

Preparation, characterization, evaluation of biological activity and cytotoxicity study against breast cancer cells (MCF-7) of Pd(II) dinuclear complexes with Schiff base and tertiary phosphines.

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Abstract :

The Schiff base ligand (1E,1'E)-N,N'-(hexane-1,6-diyl)bis(1-(4-bromophenyl)methanimine)(L) was prepared by reacting one mole of 1,6-diaminohexane with two moles of para bromo benzaldehyde the ligand was characterized by (CHN) elemental microanalysis and spectral measurements including UV-VIS, FTIR, ¹H-NMR, and ¹³C-NMR, some mixed ligand Pd(II) Complexes with this ligand and tertiary phosphine were synthesized and characterized by UV-VIS, FTIR, ¹H-NMR, ¹³C-NMR, ³¹P-NMR spectra, conductivity measurements, XRD and EDX. From the obtained results the molecular formula of synthesized complexes were [Pd₂(L)(H₂O)₂Cl₄] and [Pd₂(L)(diphosphine)_n(H₂O)₄]Cl₄. Diphosphines = pph₃, dppm, dppe, dppp and dppb; n=2 or 4.

The proposed geometrical structure for all complexes were square planar. Antibacterial activity and cytotoxicity of breast cancer cell for these prepared compounds were also studied.

Keywords: (Schiff Base), (1,6-Diaminohexane), Palladium(II), (Tertiary Phosphine).

تحضير و تشخيص و تقييم الفعالية الحيوية و دراسة السمية الخلوية اتجاه خلايا سرطان الثدي (MCF-7) لمعقدات ثنائية النوى متجانسة للبلاديوم Pd(II) مع قاعدة شف و الفوسفينات الثلاثية

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مستخلص

تضمن البحث تحضير ليكاند قاعدة شف (1E,1'E)-N,N'-(hexane-1,6-diyl)bis(1-(4-bromophenyl)-methanimine)(L) من خلال تفاعل مول واحد من (1,6 - ثنائي امين هكسان) مع مولين من بارا بروموبنزالديهايد، شخص الليكاند بالتحليل الدقيق للعناصر (CHN) و القياسات الطيفية بما في ذلك الاشعة فوق البنفسجية - المرئية (UV-Vis)، الاشعة تحت الحمراء (FTIR) و اطياف الرنين النووي المغناطيسي (¹H-NMR، ¹³C-NMR)، حضرت بعض معقدات الليكاند من مزج ملح البلاديوم Pd(II) مع هذا اليكاند وبعض الفوسفينات الثلاثية و شخصت عن طريق اطياف الاشعة فوق البنفسجية - المرئية (UV-Vis)، الاشعة تحت الحمراء (FTIR) و اطياف الرنين النووي المغناطيسي (¹H-NMR، ¹³C-NMR، ³¹P-NMR)، و قياسات الموصلية الكهربائية المولارية، وتقنية حيود الاشعة السينية (XRD)، والتشتت في طاقة حيود الاشعة السينية (EDX). من النتائج التي تم الحصول عليها كانت الصيغة الجزيئية للمعقدات المحضرة [Pd₂(L)(H₂O)₂Cl₄] و [Pd₂(L)(diphos.)_n(H₂O)₄]Cl₄ Diphosphines = pph₃, dppm, dppe, dppp ; n=2 or 4 and dppb.

كانت الصيغ الهندسية المقترحة لجميع المعقدات شكل المربع المستوي. كما تم دراسة الفعالية الحيوية المضادة للبكتيريا والسمية الخلوية لخلايا سرطان الثدي لهذه المركبات المحضرة.
الكلمات المفتاحية: (قاعدة شف)، (1,6-ثنائي امينو هكسان)، البلاديوم (II)، (الفوسفين الثلاثي).

Introduction:

Palladium (II), forms many organo-metallic compounds, and these compounds are stable towards oxidation processes, and are common homogeneous catalysts. Usage^[2], as laboratory tests confirmed that palladium is toxic that hinders the work of important enzymes from performing their role and functions inside the body such as (trypsin, alkaline phosphatase) and causes disturbances in the synthesis of collagen in bones and cartilage and causes allergies. Schiff bases are one of the important ligands in Coordination chemistry ^[3], as it invoked in many complexes with metal ions in general and transitional elements in particular, due to its ability to coordinate. Schiff base compounds have many application in fields, including catalysis, molecular magnetism, nonlinear optical molecular sensing of materials, porous and energy materials, have bases of liposuction; Because of the presence of electron pair on the nitrogen atom ^[4] Recently , we reported several new mixed ligand complexes of Pd (II) with schiff base as primart ligand and diposphine as ligands .

Physical measurements

The melting points were obtained from an electrothermometer 9300, and the molar electrical conductivity of the prepared complexes was measured using a Starter 3100 C conductivity meter) and using DMSO as a solvent) and the concentration of the solutions (1×10^{-3}) mol/L , at room temperature, Elemental analysis of the elements (C.H.N) were carried out on using an Elemental vario El III. In addition, the electronic spectra were Recorded . by shimmed Zn –UV-VIS 160 Aultra violet spectrophotometer at 25 °C at range of (200 -800) nm .

The FT-IR infrared spectra were recorded using KBr discs within the range between(400-4000) cm^{-1} The NMR spectra were also recorded for the prepared complexes ^1H -NMR , ^{13}C –NMR and ^{31}P - NMR using an Origin Bruker Bio Spin spectrometer .

Experimental

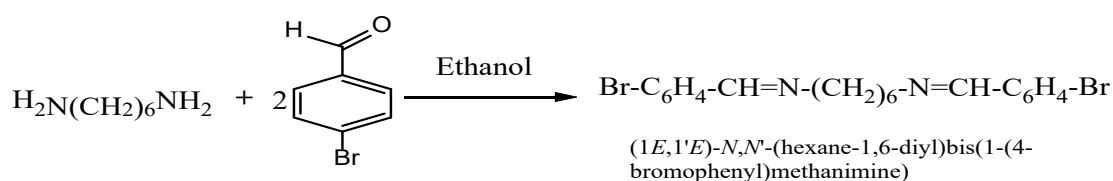
Preparation of Shiff Base ligang (L)

1) Eel,1>E)-N,N>-(hexane-1,6-diyl) bis (1-(4-bromophenylmethanimine(

In a round flask a solution of 1.5) g 12.9,mmole (of-1,6 diamine hexane diamino hexane in 15 ml of ethanol

was added gradually with stirring to 4.77) g 12.9 , mmole (of g (of -4bromobenzaldehyde dissolved in 15 ml of ethanol ,then 2 ml of glacial acetic acid was added ,the mixture was stirred for three hours a white precipitate was formed ,after that the volume of the

solution was reduced to a quarter ,then the formed precipitate was filtered off ,washed with ethanol and dried using An electric oven for three hours at a temperature of 50 ° C, the weight of the product was (2.23 g), as shown in the following reaction:

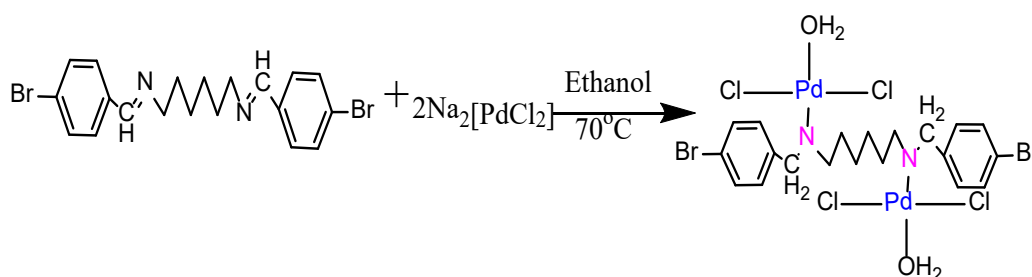


Preparation of complexes

Preparation of $[\text{Pd}_2(\text{L})(\text{H}_2\text{O})_2\text{Cl}_4]$

A solution of palladium salt Na_2PdCl_4 (0.17g , 0.6mmol) in 15ml of ethanol was added to a solution of the Schiff Base ligand (0.2g , 0.3mmol) in 15ml of ethanol. The mixture was refluxed with stirring for three hours. A

nutty dark precipitate was observed., then the volume of the solution was reduced in a water bath at a temperature of 70 ° C. The formed product was filtered off, washed with ethanol, and dried using an electric oven for three hours at 50 ° C, and the weight was (0.23 g) as shown in the following reaction :



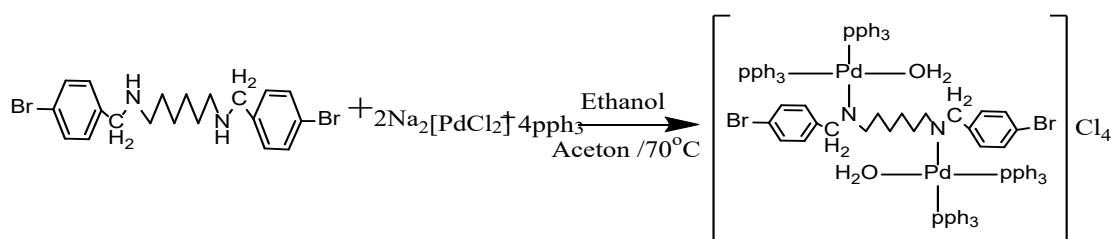
preparation of $[\text{Pd}_2(\text{L}) (\text{pph}_3)_4 (\text{H}_2\text{O})_2]\text{Cl}_4$

A solution of $\text{Na}_2[\text{PdCl}_2]$ (0.17g , 0.6mmol) in 15ml of ethanol was added to a solution of Schiff base ligand

(0.2g ,0.44mmol) in 15ml of ethanol, the mixture was refluxed with continuous stirring for an hour after that a solution of Triphenylphosphine (1.2mmol , 0.34g) in 10ml of acetone was the

mixture was refluxed add with stirring for three hours. a color precipitate was formed, then the volume of the solution was reduced by evaporation. Then the formed precipitate was filtered and

washed with ethanol, and dried using an electric oven for three hours at a temperature of 50 ° C, the weight was (0.26 g). As shown in the following interaction:



The related complexes $[Pd_2(L)(\text{phosphine})_2(H_2O)_2]Cl_4$; phosphine = dppm, dppe, dppp and dppb were prepared and isolated by similar meth-

od for preparation of $[Pd_2(L)(pph_3)_4(H_2O)_2]Cl_4$ complex by using a molar ratio of (2: 1: 2); Pd salt : ligand : phosphine.

Table: (1) shows some physical properties, percentages and molecular weights of the prepared ligands and complexes.

NO	Compound	M. Wt g / mole	M.P °C	Color	Yield %
	L	454.25	245-247	White	69
1	$[Pd_2(L)(H_2O)_2]Cl_4$	845.09	162-165	Dark nutty	61
2	$[Pd_2(L)(pph_3)_4(H_2O)_2]Cl_4$	1894.25	168-170	Light nutty	68
3	$[Pd_2(L)(dppm)_2(H_2O)_2]Cl_4$	1613.87	201-203	Light nutty	83
4	$[Pd_2(L)(dppe)_2(H_2O)_2]Cl_4$	1641.93	206-208	Nutty	89
5	$[Pd_2(L)(dppp)_2(H_2O)_2]Cl_4$	1669.97	200-203	Light nutty	77
6	$[Pd_2(L)(dppb)_2(H_2O)_2]Cl_4$	1698.05	211-213	Nutty	87

Evaluation of biological activity:

The biological activity of the compounds was studied on two bacterial models, which are Gram-positive bacteria *Staphylococcus aureus*.

and Gram-negative bacteria, *Escherichia coli*.

Test solutions for some of the prepared compounds to be evaluated for their biological activity against the two types of bacteria above were prepared using a solvent, dimethyl sulfoxide (DMSO), where the solutions were prepared with three different concentrations (0.01, 0.001, 0.0001 mg / ml) for each prepared compound. The biological activity was measured by (Agar-well diffusion method) ⁽¹⁰⁾, and standard antibiotics (such as OX-oxacillin, CX-cefexitim, Met-methicillin) were used as control samples, depending on what is used in the Ministry of Health laboratories that are based on WHO tests. global ⁽¹¹⁾ .

Cytotoxicity of the prepared compounds towards breast cancer cells (MCF-7)

Breast cancer cells (MCF-7) were cultured and cultured on Dulbecco's Modified Eagle's Medium (DMEM) culture medium supplemented with streptomycin (100 units/ml), gentami-

cin (100 µg/ml), 10% FBS (fetal bovine serum). Serum) at 37°C and an atmosphere of 5% carbon dioxide to protect cells from contamination. The MTT method ((3-[4,5-dimethylthiazol-2-yl]-2,5 diphenyl tetrazolium bromide)) was used to evaluate the efficacy of the compounds against cancer cells in vitro.

Results And Discussion

Physical and spectroscopic measurements were performed determine the composition of the structure of ligand and its prepared complexes . All complexes are stable in air having relatively high melting points .they are partially soluble in some common solvents such as DMF , DMSO , but they are slightly soluble in ethanol and insoluble in water , and their elemental microanalyses are in a good agreement with the suggested for mutations showed in the above reaction and table (1). The electrical conductivity measurements in DMSO for phosphine complexes give Λ_M values of (--) $\Omega^{-1}\text{cm}^{-1}\text{mole}^{-1}$ confirming that they are ionic and 1:4 electrolytes .

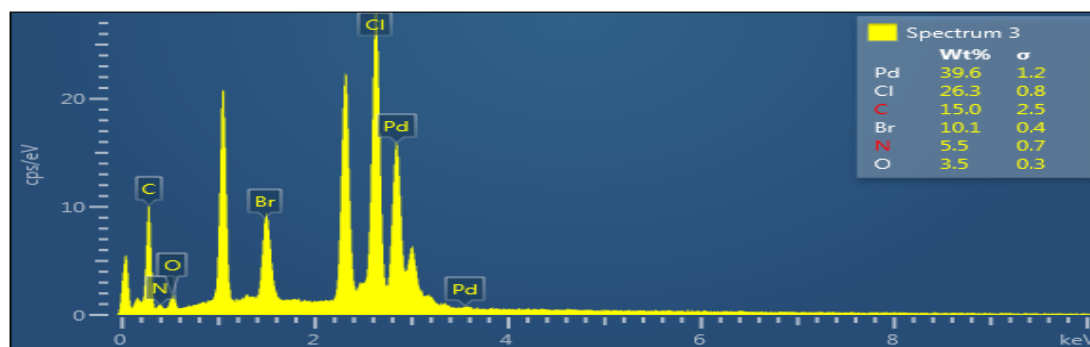
**Table (2) the results of the micro-analysis of the elements (C.H.N)
and some physical properties of the prepared complexes.**

NO	Complexes	Color	M.P. C°	Yield %	(ohm ⁻¹ .cm ² . mol ⁻¹) Δ	Found(cal)%		
						C	H	N
	L	White	245-247	68.95	-----	52.83 (52.88)	4.69 (4.77)	6.15 (6.17)
1	[Pd ₂ (L)(H ₂ O) ₂ Cl ₄]	Dark nutty	168-170	60.88	29	28.51 (28.53)	3.7 (3.12)	3.29 (3.33)
2	[Pd ₂ (L) (pph ₃) ₄ (H ₂ O) ₂]Cl ₄	Light nutty	168 - 170	57.53	291	60.09 (60.68)	4.53 (4.87)	1.48 (1.54)
3	Pd ₂ (L) (dppm) ₂ (H ₂ O) ₂]Cl ₄	Light nutty	201 - 203	83.24	295	51.98 (52.04)	4.70 (4.74)	1.69 (1.73)

**Energy dispersive X-ray EDX/
EDS spectroscopy analysis**

This technique is an excellent qualitative and good quantitative analysis technique, especially for atoms with

High atomic weights. The composition of [Pd₂(L)(H₂O)₂Cl₄] was obtained, as shown in the figure (1) and table (3) the presence of peaks indicating the presence of Pd, Br, Cl, O, N, C.

**Figure (1) Energy dispersive spectrum EDS for obtaining the composition or
chemical analysis of complex [Pd₂(L)(H₂O)₂Cl₄]****Table (3) practical, theoretical, and atomic weight percentage of the palladium complex .**

Complex	Element	C		O	Cl	Br	Pd	Total wt% Atomic% Elem(%)
[Pd ₂ (L)(H ₂ O) ₂ Cl ₄]		14.99	5.54	3.52	26.33	10.07	39.56	100
		40.21	12.73	7.09	23.92	4.06	11.98	100
		29.73	3.47	7.92	8.77	19.78	26.34	96.01

Electronic spectra



The spectrum of the prepared ligand L-Schiff base showed a distinctive ab-

sorption, the prepared ligand showed absorption bands at the location (35087 - 35335) cm^{-1} that are due to the two transitions ($n \rightarrow \pi^*$, $\pi \rightarrow \pi^*$) respectively, as shown in the figure. (2).

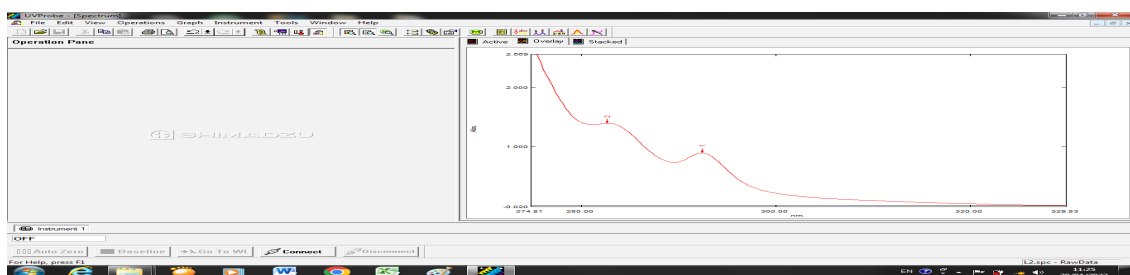


Figure (2) shows the UV-visb spectrum (L).

The electronic spectra of Pd(II) Complexes showed bands in the region between (21551 - 26385) cm^{-1} that are due to the transitions ($^1A_1 g \rightarrow ^1A_2 g$), ($^1A_1 g \rightarrow ^1B_1 g$) of square planar

environment(--) transitions in the region within the range (33333 - 41666) cm^{-1} , are due to ligand transitions $n \rightarrow \pi^*$, $\pi \rightarrow \pi^*$) table (4) .

Seq	Complexes	height waveform λ (nm)	the number waveform (cm^{-1}) ν	Abs	Possible trans- fers	proposed geometry
1	$[\text{Pd}_2(\text{L})(\text{H}_2\text{O})_2\text{Cl}_4]$	465 393 300	21739 25445 33333	1.266 0.514 0.906	$^1A_2 g \rightarrow ^1A_1 g$ $n \rightarrow \pi^*$ $\pi \rightarrow \pi^*$	Sq.P.
2	$[\text{Pd}_2(\text{L})(\text{pPh}_3)_4(\text{H}_2\text{O})_2]\text{Cl}_4$	416 379 300	24038 26385 33333	0.939 0.521 0.907	$^1A_2 g \rightarrow ^1A_1 g$ $n \rightarrow \pi^*$ $\pi \rightarrow \pi$	Sq.P.
3	$[\text{Pd}_2(\text{L})(\text{dppm})_2(\text{H}_2\text{O})_2]\text{Cl}_4$	464 393 300	21551 25445 33333	1.232 0.513 0.905	$^1A_2 g \rightarrow ^1A_1 g$ $n \rightarrow \pi^*$ $\pi \rightarrow \pi$	Sq.P.
4	$[\text{Pd}_2(\text{L})(\text{dppe})_2(\text{H}_2\text{O})_2]\text{Cl}_4$	400 240	25000 41666	0.193 1.122	$^1A_1 g \rightarrow ^1B_1 g$ $\pi \rightarrow \pi^*$	Sq.P
5	$[\text{Pd}_2(\text{L})(\text{dppp})_2(\text{H}_2\text{O})_2]\text{Cl}_4$	408 393 379	24509 25445 26385	0.775 0.511 0.521	$^1A_1 g \rightarrow ^1B_1 g$ $n \rightarrow \pi^*$ $\pi \rightarrow \pi^*$	Sq.P.

Infrared Spectrum

The IR spectra of the complexes were interpreted by comparing the spectra with that of the free ligand the complexes exhibit bands at $(3400 - 3480) \text{ cm}^{-1}$, $(817 - 871) \text{ cm}^{-1}$ and $(445 - 534) \text{ cm}^{-1}$ indicating the involvement of H_2O in the bonding^(15,14). The isomethine bond occurred in the IR spectrum of the free ligand at 1643 cm^{-1} is shifted down $(2 - 60) \text{ cm}^{-1}$ in the IR spectra of the complexes. This shift of $\text{C}=\text{N}$ bands suggested additional coordination through this group. A new bands were observed in the IR spectra of $[\text{Pd}_2(\text{L})(\text{dppm})_2(\text{H}_2\text{O})_2]\text{Cl}_4$; phosphine= pph_3 , dppm , dppe , dppp and dppb ; $n=4$ or 2 which are $\nu(\text{p-ph})$, $\nu(\text{p-c})$ observed with in $(1427 - 1533) \text{ cm}^{-1}$ and $(675 - 696) \text{ cm}^{-1}$, respectively.

It is thought that this vibration arises from the deformation of the planarity of the phenyl ring bonding to the phosphorus atom.

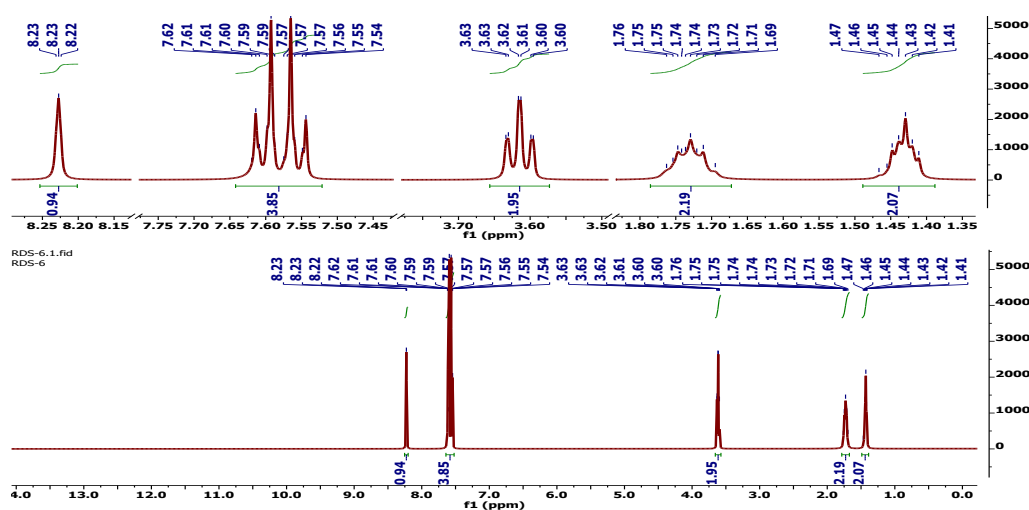
Table (5) the values of the frequencies of some bands of the infrared spectrum in Cm^{-1} for the prepared complexes

Sqe	Compound	$\nu(\text{C-H})/\text{Alph}$		M-N	M-O	H_2O		$\nu(\text{C-C})$	$\nu(\text{C-N})$	$\nu(\text{P-Ph})$	$\nu(\text{P-C})$	$\nu(\text{P-C})^b$	$\nu(\text{M-P})$
		Sym	Asym			Y	r						
	L-Schiff Base	2852 (m)	2933 (m)	-----	-----	-----	-----	1004 (m)	1643 (s)	-----	-----	-----	-----
1	$[\text{Pd}_2(\text{L})(\text{H}_2\text{O})_2\text{Cl}_4]$	2854 (m)	2927 (m)	472 (w)	534 (w)	3417 (m)	871 (w)	1101 (m)	1631 (m)	1533 (m)	1064 (m)	696 (s)	617 (m)
2	$[\text{Pd}_2(\text{L})(\text{pph}_3)_4(\text{H}_2\text{O})_2]\text{Cl}_4$	2852 (m)	2929 (m)	422 (w)	513 (w)	3400 (w)	817 (w)	1159 (w)	1639 (m)	(s) 1433	1097 (s)	675 (m)	615 (m)
3	$[\text{Pd}_2(\text{L})(\text{dppm})_2(\text{H}_2\text{O})_2]\text{Cl}_4$	2850 (m)	2923 (m)	424 (w)	445 (w)	3417 (m)	821 (w)	1157 (w)	1643 (m)	(s) 1479	1097 (s)	690 (s)	611 (w)
4	$[\text{Pd}_2(\text{L})(\text{dppe})_2(\text{H}_2\text{O})_2]\text{Cl}_4$	2850 (m)	2921 (m)	435 (w)	480 (w)	3413 (s)	871 (w)	1064 (w)	1635 (w)	(m) 1427	1008 (m)	696 (m)	617 (m)
5	$[\text{Pd}_2(\text{L})(\text{dppp})_2(\text{H}_2\text{O})_2]\text{Cl}_4$	2854 (m)	2914 (m)	430 (w)	486 (w)	3421 (m)	818 (w)	1157 (m)	1643 (m)	1481 (s)	1099 (s)	694 (s)	617 (m)
6	$[\text{Pd}_2(\text{L})(\text{dppb})_2(\text{H}_2\text{O})_2]\text{Cl}_4$	2860 (m)	2923 (m)	432 (w)	509 (w)	3480 (s)	823 (m)	1099 (m)	1643 (m)	1477 (m)	1006 (m)	694 (s)	609 (m)

1H-NMR , $^{13}\text{C-NMR}$ spectrum of ligands (L-Schiff Base)

The $^1\text{H-NMR}$ spectrum of the ligand showed multiplet at ($\delta\text{H} = 1.43$ ppm) that belonged to the (c) protons, and the spectrum showed multiple signal at ($\delta\text{H} = 1.73$ ppm) refer to the protons

(b).), also the spectrum showed a triplet signal at ($\delta\text{H} = 3.61$ ppm) belonging to the protons (a) another multiplet appeared at ($\delta\text{H} = 7.58$ ppm) for the protons (d) the (H-C=N)⁽¹⁸⁾ showed a singlet at ($\delta\text{H}=8.23$ ppm) , figure (3).



Proton NMR spectrum of the prepared $^1\text{H-NMR}$ ligand (L)

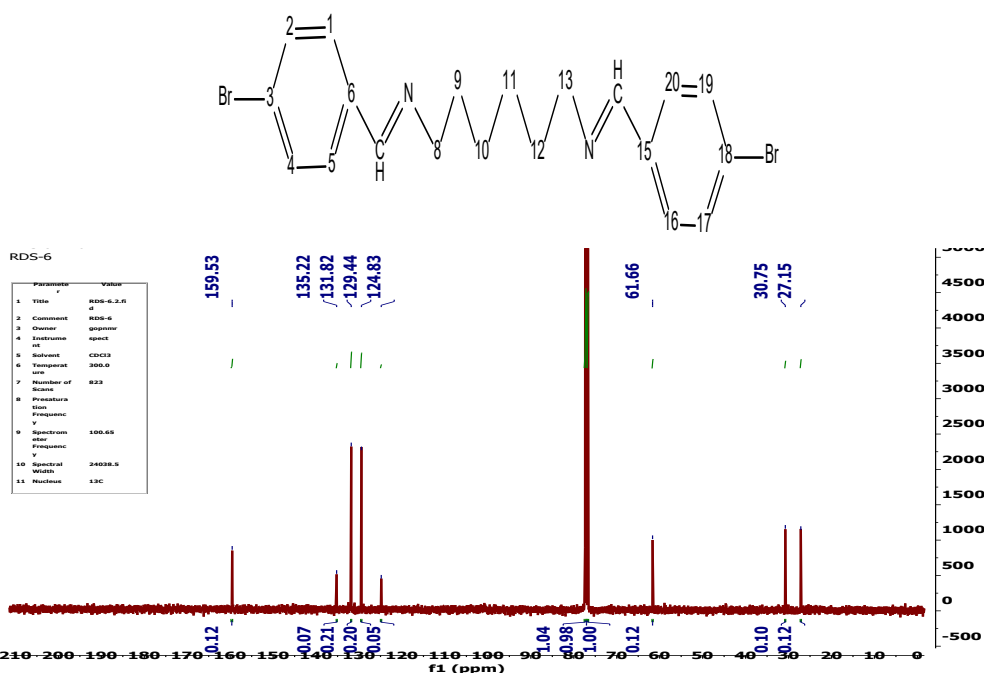


Figure (3) Proton NMR spectrum of the prepared $^{13}\text{C-NMR}$ ligand (L)

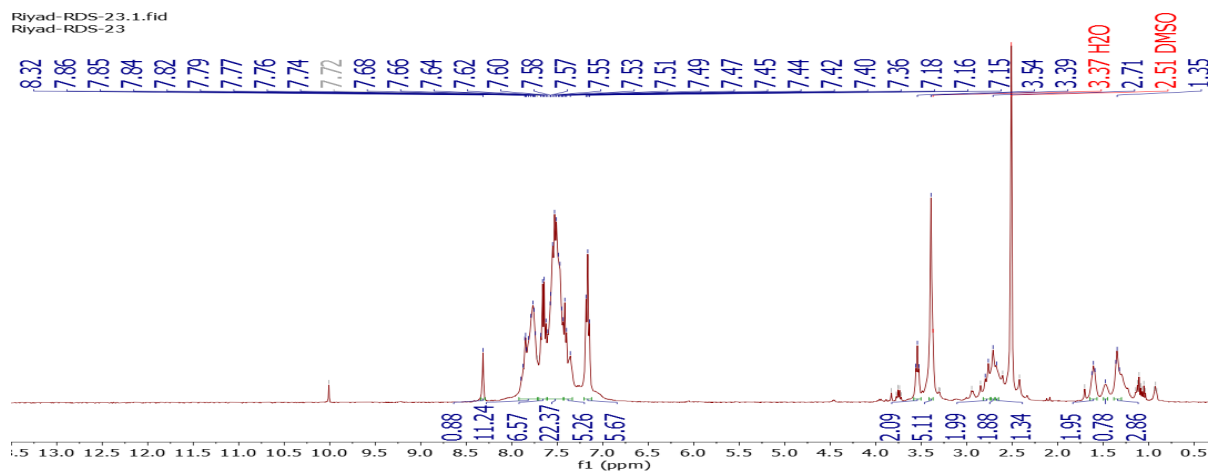


Figure (4): ^1H -NMR spectrum of $[\text{Pd}_2(\text{L}_2)(\text{dppe})_2(\text{H}_2\text{O})_2]\text{Cl}_4$

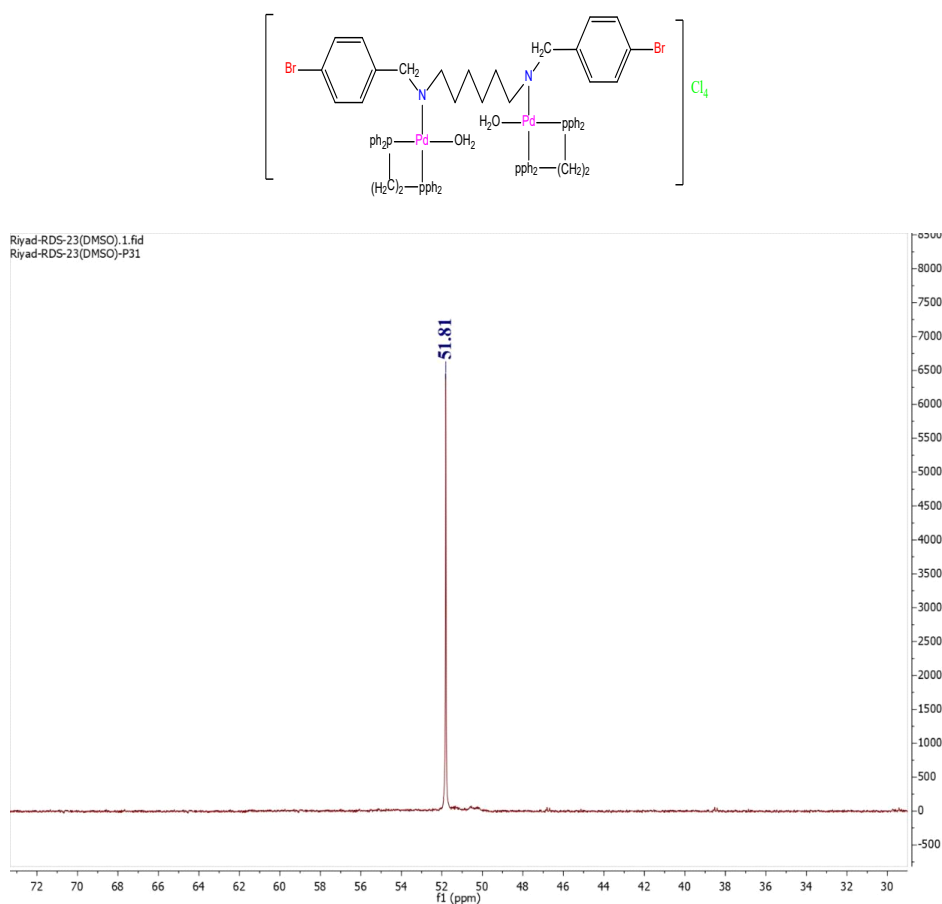


Figure (5): ^{31}P -NMR spectrum of $[\text{Pd}_2(\text{L})(\text{dppe})_2(\text{H}_2\text{O})_2]\text{Cl}_4$ complex

The collect NMR data for ligand and complexes are listed in table (6)

Table (6) ^1H , ^{13}C , ^{31}P -NMR spectra of the ligand and its complexes

Seq	Compound	Type of NMR	Chemical Shift (ppm)
	L-Schiss Base	^1H ^{13}C	(c)=1.43; (b)=1.73; (a)=3.61; d)=7.58; (HC=N)=8.23 (C ₁₀)=27.13; (C ₉)=30.87; (C ₈)=58.5; (C ₃)=124.31; (C ₁)=129.8; (C ₂)=131.32; (C ₆)=133.55; (C=N)=161.73
1	[Pd ₂ (L ₂)(H ₂ O) ₂ Cl ₄]	^1H ^{13}C	(c)= 1.06 -1.6; (b)= 2.19; (a)=2.95; (HC=N)=3.54; (d)=7.66 – 7.88 ; (e)=8.20- 8.33 (C ₁₁)= 19.27; (C ₁₀)=26.17 ; (C ₉)=30.97; (C ₈)=56.42; (C ₂₄)=60.88; (C ₃)=124.4; (C ₁)=130.24 ; (C ₇)=132.60; (C ₆)=135.72
2	[Pd ₂ (L ₂)(pPh ₃) ₄ (H ₂ O) ₂ Cl ₄]	^1H ^{31}P	(C)=1.06 – 1.34; (b)=1.61 ; (a)=1.58; (HC-N)=3.44 – 3.56 ; pPh ₃ =6.98 – 7.67 42.28
3	[Pd ₂ (L ₂)(dppm) ₂ (H ₂ O) ₂ Cl ₄]	^1H ^{31}P	(c)=1.11; (b)=1.35; (a)=1.56 ; (HC-N)=3.44 – 3.56; (dppm)=7.03 – 8.01 24.61 ; 34.09
4	[Pd ₂ (L ₂)(dppe) ₂ (H ₂ O) ₂ Cl ₄]	^1H ^{31}P	(c)=1.15- 1.46 ; (b)=1.61 ; (a)=2.58 -2.86; (HC –N)=3.54 ; (dppe)=7.36 – 7.89 51.81
5	[Pd ₂ (L ₂)(dppp) ₂ (H ₂ O) ₂ Cl ₄]	^1H ^{31}P	(C)=1.09-1.48) ; (b)=1.62-2.1 ; (a)=2.57 -2.95; (HC-N)=3.51; (dppp)=7.23 -7.95 (d,j=28HZ) , ^{31}P =1.61 -1.01 ; (d,j=28.1HZ) , ^{31}P =13.02
6	[Pd ₂ (L ₂)(dppb) ₂ (H ₂ O) ₂ Cl ₄]	^1H ^{31}P	(c)=1.12 -1.72 ; (b)=2.1; (a) =2.95 ; (HC-N)=3.55 ; (dppb)=6.96 -7.92 43.25 ; 30.24 ; 24.44

X-ray diffraction (XRD)

X-ray diffraction (XRD) technique is widely used to study the crystal structure of solids, defects, and stresses. Where the (XRD) process, which has

(a wavelength ranging between 0.07 - 0.2 nanometers) occurs by the crystalline sample according to Bragg's Law:

$$= \lambda 2d \sin \theta$$

Table (7) shows the X-ray diffraction of the powder of some prepared complexes

Seq	Complexes	The Total area under the crystalline peaks (A_c)	The total area ($A_c + A_a$)	Degree of crystallization $\% A_c / (A_c + A_a) \times 100$
1	$[\text{Pd}_2(\text{L}_2)(\text{dppm})_2(\text{H}_2\text{O})_2]\text{Cl}_4$	10010.665	10675.665	93.7708
2	$[\text{Pd}_2(\text{L}_2)(\text{dppe})_2(\text{H}_2\text{O})_2]\text{Cl}_4$	11895.205	22736.705	52.317

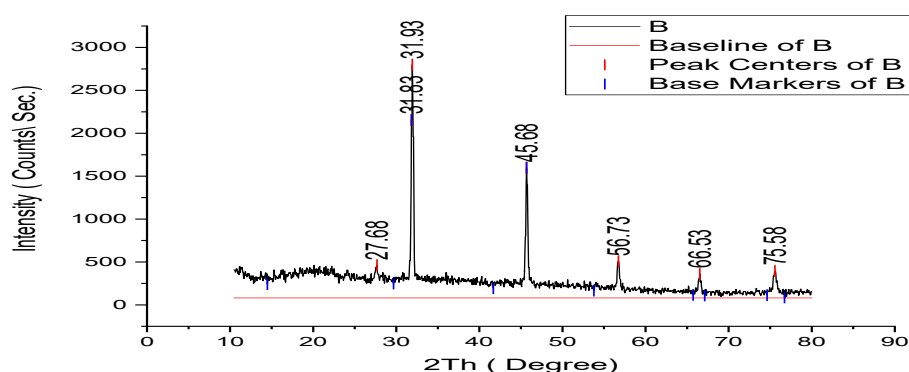


Figure (6) X-ray diffraction spectrum of complex $[\text{Pd}_2(\text{L})(\text{dppm})_2(\text{H}_2\text{O})_2]\text{Cl}_4$

Table (8) average size and crystallite size of some palladium complexes prepared according to Scherrer's equation

Seq	المعقد	2Theta	FWHM	D(size)nm	D(Averag)
1-	$[\text{Pd}_2(\text{L}_2)(\text{dppm})_2(\text{H}_2\text{O})_2]\text{Cl}_4$	20.70225	3.3711	2.395574307	74.69406
		20.70226	108.7345	0.074270086	
		31.84179	0.36973	22.34380957	
		45.61767	0.35927	23.98809623	
		56.69631	0.0025	3610.718003	
		57.45889	68.37523	0.132497149	
		73.38747	27.76314	0.356860271	
2-	$[\text{Pd}_2(\text{L}_2)(\text{dppe})_2(\text{H}_2\text{O})_2]\text{Cl}_4$	31.94174	0.29997	7.382154912	0.674773773
		45.70468	0.29345	10.79764304	
		46.17237	0.26774	11.95559832	
		75.09084	2426.85751	0.002145088	
		75.09084	65.48895	0.079491619	
		-5.61006	0.06564	-5.925177173	

Evaluation of the bacterial activity of the prepared compounds

The anti-bacterial activity of the prepared ligand and Pd(II) complexes were evaluated against selected types of micro organisms which included gram positive bacteria (*Staphylococcus aureus*) and gram negative bacteria (*Escherichia coli*) Dimethyl sulfoxide used as solvent, the antibacterial results also indicated that the palladium complexes displayed the same activity or slightly better antimicrobial activity as compared to schiff base ligand table

(9) and figure (7), The biological effectiveness of some of the prepared complexes was evaluated using the drilling method⁽¹⁹⁾

Which controls the anti-bacterial activity and then the complex spreads faster through the cell membrane and these complexes are non-polar and thus are more permeable through the fatty layers of the cover of microorganisms and then enter into the bacterial cell and destroy it, in addition to that the transition metals have an anti-microbial inhibitory effect⁽²⁰⁾.

Table (9) the antibacterial activity of the prepared compounds in the growth of a number of negative and positive bacteria (the diameter of the microbial inhibition zone ranges from 7 to 18.5 mm)

Seq	Compounds	Conc. (mg/ ml)	Escherichia coli	Staphylococcus aureus
	L_2	1×10^{-2} 1×10^{-3} 1×10^{-4}	12 5 NIZ	13 NIZ NIZ
1	$[Pd_2(L_2)(H_2O)_2Cl_4]$	1×10^{-2} 1×10^{-3} 1×10^{-4}	12.3 NIZ NIZ	14 7.5 5
2	$[Pd_2(L_2)(dppe)_2(H_2O)_2]Cl_4$	1×10^{-2} 1×10^{-3} 1×10^{-4}	17.9 10 10	11 6 NIZ
3	$[Pd_2(L_2)(dppb)_2(H_2O)_2]Cl_4$	1×10^{-2} 1×10^{-3} 1×10^{-4}	17.7 12 NIZ	14 14 NIZ

NIZ (No Inhibition Zone)*

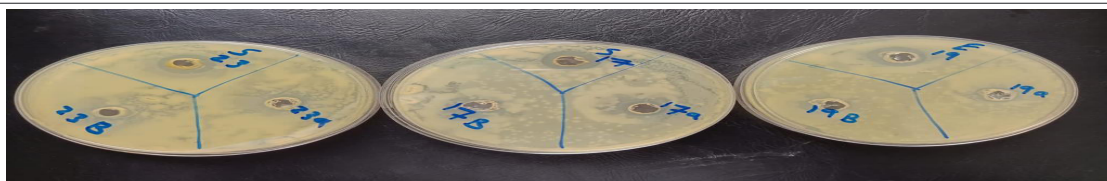


Figure (8) Inhibition activity of complexes 1,2, 3 and complex 2 is $Cl_2 [Pd_2(L)(dppe)_2(H_2O)_2]Cl_2$ against S.a.))

Cytotoxicity study of prepared compounds towards breast cancer cells (MCF-7)

Many published studies on transition metal ion complexes showed Schiff bases and their biological activity against many cancer cells, bacteria and fungi. In particular, the complexes of transition metal ions of Schiff bases dominated medicinal chemistry because of their distinctive properties and high effectiveness^(21,22). Inhibiting the growth of bacteria or cancer cells, as researchers developed many Schiff bases or their complexes and used them as antimicrobial and anticancer agents⁽²³⁾. Shown a lot The prepared lip bases are [N-(1-phenyl-2-hydroxy-2-phenyl ethyldine)-2', 4'dinitrophenyl hydrazine] [N-(1-phenyl, 2-hydroxy-2-phenyl ethylidene)-2' hydroxy phenyl imine] and [N-(2-hydroxy benzylidene)-2' hydroxy phenyl imine], or their complexes with a number of metal ions with Co (II), Cu (II), Ni (II) and Zn (II) number potencies types of cancer cells, whether in laboratory experiments or when tested on laboratory animals.⁽²⁴⁾

Accordingly, the activity of the Schiff base ligand prepared with its complexes with palladium (II) ion Pd against breast cancer cell line (MCF-7) was studied using concentrations

that ranged between (12.5, 25, 50, 100, 200, 400 micrograms). Evaluating its toxic effect and calculating the rate of inhibition of cell growth and comparing it with the drug Alss Platinum. The obtained results have been included in Table (10) and (11) and Figures (9) to (11).

1- Effect of N,N'-(hexane-1,6-diyl) bis(1-(4-bromophenyl)methanimine on MCF-7

Table(10and11)andFigure(9,10,11) show the effect of N,N'-(hexane-1,6-diyl)bis(1-(4-bromophenyl) methanimine $[\text{Pd}_2(\text{L})(\text{dppm})_2(\text{H}_2\text{O})_2]\text{Cl}_4$ and $[\text{Pd}_2(\text{L})(\text{dppp})_2(\text{H}_2\text{O})_2]\text{Cl}_4$ on the growth of breast cancer (MCF-7) , where it was found that the effect The inhibition of the prepared compound increases with increasing the concentration of this compound, as the lowest inhibitory concentration was at the lowest concentration (12.5 micromolar) and the highest inhibition to be at the highest concentration (400 micromolar), where the percentage of remaining cells was 22.17% , 18.53% and 16.3% respectively. The value of IC50 (which represents half of the inhibitory concentration for the growth of cancer cells) 118.30 ± 3.826 , 98.45 ± 1.932 and 109.31 ± 1.73 micromolar respectively.

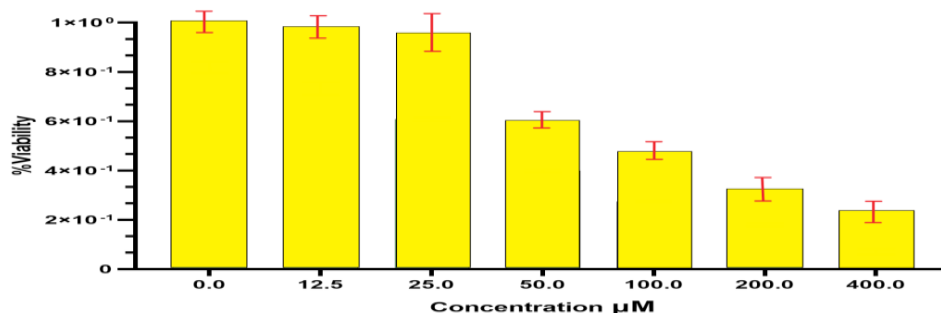


Figure 9: Inhibitory activity of the Schiff base L ligand

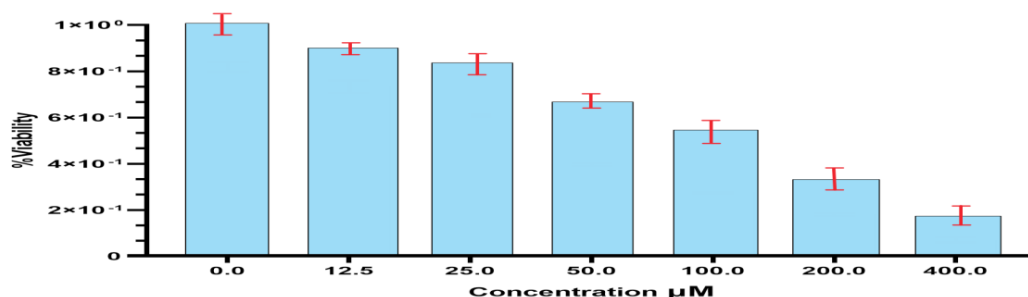


Figure (10): The inhibitory activity of the complex $[\text{Pd}_2(\text{L}) (\text{dppm})_2(\text{H}_2\text{O})_2]\text{Cl}_4$.

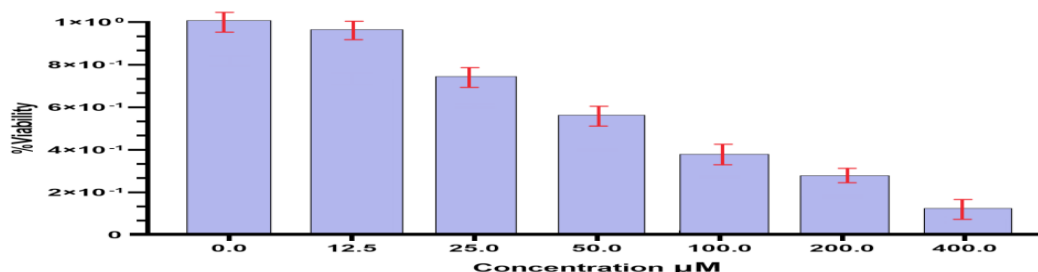


Figure 11: Inhibitory activity of $[\text{Pd}_2(\text{L}_2) (\text{dppp})_2(\text{H}_2\text{O})_2]\text{Cl}_4$

According to the Prayong classification regarding the IC_{50} standard for cancer cytotoxic samples, the IC_{50} value of the studied compounds belonged to the intermediate cytotoxic category since the obtained IC_{50} value was approximately between 100 and 1000 micromolar. In addition, the activities of the studied compounds towards cancer

cells could be considered as a result of the composition of these compounds or the biological activity of the metal ions used in The body, where palladium ion is one of the ions that showed good efficacy against many cancer cells and its high antibacterial and antifungal activity, as it is noted through the values obtained and shown in Tables (10) and

(11) the effect of the prepared compounds against this type of cells carcinogenicity, through the ability of Schiff bases ligands and complexes of Pd(II) interacts with DNA strands and forms bonds. The results also showed that the compounds used through this association with DNA strands prevented the

division of cancer cells, which leads to programmed cell death. It is noted from the results that the palladium complex containing the dppp ligand as a participant has the lowest value of IC₅₀ and the most effective among the three studied compounds.

Table (10): Viability values (cell growth) for the studied compounds

Conc.	%Viability –Schiff base L	%Viability – [Pd ₂ (L) (dppm) ₂ (H ₂ O) ₂]Cl ₄	%Viability – [Pd ₂ (L) (dppp) ₂ (H ₂ O) ₂]Cl ₄
0	100	100	100
12.5	97.09	94.56	94.37
25	93.76	78.04	91.05
50	60.13	58.19	73.21
100	54.23	37.68	57.19
200	37.41	31.78	36.81
400	22.17	16.43	18.53

**Table (11): The IC₅₀ values of the prepared compounds
in comparison with SZ Platinum Breast Cancer Growth (MCF-7)**

Compounds	IC ₅₀ ^{a,b} of MCF-7± SD (mM)
Schiff base- L	118.30± 3.826
Cis-platin ^c	39.26± 0.92

a- The IC50 half of the concentration inhibiting the growth of cancer cells was calculated after 24 hours using different concentrations and three replicates of the experiment, depending on the MTT method.

b- The IC50 was calculated in mM units of the dose-response curve.

c- Cis-platin was used as a positive reference

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