. Некоторые из синтезированных соединений проявили значительную ингибирующую активность против тестируемых бактериальных штаммов.

**Ключевые слова:** хлорхинолин-8-ол, эфир, третичные дифосфины, комплексы, биологическая активность.