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Cytotoxicity of Fe2+, Cu2+, and Ni2+ metal complexes of thiosemicarbazide Schiff bases with dibenzalcyclohexanone & Di-o-bromobenzalcyclohexanone

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***Abstract*---**The work included the synthesis and characterization of two ketones (chalcones) through the reaction of cyclohexanone with benzaldehyde in the presence of a strong base, as well as ketones were prepared replaced with bromine in the ortho position from the reaction of brominated benzaldehyde in the ortho site with cyclohexanone. The first ligand prepared through the reaction of the thiosemicarbazide compound with dibenzalcyclohexanone, while the second ligand was prepared by reacting di-o-bromobenzalcyclohexanone. The resulting ligands are bi-dentate ligands that can bind to transition metal ions in a molar ratio (ligand:metal) 2:1. As mononuclear complexes were prepared through the reaction of these ligands with the divalent metallic elements under study, which are copper(II), iron(II) and nickel(II). The novel complexes have been characterized by 1H&13C-NMR, (Mass Spectra), magnetic susceptibility and molar conductivity. And through spectroscopic studies and magnetic susceptibility, the geometry of the prepared complexes were suggested. The iron and copper complexes are paramagnetic complexes, and the magnetic moment values are within the range of the distorted tetrahedral. While for the nickel complexes, they are diamagnetic complexes, and the magnetic moment values are within the range of the distorted square planar shape. The biological activity of the prepared complexes against breast cancer cells type MDA-MB231 was evaluated. It was found that two complexes were effective against cancer cells with a concentration less

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than (50) µmolar , copper complex of di-o-bromobenzalcyclohexanone-thiosemicarbazide with a value of IC50 equal to 41.1 micromolar and copper complex with dibenzalcyclohexanone-thiosemicarbazide with a value of IC50 equal to 24.3 micromolar.

***Keywords*---**cytotoxicity, metal complexes, thiosemicarbazide, Schiff bases, chalcones.

Introduction

Published statistics of people infected and died of cancer in the last thirty years indicate a significant increase in relation to the rest of the diseases that afflict humans and that cause cancer . Huge human and economic losses and even drain poor countries, causing the inability of the governments of those countries to provide appropriate treatments for various cancerous diseases. The published research indicates the effectiveness of many metal complexes in the treatment of various cancerous diseases. The current study is an attempt to enter into this battlefield in an attempt to study certain types of compounds that we expect to have good efficacy in this field by preparing fourteen new compounds prepared for the first time and evaluating their effectiveness against breast cancer cells. The results obtained are used to set future goals and prepare new compounds that have much better efficacy than these compounds, in an attempt to reach the preparation of metal complexes with better efficacy than the currently used treatments[1-8].

The metal complexes targeted in this study are compounds consisting of transitional elements bound to the bases of Schiff- calcanades prepared from the thiosemic reactor. Carbazide (Thiosemicarbazide) as an amino compound with symmetric galcones as a ketone compound prepared by reacting benzaldehyde with cyclohexanone[9-12] .

Chalcones

They are unsaturated ketones at alpha and beta positions (trans-1-3-diaryl-2-propen-1-one) consists of two aromatic rings attached to the carbonyl system. [13] These compounds are in the form of solids, and their color is mostly yellow. Where chemically they belong to the ketones and ions , and is the nucleus of a group of compounds of vital importance known as chalcones. It is considered one of the natural compounds that are used in various applications due to its biological activity, such as anti-inflammatory[14] and sunscreen for the human body[15] and antioxidants[16] and carcinomas[17] and malaria[18].

Schiff Bases

Schiff bases are organic nitrogen compounds analogous to aldehydes and ketones when replaced the carbonyl group Carbonyl C=O) (substituted azomethine C=N) [19] .It is called another name, imines, and was named after the chemist Hugo Schiff synthesised this type of compounds through the reaction of an aldehyde or ketone with a primary amine [20] . Schiff bases are one of the chemical compounds that have received great and wide attention in terms of chemical, applied and biological terms . Condensation of an aldehyde or a ketone with the primary amine with the deletion of a water molecule, these reactions are the most common in the preparation of Schiff bases, as shown below [21,22] :

Materials and Methods

Preparation of ketones

Mix in a baker 2.325 g of cyclohexanone and 14.9 grams of ortho-bromobenzaldehyde dissolved in 100 mL of ethanol while stirring with a glass stirrer. An aqueous solution of potassium hydroxide consisting of 4 grams of potassium hydroxide in 20 ml of water was gradually added to the mixture with stirring for half hour, a yellowish precipitate is observed. Then 50 ml of water was added to the mixture with stirring for 15 minutes. The mixture was filtered, recrystallized with ethanol and dried to obtain a pure precipitate. The resulting substance is yellow in color, its weight is (14.5) grams, and the melting point of the resulting compound is (132-135)°C. The bellow table, table (1), shows the amount of prepared ketones, yield percentage, color and melting points of the synthesised ketones.

Table (1)
Quantity of prepared ketones, percentage, color and melting point

No.	Ketone	Weight of Chalcones (g)	Yield%	Color	mp . °C
1	DBA	8.5	90%	Yellow	118-121
2	Do -Br-BA	14.5	92.4%	Yellow	132-135

Preparation of Schiff bases (-L_2 -L_1)

In a round bottom flask, 7.84g of ortho-bromobenzalcyclohexanone dissolved in 50 ml ethanol and 1.82 g of thiosemicarbazide dissolved in 25 ml of ethanol was mixed and 3 to 5 drops of concentrated hydrochloric acid was added. Then the mixture was refluxed for (1-3) hours. After that, the solution was cooled, filtered and left to dry. Re-crystallization was done using ethanol to obtain a pure precipitate. The below table, table (2), shows the Schiff bases that were prepared in this study with some of their physical properties such as color and melting point in addition to the weight of the resulting materials and the transformation ratio.

Table (2)
quantity of prepared Schiff bases, percentage, color and melting point

No.	Schiff Base	Weight of Schiff Base (g)	Yield%	Color	mp . °C
1	DBC-TSC	5.9	96%	Orange	88-90
2	Do -Br-BC-TSC	9.2	98.9%	Yellow	129-132

Preparation of metal complexes

Preparation of nickel complexes

In a round bottom flask, 1.5 g of Schiff base dissolved in 100 ml ethanol was added to 0.45 g of nickel salt dissolved in 50 ml of ethanol with stirring and heating for one hour. Then the solution was filtered and left to dry to give a precipitate its color (green yellowish), weight (1.9g), and no clear melting point for the compound was shown, as the compound melting point at (226-229)°C.

Preparation of copper complexes

In a round bottom flask, dissolve 1.5 g of Schiff base in 100 ml of ethanol with stirring and heating. Heat in a second baker 0.54 g of copper salt dissolved in 50 ml of ethanol . The copper salt was added to the base gradually. Leave the mixture to rise for an hour to obtain a precipitate. Then the solution was filtered and left to dry to give a precipitate of color (dark brown), weight (1.76) grams , and the melting point of the complex is (173 - 176)°C.

Preparation of iron complexes

In a circular flask, dissolve 1.5 g of Schiff base in 100 ml of ethanol with stirring and heating. Heat in a second baker 0.4 g of iron salt dissolved in 50 ml of ethanol . Iron salt was added to the base gradually. Leave the mixture to rise for an hour to obtain a precipitate. Then the solution was filtered and left to dry to give a precipitate its color (red), weight (1.7) grams , and the melting point of the complex is (244-246)°C. The bellow table, table (3), shows the metallic complexes that were prepared in this study with some of their physical properties such as color and melting point in addition to the weight of the resulting materials and the transformation ratio of each of these complexes.

Table (3)
Amount of prepared complexes, percentage, color and melting point

No	Schiff Base	Metal Complex	Weight of Complex (g)	Yield%	Color	mp. °C
1	DBA-TSC	Ni-DBA-TSC	2.2	67%	Light green	122-124
2		Cu-DBA-TSC	1.83	55%	dark brown	159 d
3		Fe-DBA-TSC	1.9	58%	Dark red	179-182
4	Do-Br-BA-TSC	Ni-Do-Br-BA-TSC	1.9	59%	Yellowish green	226-229
5		Cu-Do -Br-BA-TSC	1.76	55%	dark brown	173-176
6		Fe-Do-Br-BA-TSC	1.7	53%	Red	244-246

Results and Discussions

Physical properties

symmetrical ketones were prepared consisting of a carbonyl group located in the middle of the ketone compound . This ketone also contains two substituted or uncompensated benzene rings with predetermined positions and numbers according to the raw materials used in the preparation. The carbonyl group and the two benzene rings are linked to an unsaturated hydrocarbon chain containing two double bonds. It works on the formation of a successive system consisting of a single bond and a double bond connected with the double bonds in the two gasoline rings, and this successive electronic system is relatively long to the point that the appearance of this ketone compound in a yellow or orange color is due to the existing electronic transitions that compose this successive electronic system. The reason for preparing this type of ketones is to control the electron density on the metallic metal as a final result. Schiff bases were prepared from these symmetrical ketones by reacting them with thiosemia Carbazide to form bi- dental ligands that can interact with metal ions from two sites in the ligand : sulfur from the (C=S) group, a sigma-type ligand, and the electron pair on the imine group (C=N) with a coordination bond (Coordination Bond) . According to the published sources about this type of ligand , it is possible to prepare metal complexes through the reaction of two moles of the ligand with one mole of the metal ion (the central atom). It can be either a tetrahedron, a deformed tetrahedron, a square planar, or a deformed planar square. The ketones , Schiff bases (ligands) and metal complexes were successfully prepared by analyzing these compounds by physical and spectroscopic methods and comparing each of the physical properties of the reactants and products, which showed very clear differences in these properties between the reactants and the required products, as shown below. It is worth noting that the raw materials used in the preparation of ketones (chalcones) are liquid materials, while the resulting ketone is a solid substance, and the resulting ketone is called by several names, including chalcon (Chalcone) or dibenzylcyclohexanone (Dibenzalcyclohexanone).

The electrical conductivity of the complexes was measured at (10^{-3} M) concentration in the solvent dimethyl sulphoxide after allowing the solution to be in equilibrium at 25°C. has been shown One of the results of electrical conductivity measurements is that they agree with the structural formulas of the prepared complexes that all the complexes have neutral behavior (non-electrolyte). Also, the magnetic sensitivity of the prepared complexes was measured. After applying the calculations and comparing the practical results of the magnetic susceptibility values with the theoretical results, the results showed that the complexes Iron and copper are paramagnetic complexes and the magnetic moment values fall within the range of the deformed tetrahedron, while the nickel complexes are diamagnetic complexes and the magnetic moment values fall within the range of the distorted square plane shape [23]. The bellow table, table (4), shows the values of electrical conductivity, magnetic susceptibility and physical properties.

Table (4)
values of electrical conductivity, magnetic susceptibility and physical properties

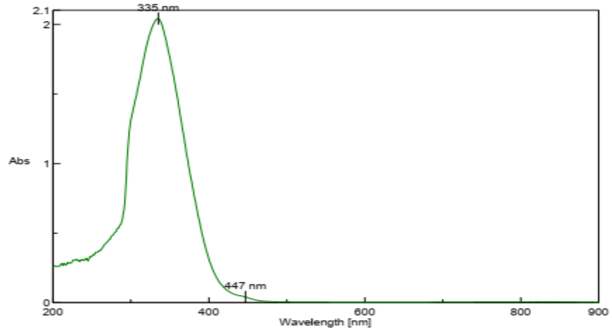
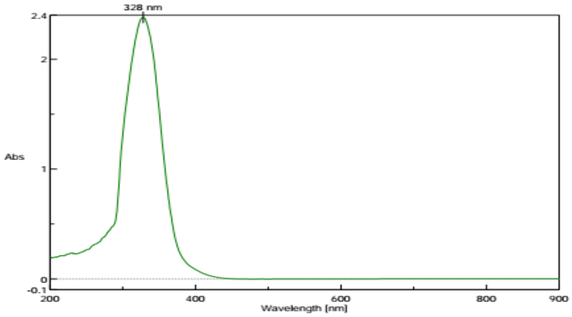
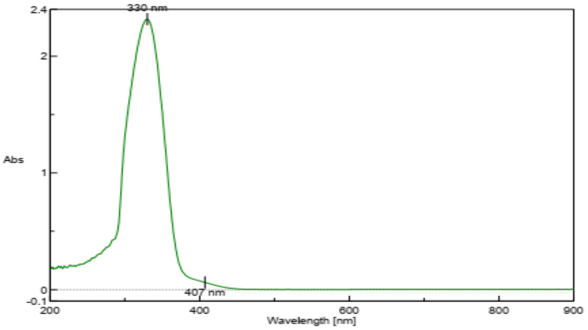
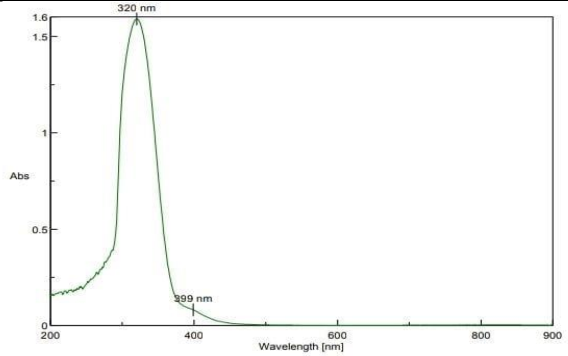
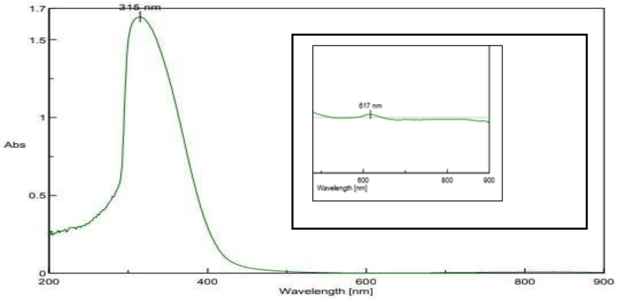
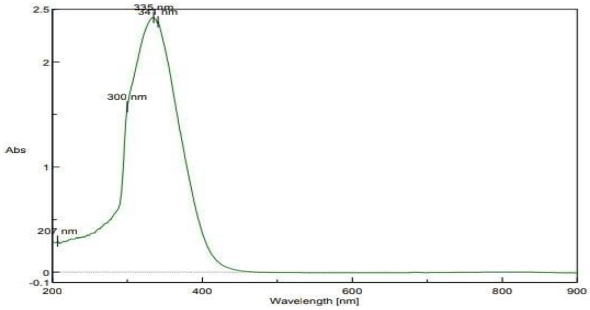
No	Complex	Yield%	μ_{eff} (BM) calc.	μ_{eff} (BM) found	Cod. S.cm .mole^{-1}	μ ^{2}	Type of complex	Expected shape
1	$Cu(L1)_2$	55	1.73	1.49	12		Non-electrolyte	Distorted tetrahedral
2	$Cu(L2)_2$	55	1.73	1.49	6		Non-	Distorted

						electrolyte	tetrahedral
3	$Cu(L3)_2$	53	1.73	1.49	12	Non-electrolyte	Distorted tetrahedral
4	$Ni(L1)_2$	67	0	0	2	Non-electrolyte	Distorted square planar
5	$Ni(L2)_2$	59	0	0	2	Non-electrolyte	Distorted square planar
6	$Ni(L3)_2$	57	0	0	2	Non-electrolyte	Distorted square planar
7	$Fe(L1)_2$	58	1.73 Fe^{3+}	1.49	10	Non-electrolyte	Distorted tetrahedral
8	$Fe(L2)_2$	53	4.9	3.3	6	Non-electrolyte	Distorted tetrahedral
9	$Fe(L3)_2$	52	4.9	4.8	0	Non-electrolyte	Distorted tetrahedral

Spectroscopy

UV-Visible Spectra

Ultraviolet and visible spectra were determine to the synthesised compounds with (10^{-3}M) solution concentration dissolved in DMSO. UV-Vis spectra of DBC ketone showed wide absorption peak at wavelength equal to (328nm) (29579Cm^{-1}) which belongs to the $n\rightarrow\pi^*$ and $\pi\rightarrow\pi^*$ electron transitions overlapped together. As for the spectrum of the ligand (L1), Schiff base, product of the reaction of ketones with thiosemicarbazide showed a clear difference from the ketone spectrum, where we notice a partial separation of the $\pi\rightarrow\pi^*$ type transition with the appearance of a shoulder peak at the wavelength (300nm) with the appearance of a clear peak for the $n\rightarrow\pi^*$ type electronic transition at the wavelength (333nm) and the difference in the displacement of the absorption peaks of each of the ketones And the liked is evidence of the occurrence of the reaction and the formation of the products required to be prepared in this study. The UV-visible spectrum of di-o-bromobenzalcyclohexanone was also showed wide absorption peak at (320nm) (29120Cm^{-1}) which belongs to the $n\rightarrow\pi^*$ and $\pi\rightarrow\pi^*$ electron transitions overlapping together due to the existence of a successive system of electronic transitions between the symmetric and pi-bonds, and this successive system is long as it can be observed from the structural structure and the geometrical shape of the particle as in figure (1). As for the spectrum of the ligand (L2) , a Schiff base, resulting from the reaction of a di-o-bromobenzalcyclohexanone with thiosimecarbazide showed a clear difference from the spectrum of di-o-bromobenzalcyclohexanone, where a partial separation of the $\pi\rightarrow\pi^*$ type transition is observed with the appearance of a shoulder peak at the wavelength (300 nm) with the appearance of a clear peak of the $n\rightarrow\pi^*$ type electronic transition at the wavelength (330 nm) as shown in figures (1) to (7). And the difference in the displacement of the absorption peaks of each of the ketones The ligand is evidence of the occurrence of the reaction and the formation of the products required to be prepared in this study , and the following, table (Table 5), shows the ultraviolet spectrum of the prepared compounds.

 Figure (2): UV-Visible Spectrophotometer for DBC-TSC	 Figure (1): UV-Visible Spectrophotometer for DBC
 Figure (4): UV-Visible Spectrum of 2-Br-DBC-TSC	 Figure (3): UV-visible spectrum of 2-Br-DBC
 Figure (6): UV-visible spectrum of the complex [Cu(L1)$_2$]	 Figure (5): UV-visible spectrum of the complex [Ni(L1)$_2$]

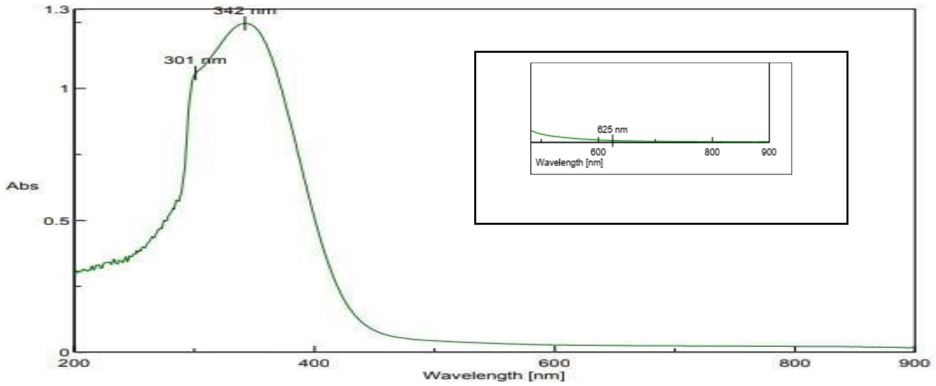


Figure (7): UV-visible spectrum of the complex [Fe(L1) 2]

The following table, table (5), shows the most important peaks and spectral bands of the UV-visible spectrum of the prepared compounds.

Table (5) the most important peaks and spectral bands of the UV-visible spectrum of the prepared compounds

Complex	λ (nm)	υ (cm^{-1})	Assignment	Proposed Structure
$[Ni(L1)_2]$	300 335 341	33333 29850 29325	$\pi \to \pi^*$ $n \to \pi^*$ $n \to \pi^*$	Distorted square planar
$[Ni(L2)_2]$	301 342	33222 29239	$\pi \to \pi^*$ $n \to \pi^*$	Distorted square planar
$[Cu(L1)_2]$	315 617	31746 16207	$n \to \pi^*$ d-d transition $^2B_1 \to {}^2A_1$	Distorted tetrahedral
$[Cu(L2)_2]$	305 341 615	32787 29325 16260	$\pi \to \pi^*$ $n \to \pi^*$ d-d transition $^2B_1 \to {}^2A_1$	Distorted tetrahedral
$[Fe(L1)_2]$	301 342 625	33222 29239 16000	$\pi \to \pi^*$ $n \to \pi^*$ d-d transition $^5E \to {}^5T_2$	Distorted square planar
$[Fe(L2)_2]$	333 342 594	30030 29239 16835	$\pi \to \pi^*$ $n \to \pi^*$ d-d transition $^5E \to {}^5T_2$	Distorted tetrahedral

Infrared Spectra (FT-IR)

The prepared compounds were spectroscopically characterized by FT-IR and Figures (2) and (3) are the infrared spectra of the prepared ketones in this study, where the appearance of the stretch-vibration absorption bands (νC) can be observed. -H $_{\text{aromatic}}$) within the range $^{-1}$ cm (3165 - 3140), the appearance of stretchable vibration absorption bands (νC -H $_{\text{Aliphatic}}$) within the range $^{-1}$ (2866-2940) and the appearance of rubber vibration absorption bands (νC=C$_{\text{ring \&alkene}}$) within the range cm^{-1} (1608 - 1463) for the compounds, and the table (6) shows the values of the absorption bands of the FT-IR spectrum for the prepared compounds (ketones):

Table (6): values of the absorption bands for the infrared spectrum FT-IR The prepared ketones are measured in cm $^{-1}$.

Comp. Symb .	ν C -H Arom.	ν C -H Aliph.		ν C = O Ketone	ν C=C $_{\text{ring}}$		Others
		Asym.	Sym.				
DBC	3140	2933	2866	1661	1608	1485	………….
2 -Br-DBC	3155	2932	2868	1663	1606	1463	C-Br at 767

The following table, table (7), shows the values of the absorption bands for the infrared spectrum of the complexes.

Table (7) the values of the absorption bands for the infrared spectrum of the complexes

Comp. Symb .	ν C –H Arom .	ν C –H Aliph .		ν C = N	ν C=C $_{\text{ring}}$		Others	MN
		Asym .	Sym.					
DBC-Ni	3156	2936	2863	1606	1606	1494	NH$_2$, 3411,3280	570
2-Br-DBA-Ni	3148	2936	2865	1610	1599	1487	NH$_2$, 3403,3285	573
DBC-Cu	3150	2929	2866	1615	1599	1497	NH$_2$ 3435,3270	565
2-BrDBA-Cu	3140	2929	2870	1632	1599	1466	NH$_2$ 3435,3252	527
DBC-Fe	3090	2918	2850	1628	1599	1474	NH$_2$ 3435,3255	520
2-BrDBC-Fe	3157	2936	2862	1610	1593	1468	NH$_2$ 3402,3278	534

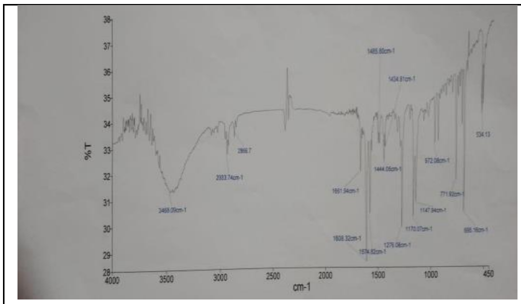


Figure (8): FT-IR spectrum of DBC

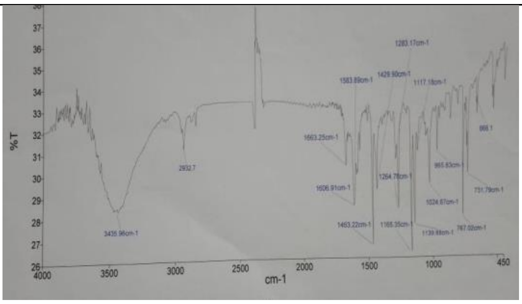


Figure (9): FT-IR spectrum of 2-Br-DBC

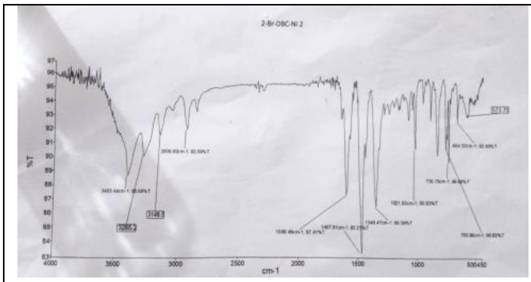


Figure (11): FT-IR spectrum for Ni-o-Br-DBC complex

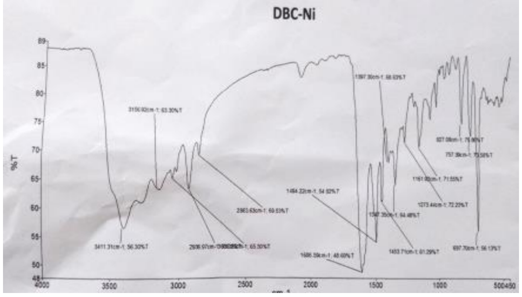


Figure (10): FT-IR spectrum for Ni-DBC complex

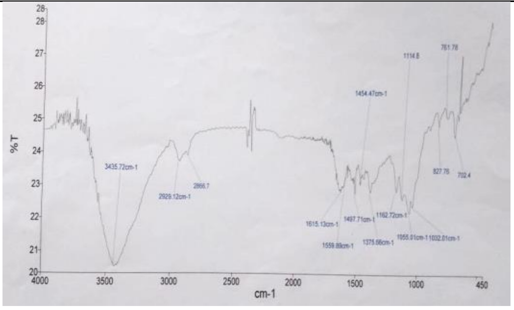


Figure (12): FT-IR spectrum for Cu-DBC complex

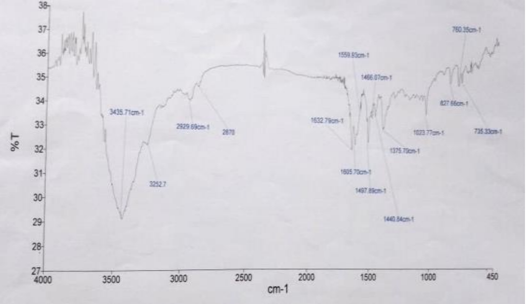


Figure (13): FT-IR spectrum for Cu-o-Br-DBC comple

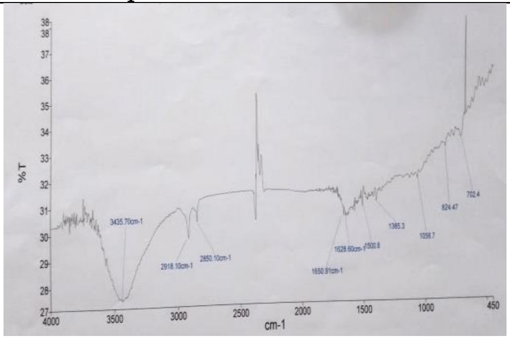


Figure (14): FT-IR spectrum for Fe-DBC complex

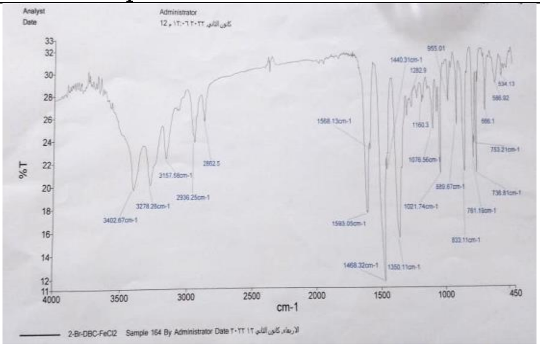


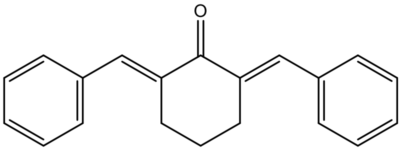
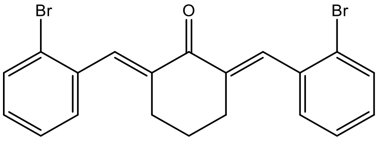
Figure (15): FT-IR spectrum for Fe-o-Br-DBC complex

Nuclear Magnetic Resonance Spectra

The structural formula of the compounds was also confirmed by H-NMR spectroscopy of the proton . In general, Figures (16) and (17) indicated the following beams and displacements. Where the binary benzalcyclohexanone (DBC), Figure No. (16), the prepared showed a multiple signal at [δ =(1.69-1.73) ppm, (m,2H)] belonging to the alkane group of the saturated hexagonal ring, and a triple signal appeared at [δ=(2.51-2.53) ppm,(t,2H)] refers to the alkane group in the saturated hexagonal ring, and showed a triple signal at [δ=(2.87-2.90)ppm,(t,2H)] back to the alkane group in the ring saturated hexagram, and a single signal appeared at [δ=(7.40) ppm, (s,2H)] due to belonging to the alkyl group , and a multiple signal appeared at [δ=(7.42-7.65) ppm , (m,10H), - Ar - H.] belongs to the protons of the aromatic ring .

compound, ortho-bromobenzalcyclohexanone (o-Br-DBC), was shown, Figure No. (17), the prepared multi-signal at [δ=(1.66-1.70) ppm, (m,2H)] belongs to the alkane group of the saturated hexagonal ring, and a triple signal appeared at [δ=(2.50-2.52) ppm,(t,2H)] belongs to the alkane group in the saturated hexagonal ring, and shows a triple signal at [δ=(2.74-2.76) ppm,(t,2H)] back to the alkane group in the ring The saturated hexagonal, and a single signal appeared at [δ=(7.35) ppm,(s,2H)] due to belonging to the alkene group , and a multiple signal appeared at [δ=(7.48-7.76) ppm,(m,10H)], -Ar- H.] belongs to the protons of the aromatic ring . Bellow table shows the chemical displacement of ketone compounds Diagnosed by nuclear magnetic resonance spectrometry, measured in ppm.

Table (8) shows the chemical displacement of compounds (ketones) diagnosed by nuclear magnetic resonance spectroscopy

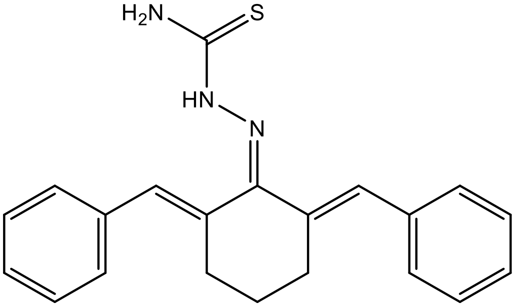
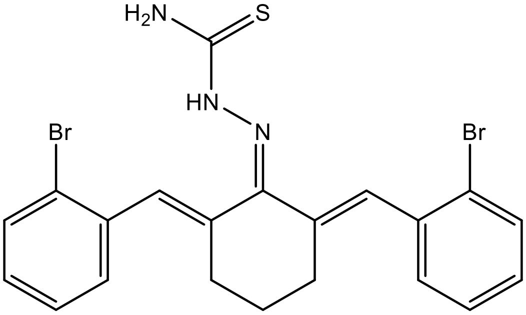
Comp. Symb .	Structure	Chemical Shift (ppm)	No. of Protons	Type of signal	Group
DBC		1.69-1.73	2	M	Aliphatic protons
		2.51-2.53	2	T	
		2.87-2.90	2	T	
		7.40	2	S	C H = C -
		7.42-7.65	10	M	Aromatic Protons
O-Br-DBC		1.66-1.70	2	M	Aliphatic protons
		2.50-2.52	2	T	
		2.74-2.76	2	T	
		7.35	2	S	C H = C -
		7.48-7.76	8	M	Aromatic Protons
		7.41-7.72	8	M	Aromatic Protons

NMR spectrum of Schiff bases

The structural formula of the compounds was also confirmed by the H-NMR spectrum of the proton . In general, Figures (18) and (19) indicated the following bands and absorptions. Where the prepared compound (DBC-TSC), Figure No. (18) showed multiple signs at [δ=(1.62-1.67) ppm,(m,2H)] It belongs to the alkane group in the saturated hexagonal ring, and a single signal appeared at [δ=(1.67) ppm,(s,2H), -N H_2] belongs to the protons of the terminal amine group, and a triple signal appeared at [δ=(2.90-2.93) ppm,(t,4H),] belongs to the two alkane groups of the saturated hexagonal ring, and it showed a single signal at [δ=(7.10) ppm,(s,2H) , = C H] belongs to the alkene group , and a multiple signal appeared at [δ = (7.33-7.41) ppm, (m,10H), - Ar - H. _] belongs to the aromatic ring protons , and it shows a single signal at [δ = (7.91) ppm , (s, 1H) , -N H -N] belongs to the amine group.

As for the prepared compound (o-Br-DBC-TSC), Figure No. (19), it showed multiple signs at [δ=(1.69-1.74) ppm, (m,2H)] It belongs to the alkane group in the saturated hexagonal ring, and a single signal appeared at [δ=(1.72) ppm,(s,2H), -N H $_2$.] belongs to the protons of the terminal amine group, and a triple signal appeared at [δ = (2.57-2.59) ppm, (t,2H)] It belongs to the alkane group in the saturated hexagonal ring, and a triple signal appeared at [δ=(2.75-277) ppm,(t,2H) ,] it belongs to the alkane group of the saturated hexagonal ring, and a single signal appeared at [δ=(6.83) ppm,] (s,2H) , = C H] belongs to the alkene group , and a multiple signal appeared at [δ = (7.28-7.71) ppm, (m,10H), -Ar - H. _] belongs to the aromatic ring protons , and shows a single signal at [δ = (7.75) ppm, (s, 1H) , -N H -N] belongs to the amine group. Table (9) shows the chemical displacement of compounds (Schiff bases) diagnosed by nuclear magnetic resonance spectroscopy.

Table (9): shows the chemical displacement of compounds (Schiff bases) diagnosed by NMR spectrum measured in ppm

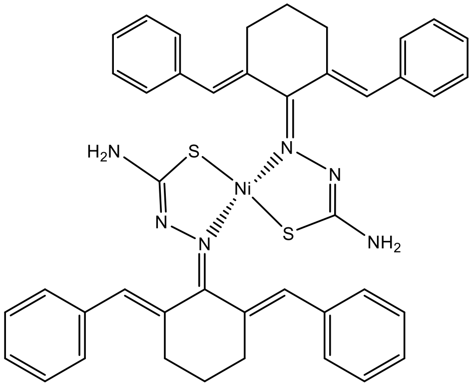
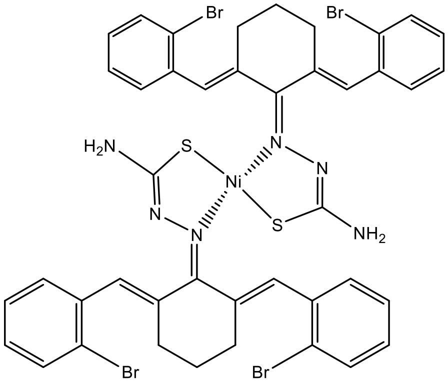
Comp. Symb .	Structure	Chemical Shift(ppm)	No. of Protons	Type of signal	Group
DBC-TSC		1.62-1.67	2	M	Aliphatic protons
		2.90-3.93	4	M	
		1.67	2	S	-N H $_2$
		7.10	1	S	C H = C -
		7.33-7.46	10	M	Aromatic Protons
		7.91	1	S	-N H -
o-Br-DBC-TSC		1.69-1.74	2	M	Aliphatic protons
		2.57-2.59	2	T	
		2.75-2.77	2	T	
		1.72	2	S	-N H $_2$
		6.83	1	S	C H = C -
		7.28-7.71	8	M	Aromatic Protons
		7.75	1	S	-N H -

NMR spectrum of complexes

The structural formula of the compounds was also confirmed by the H-NMR spectrum of the proton. In general, Figures (20) and (21) indicated the following bands and absorptions. The prepared compound (DBC-Ni Complex), Figure No. (20), showed multiple signs at [δ=(1.62-1.64) ppm,(m,4H)] It belongs to the alkane group in the saturated hexagonal ring, and a triple signal appeared at [δ=(3.09-3.11) ppm,(t,8H)] back to the two alkane groups of the saturated hexagonal ring, and it showed a single sign at [δ=(6.87) ppm,(s,4H) , = C H] belongs to the alkene group , and a multiple signal appeared at [δ = (7.33-7.46) ppm, (m,20H), - Ar - H. _] belongs to the aromatic ring protons , and it shows a single signal at [δ = (9.46) ppm, (s,4H), $-NH_2$] belonging to the amine group.

As for the prepared compound (2-Br-DBC-Ni complex), Figure (21), it showed a multiple signal at [δ=(1.59-1.64) ppm, (m,4H)] It belongs to the alkane group in the saturated hexagonal ring, and a triple signal appeared at [δ=(3.12-3.15) ppm,(t,8H)] It belongs to the two alkane groups of the saturated hexagonal ring, and a single signal appeared at [δ=(6.97) ppm,(s,4H) , = C H] belongs to the alkene group , and a multiple signal appeared at [δ = (7.24- 7.67) ppm, (m, 16H), - Ar - H. _] belongs to the aromatic ring protons , and a single signal appeared at [δ = (9.49) ppm, (s,4H), $-NH_2$] belonging to the amine group. Table (10) shows the chemical displacement of the compounds (complexes) diagnosed by nuclear magnetic resonance spectroscopy.

Table (10): The chemical displacement of the compounds (complexes) diagnosed by nuclear magnetic resonance spectroscopy, measured in ppm

Comp. Symb .	Structure	Chemical Shift(ppm)	No. of Protons	Type of signal	Group
[Ni(L1)2]		1.61-1.64	4	M	Aliphatic protons
		3.09-3.11	8	T	
		6.87	4	S	C H = C -
		7.33-7.46	20	M	Aromatic Protons
		9.46	4	S	$-NH_2$
[Ni(L2)2]		1.59-1.64	4	M	Aliphatic protons
		3.12-3.15	8	T	
		6.97	4	S	C H = C -
		7.24-7.67	16	M	Aromatic Protons
		9.49	4	S	$-NH_2$

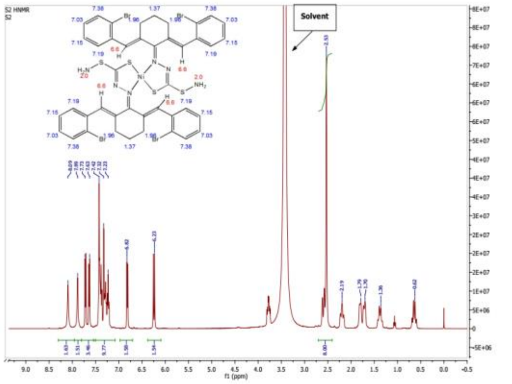


Figure (21): Expanded and condensed ¹ H-NMR spectrum of Ni-o-Br-DBC complex

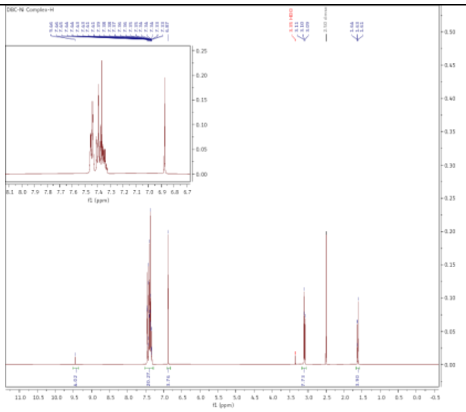


Figure (20): Expanded and condensed ¹ H-NMR spectrum of the DBC-Ni Complex

Mass Spectra

Most Research and studies that care preparing ligands and complexes for items transition Depends on me ghost Bloc Where Give clues confirmed and clear on me formulas synthetic for vehicles isomethine prepared and its complexes And that From During note Package ion Molecular (M^+) and basic bundles of ligands and some complexes prepared Appearance of strap represent Lc -mass - pint consequences diagnosis Lc -mass for ligands and some complexes prepared Appearance of Weight packs molecular And from that proven health formulas proposed that correspond with consequences Measurements The other , and the following figures from (22) to (30) show abundance relativity. The energetic ligands and complexes which are available with formulas proposed that I explained as such flower in Literature [24,25] .

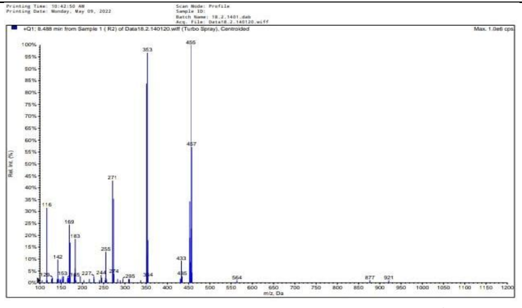


Figure (23): Mass spectrometry of 2-Br-DBC

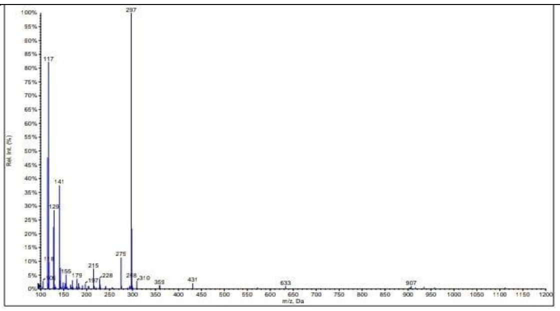


Figure (22): Mass spectrum of the compound DBC

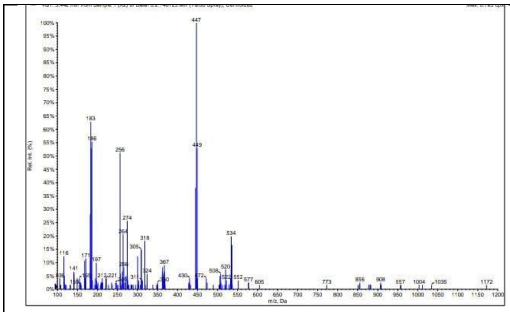


Figure (25): Mass spectrum of 2-Br-DBC-TSC-

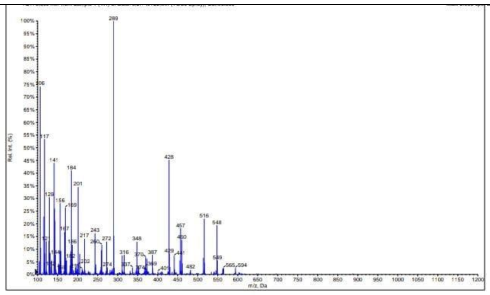


Figure (24): Mass spectrum of DBC-TSC

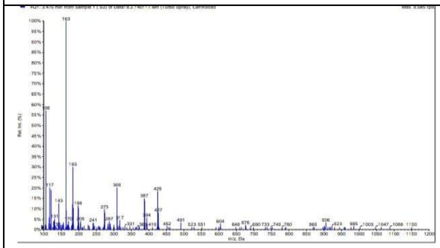


Figure (27): Mass spectrum of Cu-DBC complex

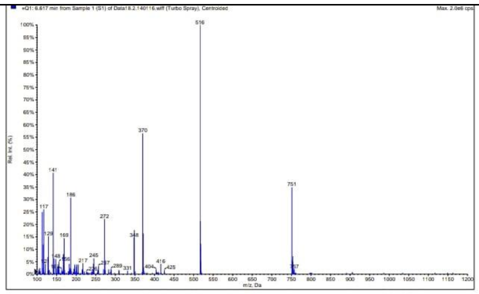


Figure (26): The mass spectrum of the complex Ni-DBC

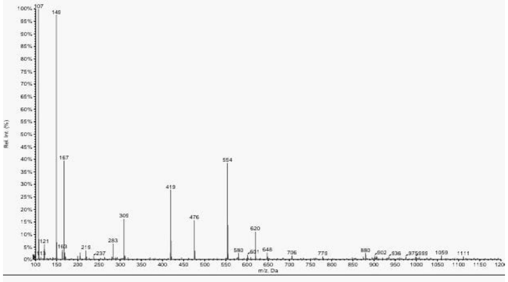


Figure (29): Mass spectrum of Cu-o-Br-DBC complex

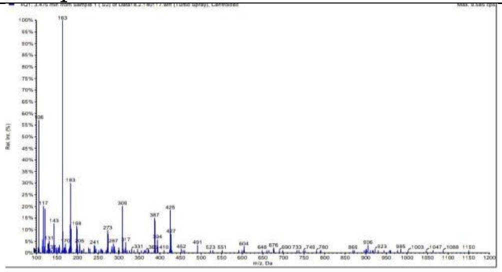


Figure (28): Mass spectrum of the Fe-DBC complex

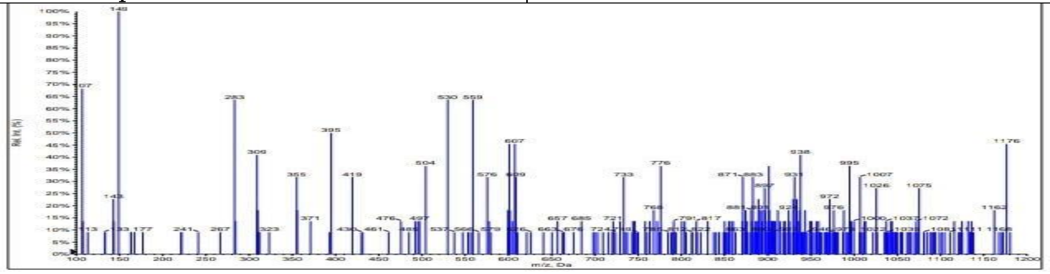


Figure (30): Mass spectrum of Fe-o-Br-DBC complex

Biological activity against breast cancer cells type MDA-MB231

From the table it is clear that four metal complexes have been effective against cancer cells with a concentration of less than (50) micromolar. Copper complex with Schiff base derived from di-o-benzalcyclohexanone-thiosemicarbazide shows moderate cytotoxicity with IC_{50} value equal to 41.1 micromolar. While copper complex with dibenzalcyclohexanone-thiosemicarbazide shows better cyctotoxicity with IC_{50} value equal to 24.3 micromolar.

Conclusion

From these results, we expect that preparing metal complexes from Schiff bases replaced by more than one bromine group will certainly lead to obtaining compounds with very strong efficacy against cancer cells, especially breast cancer type MDA-MB231 .The results are shown in the following table, table (11).

Table (11) Cytotoxicity of the synthesised compounds with IC_{50} values against breast cancer cells type MDA-MB231

IC_{50}	Compound name	compound symbol
>50μM	Ni-DBC-TSC	1
24.3μM	Cu-DBC-TSC	2
>50μM	Fe-DBC-TSC	3
>50μM	Ni-o-Br-DBC-TSC	4
41.1μM	Cu-o-Br-DBC-TSC	5
>50μM	Fe-o-Br-DBC-TSC	6

References

A. Olyaei, M. Vaziri, R. Razeghi, B. Shams, and H. Bagheri, Anovel Approach to bis (Indolyl) Methanes Using Nickel Nanooparticles as Areusable Catalyst Under Solvent – Free Conditions; *Journal of the Serbian Chemical Society*, 78,4, 463-468, (2013).

Al-Adely, K. J. K. (2000). *Synthesis and spectroscopic Study of Group (IIB) and (IIIB) Metal Ion Complexes With New Azo Compounds and With 1-(2-Pyridyl azo)-2-naphtho* (Doctoral dissertation, Ph. D. Thesis)

Al-Jeboori, M. J., Hasan, H. A., & Jaafer Al-Sa'idy, W. A. (2009). Formation of polymeric chain assemblies of transition metal complexes with a multidentate Schiff-base. *Transition metal chemistry*, *34*(6), 593-598.

Chopra, P. G. (2016). Chalcones: a brief review. *Int J Res Eng Appl Sci*, *6*, 173-85.

Gao, C., Wang, J., Xu, H., & Xiong, Y. (2017). Coordination chemistry in the design of heterogeneous photocatalysts. *Chemical Society Reviews*, *46*(10), 2799-2823.

Gross, J. H. (2006). *Mass spectrometry: a textbook*. Springer Science & Business Media.

Huheey, J. E., Keiter, E. A., Keiter, R. L., & Medhi, O. K. (2006). *Inorganic chemistry: principles of structure and reactivity*. Pearson Education India.

Kajal, A., Bala, S., Kamboj, S., Sharma, N., & Saini, V. (2013). Schiff bases: a versatile pharmacophore. *Journal of Catalysts*, *2013*.

Lawrance, G. A. (2013). *Introduction to coordination chemistry*. John Wiley & Sons.

Lin, Y., Zhang, M., Lu, Q., Xie, J., Wu, J., & Chen, C. (2019). A novel chalcone derivative exerts anti-inflammatory and anti-oxidant effects after acute lung injury. *Aging (Albany NY)*, *11*(18), 7805.

Nicholls, D. (2017). *Complexes and first-row transition elements*. Macmillan International Higher Education.

Oyama, H., Ohashi, A., & Watarai, H. (2004). Complex formation of copper (II) and iron (II) with octadecyloxythiazolylazophenol at the heptane-water interface. *Analytical sciences*, *20*(11), 1543-1547.

Papakyriakou, A., Bratsos, I., & Katsaros, N. (2003). Structural studies on metallobleomycins: The interaction of Pt (II) and Pd (II) with bleomycin. *Journal of the Serbian Chemical Society*, *68*(4-5), 339-348.

Porterfield, W. W. (2013). *Inorganic chemistry*. Academic press.**5**-

Qin, W., Long, S., Panunzio, M., & Biondi, S. (2013). Schiff bases: A short survey on an evergreen chemistry tool. *Molecules*, *18*(10), 12264-12289.

Raut, N. A., Dhore, P. W., Saoji, S. D., & Kokare, D. M. (2016). Selected bioactive natural products for diabetes mellitus. *Studies in Natural Products Chemistry*, *48*, 287-322.

Silverstein, R. M., & Bassler, G. C. (1962). Spectrometric identification of organic compounds. *Journal of Chemical Education*, *39*(11), 546.

Suijkerbuijk, B. M., Aerts, B. N., Dijkstra, H. P., Lutz, M., Spek, A. L., van Koten, G., & Gebbink, R. J. K. (2007). “Click” 1, 2, 3-triazoles as tunable ligands for late transition metal complexes. *Dalton Transactions*, (13), 1273-1276.

Sunday, N. F. (2020). Chemometrics of solvent extraction of Mn (II) and Fe (III) bis (salicylidene) ethylenediamine complexes in acid medium. *Journal of Human, Earth, and Future*, *1*(2), 71-77.

Suryasa, I. W., Rodríguez-Gámez, M., & Koldoris, T. (2022). Post-pandemic health and its sustainability: Educational situation. *International Journal of Health Sciences*, *6*(1), i-v. https://doi.org/10.53730/ijhs.v6n1.5949

Susilo, C. B., Jayanto, I., & Kusumawaty, I. (2021). Understanding digital technology trends in healthcare and preventive strategy. *International Journal of Health & Medical Sciences*, *4*(3), 347-354. https://doi.org/10.31295/ijhms.v4n3.1769

Syahri J, Yuanita E, Nurohmah BA, Armunanto R, Purwono B. Chalcone analogue as potent anti-malarial compounds against Plasmodium falciparum: Synthesis, biological evaluation, and docking simulation study. Asian Pacific Journal of Tropical Biomedicine. 2017;7(8):675-679

Tawfeeq, N. A.(2019). Synthesis of transition metal complexes containing symmetrical chalcone-derived Schiff bases and cytotoxic studies against bladder cancer cells - Universiti Putra Malaysia Institutional Repository. http://psasir.upm.edu.my/id/eprint/83237/. Accessed July 22, 2022.

Vásquez-Martínez, Y. A., Osorio, M. E., San Martín, D. A., Carvajal, M. A., Vergara, A. P., Sanchez, E., ... & Martín, C. S. (2019). Antimicrobial, anti-inflammatory and antioxidant activities of polyoxygenated chalcones. *Journal of the Brazilian Chemical Society*, *30*, 286-304.

Wijayanti, L. W., Swasono, R. T., Lee, W., & Jumina, J. (2021). Synthesis and evaluation of chalcone derivatives as novel sunscreen agent. *Molecules*, *26*(9), 2698.

Xu X, Qiu G, Ji L, Ma R, Dang Z, Jia R, et al. Research and development of anticancer agents under the guidance of biomarkers. Cancer Traditional Medicine. 2019;5(1):17-21

Xu, Y., Shi, Y., Lei, F., & Dai, L. (2020). A novel and green cellulose-based Schiff base-Cu (II) complex and its excellent antibacterial activity. *Carbohydrate polymers*, *230*, 115671.