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Synthesis and Characterization of A New Ligand (DPTYEDAPIBO) Derived from 2-Aminothiazole and Preliminary MCF-7 Cytotoxicity Evaluation

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Abstract

A series of new complexes were prepared by ligand (2E,3E)-3-((2-(((1E,2E)-1,2-diphenyl-2-(thiazol-2-ylimino) ethylidene) amino) phenyl) imino) butan-2-one oxime (DPTYEDAPIBO) interaction with the following metal chlorides: Ni (II), Cu (II), and Pt (IV), as well as AgNO3 dissolved in ethanol. The ligand (DPTYEDAPIBO) is prepared in three steps: The first step is the preparation of compound (A) (E)-1,2-diphenyl-2-(thiazol-2-ylimino) ethan-1-one which is prepared from the reaction of 2-Aminothiazol and benzil. The second step involves the reaction of benzene-1,2-diamine with (E)-3-(hydroxyamino) butan-2-one to form compound (B). As for the third step, it involves the reaction of compound (A), with compound (B), to form the ligand. The structures of the ligand and its complexes are confirmed by FTIR, 1H,13CNMR, and UV-Vis spectra, melting points, molar conductivity, elemental analyses (C.H.N), and magnetic susceptibility measurements. The synthesized complexes are prepared in a (1:1) ratio (M: L). These measurements suggest octahedral geometry for each of the Ni (II), Cu (II), and Pt (IV) complexes and tetrahedral geometry for the Ag (I) complexes. Each of the ligands and the platinum complex were tested for cytotoxic activity, and it was discovered that the platinum complex is more effective against breast cancer cells (MCF-7) while having less effect on normal cells (WRL-68) than (DPTYEDAPIBO) ligand. An antioxidant test was also performed for the prepared compounds.
Keywords: 2-aminothiazoles, Antioxidant, Breast anticancer, platinum (IV) complex.

تحضير ووصف الليكاند الجديد (DPTYEDAPIBO) المشتق من ٢-أمينوثيازول مع دراسة التأثير السمي على خلايا سرطان الثدي

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الخلاصة

تم تحضير سلسلة من المعقدات الجديدة عن طريق تفاعل الليكاند(3E,2E) -٣-((2E,1E)) -2,1-داي فنيل-٢-(ثيازول-٢-يل امينو) اثيل أدين) امينو) فينول (DPTYEDAPIBO) مع كلوريدات المعادن التالية: النيكل(II) والنحاس(II) والبلاتين(IV) بالإضافة إلى نترات الفضة (I) المذاب في الإيثانول.. تم تحضير الليكاند (DPTYEDAPIBO) في ثلاث خطوات: الخطوة الأولى هي تحضير المركب(A) 2,1-داي فنيل-٢-(ثيازول-٢-يلامينو) ايثان-١-ون) الناتج من تفاعل ٢-أمينوثيازول المذاب في الإيثانول مع البنزيل. فيما تضمنت الخطوة الثانية تحضير مركب ((2)-3 B-امينوفنيل) امينوبيوتان-٢-ون اوكسيم) الناتج من تفاعل (بنزين١,٢-داي امين) مع (-٣ (هيدروكسي امينو) البيوتان-٢-ون. أما بالنسبة للخطوة الثالثة، فهي تفاعل ناتج الخطوة الأولى، المركب (A)، مع ناتج الخطوة الثانية، المركب (B)، لتكوين الليكاند (DPTYEDAPIBO). تم تشخيص الليكاند ومعقداته بواسطة كل من FTIR، ^{1}H، $^{13}CNMR$، أطياف الاشعة فوق البنفسجية والمرئية، نقاط الانصهار، التوصيلية المولارية، التحليل العنصري (C.H.N)، الامتصاص الذري وقياسات الحساسية المغناطيسية. تم تحضير المعقدات بنسبة (١: ١) (M: L). تشير القياسات إلى ان الشكل الهندسي يكون ثماني السطوح لكل من معقدات النيكل (II) والنحاس (II) والبلاتين (IV); بينما يكون رباعي السطوح لمعقد الفضة (I). اجري اختبار الليكاند ومعقد البلاتين لنشاط مضاد السرطان، واكتشف أن معقد البلاتين أكثر فعالية ضد خلايا سرطان الثدي (MCF-7) بينما يكون له تأثير أقل على الخلايا الطبيعية (WRL-68). كذلك تم إجراء اختبار مضادات الأكسدة للمركبات المحضرة.
الكلمات المفتاحية: ٢-امينوثيازول، مضادات الاكسدة، مضاد لسرطان الثدي، معقد البلاتين. Pt (IV).

Introduction

Heterocyclic compounds are the most important class of organic compounds that have a ring system, and which contains carbon atoms as well as at least one heterogeneous atom, including (nitrogen, oxygen, sulfur, boron, phosphorous, arsenic, silicon, and antimony[(1)] .

These compounds include quaternary, pentagonal, hexagonal and heptagonal, some of which are aromatic and some are non-aromatic[2]. Heterocyclic compounds are naturally present and have biological activity, and they are present in vitamins, including (vitamin C, vitamin B1,B2)[3], as well as in antibiotics such as penicillin and tetracycline, and in hemoglobin and chlorophyll. Heterocyclic rings are also found in the synthesis of nucleic acids (RNA, DNA)[4]. There are many prepared cyclic compounds of greatimportance in the field of medicinal chemistry[1] and pharmaceutical preparations[5], as it is found that 90% of the prepared medicines contain heterogeneous rings because they have biological activity[6] as an antibacterial[7], Anti-vascular disease and an anticancer[8] .

Compound 2-aminothiazole is one of the Penta-Heterocyclic compounds that contains in its composition two heterogeneous atoms: the sulfur atom and the nitrogen atom, in addition to carbon atoms[9] .The thiazole ring is flat, aromatic, and possesses a non-bonding electron pair. It possesses a degree of delocalization, which makes the aromatic ring higher than that of the oxazole ring[10] . Thiazoles are present in many natural compounds, with biological activity, including vitamin B1 and penicillin[11]. The thiazole ring has shown different biological activities[12], including anti-bacterial, anti-fungal, anti-viral[13], anti-inflammatory, anti-tumor, anti-cancer[14][15], and anti-oxidant[16]. It is essential for generating biologically active molecules and is considered the cornerstone in the preparation of drug therapies[17], such as sulfur drugs, insecticides, and fungicides, in addition to its formation of different types of dyes, as well as entering into the composition of chemical accelerators, and a corrosion inhibitor which is used to protect mild steel[18]. The aim of this study is to synthesize ligand of aminothiazoles and its platinum (IV) complex. Then evaluate the antioxidant activity and the cytotoxicity against MCF-7.

Materials and Methods

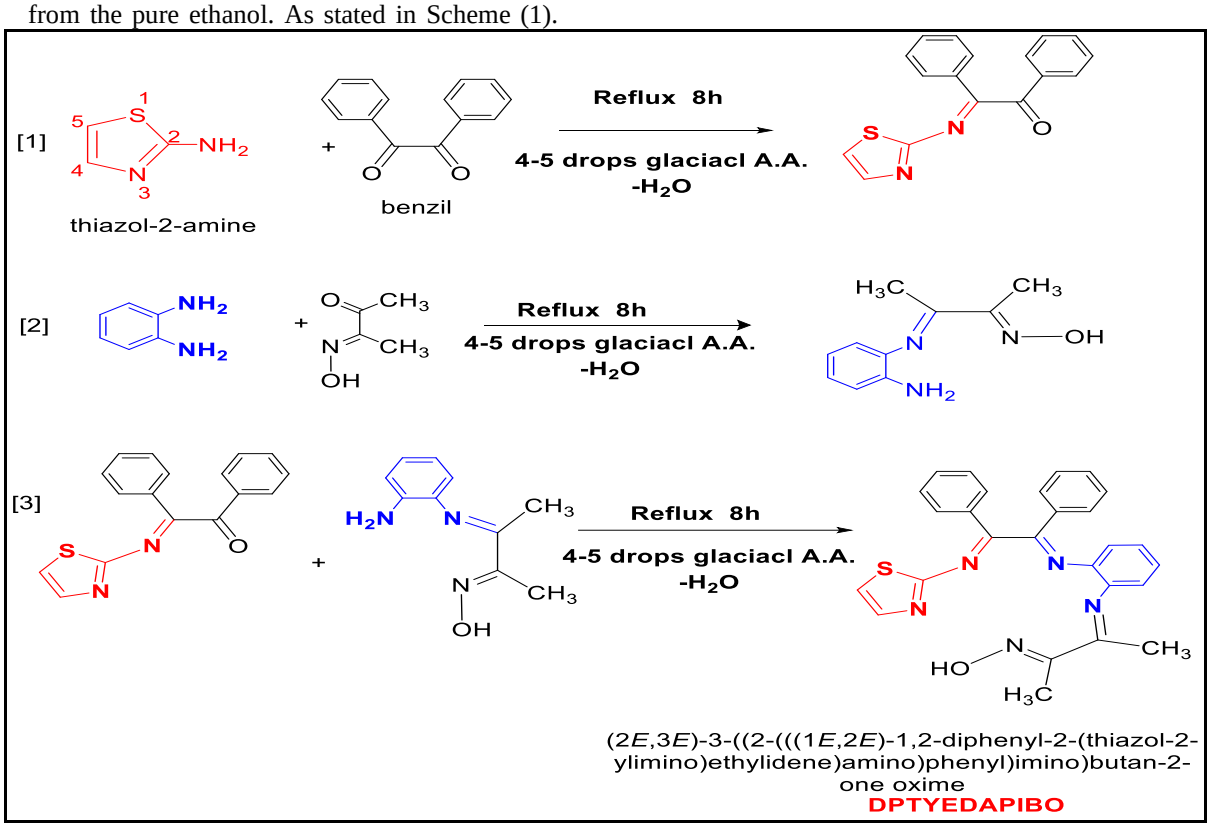
All chemicals are provided by HIMEDIA, BDH, Merck, and Al-Drich, ^{1}H,^{13}CNMR spectra are recorded on the Fourier Transform Varian Spectrometer, operating at 300 MHz with a standard internal reference in DMSO-d_6 solvent, measured in Iran-Tehran. Utilizing UV-Vis spectroscopy, wave numbers between (200-1000) nm have been recorded (Shimad-zuU.V-165PCS spectrophotometer), The measurement was done at Al-Qadisiyah University - College of Education. FTIR Spectra with the range of (400-4000 cm-1) is recorded by using FTIR 8400S Shimadzu Spectrophotometer (Japan), The measurement was done at Al-Qadisiyah University - College of Education. Elemental analyses (C.H.N) was determined by using an EA 300 C.H.N Element Analyzer's micro analytical unit, Measured in Iran-Tehran. X-ray diffraction was performed on a Bestec Germany Aluminum anode type X-Petro with a wavelength of 1.54A°, X-ray beam (Cu k), material=Cu, potential = 40KV, and supply = 30Ma, Measured in Iran-Tehran. Melting points of all compounds were determined by the Stuart melting point. Magnetic susceptibility measurements were obtained at room temperature applying method using Balance Magnetic Susceptibility Model MSB-MKI, Measured in Iran-Tehran. Flame atomic absorption spectrophotometer, Shimadzu. AA-6300 was used to determine metal percentage in the complexes, Measured in Iran-Tehran. Images from the HITACHI S-4160's field scanning electron microscopy (FE-SEM) were collected, Measured in Iran-Tehran. While a toxicological study was conducted at the Microtechnology Research Center - Al-Nahrain University – Baghdad

Preparation of the ligand (DPTYEDAPIBO)

Three stages are used to prepare the (DPTYEDAPIBO) Ligand.

- The first stage: involves creating (compound A) of (E)-1,2-diphenyl-2-(thiazol-2-ylimino) ethan-1-one from the reaction (2.00 g, 0.02mole) 2-aminothiazol dissolved in 25 mL of the absolute ethanol with (4.20 g, 0.02mole) Benzil which is also dissolved in 25 mL ethanol and drops of glacial acetic acid with continuous stirring. The mixture is refluxed for 8 hours. After that, it is cooled, filtered, and collected. Then, it is recrystallized by using pure ethanol. Then the precipitate is left to dry, collected, and weighed so that it will be employed in the second stage, to get an 84% yield percentage and the melting point is (96-94).
- The second stage: includes the preparation of (2E,3E)-3-((2-aminophenyl) imino) butan-2-one oxime (compound -B) from the reaction (3.24 gm, 0.03mmole) benzene-1,2-diamine dissolved in 25 mL of the absolute ethanol with (3.033 g, 0.03mole) (E)-3-(hydroxyamino) butan-2-one also dissolved in 25 mL ethanol and drops of glacial acetic acid with continuous stirring. The mixture is refluxed for 8 hours. After that, it is cooled, filtered, and collected.
- The third stage preparation of the (DPTYEDAPIBO) ligand (2E,3E)-3-((2-((1E , 2E) - 1,2- dipheny l-2-(thiazol-2-ylimino) ethylidene) amino) phenyl) imino) butan-2-one oxime. Ligand is prepared by a solution (4.38 g, 0.015mole) of the A-compound in 25 mL of ethanol with a solution (2.87 g, 0.015 mol) of the (compound -B) in 25 mL of ethanol, with the addition of (5-6) drops of glacial acetic acid to the mixture. The mixture is refluxed for 8 hours, then

cooled. Re-crystallization of precipitation by ethanol, filtration, and drying are seen to occur from the pure ethanol. As stated in Scheme (1). The yield is 79 %, and the melting point is (111 °C).



Scheme 1. Synthesis of the 2-(1E,2E)-1,2-diphenyl-2-(thiazol-2-ylimino) ethylidene) amino) phenol (DPTYEDAPIBO) ligand.

Synthesis of the Complexes

The complexes of Ni (II), Cu (II), Ag(I) and Pt (IV) are prepared with (DPTYEDAPIBO) ligand by a ratio (1: 1), (M: L). The complexes are prepared from a reaction of (0.372 g, 0.8 mole) of (DPTYEDAPIBO) ligand solvent in 10mL of ethanol, with 0.8 mole chlorides of each of Ni (II), Cu (II), Pt (IV) and $AgNO_3$ which are dissolved in 5mL absolute ethanol. The mixture then, is refluxed with stirring for 2 hours and cooled, filtrated and dried[19].

Measuring antioxidant capacity

Using a spectrophotometric method, the ligand (DPTYEDAPIBO) and metal complexes were tested for radical scavenging activity against the stable free radical 1,1-diphenyl-2-picrylhydrazyl (DPPH). In practice, 1 mL of the ligand and metal complexes in DMSO were mixed with 1 mL of 0.1 mM DPPH in methanol at various concentrations (3.90-500 g/mL). The tested samples were allowed to react for 30 minutes with (DPPH). The absorbance at 517 nm was measured after 30 minutes of incubation in the dark at room temperature (ShimadzuU.V-165PCS spectrophotometer). The linear regression analysis was used to determine the IC_{50} value (which is defined as the concentration of the tested compound that causes 50% of RSA, the lower the value of IC_{50}, the more efficient the antioxidant) from the obtained RSA values (GraphPad Prism 8.3.1 software)[20].

(Cytotoxic assay MTT)

The breast cancer cell line (MCF-7) and the normal human liver cell line were used in this study (WRL 68). Cell lines were stored in liquid nitrogen and maintained and tested at Al-Nahrain University's Biotechnology Research Center. After completely preparing the cells of cancer lines (MCF-7) and the suspension at a concentration of ($1*10^5$ cells/well), the cell suspension was placed in a plate with 96 holes and a flat base, and it was incubated in an incubator with 5% carbon dioxide (CO_2) at 37°C for 24 hours. Then pour 100 microliters of this suspension into each well. Following that, the concentrations prepared for each of the ligands and the platinum complex (25, 50, 100, 200, and 400 µg/mL) were added to those wells at a rate of three wells for each concentration. The plate was then incubated for a full day at 37 °C, with 10 mL of MTT solution at a concentration of 0.45 mg/mL added to each hole. The plate was then incubated at 37 °C for four hours. Each hole was filled with 100 L of DMSO solution and incubated for 5 minutes[21]. Finally, the absorbance of that sample was measured at 570 nm using the ELASIS device, and the optical density readings were statistically analyzed to calculate the IC_{50}.

Results and Discussion

The new (DPTYEDAPIBO) ligand (2E,3E)-3-((2-(1E,2E)-1,2-diphenyl-2-(thiazol-2-ylimino) ethylidene) amino) phenyl) imino) butan-2-one oxime is synthesized from the reaction of 2-aminothiazol with Benzil. Then, this product reacts with(2E,3E)-3-((2-aminophenyl) imino) butan-2-one oxime to form a ligand. The complexes have been prepared from reaction of the ligand (DPTYEDAPIBO) with metal chlorides hydrate which is solved in ethanol. Table (1) shows the physical attributes and the elemental analyses. All the synthesized complexes (Ni (II), Pt (IV), Cu (II) and Ag (I)) are created in a (1:1) ratio (M: L) complexes.

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Table1. Elemental analysis and some physical properties of the ligand (DPTYEDAPIBO) and its metallic complexes.

Compound	Color	M P (^{0}C)	Yield %	M. W *(gm/mole)*	*Calc. (Found)%* C	H	N	M
Ligand (DPTYEDAPIBO)	Brown	111	79	465.16	69.66 (71.97)	4.98 (5.56)	15.04 (14.32)	---- (----)
[Ni (DPTYEDAPIBO)Cl_2]. H_2O	Dark green	120	67	613.2	52.89 (53.17)	4.11 (4.81)	11.42 (10.00)	9.57 (9.98)
[Cu (DPTYEDAPIBO)Cl_2]. H_2O	Dark Brown	118	72	547.1	59.27 (61.64)	4.48 (4.61)	12.80 (11.87)	10.90 (11.61)
[Ag (DPTYEDAPIBO)].NO_3	green	123	69	591.5	54.83 (55.58)	4.12 (4.26)	11.84 (10.89)	17.79 (18.24)
[Pt (DPTYEDAPIBO)Cl_2] $Cl_2.H_2O$	purple	114	77	749.6	43.26 (44.11)	3.36 (4.05)	9.34 (8.77)	25.70 (26.03)

Mass spectrum of the (DPTYEDAPIBO) ligand

Mass spectrum is one of the analytical techniques that is used in accurate diagnosis to know the prepared compound and what it contains of the elements included in its composition and its molecular and structural formula. The main function of this apparatus is the fragmentation of ions, which is dependent on the ratio of mass to charge, which is measured by a mass spectrometer. Figure (1) shows the (DPTYEDAPIBO) ligand fragmentation and exhibited peak at (464.3 = m/z$^+$) for M-1$^+$.

1H and ^{13}CNMR Spectra of the Ligand (DPTYEDAPIBO)

The ^{1}HNMR Spectrum of the (DPTYEDAPIBO) Ligand exhibits several signals at the two methane groups (s, 6H, δ = 1.956 ppm) due to the protons of methane found in the 3-(hydroxyamino) butan-2-one. while the multiple signals are observed at the range (m, 4H, δ = 7.396-7.858 ppm) due to the protons of phenyl group(benzene-1,2-diamine)[22], where the multiple signals at (m, 5 H, δ = 7.796-7.453 ppm) and (m, 5 H, δ =7.464-8.097 ppm) attributed to ring's protons found in Benzil[23] . While doublet signals at (d, 2H, = 7.176-7.565 ppm) were attributed to Thiazole ring protons[24], A singlet other signal appeared at (s, 1H, δ= 11.439 ppm) due to Hydroxyl proton (OH)[25],as shown in Figure (2).

The ^{13}CNMR Spectrum of the Ligand (DPTYEDAPIBO

The ^{13}CNMR spectrum of the ligand exhibited the signal at (9.811,23.209 ppm) belongs to carbon (C_{33},C_{32}) of the two group (CH_3) found in the 3-(hydroxyamino) butan-2-one[26]. while signal at (40.111 ppm), was due to DMSO, whereas carbon (C_9) of the group (CH) gave the signal at (128.456 ppm) due to thiazole[27]. Several signals at (129.273-130.837ppm), (129.001-130.068ppm) and (128.982-128.457ppm) belonging to the carbon atoms (C_{12}-C_{16}), (C_{17}-C_{21}) and (C_{24}-C_{27}) respectively is found in each of the Phenyls of Benzil and the benzene-1,2-diamine[28]. As for these three signals at (132.665,135.992 ,139.208-ppm) exhibited in the carbon atoms (C_{10},C_{25},C_{26}) is due to the connection of carbon atoms with nitrogen atoms[29]. The following five carbon atoms (C_1, C_2, C_7, C_{29}, C_{30}) gave the values between (140.922-195.272ppm) due the group azomethane carbon (-C = N-)[30] . as shown in Figure (3).

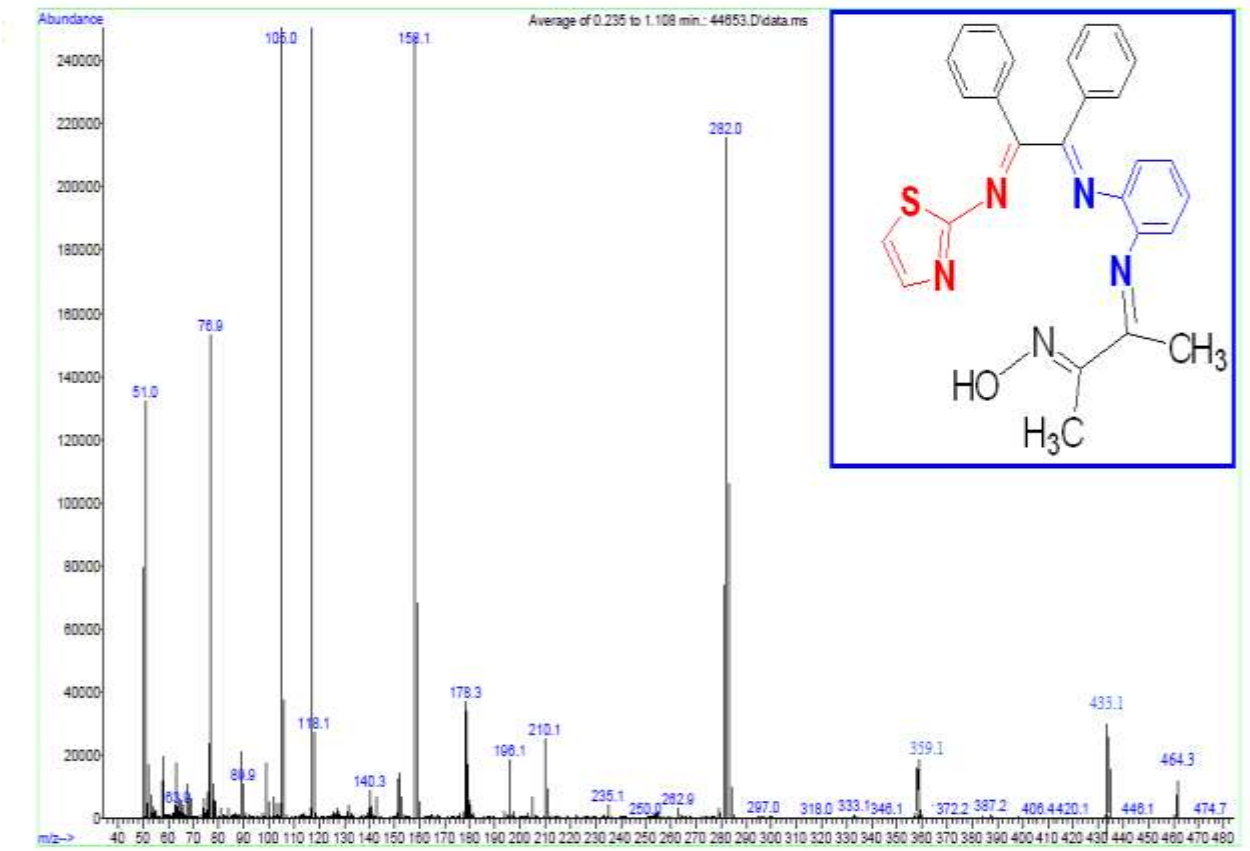

Figure 1. Mass spectrum of schiff base (DPTYEDAPIBO) ligand.

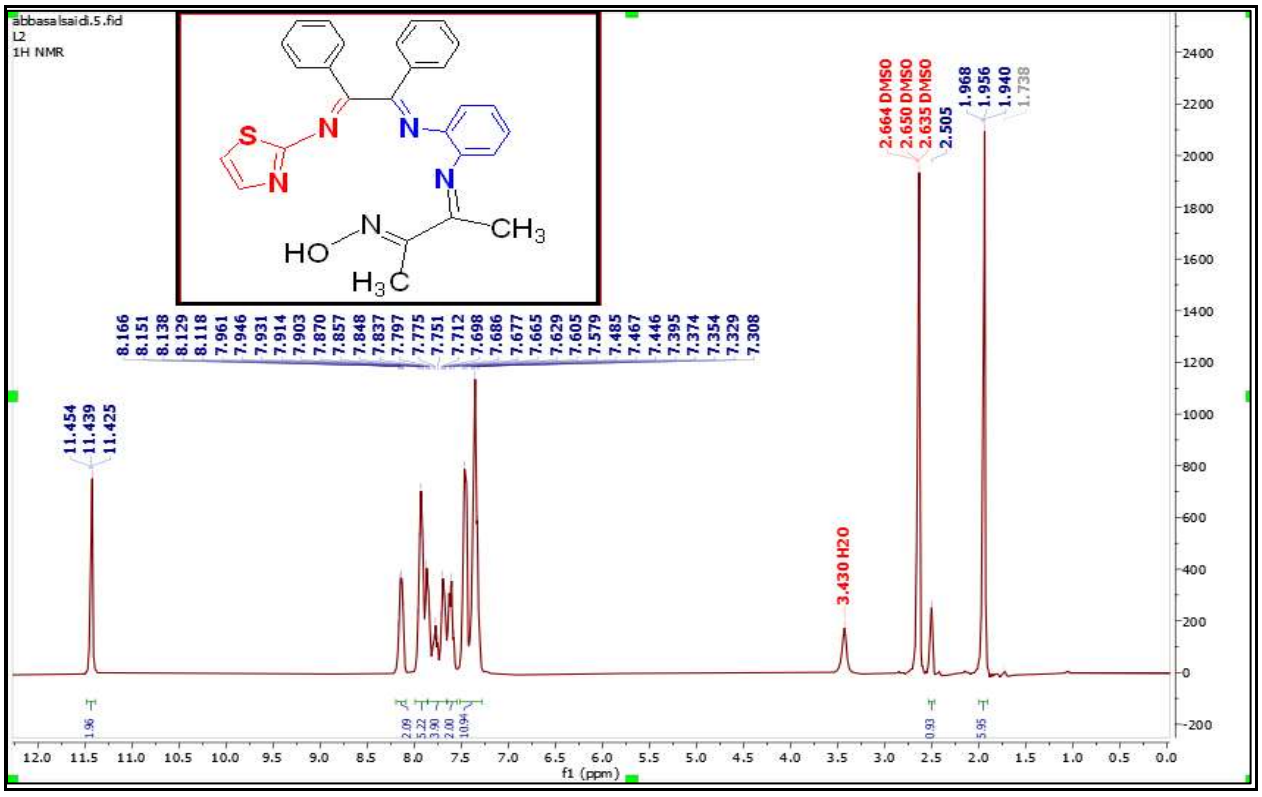

Figure 2. 1HNMR spectra of the (DPTYEDAPIBO) ligand .

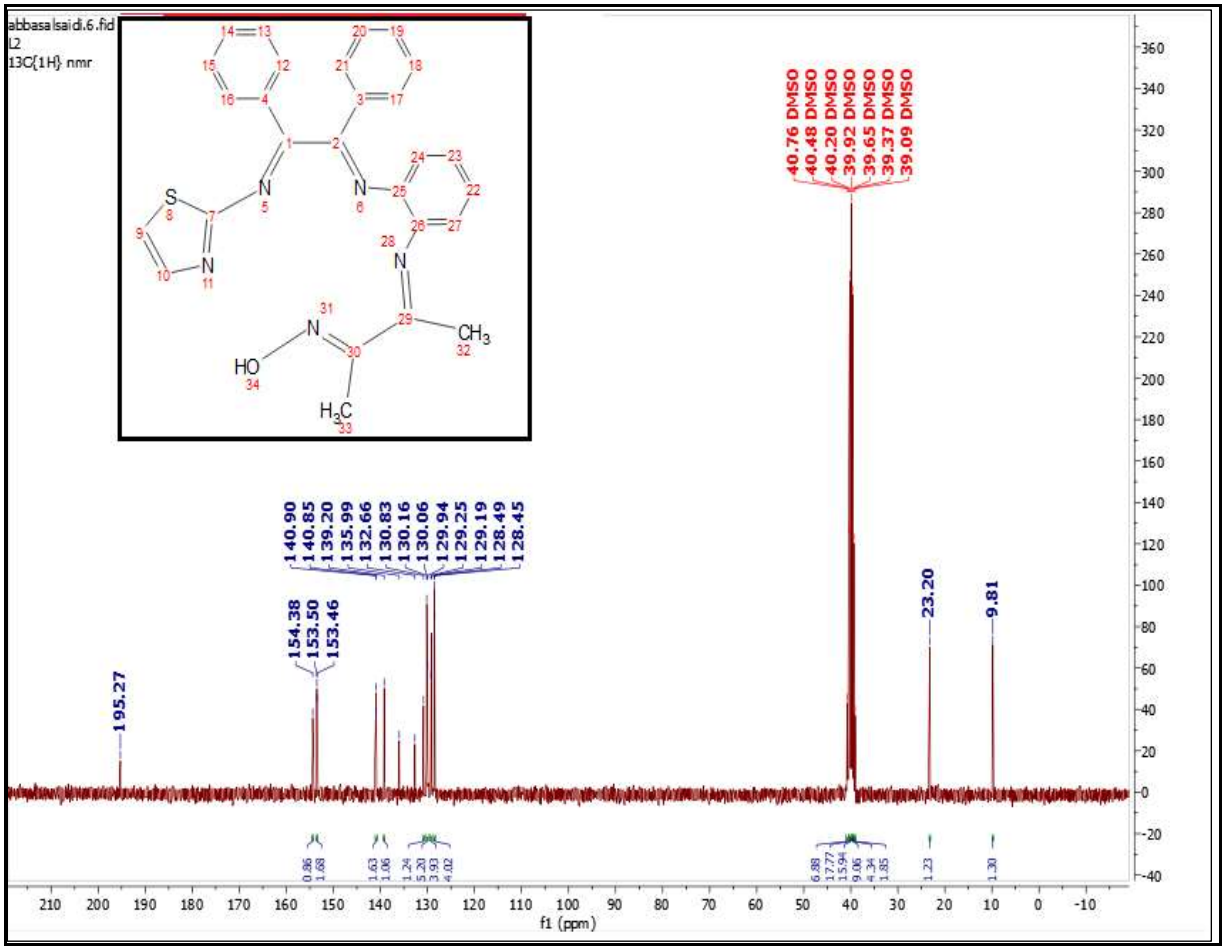

Figure 3. 13CNMR spectra of the (DPTYEDAPIBO) ligand .

The FTIR Spectra

Following the diagnostic of the free ligand (DPTYEDAPIBO) by infrared spectrum, it was discovered to have several functional groups, which came as Figure (4) showed many bands, the most important of which is a band at the wave number (3186, 3062, 2885 cm^{-1}) which belongs to each of the hydroxyl group (O-H) and two groups of (C-H) aromatic and aliphatic, respectively. An important band belonging to the azomethine group (C=N) also appeared, indicating the formation of the Schiff base in the ligand at the wave number (1658 cm^{-1})[31] .

The FTIR Spectra of the Complexes

A comparison was made between the (DPTYEDAPIBO) free ligand before binding to any metal and the formed complexes through the spectra, the Table (2) and Figures (5.1-5.4) show this comparison. It was observed that the uptake of the hydroxyl group (υ (O-H) in the spectrum of the complexes was shifted to higher frequencies from where it was in the ligand spectrum and also it was found that the azomethine 'υ (C = N) groups in the complexes was also shifted to higher frequencies from where it was in the free ligand[32]. This proves the occurrence of coordination process between the ligand and the metal. Finally, the appearance of bands for all the complexes except for the silver complex at the wave number (3317-3379 cm^{-1}), which belongs to the hydroxyl group (O-H) within the water of crystallization molecules[33].

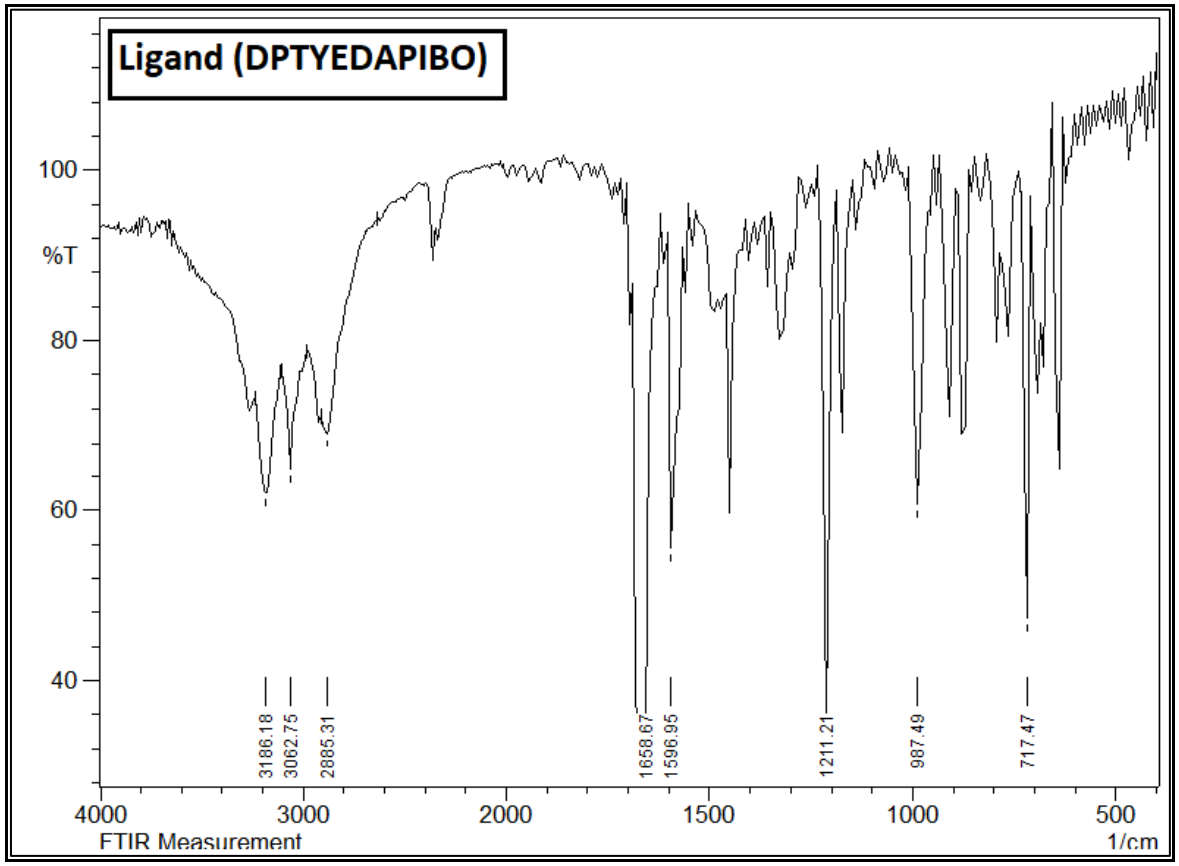

Figure 4. FTIR spectra of the synthesized(DPTYEDAPIBO) ligand.

Table 2. The important infra-red spectral bands for the synthesized ligand (DPTYEDAPIBO) and its metallic complex.

Compound	***υ(O-H) of water molecules***	***υ(O-H)***	***υ(C=N)***		**υ(C-H) Aromatic υ(C-H) Aliphatic**	***υ(M–N)***	***υ(M–O)***
			Imine	**Thiazole**			
Ligand (DPTYEDAPIBO)	----------	3186 (bro)	1658 (s)	1596 (s)	(3062) (2885)	-------	------
[Ni (DPTYEDAPIBO)Cl_2]. H_2O	3379 (bro)	3209 (w)	1666 (w)	1596 (s)	(3031) (2970)	516 (w)	462 (m)
[Cu (DPTYEDAPIBO)Cl_2]. H_2O	3301 (bro)	3206 (bro)	1674 (w)	1596 (s)	(3008) (2916)	524 (w)	462 (s)
[Ag (DPTYEDAPIBO)].NO_3	--------	3193 (bro)	1666 (w)	1596 (s)	(3062) (2885)	547 (m)	470 (m)
[Pt (DPTYEDAPIBO)Cl_2] $Cl_2.H_2O$	3317	3193	1666	1596	(3062) (2893)	516 (w)	470 (m)

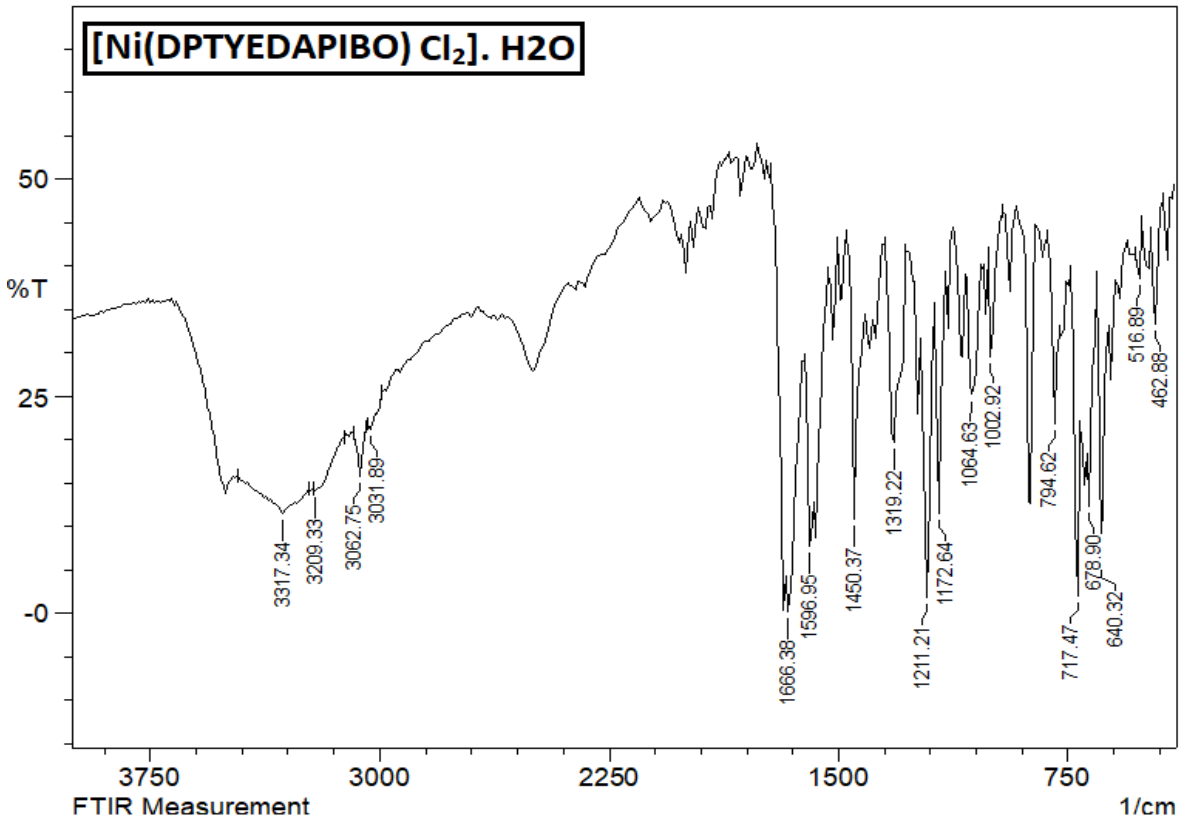

Figure 5.1. FTIR spectra of the Ni (II) complex.

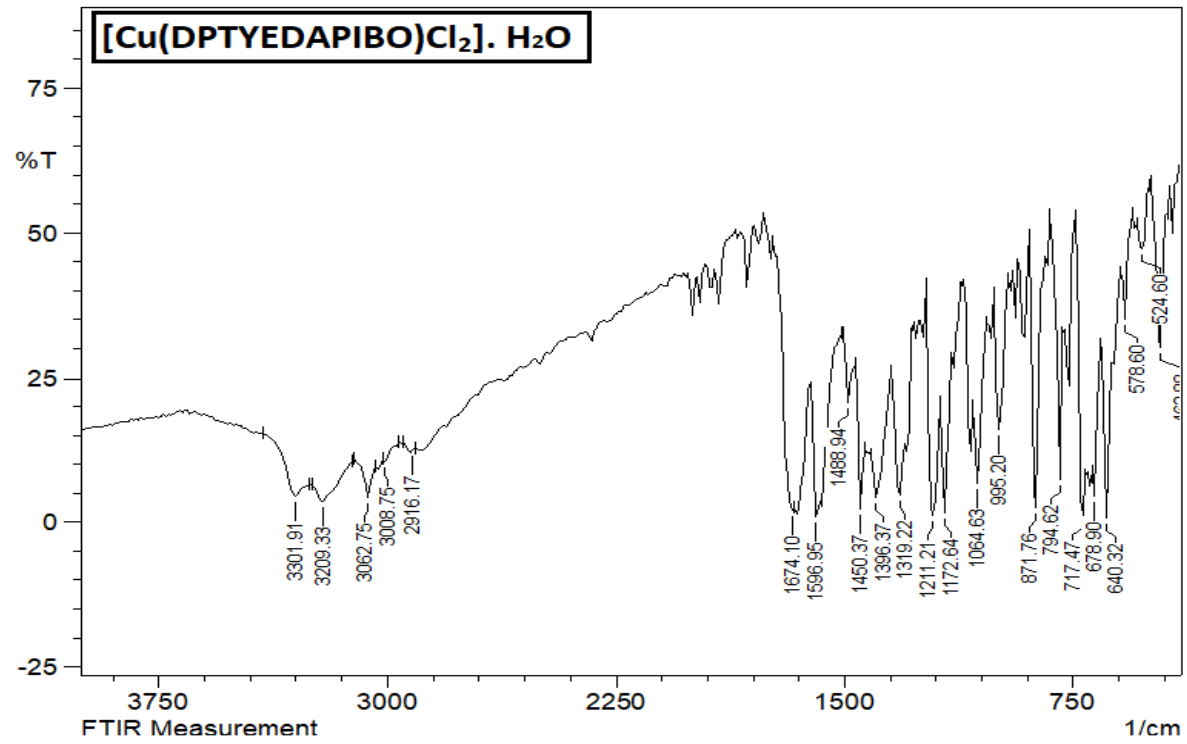

Figure 5.2. FTIR spectra of the Cu (II) complex.

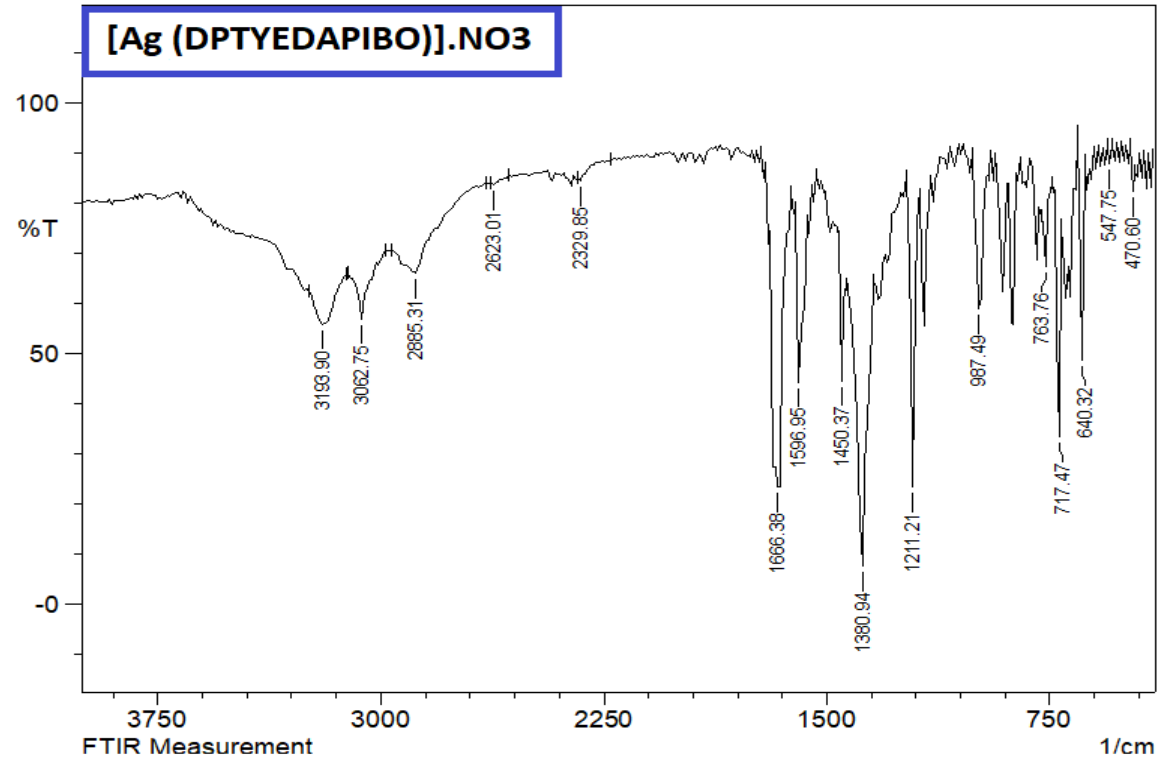

Figure 5.3. FTIR spectra of the Ag (I) complex.

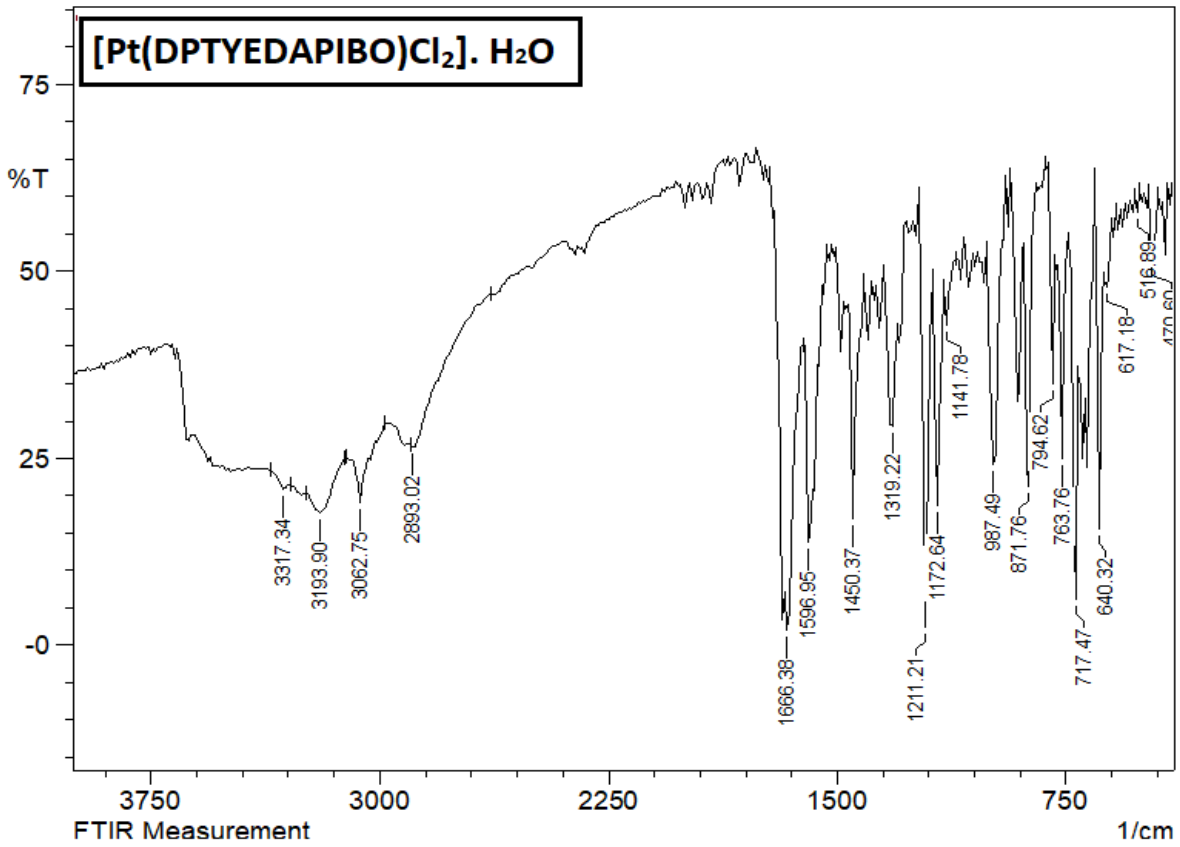

Figure 5.4. FTIR spectra of the Pt (IV) complex.

Electronic spectra

The spectra of the (DPTYEDAPIBO) free ligand in Figure (6) includes three absorption peaks, two of which are two peaks at 206 nm (48543 cm^{-1}) and 237 nm (42194 cm^{-1}) which are due to the π-π* transition type resulting from the presence of vinyl rings. While the third peak at 259 nm (38610 cm^{-1}) indicates the n-π* transition type, and this is due to each of the azomethine groups of the Schiff base and the thiazole ring[34].

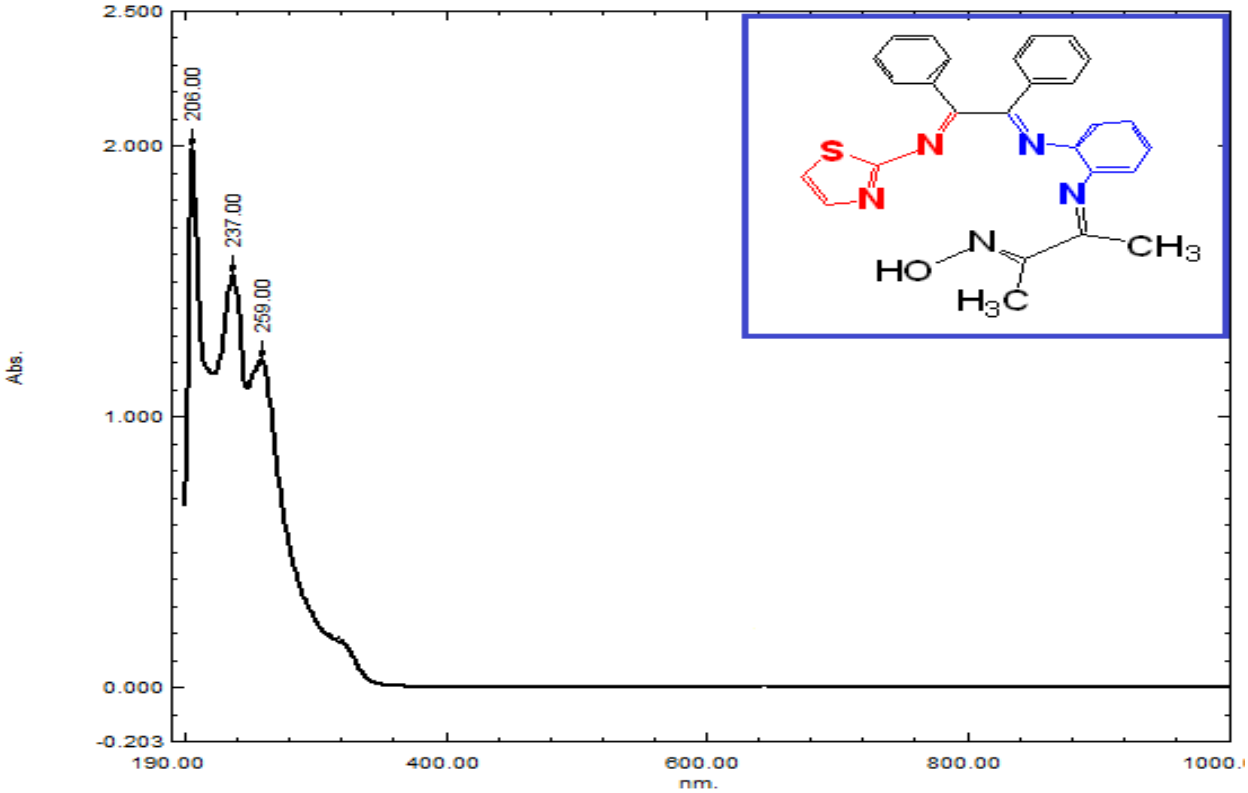

Figure 6. Electronic spectra of the synthesized (DPTYEDAPIBO) ligand.

The Electronic Spectra of the Synthesized Metallic complexes

The spectrum of the nickel (II) complex in Figures (7.1-7.4) shows multiple peaks, three of which belong to the ligand at 213 nm (46948 cm^{-1}), 245 nm (40816 cm^{-1}) and 267 nm (37453 cm^{-1}). Which shifted to higher wavelengths compared to the free ligand and this is clear evidence that the metal and the ligand are linked. There are other absorption peaks at 407 nm (24570 cm^{-1}) and 527 nm (18975 cm^{-1}) which indicate the following transitions ^3A_2g (F) $\rightarrow ^3T_2g$ (F), ^3A_2g (F) $\rightarrow ^3T_1g$ (F) respectively, confirming the regular octahedral geometry of the nickel complex μeff = 3.87 BM[35]. While the copper complex showed four peaks as shown in the Table (3), three of them belong to the ligand field, while the fourth peak has appeared at 447 nm (22371 cm^{-1}),which gave the transition type $^2B_1g \rightarrow ^2Eg$ and this shows that it has an octahedral geometric shape Surfaces and magnetic sensitivity of 1.74 BM[36] . There are no (d-d) transitions in the electronic spectrum of the silver (I) complex, the explanation for this is the saturation of orbital (d) with electrons. The silver (I) spectrum shows the appearance of multiple absorption peaks, three of which are due to the ligand field. While the peak at 331 nm (30,211 cm^{-1}) indicates a charge transfer transition (M−L) and shows that the silver complex possesses a tetrahedral geometry, μe ff = 0.0 BM[37] . Finally, the spectrum of the platinum (IV) complex shows multiple peaks, the first three peaks belong to the ligand field and the other three absorption peaks at 534 nm (18726 cm^{-1}) and 731 nm (13679 cm^{-1}) indicate the following transitions $^1A_1g \rightarrow ^1T_1g$,$^1A_1g \rightarrow ^1T_2g$, respectively . This confirms the regular octahedral geometry of the platinum (IV) complex, μe ff = 0.0 BM[38]. The proposed chemical structure formula of the complexes is depicted in Figure (7.5).

Table 3. Electronic spectra and Magnetic Moments of the ligand (DPTYEDAPIBO) and its metallic complexes.

Compounds	λ (nm)	υ⁻ (cm^{-1})	Transitions	μeff (B.M)	Hyperdization And Geometry
Ligand (DPTYEDAPIBO)	206 237 259	48543 42194 38610	π-π* π-π* n-π*	——	——
[Ni (DPTYEDAPIBO)Cl_2]. H_2O	213 245 267 407 527	46948 40816 37453 24570 18975	Ligand Field Ligand Field Ligand Field ^3A_2g (F) →^3T_2g (F) ^3A_2g (F) →^3T_1g (F)	3.87)Para.(	sp^3d^2 Octahedral Distorted
[Cu (DPTYEDAPIBO)Cl_2]. H_2O	216 248 270 447	46296 40322 37037 22371	Ligand Field Ligand Field Ligand Field ^2B_1g →^2Eg	1. 74)Para.(	sp^3d^2 Octahedral Distorted
[Ag (DPTYEDAPIBO)].NO_3	219 250 272 331	45662 40000 36764 30211	Ligand Field Ligand Field Ligand Field Charge transfer (MLCT)	0.00 (Dia.)	sp^3 Tetrahedral
[Pt (DPTYEDAPIBO)Cl_2] Cl_2.H_2O	220 252 274 534 731	45454 39682 36496 18726 13679	Ligand Field Ligand Field Ligand Field ^1A_1g →^1T_1g ^1A_1g →^1T_2g	0.00)Dia.(	d^2 sp^3 Octahedral Distorted

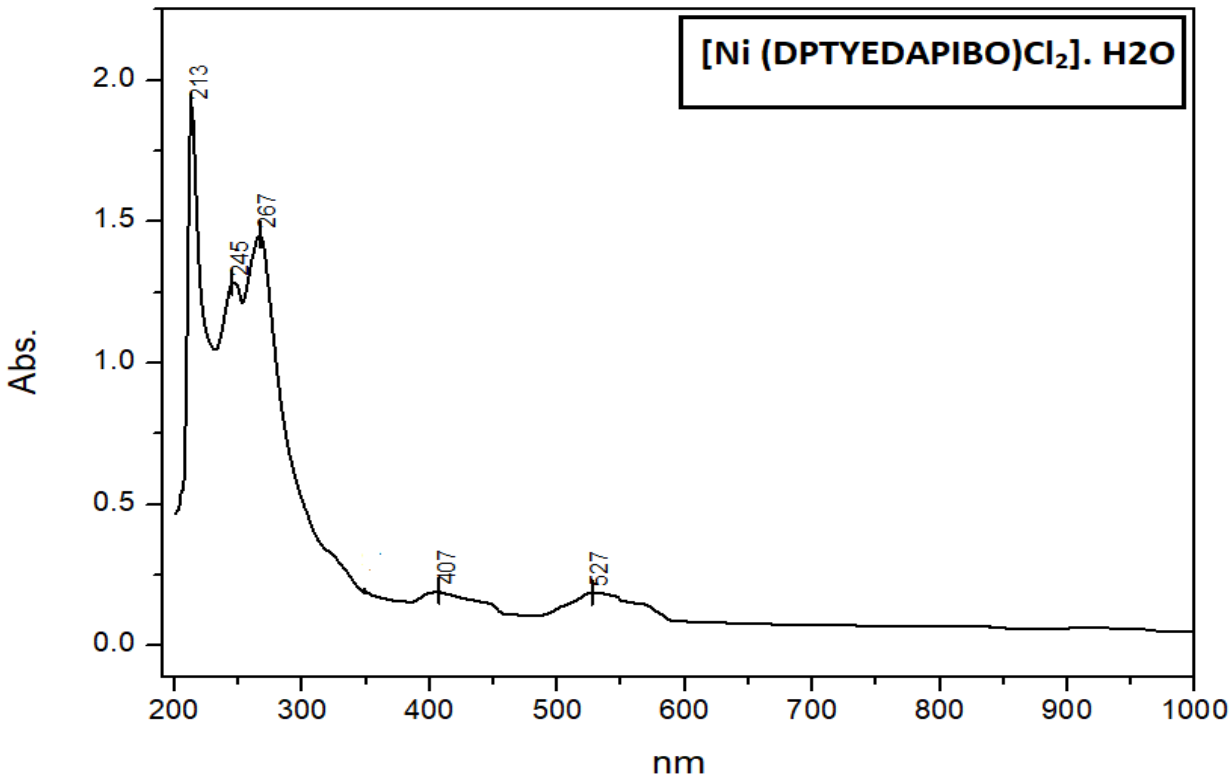

Figure 7.1. The absorption peaks of each of the Ni (II)complexes.

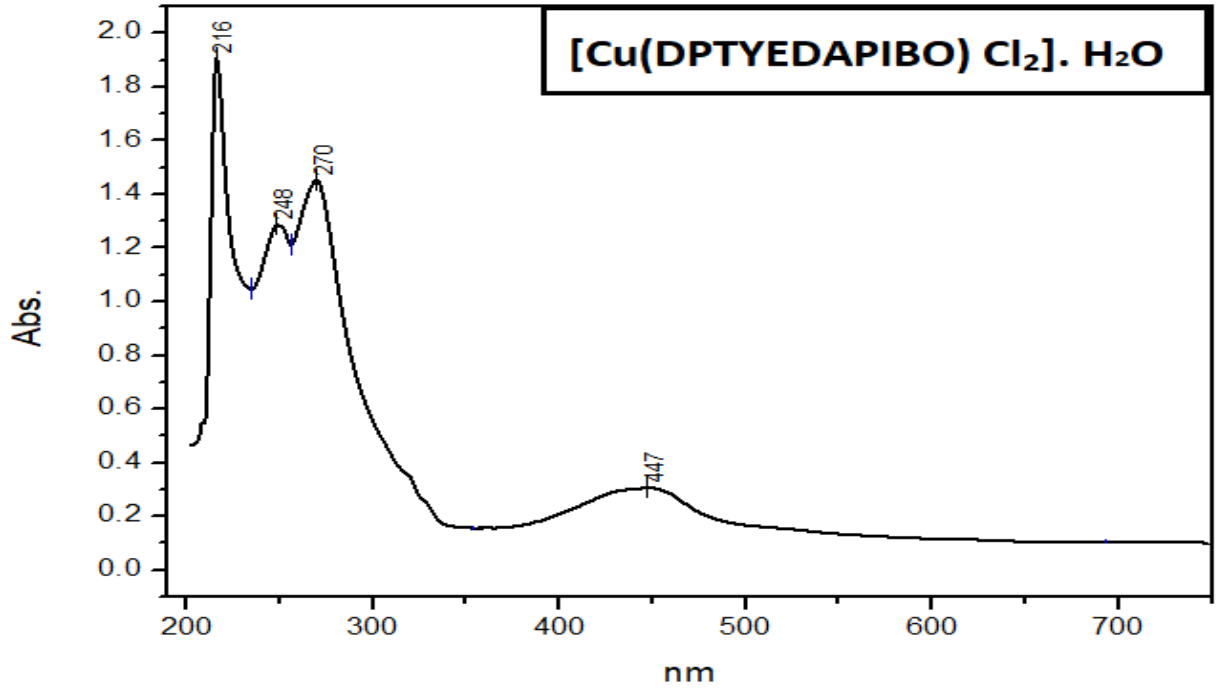

Figure 7.2. The absorption peaks of each of the Cu (II)complexes.

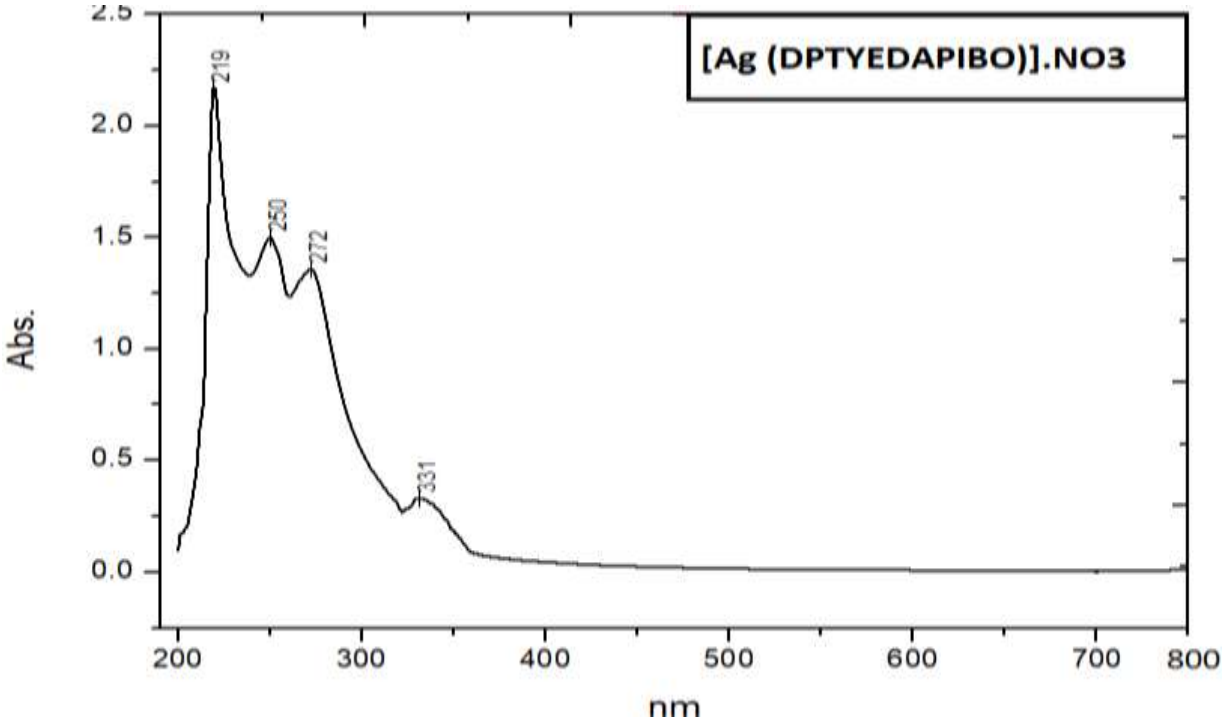

Figure 7.3. The absorption peaks of each of the Ag (I)complexes.

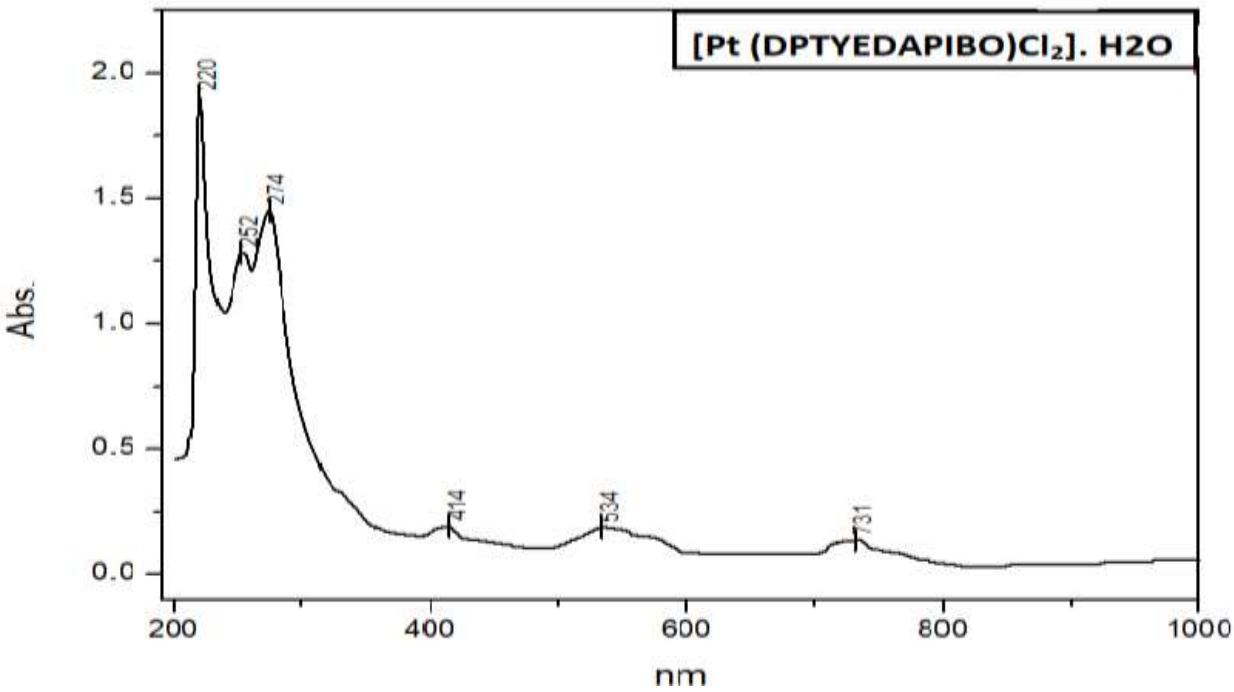

Figure 7.4. The absorption peaks of each of the Pt (IV)complexes.

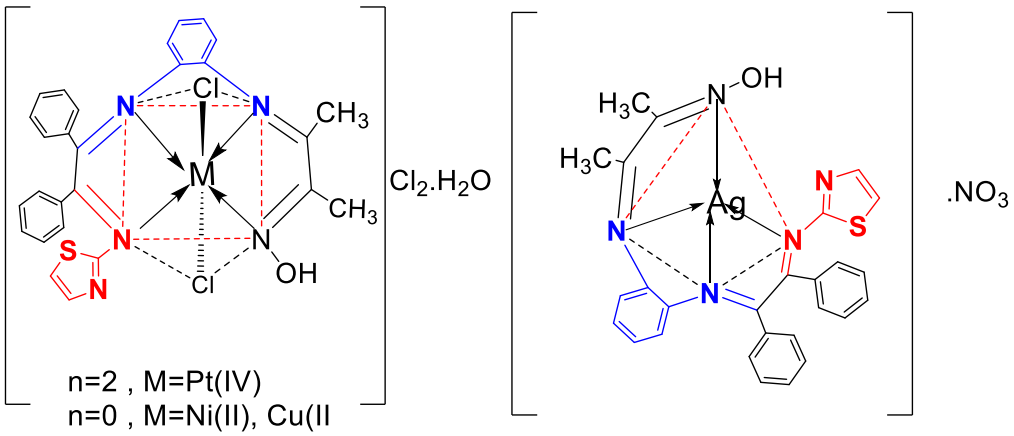

Figure 7.5. The proposed chemical structure formula of the complexes.

The molar electrical conductivity measurement is one of the important means by which it is possible to know the ionic formula of the metal complexes in their solutions from which can be used to suggest the stereoscopic forms of the complexes and figuring their structural formulas. The measure of molar conductivity depends on the number of ions liberated from the complex in the solution, the smaller the size the less electrical conductivity, in this case it can be neglected, but if the size is bigger, the degree of electrical conductivity will be high. It is best to not use water as a solvent in measuring the molar electrical conductivity of coordination complexes, and the reason is attributed to the difficulty of dissolving the complexes in water and also water can lead to decomposing of the complexes. In order to avoid this, organic solvents are often used, such as: dimethyl sulfur dioxide, methanol, ethanol, dimethylformamide, and others, because they have high dielectric constants and low viscosity. To measure the molar electrical conductivity of these compounds at a concentration of ($1x10^{-3}$ M), and at room temperature. Ethanol was used as a solvent. Table (4) shows the molar electrical conductivity values at concentration ($1*10^{-3}$ M) for different types of complexes in ethanol solvent[39].

Table 4. Molar conductivity of the ligand (DPTYEDAPIBO) and its metallic complexes.

NO	Compound	Λ (ohm^{-1}, cm^2, $mole^{-1}$)	Ionic ratio
1.	[Ni (DPTYEDAPIBO)Cl_2]. H_2O	11.9	no ionic
2.	[Cu (DPTYEDAPIBO)Cl_2]. H_2O	8.4	no ionic
3.	[Ag (DPTYEDAPIBO)].NO_3	29.9	Ionic (1:1)
4.	[Pt (DPTYEDAPIBO)Cl_2] Cl_2.H_2O	31.5	Ionic (1:2)

X-Ray Diffraction

The ligand (DPTYEDAPIBO) and complexes of nickel, platinum, silver, and copper were found to have crystal structures, which means they have a crystalline level and a crystal lattice, by studying the X-ray diffraction spectra. This was also demonstrated in the Figures (8.1-8.2) and Table (5) below. by comparing the intensity and locations of the data's peaks with the international standard cards.it was found that there is no presence of any odd locations or peaks that belonged to a substance that was not initially present in the basic compounds, the reason for that is that the compounds are new and also due to the lack of comparison with the various international standard cards. It was found that the manufactured materials can be categorized as nanoscale compounds.

Table 5. Crystallographic data for (DPTYEDAPIBO) ligand and its complexes.

Compound	No.	Peak Position °2Θ	Height [cts.]	Peak Width (FWHM)	d-spacing [Å]	Rel. Int . [%]	D Crystal-lite size(nm)
Ligand (DPTYEDAPIBO)	1-	25.1721	961.39	0.1574	3.53795	100.00	54.04
	2-	12.4392	899.50	0.2362	7.11596	93.56	35.35
	3-	26.5790	782.58	0.2755	3.35378	81.40	30.96
	4-	17.6751	526.97	0.1574	5.01802	54.81	53.37
	5-	16.3025	491.10	0.1968	5.43731	51.08	42.61
	6-	22.7734	377.65	0.1574	3.90486	39.28	53.80
[Ni(DPTYEDAPIBO)Cl_2].H_2O	1-	12.1687	1994.35	0.1181	7.27353	100.00	70.69
	2-	25.2797	1861.02	0.1574	3.52312	93.31	54.05
	3-	17.7639	744.97	0.1181	4.99315	37.35	71.14
[Cu(DPTYEDAPIBO)Cl_2].H_2O	1-	25.2672	2679.29	0.1181	3.52484	100.00	72.03
	2-	12.1183	1614.55	0.1181	7.30366	60.26	70.69
	3-	24.4079	1315.47	0.1574	3.64696	49.10	53.96
[Ag(DPTYEDAPIBO)].NO_3	1-	9.4838	735.76	0.1181	9.32575	100.00	70.53
	2-	25.2759	639.62	0.1181	3.52365	86.93	72.03
	3-	24.4360	373.27	0.1181	3.64282	50.73	71.92
[Pt(DPTYEDAPIBO)]Cl_2.H_2O	1-	25.2550	681.08	0.1181	3.52651	100.00	72.03
	2-	24.4253	623.68	0.1181	3.64440	91.57	71.92
	3-	17.7967	297.62	0.1574	4.98401	43.70	53.37

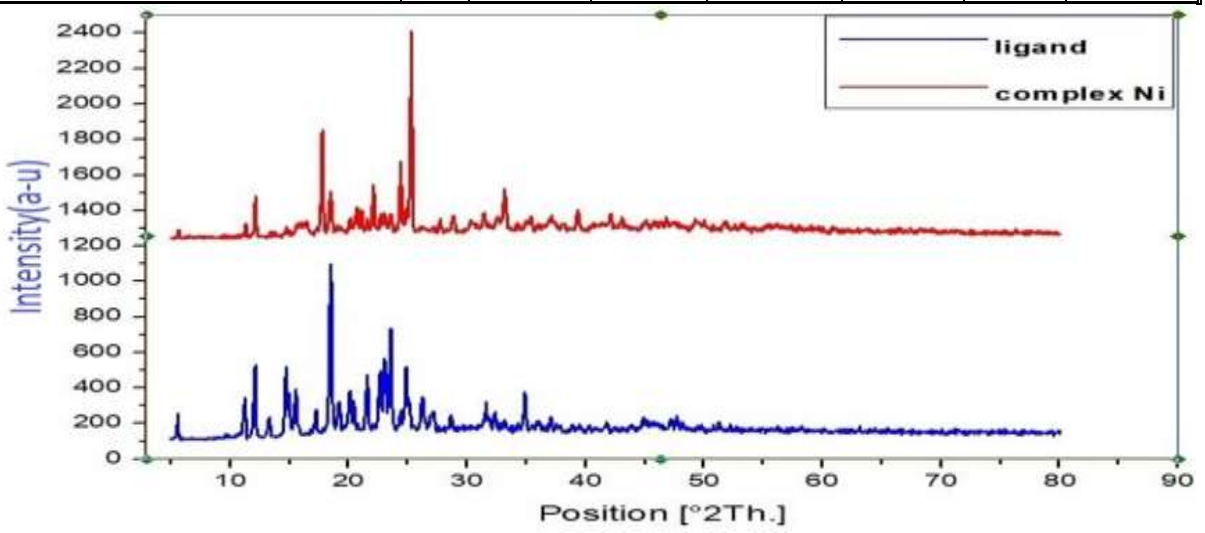

Figure 8.1. XRD patterns for ligand (DPTYEDAPIBO) and Ni (II) complexes.

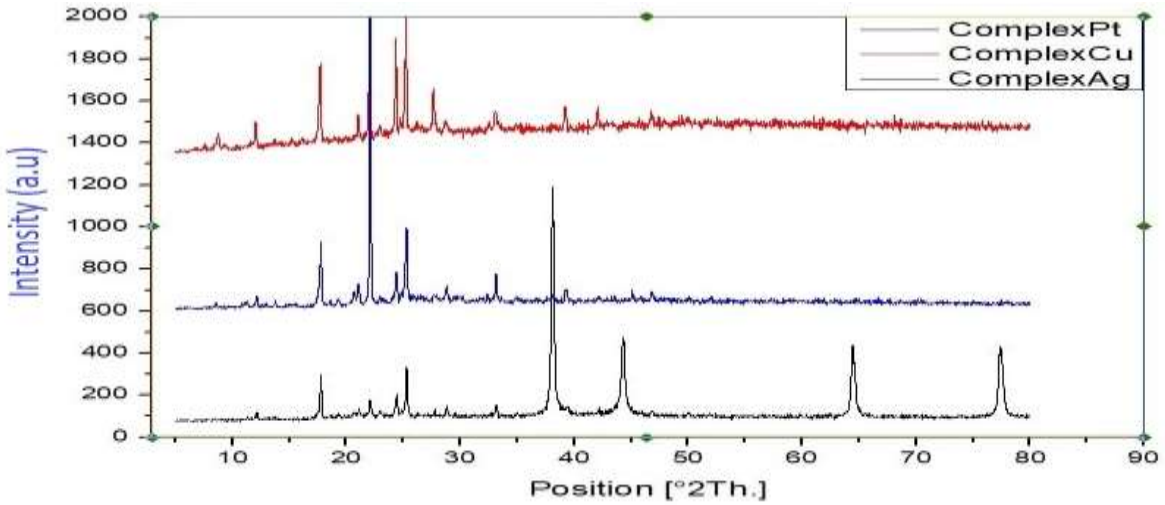

Figure 8.2. The XRD patterns for the Cu (II), Ag (I) and Pt (IV) complexes.

Scanning Electron Microscopy (FESEM)

Through the scanning microscopy technique, the surface properties (morphology), the shape and size of the particles, and the crystal structure of each of the (DPTYEDAPIBO) ligand and its complexes were known and studied. The ligand has a circumferential shape similar to a spherical shape and the average size of the particles was 69.19 nm, while the (FESEM) image of the nickel (II) complexes showed that it was completely spherical and homogeneous, and the size of the particles was 71,572 nm. It was found that the (FESEM) image For platinum (IV) complexes have a heterogeneous shape and the size of particles was 88.678 nm, as well as a (FESEM) image appeared for silver (I) complexes showed a granular and spherical shape with an average particle size of 86.316 nm , Finally the (FESEM) image of the copper (II) complexes showed that they have square shapes and that they are not within the nanoscale as shown in the Figures (9.1-9.5) below .Through what has been studied for (FESEM) technology, it was found that compounds whose crystal shape or size is granular, i.e. within the nanoscale, are compounds of importance because of the properties that it possesses that enable us to benefit from it in the fields of industry such as thermal or electrical conduction or in the fields of medicine and pharmacology in the treatment of Some types of cancer or some harmful bacteria.

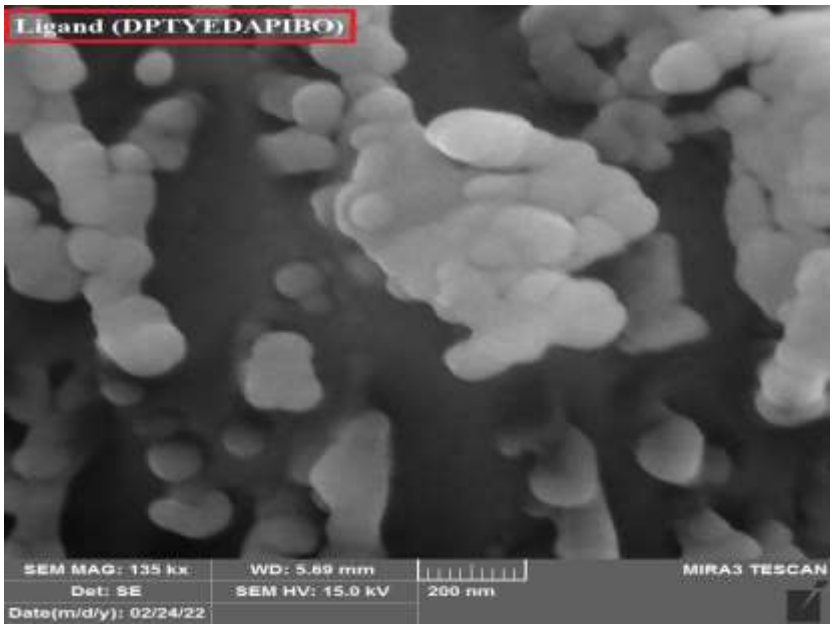

Figure 9.1. The FESEM image of the synthesized (DPTYEDAPIBO) ligand.

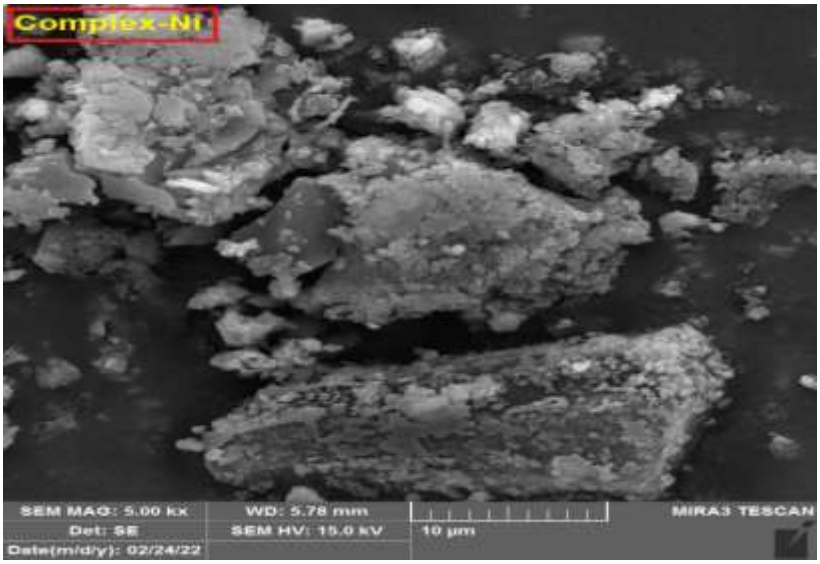

Figure 9.2. The FESEM image of the Ni (II) complex.

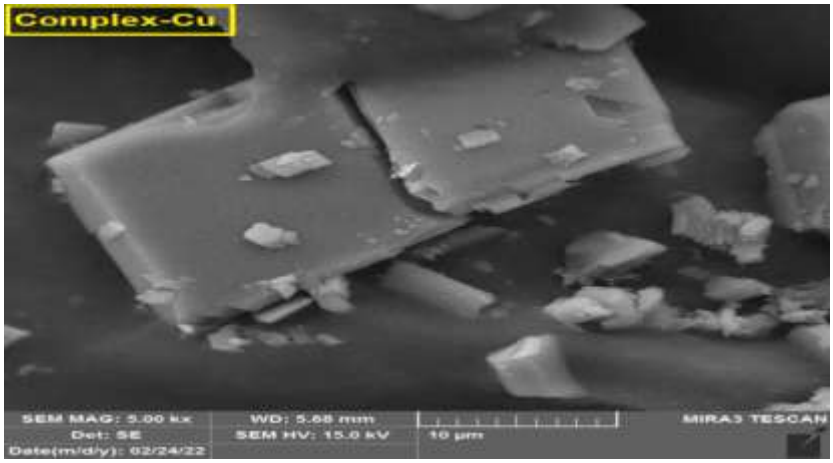

Figure 9.3. The FESEM image of the Cu (II) complex.

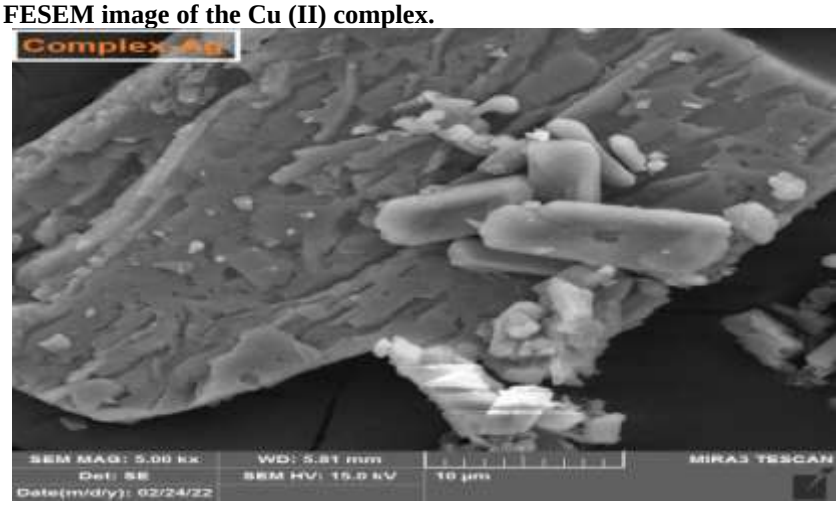

Figure 9.4. The FESEM image of the Ag(I) complex.

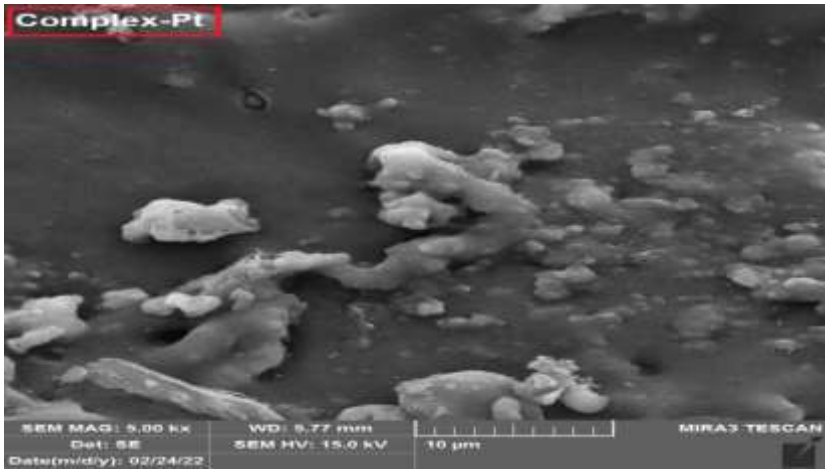

Figure 9.5. The FESEM image of the Pt (IV) complex.

Antioxidant Activity

The anti-free radical test was performed on each of the ligands (DPTYEDAPIBO) and all of the prepared metal complexes, which have been widely used in recent years to estimate antioxidant activity. This test is based on the presence of an antioxidant compound that can donate an electron or a hydrogen radical to the compound (DPPH), which has a violet color. The interaction of the prepared compounds with the compound (DPPH) and the disappearance of the violet color and transformation into a more sTable compound indicates that the compounds have high antioxidants. The measurements for each ligand (DPTYEDAPIBO), platinum (IV), nickel (II) and copper (II) complexes revealed a high antioxidant activity towards (DPPH). The prepared compounds achieved the highest inhibition percentage at a concentration of (500 µg. mL−1), which ranged between (64.16% -88.91%). While the lowest inhibition percentage ranged between (32.5% - 64.5%) at a concentration of 3.9 (µg. mL−1). while the silver(I) complex exhibited no antioxidant activity. The half inhibitory concentration (IC50) for each ligand (DPTYEDAPIBO) and all metal complexes under study, on the other hand, ranged between (0.4148-112.7885), as shown in Table (6), and Figure (10) depicts the antioxidant activity of DPPH scavenger radical for (DPTYEDAPIBO) ligand and its complexes.

Table 6. Antioxidant activity from the analysis in vitro for ligand (DPTYEDAPIBO) and its metal complexes.

Compound	Concentration (µg. mL−1)									IC_{50}
	0.000	**3.900**	**7.810**	**15.620**	**31.250**	**62.500**	**125.00**	**250.00**	**500.000**	
Ascorbic Acid	0.000	64.5	68.12	72.24	78.66	80.02	85.33	89.66	95.54	0.9819
Ligand (DPTYEDAPIBO)	0.000	56.66	57.5	58.33	60.83	66.66	68.33	69.16	78.33	0.4148
[Ni (DPTYEDAPIBO)Cl_2]. H_2O	0.000	46.11	51.33	56.76	59.89	60.45	66.12	67.86	74.33	2.2462
[Cu (DPTYEDAPIBO)Cl_2]. H_2O	0.000	32.5	33.14	35.16	45.25	45.75	56.91	85.33	88.91	112.788
[Ag (DPTYEDAPIBO)].NO_3	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	no value
[Pt (DPTYEDAPIBO)Cl_2] $Cl_2.H_2O$	0.000	42.5	45	47.5	49.16	51.66	52.5	58.33	64.16	83.4836

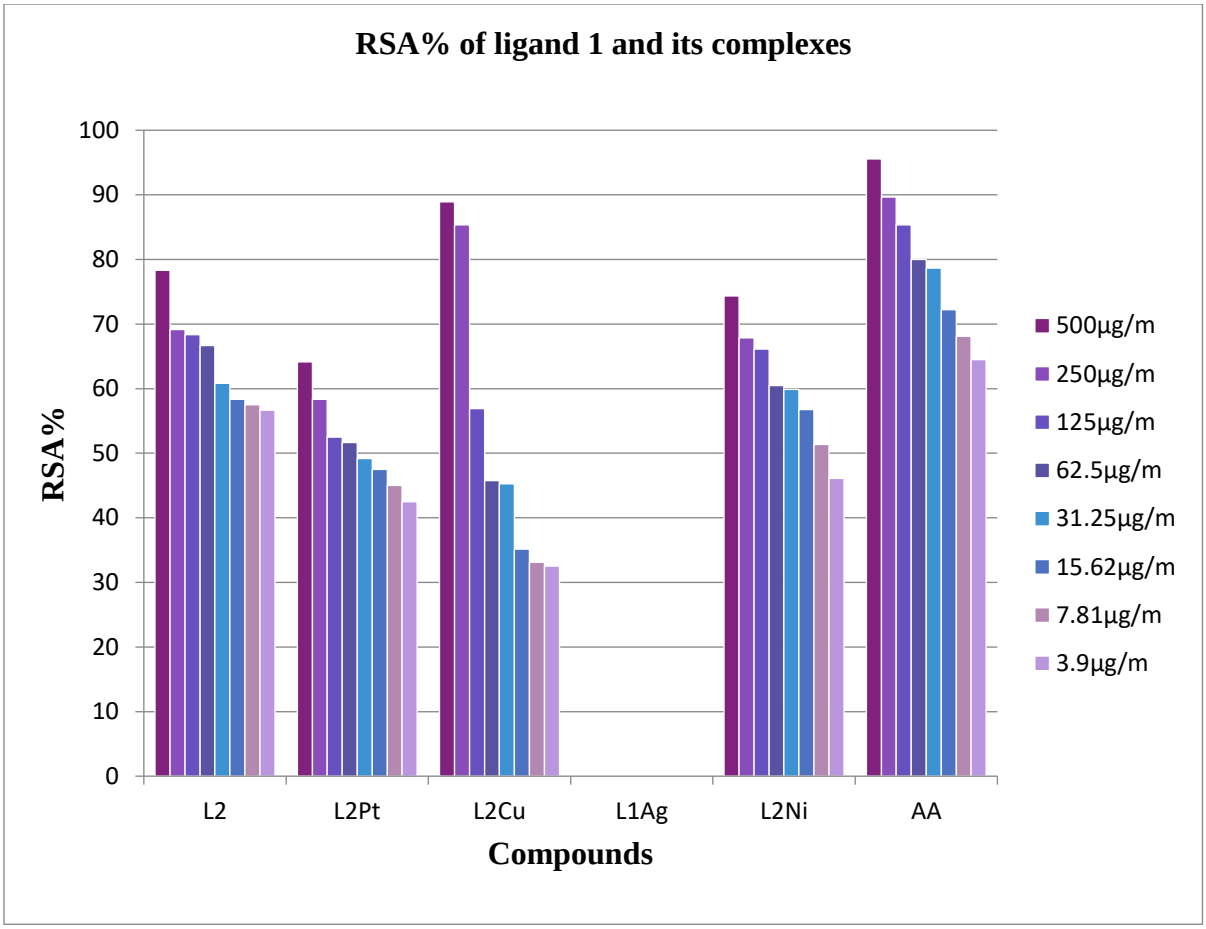

Figure 10. Antioxidant activity of DPPH scavenger radical for (DPTYEDAPIBO) ligand and its complexes.

In vitro cytotoxicity evaluation

The MTT cytotoxicity assay for both the (DPTYEDAPIBO) ligand and the platinum (IV) complex was performed on the (MCF-7) breast cancer cell line as it is the most common type of cancer in women. As well as with the normal cell line (WRL68) for the purpose of knowing the effect of the (DPTYEDAPIBO) ligand and the platinum (IV)complex on healthy cells. By integrating (MCF-7) cancer cells as well as WRL68 normal cells with the prepared compounds separately at 5% CO_2 atmosphere and 37°C temperature for 24 hours at different concentrations ranging from (400 -25) µg /ml and through the ELISA device, the absorbance was calculated. At the wavelength of 570 nm and by means of the statistical program and IC_{50} calculation, it was found that the effect of the ligand on the (MCF-7) cancer cell line is less than that of the platinum complex, as it inhibited cells by 56.83%, 41.9%, 24.38%, 11.92%, 5.4% at concentrations 400, 200, 100, 50, 25 µg /ml respectively. While it gave the platinum (IV)complex inhibition rate on the normal cell line (WRL68) by (50.31 - 3.5%%) at concentrations of (400 -25) µg /ml respectively, it showed good results than it is in the ligand, as it inhibited (MCF-7) cancer cells with a rate ranging between (71.59% - 3.78%), while the percentage of inhibiting normal cells (WRL68) ranged between (34.61% - 4.78%). The Table (7) and the Figures (11.1-11.2) shows the IC_{50} value of both the ligand and platinum (IV) complex.

Table 7. Evaluation of the cytotoxicity of both the ligand and the Pt (IV) complex against the MCF-7 cancer cell line after incubation (24 h) at (37 °C).

Conc.	Viability% mean ± SD							
	MCF-7 L2 Mean ± SD	Inhibition of dead cells% MCF-7	WRL68 L2 Mean ± SD	Inhibition of dead cells% WRL68	MCF-7 L2Pt Mean ± SD	Inhibition of dead cells% MCF-7	WRL68 L2Pt Mean ± SD	Inhibition of dead cells% WRL68
400	43.17 ±3.64	56.83%	49.69 ±3.51	50.31%	28.41 ±4.79	71.59%	65.39 ± 6.90	34.61%

200	58.10 ±2.37	41.9%	74.46 ±0.85	25.54%	37.85 ±1.74	62.15%	73.23 ±1.20	26.77%
100	75.62 ±3.47	24.38%	92.13 ±1.56	7.87%	57.15 ± 6.72	42.85%	93.60 ± 2.10	6.4%
50	88.08 ±3.28	11.92%	96.18 ±1.25	3.82%	80.05 ± 8.57	19.95%	95.33 ± 1.18	4.67%
25	94.60 ±2.17	5.4%	96.95 ±1.14	3.05%	96.22 ± 068	3.78%	95.22 ± 0.82	4.78%

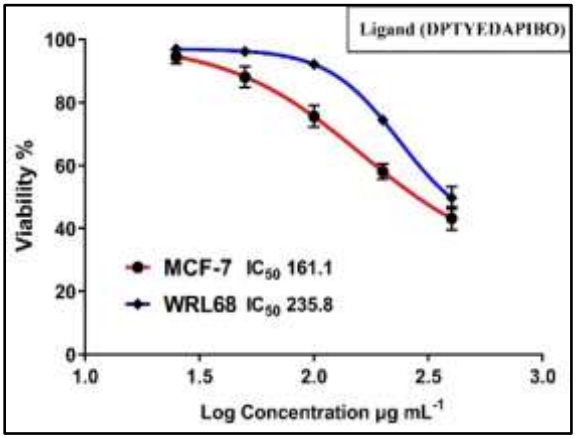

Figure 11.1. IC_{50} for (DPTYEDAPIBO) ligand in (MCF-7) cancer cell line and (WRL68) natural cell line

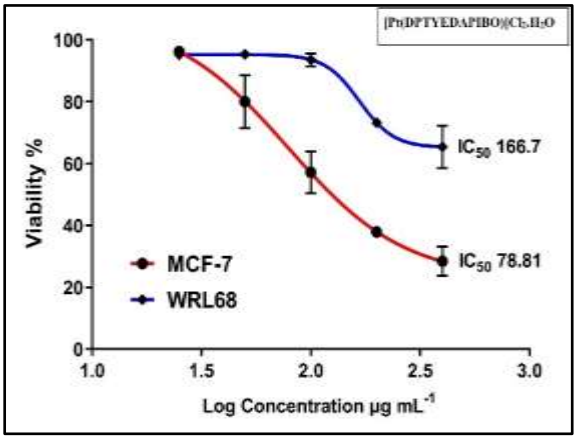

Figure 11.2. IC50 for the Pt(IV) complex in (MCF-7) cancer cell line and (WRL68) natura

Conclusion

The measurements which were used to determine the geometry of the compound were (elementary analysis, electronic, atomic absorption spectroscopy, infrared spectroscopy, molar conductivity, and magnetic susceptibility). These observations were also supported by the octahedral geometry of the Ni (II), Cu (II), and Pt (IV) complexes, as well as the tetrahedral geometry of the Ag(I) complexes. Also, we learned via toxicity testing (MTT) that they have effectiveness against breast cancer cells (MCF-7). By this research, it will be feasible to work closely and precisely on these suggested chemicals in the future in order to utilize them in the medical area. All compounds were found to display nanotechnology traits, which indicates the stance and outlook of the world on these compounds, their significance, and their entry into numerous industrial, medical, and electronic domains.

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Conflicts of Interest

I hereby to certify that there is no conflict of interest regarding our paper

Funding

By first author only

Ethics Statements

The Deanship of the College of Education at Al-Qadisiyah University approved the research, which was a novel piece of work. Neither people nor animals have been subjected to it.

Author Contribution

Both authors contributed to preparing, diagnosing and reviewing the research together

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