Article

Study Of Novel Heterocyclic Ligand Derivtive From Imidazole And Its Metal Complexes: Synthesis, Spectral Characterization, Antitumor Activity And Antioxidant

Nabaa Hadeer Abd[1], Mithaq Saeed Mohammed [2]
[1,2] Department of Chemistry, College of Education for Girls, University of Kufa, Iraq
1*nabaah.khanfour@student.uokufa.edu.iq
, 2Mithaq.aldarughi@uokufa.edu.iq

Abstract:
A heterocyclic azo ligand was prepared from the conjugation of amino acid with Imidazole in alkaline media. The new compound was identified by C.H.N analysis , Mass spectrometry, Infrared spectroscopy, Ultraviolet-Visible spectroscopy, ^{1}HNMR spectroscopy and many other Physical properties. It is prepared a series of octahedral coordination complexes for the ions of cobalt(II), nickel(II), copper(II), zinc(II), cadmium(II) and mercury(II) ,The proposed geometrical of all complexes were octahedral . The prepared new compounds proved their vital activity as antioxidant and anti-cancer compounds.

Keywords:*metronidazole, Anticancer, Antioxidant, Azo dye*

1. Introduction

The metronidazole compound is an antibiotic from nitroimidazole derivatives, from its common uses as a treatment for some anaerobic bacterial infections and parasites that affect the joints, spinal cord of the brain, skin, stomach and liver [(1,2)] the physical properties of metronidazole is a white to pale yellow powder that can change to a dark color when exposed to light [(3)] As for the compound metronidazole, it has a mild odor and has a bitter, slightly salty taste [(4)] , its melting point is 158-160 degrees Celsius, it has solubility in water as well as ethanol, but its solubility in ether is slightly[(5,6)]. That is, its solubility in organic solvents is unstable at room temperature [(7)].

Chemical nitroimidazole derivatives include active Nitro groups either at positions 2 as well as 5 of the imidazole ring. While 2 - nitroimidazole carries pharmacological properties[(8)]. Metronidazole MTN. the prototype and one of the most versatile antibiotics in clinical use, is a derivative of metronidazole with antibiotics, A wide range of pharmacological effects of the microorganism is manifested with an emphasis on its antiviral, antibacterial, antiproliferative and antifungal activities in particular [(9-11).]

For azo compounds with an azo anion (–N=N -) in their structure, conjugated with heterocyclic or identical, monocyclic or polycyclic aromatic systems [12]. The presence of various functional groups in the backbone of the prepared compound can increase the impact on its electronic and structural flexibility, and therefore on the range of its possible applications [13,14].

The aim of the study preparation of a new heterocyclic azo ligand for derivative of imidazole with aromatic amine using the traditional preparation method and some selective transition ion complexes . Studying the physical and chemical properties of the prepared ligand and their metal complexes, diagnosis by available analytical means and proposing geometric shapes for them .

2. Experimental

2.1. Materials and Methods

All reagents and solvents used without purification from the companies BDH and FLUKA . Before being used, glassware was cleaned with soap, rinsed with distilled water, and dried at 110 degrees Celsius in an oven. An electric Metler balance was used for the weigh-in (BL, Satorius, 2015).The Stuart Melting Point SMP10 melting point instrument was used . Measurements of molar conductance were performed in DMSO using (Digital Conductivity Series Ino.Lab.720). Magnetic Susceptibility Measurement was conducted using Balance Magnetic Susceptibility model (M.S.B Auto) . Infrared spectral analyses were recorded using (Shimadzu FTIR 8400S Spectrophotometer) in the range of 400-4000cm-1. Elemental analysis (C.H.N.S) was carried out using Elemental Analysis System (GMBH). Using ethanol in the 200–1000 nm range, the Shiadzu 240–UV–V is spectrophotometer recorded the UV-Visible spectra of all the substances under investigation. Using DMSO as the solvent, the 1H-NMR spectra measurements were conducted on a BRUKER 500MHz using tetramethylsilane (TMS) as the internal standard. Mass Spectra Measurements were captured using the Shimadzu Instruments, Japan, QP-2010 GC-MS.

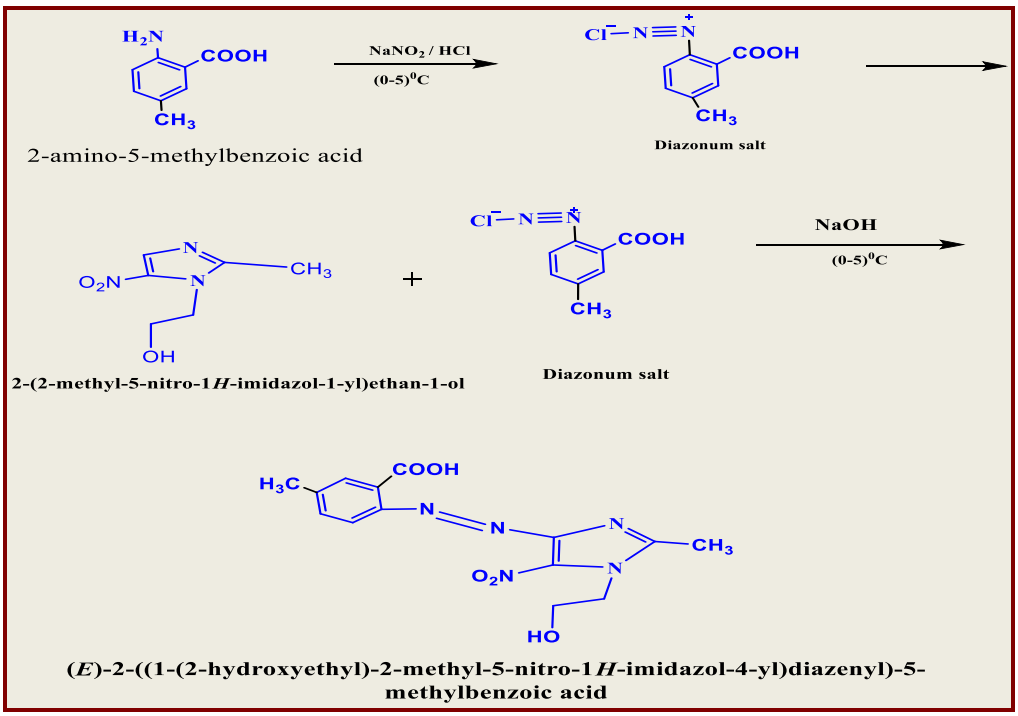
2.2. Synthesis of azo-metronidazole ligand

The preparation of this heterocyclic azo ligand was done as previously mentioned [15,16] as shown in Figure .1. 2-amino-5-methyl benzoic acid (1.51 g, 0.01mol) was dissolved in(50 mL) distal water and (5 mL) concentrated HCl (37%) by stirring the mixture until a transparent solution was achieved. After cooling this solution to between (0 and 5 °C), a drop-by-drop addition of sodium nitrite solution (0.7g, 0.01mol) in (10 mL) of water and stirring the liquid for 20 minutes in an ice bath. After cooling below 5 °C, (1.71g ,0.01mol) of metronidazole was dissolved in (150 mL) of alkaline ethanol and added to the resultant diazonium chloride solution. The mixture was acidified with (0.1 M)of HCl acid till (pH ≈ 7) after being refrigerated for a full day. After repeatedly washing with distilled- water, the red

crude precipitate was air dried, twice recrystallized from ethanol, and dried in an oven set at 45 °C.

2.3 Preparation of the azo-metronidazole complexes

Chelated complexes in their solid state have been prepared for this bonding with metal ions [Co (II),Ni(II),Cu(II),Zn(II),Cd(II), Hg(II),]. The complexes were prepared by dissolving the appropriate weights of each of the selected metal salts in (10 ml) of distilled water into ligand solution dissolved in (25 ml) of absolute ethanol,mole ratio (1:2)(metal:ligand) the reaction solution is heated for half an hour, after addition operations, precipitation of the prepared complexes is observed, which were filtered and dried with air, after which they were recrystallized using absolute ethanol [17,18].



Scheme 1: The synthesis of azo-metronidazole ligand

2.4 Antioxidant Activity

Ethanol was used as a solvent to create a (0.1 Mm) concentration DPPH solution. Three milliliters ml of the aforesaid solution were taken out and mixed with one milliliter of azo-metronidazole solution in ethanol at various concentrations. The mixes were stored at (25°C) in the dark. The absorbance at 517 nm was evaluated after 30 minutes in comparison to blank samples that lacked a scavenger. Using ethanol as a blank, the absorbance of the clear resultant solution was measured at 517 nm. Positive controls included ascorbic acid (A.A). A greater activity of DPPH free radical scavenging is shown by the reduction in absorbance of the resultant mixture [19,20].

2.5 Effectiveness of Anticancer

The produced azo-metronidazole ligand cytotoxic action on the colon cancer cell line HCT116 and the normal cell line HFF. Following a 24-hour incubation period at 37°C, the ligand was assessed using MTT assays at doses of (7.4, 22.22, 66.66, 200 and 600) μg/mL. It was found that the selected chemical inhibited the (HCT116) and (HUVEC) cell lines. The percentage of inhibition was compared to the control to determine the harmful impact's magnitude [21,22].

3. Results and Discussion

The azo-metronidazole ligand was a stable solid powder, red in color and all of the complexes are powders that are soluble in the majority of organic solvents, including methanol, ethanol, acetone, dimethylformamide, and dimethyl ulfoxide, which yield stable solutions at room temperature, but insoluble in water. The color of the complexes varies depending on the metal ions present.

3.1. Element investigation

The results show a strong correlation with the computed values that were utilized to assess the ligand purity. It implies that the coordination ratio (M:L) between the metal and the ligand is[2:1] or[1:1]. The complexes' empirical formulas are proposed based on the analytical data. In Table 1 Some analytical and physicaldata on the ligand and its complexes.

Table 1. Some analytical and physical data on the ligand and its complexes

Compound	M.wt. (g/mol)	m.p. °C	yield%	Color	M:L	Found (Caled) %			
						C	H	N	M
$C_{14}H_{14}N_5O_5$	333	215	85	Red	....	66. 66 (64.36)	5.55 (5.36)	27.77 (26.81)	…… …….
$[Co(C_{14}H_{14}N_5O_5)_2]\ H_2O$	488.993	198	75	Greenish brown	1:2	59. 68 (57. 83)	4.97 (4.81)	24.86 (24.09)	10.47 (10. 15)
$[Ni\ (C_{14}H_{14}N_5O_5)_2]\ H_2O$	408.71	300	70	Greenish brown	1:2	59.71 (57.86)	4.97 (4.82)	24.87 (24.10)	10.43 (10.11)
$[Cu(C_{14}H_{14}N_5O_5)_2]\ H_2O$	413.54	300	85	Green	1:2	59.20 (57.38)	4.93 (4.78)	24.66 (23.90)	11.19 (10.85)
$[Zn(C_{14}H_{14}N_5O_5)_2]\ H_2O$	415.38	218	75	Red	1:2	59.01 (57.20)	4.91 (4.76)	24.58 (23.83)	11.48 (11.13)
$[Cd(C_{14}H_{14}N_5O_5)_2]\ H_2O$	462.4	220	75	Red	1:2	54.51 (52.96)	4.54 (4.41)	22.71 (22.06)	18.23 (17.71)
$[Hg(C_{14}H_{14}N_5O_5)_2]\ H_2O$	550.59	300	70	Red	1:2	47.68 (46.49)	3.97 (3.87)	19. 86 (19. 37)	28.46 (27.75)

3.2 The ^{1}HNMR Spectrum of ligand

Spectra of ^{1}HNMR of this chemical were obtained using DMSO-D6, at 2.5 ppm it was caused by protons in the solvent. Multiple indicators appeared in the region of 6.8-8.5 ppm due to aromatic rings . The -CH_3 group appeared in the imidazole ring at 2.9 ppm . At δ 12.9 ppm due to (-OH) carboxcylic acid . An additional signal at δ 4.30 ppm is due to the proton active group (CH_2) aliphatic group [23,24,25]. And additional signal at δ 4.37 ppm in the ligand spectrum due to (-OH)
aliphatic group.Shown in Figure 1

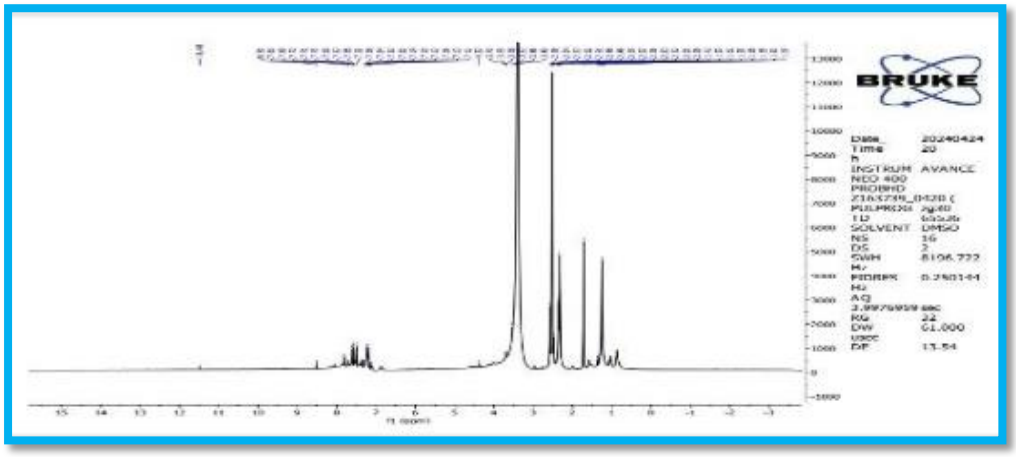


Figure 1: The ^{1}HNMR spectrum of the ligand

3.3 The azo ligand Mass Spectrum

The mass spectrum of Azo - sulfadiazine ligand showed a characteristic molecular ion peak at (M / Z = 541.3), which corresponds to its corresponding molecular mass. The fraction (M / Z = 477.3) is the azo molecule after the loss of the (sulfo group) fraction at (M/Z = 295,280) attributed to [$C_{17}H_{15}N_3O_2$]and

Figure 2: azo-metronidazole ligand mass spectrum

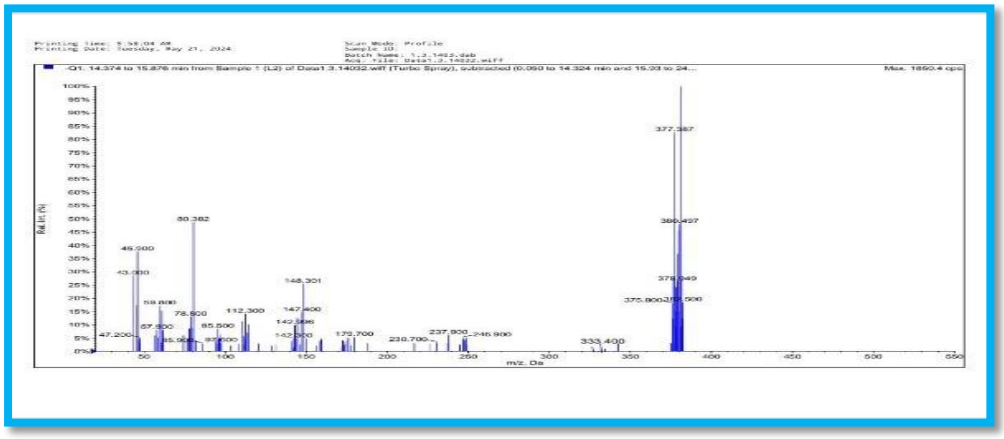
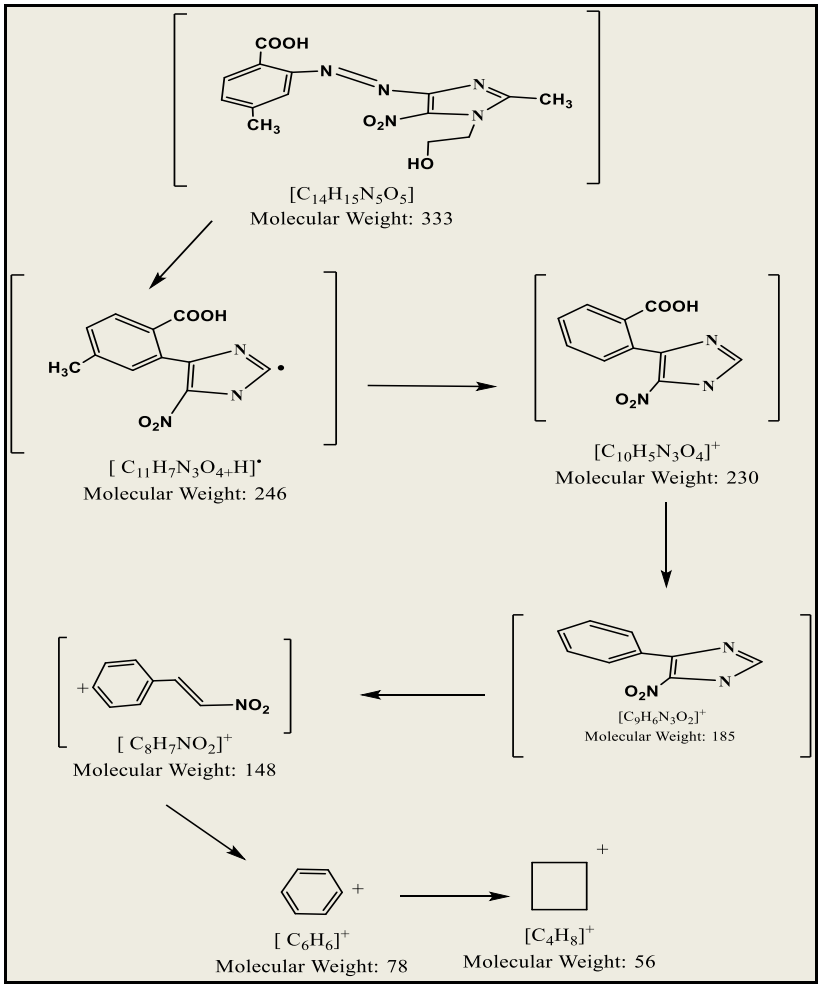


Figure 2: azo-metronidazole ligand mass spectrum

$[C_{17}H_{15}N_2O_2]$ The fragment is at (M / Z = 263) corresponding to $(C_{10}H_8N_5O_2S)$, the peak at (M/Z = 105 and 92) which is due to$(C_6H_4N_2)$ and (C_6H_4N) [26,27].



Scheme (2): Suggested mass fragmentation pathways for Azo Ligand

3.4.IR Spectra of ligand

The azo ligand and the metal complexes recorded their IR spectra as KBr pellets in the 4000-400 cm^{-1} range. The results revealed the ligand's functional group associated with the metal ions, which are shown in Table (2). The absorption band resulting from (O–H) in the imidazole ring was detected at 3290 cm^{-1} . Additionally, the band at 3454 cm^{-1} in the ligand spectrum was caused by (COOH) stretching vibration of carboxcylic acid . This band, which were absent in complexes spectra .The band at 1566 $cm^{-1}$was moved to a lower frequency in complexes and suggested that the azomethine group of imidazole ring was involved in complexation .In the

ligand, the stretching frequency resulting from the azo (N=N) was detected at 1417 cm^{-1}. The presence of one azo nitrogen atom coordinating with a metal ion is indicated by the azo group's shift to hihger frequency, appearing around 1417–1435 cm^{-1} .The presence of low intensity non-ligand bands in the range of 520–547 cm^{-1} in all complexes is further evidence that the creation of complexes between the azo ligand and metal ions through coordination bonds is caused by ν (M–N) stretching frequencies, respectively [28]. The spectra of the azo ligand and its complexes are shown in Figures 3 to 9.

Table 2: Frequencies of functional aggregates in the infrared spectrum (in cm^{-1})

Compound	ν (O─H)	υ(COOH) or H2O	υ(C=N) imidazole	ν (C═O)	ν (N═N) azo	ν (NO2)	ν (M─N)
$C_{14}H_{14}N_5O_5$	3290 br	3454	1566 s	1647	1417 s	1155m 1269	.....
$[Co(C_{14}H_{14}N_5O_5)_2]\ H_2O$	3286	3441	1579	1548	1423	1273 1155	542
$[Ni\ (C_{14}H_{14}N_5O_5)_2]\ H_2O$	3290	3439 br	1573 w	--------	1421 w	1273 1155	547
$[Cu(C_{14}H_{14}N_5O_5)_2]\ H_2O$	3358	3442m	1571 w	1630 s	1417 m	1269 1153	520
$[Zn(C_{14}H_{14}N_5O_5)_2]\ H_2O$	3394	3437 s	1591 w	---------	1406 w	1280 s	474 w
$[Cd(C_{14}H_{14}N_5O_5)_2]\ H_2O$	3346	3446 s	1570s	1640	1419 s	1284 1163	553 m
$[Hg(C_{14}H_{14}N_5O_5)_2]\ H_2O$	3286	3441 br	1564 s	1635	1417m	1267 1130	532 w

S= strong, m = medium, w = weak, br = broad

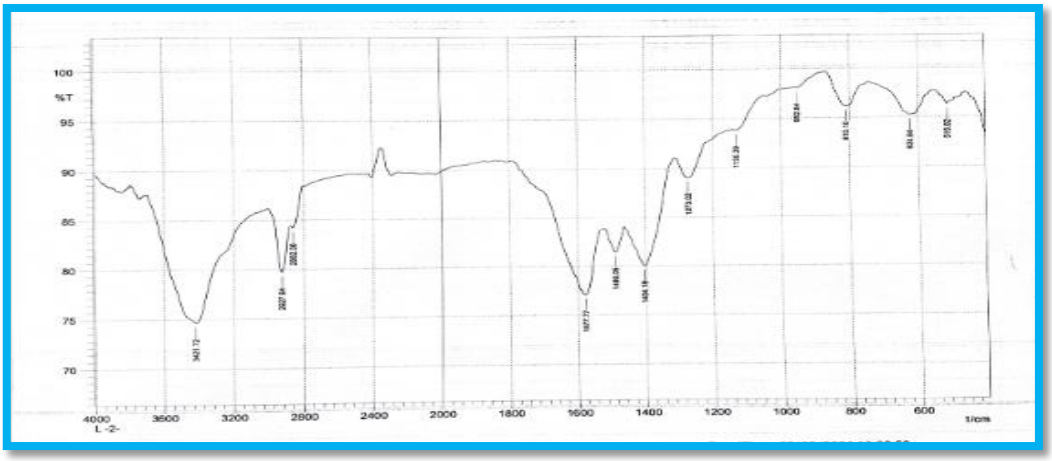


Fig. 3: IR spec.of L

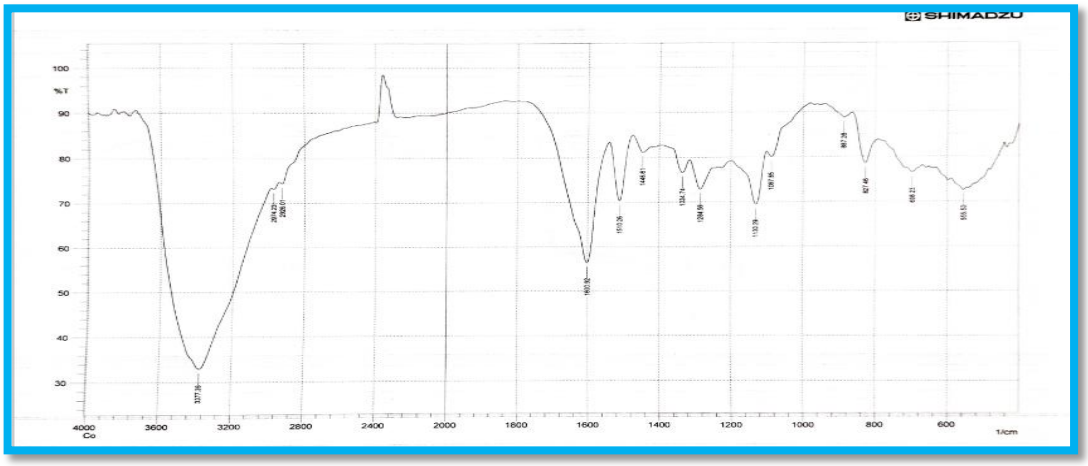


Fig. 4: IR Spec. of [Co $(L)_2$]

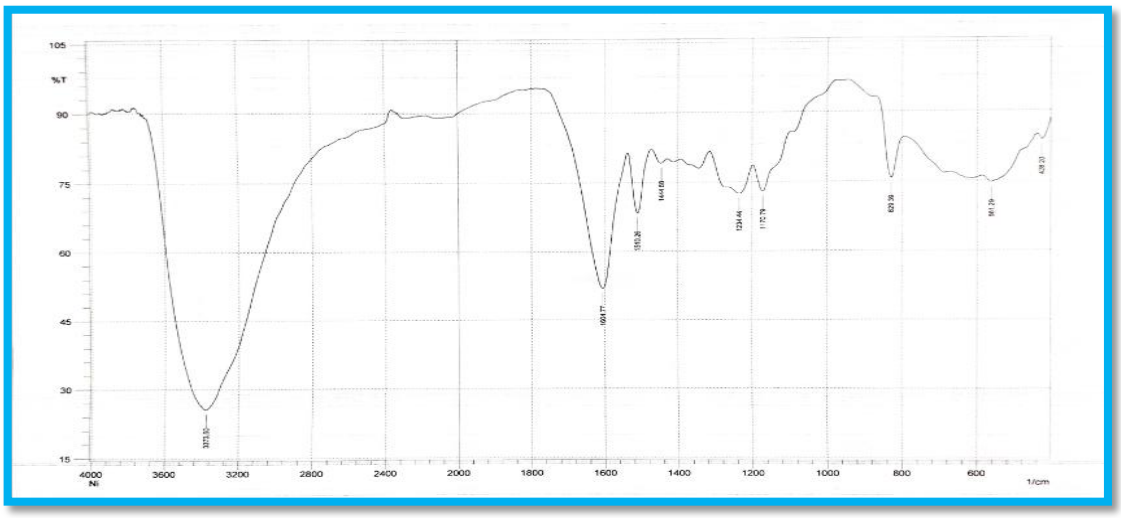


Fig.5: IR Spec. of [Ni $(L)_2$]

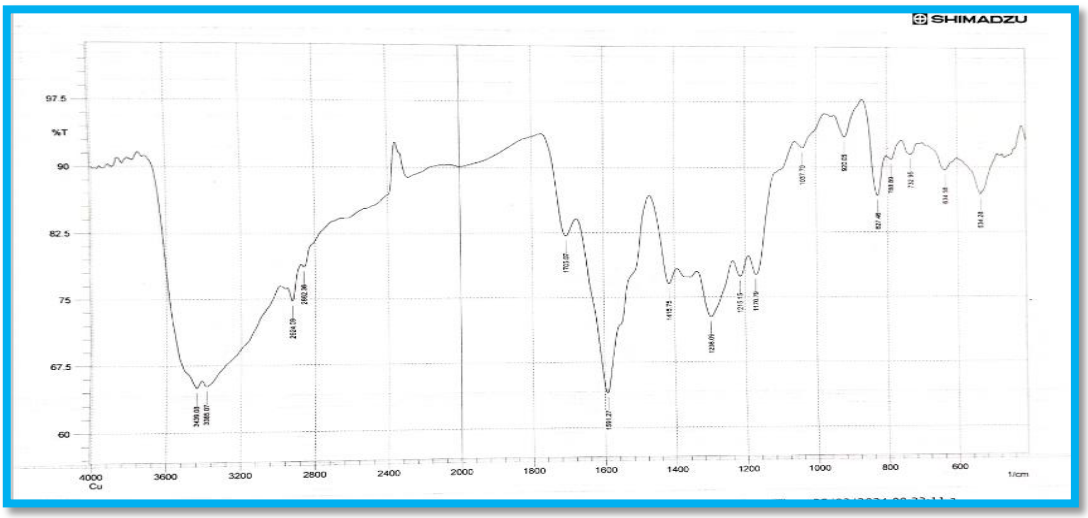


Fig. 6: IR Spec. of [Cu $(L)_2$]

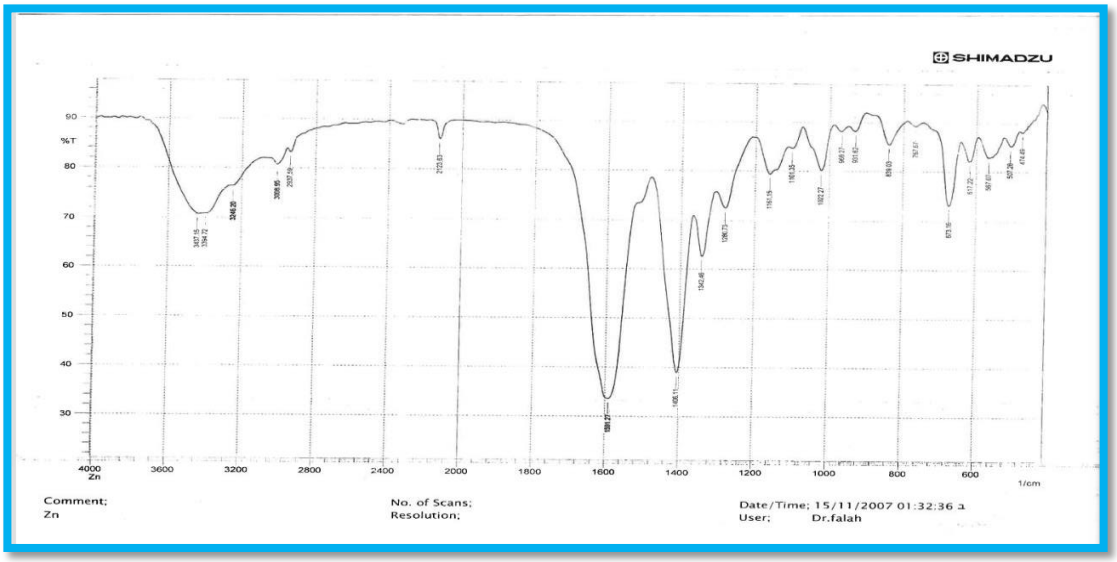


Fig. 7: IR Spec. of [Zn $(L)_2$]

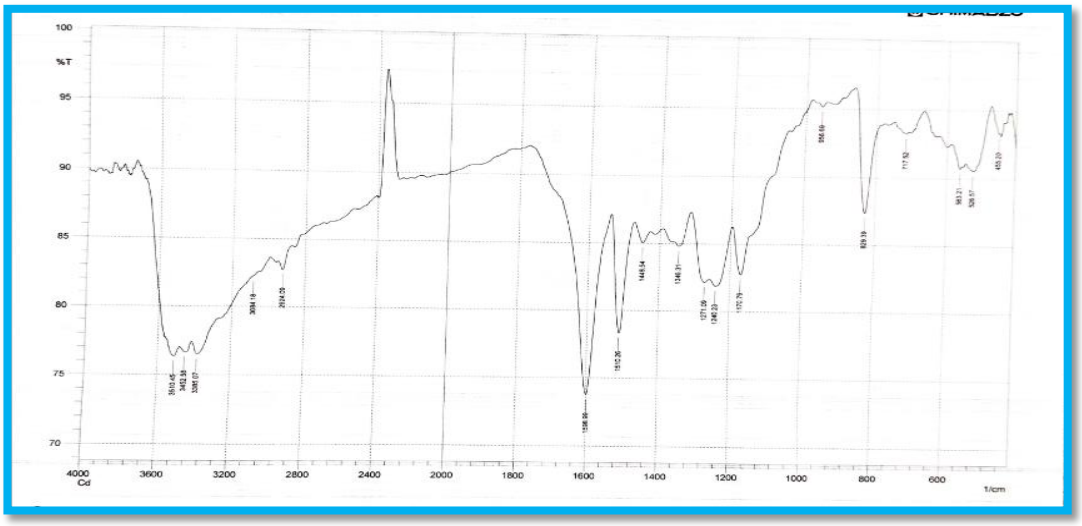


Fig. 8: IR Spec. of [Cd $(L)_2$]

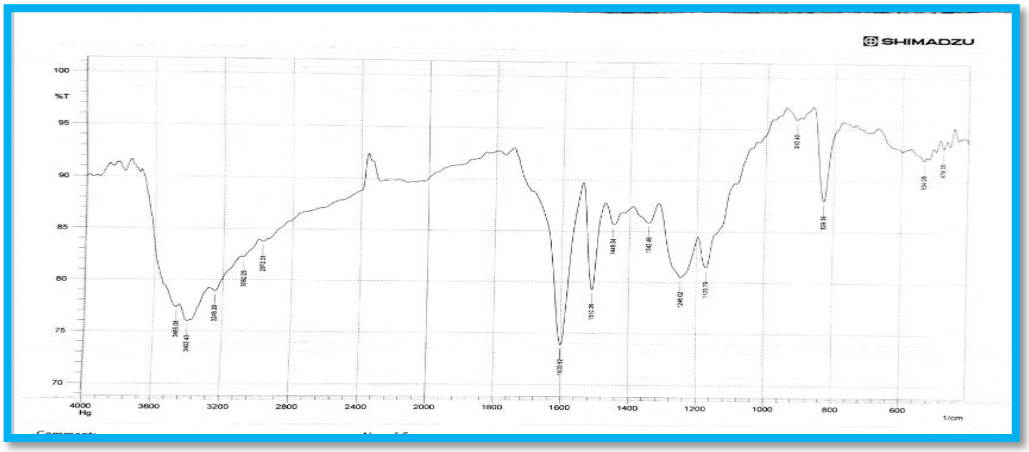


Fig. 9: IR Spec. of [Hg $(L)_2$]

3.5 Electronic Transfers

All of the compounds' electronic absorption spectra were recorded at room temperature using an ethanol exhausting solution in the(200–1100 nm)range. All of the complexes, with the exception of complex , were determined to be non-electrolytic based on molar conductance measurements recorded in the solvent DMSO. The chelate's value of conductivit [29]. and fall within the range (1.17 - 4.72) $S.cm^2.mol^{-1}$[30]. The spectra of the azo ligand and its complexes are displayed in Figures 9 to15

Table 3: Electronic data, Magnetic measurements, Geometry, Hybridization and Conductivity

Compound	Abs. Bands(n. m)	Transition	Cond. S. cm^2 $.mol^{-1}$	μeff (B.M)	Geometry	Hybridization
$C_{14}H_{14}N_5O_5$	316 464	π→ π* n→ π*		…….	.....	.....
$[Co(C_{14}H_{14}N_5O_5)_2]$ H_2O	364 625	ILCT MLCT	2.13	2.9	Octahedral	SP^3d^2
$[Ni\ (C_{14}H_{14}N_5O_5)_2]$ H_2O	382 653	ILCT MLCT	1.42	5.47	Octahedral	SP^3d^2
$[Cu(C_{14}H_{14}N_5O_5)_2]$ H_2O	317 654	ILCT MLCT	3.47	1.78	Octahedral	SP^3d^2
$[Zn(C_{14}H_{14}N_5O_5)_2]$ H_2O	347 494	ILCT MLCT	2.23	Dia	Octahedral	SP^3d^2
$[Cd(C_{14}H_{14}N_5O_5)_2]$ H_2O	316 451	ILCT MLCT	4.72	Dia	Octahedral	SP^3d^2
$[Hg(C_{14}H_{14}N_5O_5)_2]$ H_2O	330 673	ILCT MLCT	1.17	Dia	Octahedral	SP^3d^2

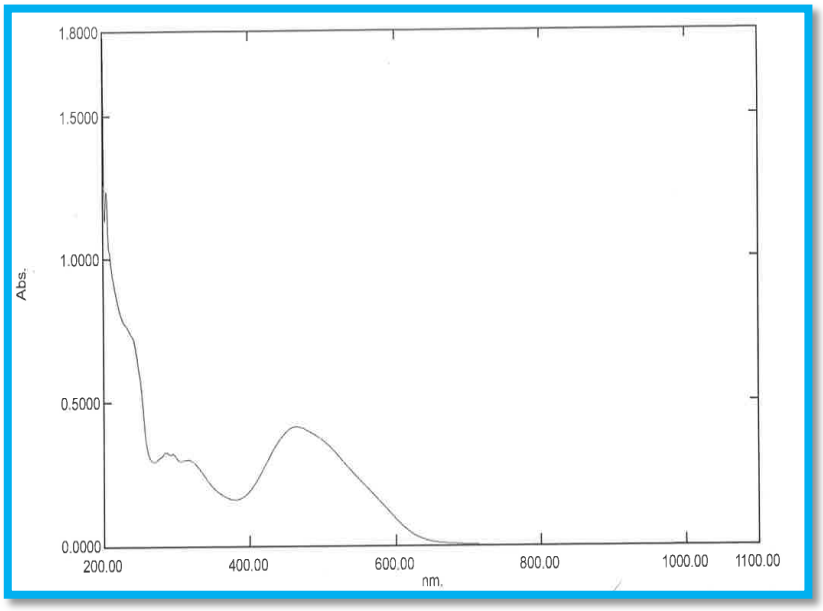


Fig. 9 : UV-Vis. of L

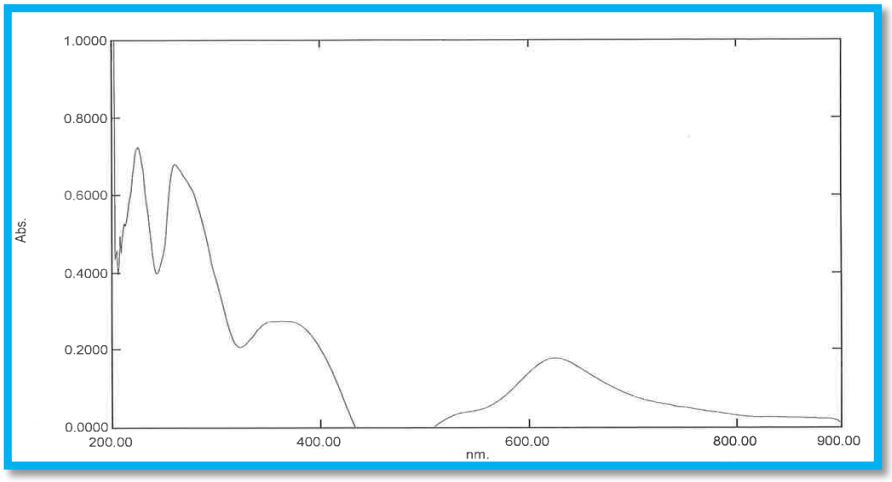


Fig.10: UV-Vis of [Co $(L)_2$]

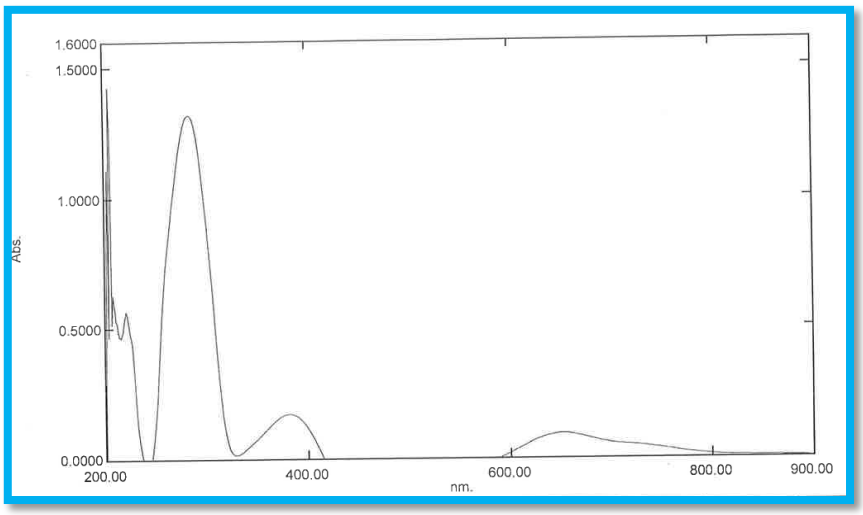


Fig.11: UV-Vis of [Ni $(L)_2$]

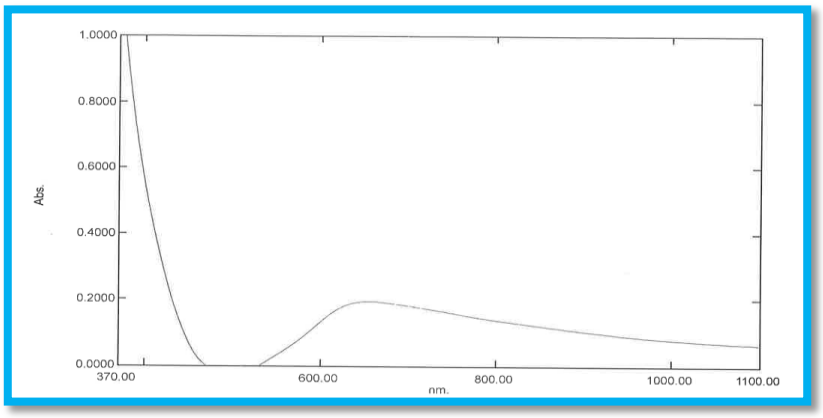


Fig. 12: UV-Vis of [Cu $(L)_2$]

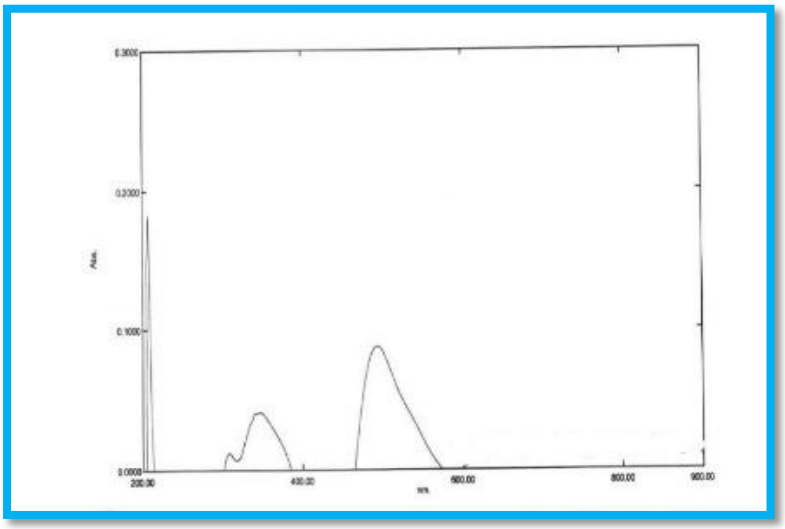


Fig.13: UV-Vis of $[Zn(L)_2]$

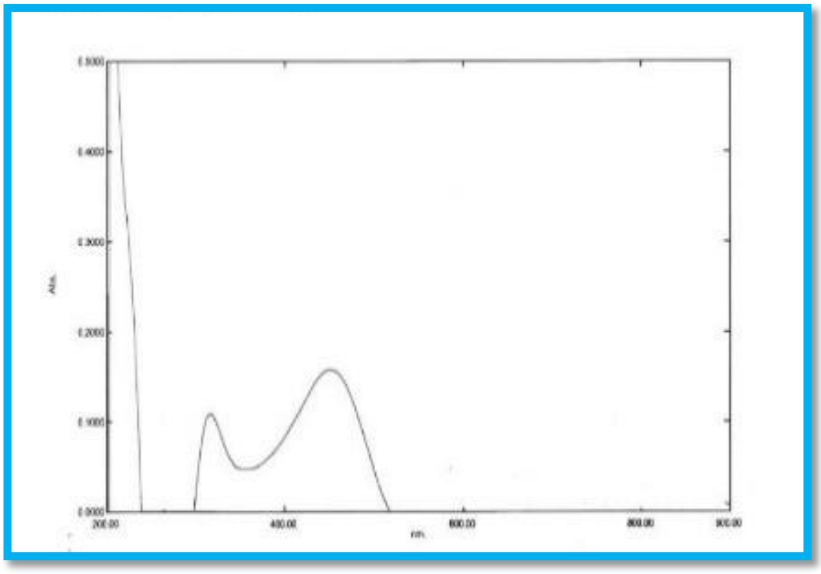


Fig.14: UV-Vis of [Cd $(L)_2$

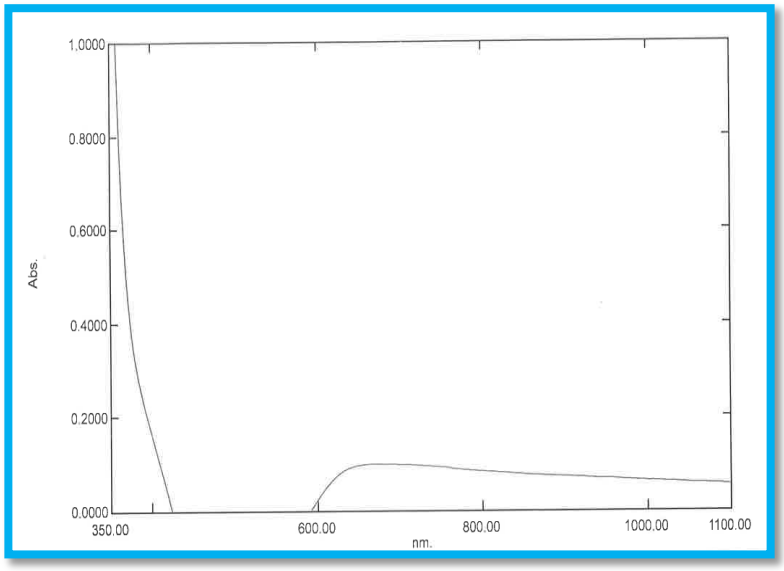


Fig.15:UV-Vis of [Hg $(L)_2$]

3.7 Anticancer effectiveness

Previous studies have shown good results for and its derivatives as pharmaceutical compounds[31]. A study was conducted of the cytotoxic effect of the ligand on treated and untreated colon cancer cells (HCT116) , then a study of the cytotoxic effect of normal cells (HUVEC) was conducted and a comparison was made between them for the purpose of demonstrating the extent of their toxic effectiveness on the cells of the human body and the possibility of using them as medicines For cancer .The azo-metronidazole ligand , proved biological effectiveness towards colon cancer, as the results of measurements on cells with colon cancer showed a clear inhibition [32]. The practical results obtained confirmed the possibility of using the ligand as a new inhibitor for this type of cancer, as it is safer for healthy cells because it has (IC50 = 98.07µg\ml) for cancer cells and (IC50 = 376,45µg\ml) for healthy cells [33]. Table 4: Biological effectiveness of ligand on cellular cells of cancer HCT116. Compare it to the normal HUVEC cellular line for the same concentration and use the test MTT for 72 hours and tem 37 °C.

Table 4: Biological effectiveness of Ligand on cellular cells of colon cancer HCT116. Compare it to the normal HUVECcellular line for the same concentration and use the test MTT for 72 h. and tem. 37 °C.

Con. ($\mu g.\ mL^{-1}$)	Percentage (%) for each cell line			
	Cancer line cells of HCT116		Normal line cells of HUVEC	
	Cell Viab.	Cell Inhib.	Cell Viab.	Cell Inhib.
7.4	93.56	6.44	106.25	6.25
22.22	81.10	18.9	100.25	0.25
66.66	67.47	32.53	90.06	9.94
200	56.03	43.97	79.17	20.83
600	41.71	58.29	71.52	28.48
IC50	98.07		376.45	

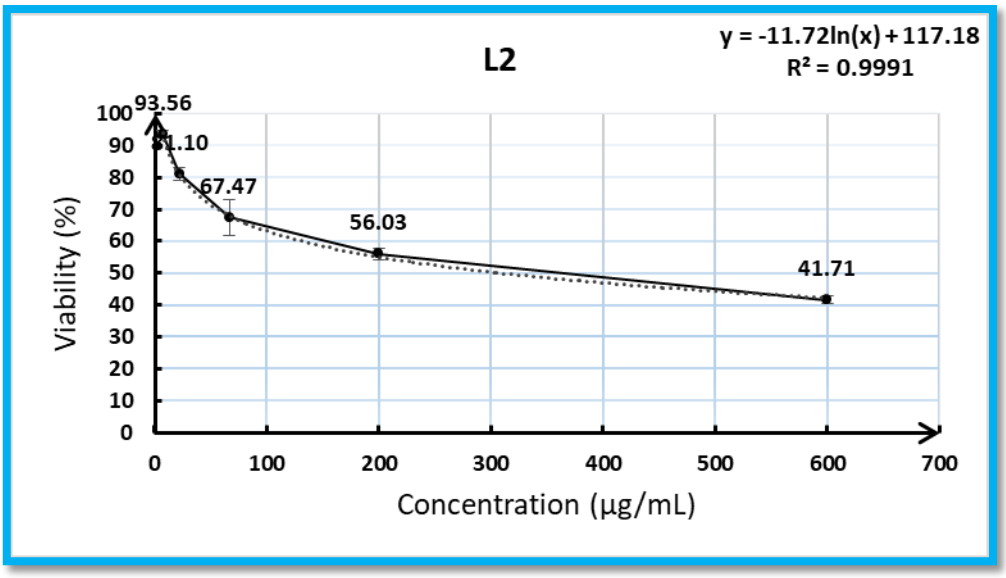
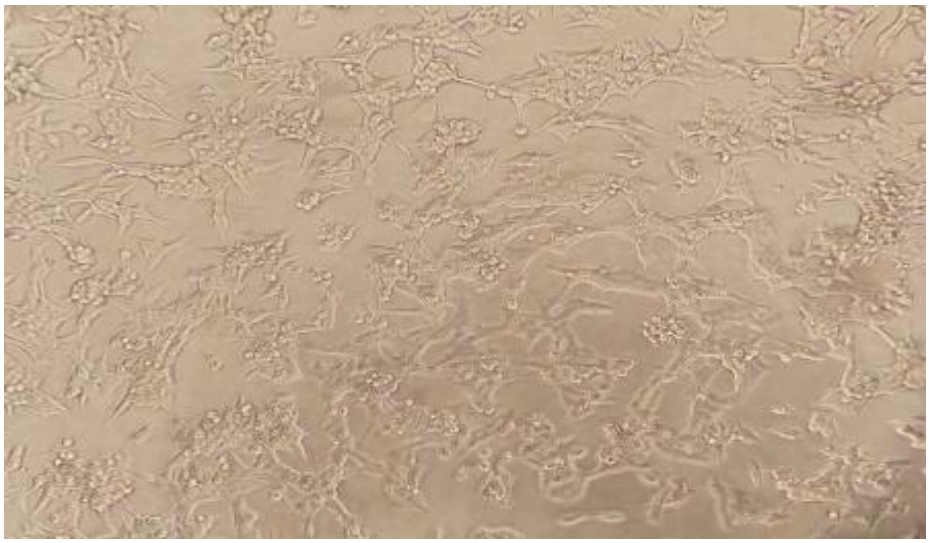
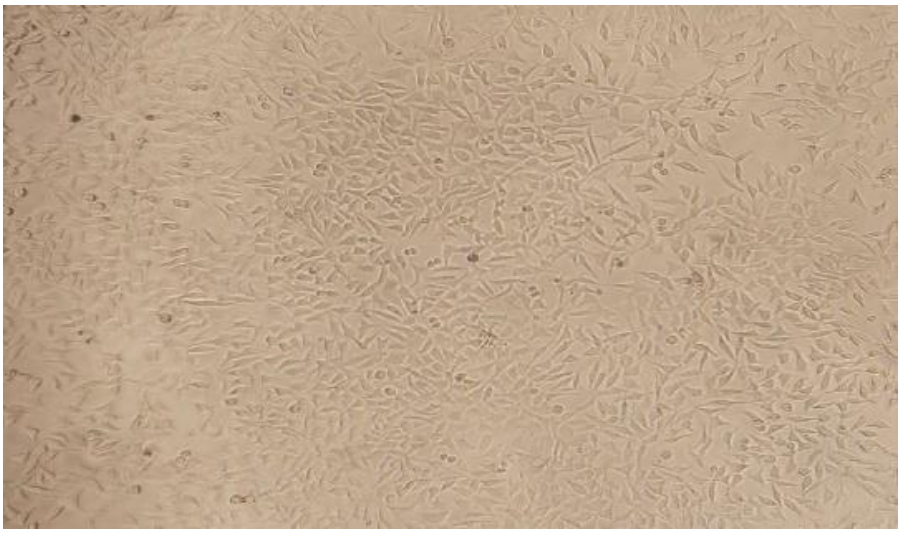


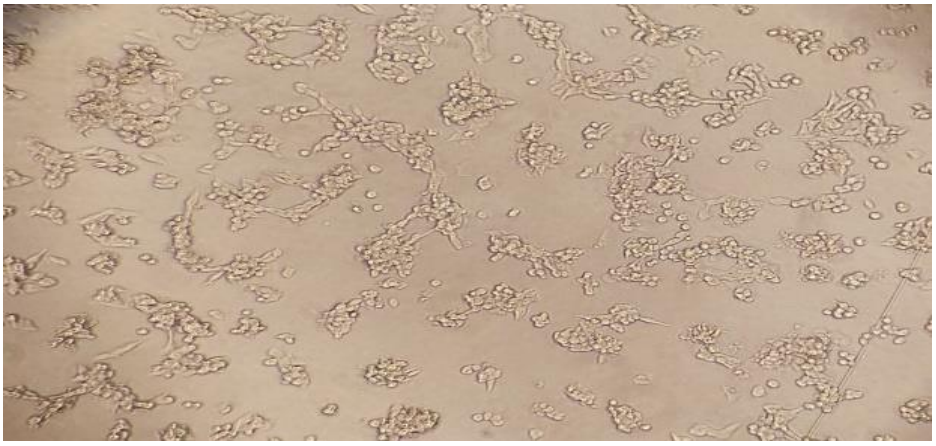
Fig.16: The half-inhibitory concentration of cancer cells (HCT116) and healthy cells (HUVEC) for ligand ,Anticancer activity data of cells against unhealthy and healthy Cells.



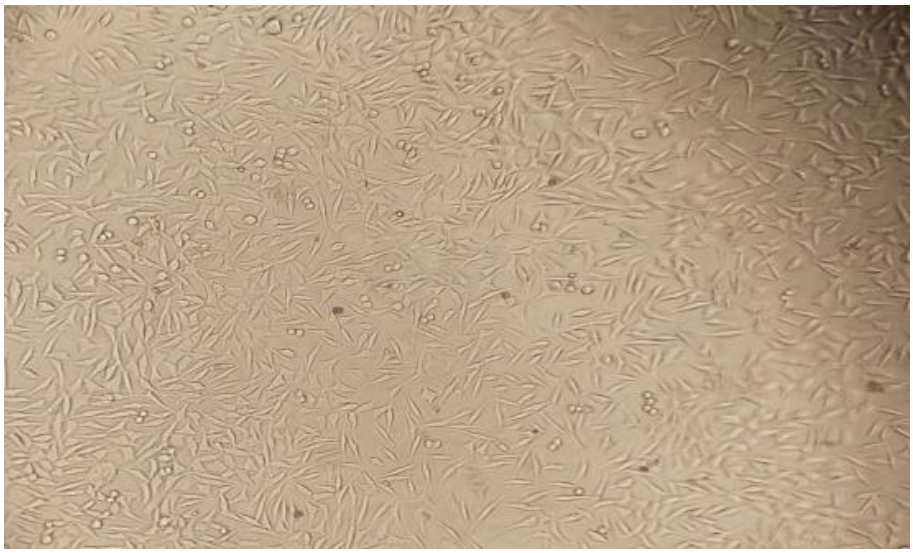
L2 (HCT116) 7.4 ug.m



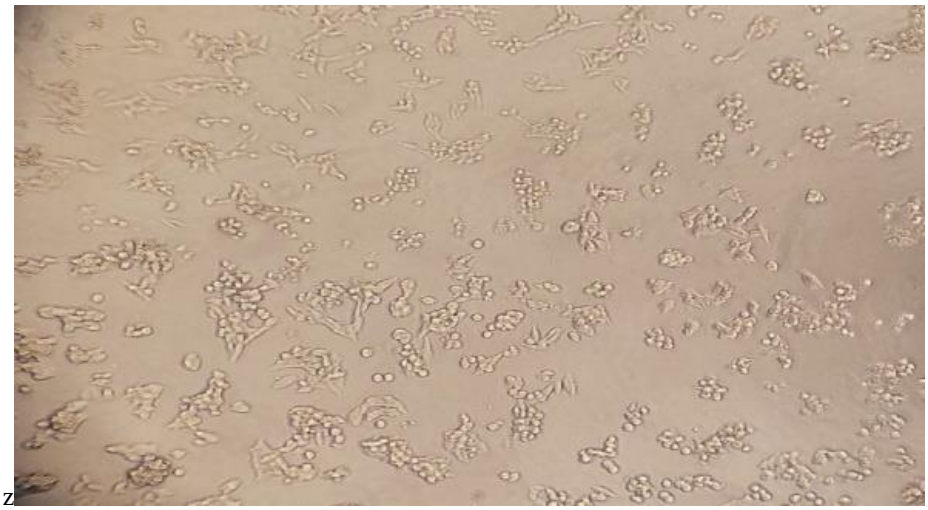
L2 (HUVEC) 7.4 ug.m



L2 (HCT116) 22.22 ug.m

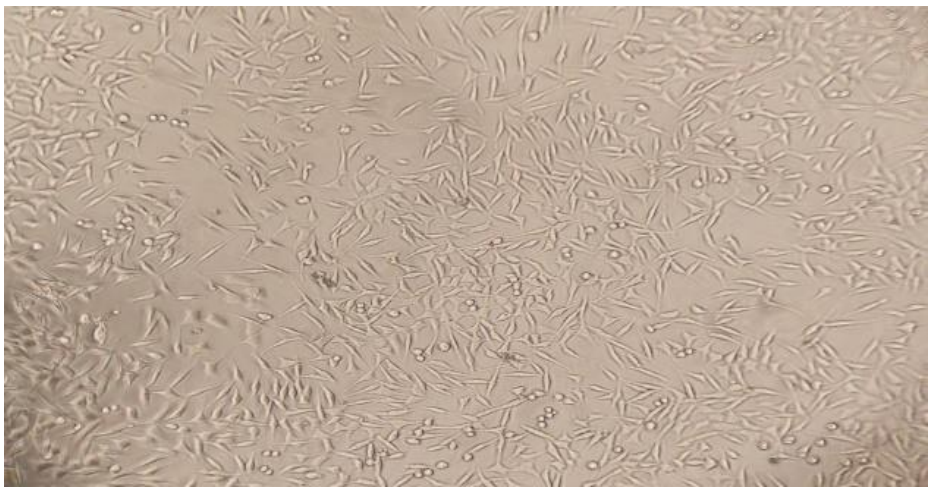


L2 (HUVEC) 22.22 ug.m

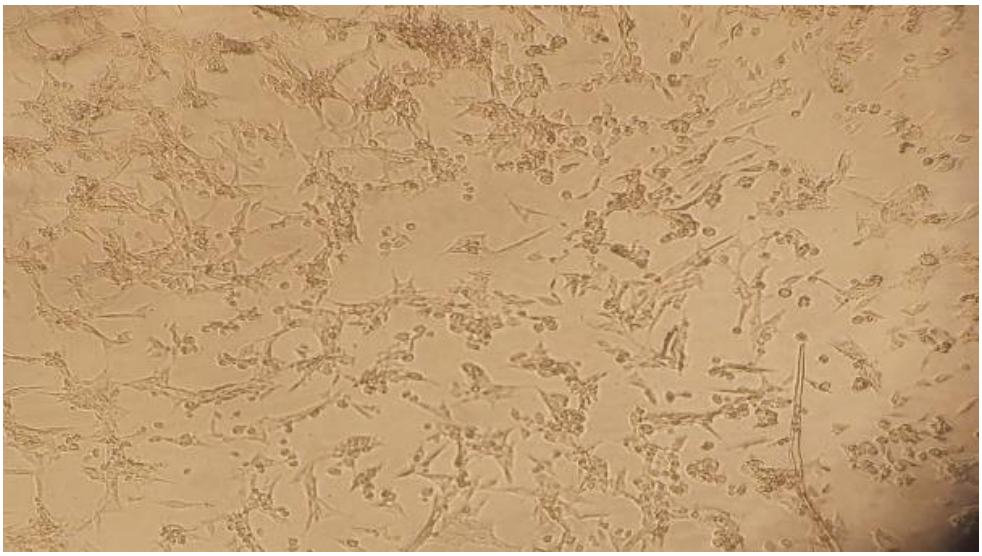


z

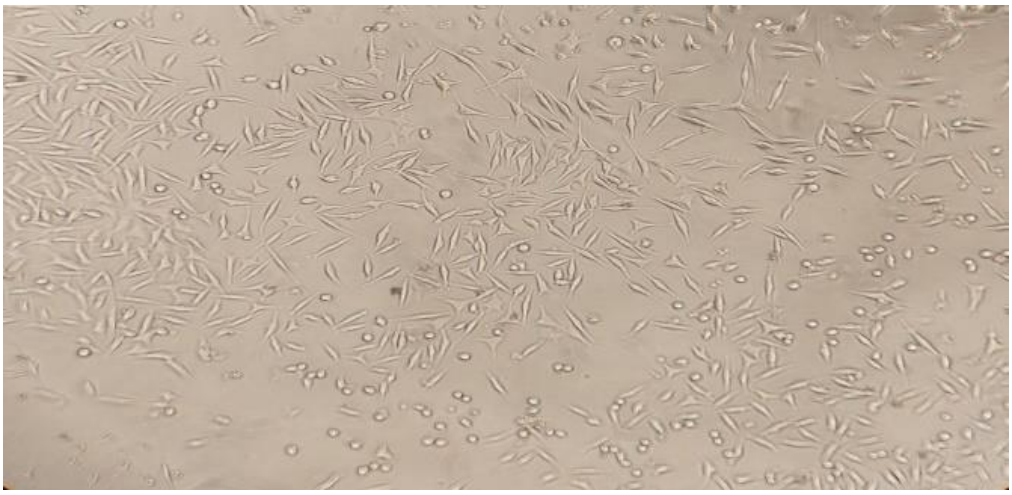
L2 (HCT116) 66.66 ug.m



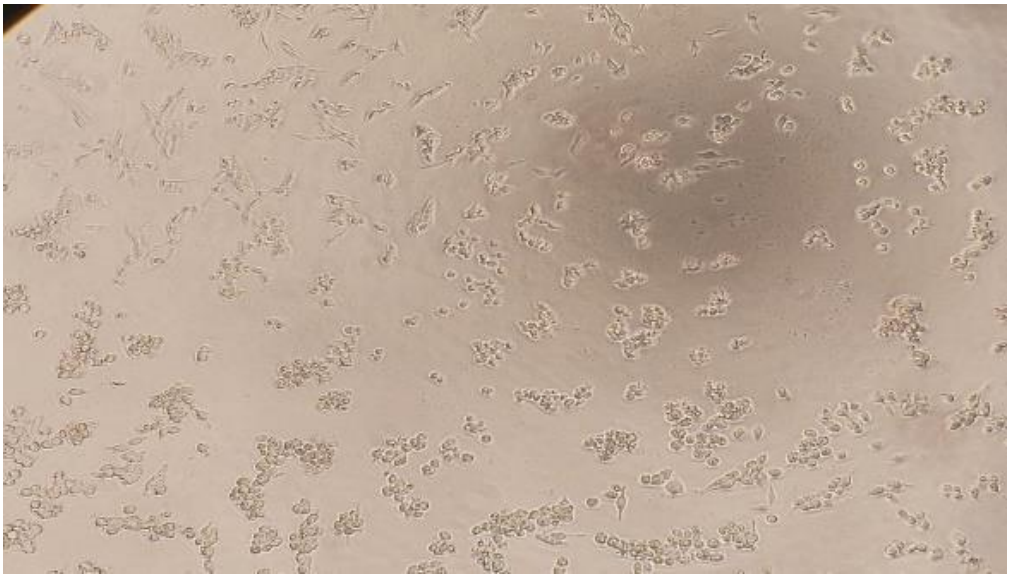
L2 (HUVEC) 66.66 ug.m



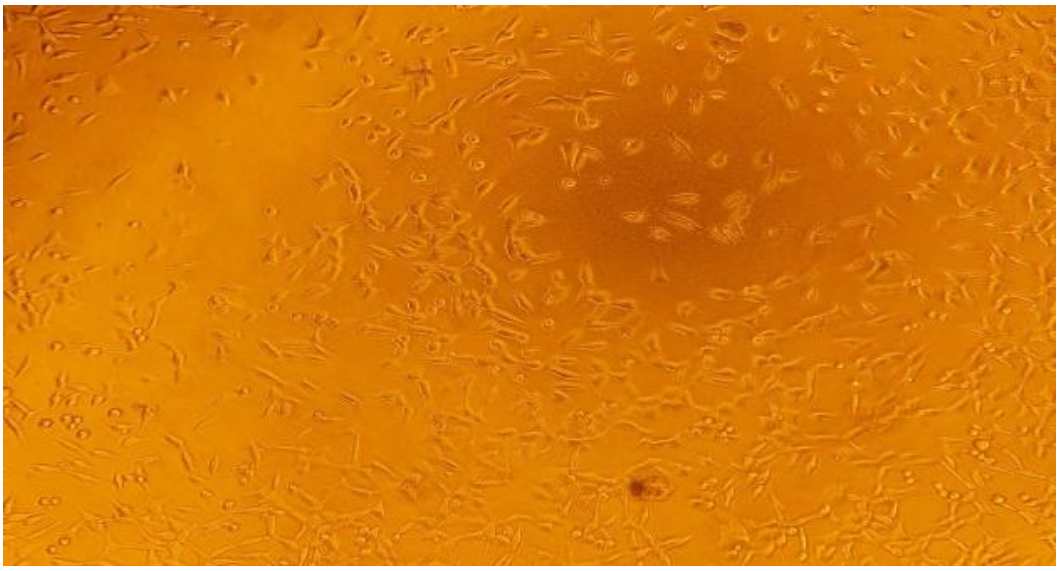
L2 (HCT116) 200 ug.m



L2 (HUVEC) 200 ug.m



L2 (HCT116) 600 ug.m



L2 (HUVEC) 600 ug.m

Fig.17: Cancer cells treating Ligand with different conc. after adding (MTT)

3.8 Activity of Antioxidants

Many biological functions, such as those that are anti-inflammatory, anti-allergic, anti-cancer, and anti-diabetic, need antioxidant activity[34]. The azo dye has strong anti-radical scavenging properties. The inclusion of sulfadiazine derivatives as bioactive elements in the structures of synthetic dyes was suggested to be responsible for these compounds' activity . A stable, comparatively free radical is DPPH. To be more stable, it takes an electron or hydrogen . Azo ligand showed high antioxidant activity towards DPPH, with the highest inhibition rate of the prepared compounds at concentration (25ppm) reaching (78.33%), while the lowest inhibition rate at concentration (5ppm) was (75.32%). As shown by the inhibition ratios in the table below[35] .Table 5 displays the azo ligand's DPPH % inhibition.

Table 5: Antioxidant activity of the azo-metronidazole ligand

Con. ($\mu g.\ mL^{-1}$)	Ligand		Ascorbic Acid	
	Absorbance	Inhibition	Absorbance	Inhibition
5	0.287	75.32	0.015	98.7
10	0.281	75.83	0.009	99.2
15	0.265	77.21	0.006	99.4
20	0.255	78.07	0.004	99.6
25	0.252	78.33	0.002	99.8

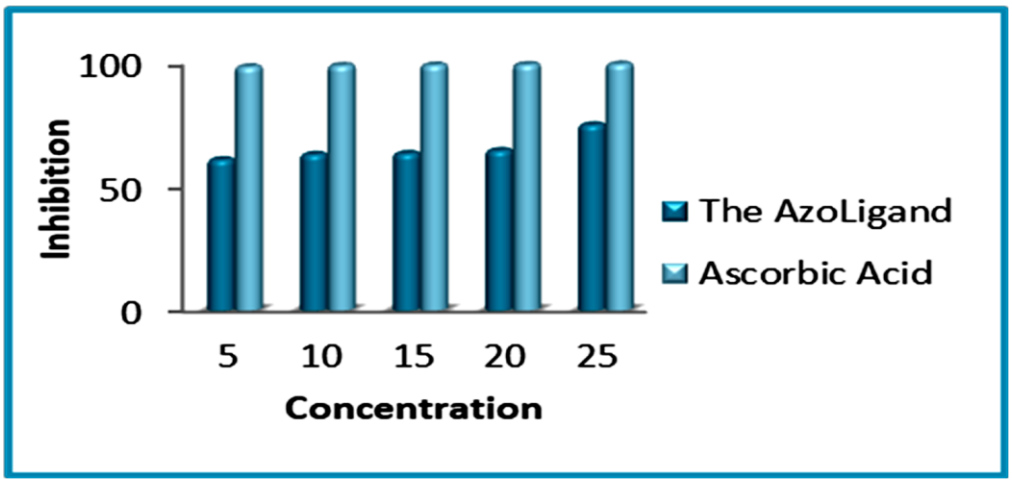
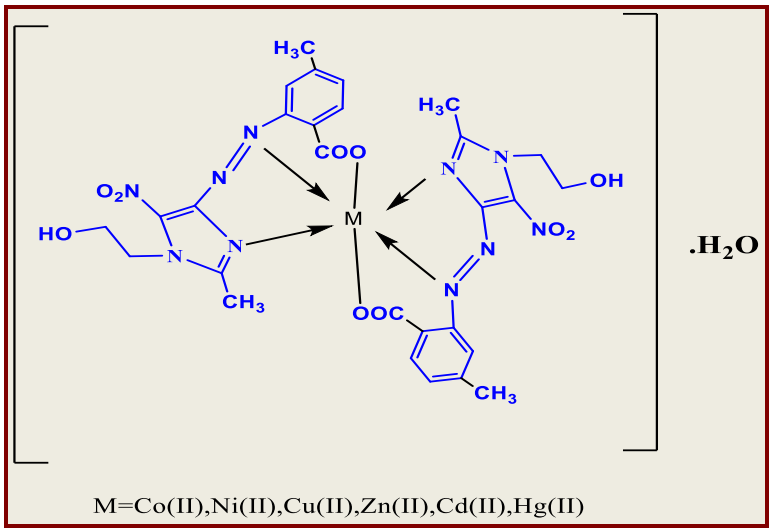


Figure 18: Scavenging activity of the azo ligand

4. Conclusion

Inferences have been reached that lead to: The ligand was produced using the diazotization process and A three-claw ligand of type (N,N,O) is a negatively charged monocoque chelating ligand that binds to metal ions in a pentagonal chelating ring. the complexes are octahedral. The generated complexes demonstrated good stability. The ligand is efficient against cancer, and antioxidants.



Scheme2 : Suggested geometries of the ligand complexes

References

[1] Löfmark, Sonja, Charlotta Edlund, and Carl Erik Nord. "Metronidazole is still the drug of choice for treatment of anaerobic infections." *Clinical infectious diseases* 50.Supplement_1 (2010): S16-S23.

[2] Moffat, Anthony C., et al. *Clarke's analysis of drugs and poisons*. Vol. 3. London: Pharmaceutical press, 2011.

[3] Fakhre, Nabil A., and Dashne M. Kokhasmail. "ZANCO Journal of Pure and Applied Sciences."

[4] Al-Sabea, N. "Assay of metronidazole from different manufacturing sources in Iraqi markets." *Al Mustansiriyah Journal of Pharmaceutical Sciences* 5.1 (2008): 16-25.

[5] Khalil, Nada Ahmadd, Hana Shuker Mahmoud, and Ahlam Ahmad Shehab. "Spectrophotometric Determination of Metronidazole in Pharmaceutical Preparations and in Human Blood samples." *Egyptian Journal of Chemistry* 65.8 (2022): 397-405.

[6] SAKIRA, Abdoul Karim, et al. "Determination of the quality of metronidazole formulations by near-infrared spectrophotometric analysis." *Talanta Open* 3 (2021): 100027.

[7] Fakhre, Nabil A., and Dashne M. Kokhasmail. "ZANCO Journal of Pure and Applied Sciences."

[8] Çelik, Ayla, and Nurcan Aras Ateş. "The frequency of sister chromatid exchanges in cultured human peripheral blood lymphocyte treated with metronidazole in vitro." *Drug and Chemical toxicology* 29.1 (2006): 85-94.

[9] Kapoor, V. K., Renu Chadha, Praveen K. Venisetty, and S. Prasanth. "Medicinal significance of nitroimidazoles—some recent advances." (2003).

[10] Radko, Lidia, et al. "Silver (I) complexes of the pharmaceutical agents metronidazole and 4-hydroxymethylpyridine: comparison of cytotoxic profile for potential clinical application." *Molecules* 24.10 (2019): 1949.

[11] Mahmoud, Simaa Safaa, and Asmaa Mohammed Noori Khaleel. "New Metronidazole Derivative and Some of Its Complexes with Antibiofilm study." *Ibn AL-Haitham Journal For Pure and Applied Sciences* 36.4 (2023): 274-287.

[12] Giovanni, D. A. R., B. Giuseppe, and F. Andrea. "Quantitative determination of 26 aromatic amines derived from banned azo dyes in textiles through the use of LC, tandem MS, and identification of some structural isomers." (2014).

[13] Hakimi, Mohammad, Boris-Marko Kukovec, and Mao Minoura. "2D s-d Mixed-Metal Coordination Polymer Containing Potassium, Chromium (III) and Dipicolinate Ions: Preparation and Crystal Structure." *Journal of chemical crystallography* 42 (2012): 290-294.

[14] Hamza, Mariam Bassem, and Enaam IsmaiI Yousif. "New Metal Complexes Derived from Azo Linked Schiff-Base ligand: Synthesis, Spectral Investigation and Biological Evaluation." *Journal of University of Anbar for Pure Science* 17.2 (2023): 154-164. Al-Khodir, Fatima AI. Ca (II), Zn (II) and Au (III) sulfamethoxazole sulfa-drug complexes: Synthesis, spectroscopic and anticancer evaluation studies. Orient. J. Chem. 2015, 31, 1277. http://dx.doi.org/10.13005/ojc/310304 .

[15] 15)Abbas, AlyaKhider, and Rafal Salam Kadhim. Metal Complexes of Proline-Azo Dyes, Synthesis, Characterization, Dying Performance and Antibacterial Activity Studies. Orient J Chem . 2017 33402-417. http://dx.doi.org/10.13005/ojc/330148 .

[16] **1**6)Al-Joboury, Wissam MR, Khalid A. Al-Badrany, and Nabeel J. Asli. Synthesis of new azo dye compounds derived from 2-aminobenzothiazole and study their biological activity. Mater. Today 202147, 5977-5982. https://doi.org/10.1016/j.matpr.2021.04.538 .

[17] 17)Patel, Khyati D., and Hasmukh S. Patel. Synthesis, spectroscopic characterization and thermal studies of some divalent transition metal complexes of 8-hydroxyquinoline. Arab. J. Chem. 2017, 10,S1328-S1335. https://doi.org/10.1016/j.arabjc.2013.03.019

[18] 18)Huo, Yanping, Jiguo Lu, Sheng Hu, Liming Zhang, Fenghua Zhao, Huarong Huang, Baohua Huang, and Li Zhang. Photoluminescence properties of new Zn (II) complexes with 8-hydroxyquinoline ligands: dependence on volume and electronic effect of substituents. Journal of Molecular Structure. 2015,1083,144-151. https://doi.org/10.1016/j.molstruc.2014.11.029 .

[19] 19)Hassan, Z. M., Alattar, R. A., Abass, S. K., Mihsen, H. H., Abbas, Z. F., & Hussain, K. A. SYNTHESIS, CHARACTERIZATION AND BIOLOGICAL ACTIVITY OF MIXED LIGAND (IMINE OF BENZIDINE AND 1, 10-PHENANTHROLINE) COMPLEXES WITH Fe (II), Co (II). Chem. Chem. Technol. 2022,16, 15-24. http://dx.doi.org/10.23939/chcht16.01.015 .

[20] 20)Dinçalp, Haluk, Fatih Toker, İnci Durucasu, Nesibe Avcıbaşı, and Sıddık Icli. New thiophene-based azo ligands containing azo methine group in the main chain for the determination of copper (II) ions. Dyes and Pigments. 2007,75, 11-24. https://doi.org/10.1016/j.dyepig.2006.05.015 .

[21] 21)Kyhoiesh, Hussein Ali Kadhim, and Khalid J. Al-Adilee. Synthesis, spectral characterization, antimicrobial evaluation studies and cytotoxic activity of some transition metal complexes with tridentate (N, N, O) donor azo dye ligand. Results Chem. 2021 ,3,100245. https://doi.org/10.1016/j.rechem.2021.100245 .

[22] 22)Mohamed, G. G., Nadia EA El-Gamel, and F. A. Nour El-Dien. Preparation, chemical characterization, and electronic spectra of 6-(2-pyridylazo)-3-acetamidophenol and its metal complexes. SYNTH REACT INORG M. 2001,31, 347-358. https://doi.org/10.1081/SIM-100002053 .

[23] 23)Al-Adilee, Khalid J., Khamis A. Abedalrazaq, and Zainab Mohsin Al-Hamdiny. "Synthesis and Spectroscopic Properties of Some Transition Metal Complexes with New Azo-Dyes Derived From Thiazole and Imidazole. Asian J. Chem. 2013,25.

[24] 24)Gaber, Mohamed, Nadia El-Wakiel, and Osama M. Hemeda. Cr (III), Mn (II), Co (II), Ni (II) and Cu (II) complexes of 7-((1H-benzo [d] imidazol-2-yl) diazenyl)-5-nitroquinolin-8-ol. synthesis, thermal, spectral, electrical measurements, molecular modeling and biological activity. J. Mol. Struct. 1180 2019,1180, 318-329. https://doi.org/10.1016/j.molstruc.2018.12.006 .

[25] 25)Jasim, Duaa Jameel, and Alyaa Khider Abbas. Synthesis, identification, antibacterial, medical and dying performance studies for azo-sulfamethoxazole metal complexes. Eurasian Chem. Commun. 2022,4, 16-40. https://doi.org/10.22034/ecc.2022.310593.1251 .

[26] 26)Lane, Andrew A., and Bruce A. Chabner. Histone deacetylase inhibitors in cancer therapy. J. Clin. Oncol.2009,27, 5459-5468. https://doi.org/10.1200/JCO.2009.22.1291 .

[27] 27)Yang, Jun, Xuanrong Sun, Weiwei Mao, Meihua Sui, Jianbin Tang, and Youqing Shen. Conjugate of Pt (IV)–histone deacetylase inhibitor as a prodrug for cancer chemotherapy. Mol. Pharmaceutics. 2012,9, 2793-2800. https://doi.org/10.1021/mp200597r .

[28] 28)Bouhdada, Mohammed, Mohamed EL Amane, and Najia El Hamzaoui. Synthesis, spectroscopic studies, X-ray powder diffraction data and antibacterial activity of mixed transition metal complexes with sulfonate azo dye, sulfamate and caffeine ligands.Inorg. Chem. Commun. 2019, 101,32-39. https://doi.org/10.1016/j.inoche.2019.01.005 .

[29] 29)Saad, Fawaz A., Jabir H. Al-Fahemi, Hoda El-Ghamry, Abdalla M. Khedr, Marwa G. Elghalban, and Nashwa M. El-Metwaly. "Elaborated spectral, modeling, QSAR, docking, thermal, antimicrobial and anticancer

activity studies for new nanosized metal ion complexes derived from sulfamerazine azodye." J. Therm. Anal. Calorim. 2018,131,1249-1267. https://doi.org/10.1007/s10973-017-6598-4 .

[30] 30)Habila, Imane, Mouna Saoudi, Fadila Berrah, Belkacem Benmerad, Mhamed Boudraa, Hocine Merazig, and Sofiane Bouacida. A new complex of Zinc (II) with sulfamethoxazole ligand: Synthesis, crystal structure, Hirshfeld surface analysis, thermal properties, DFT calculations and antibacterial/antifungal activities. J. Mol. Struct. 2021,1244,130903. https://doi.org/10.1016/j.molstruc.2021.130903 .

[31] 31)Alshibl, Hanan M., Ebtehal S. Al-Abdullah, Mogedda E. Haiba, Hamad M. Alkahtani, Ghada EA Awad, Ahlam H. Mahmoud, Bassant MM Ibrahim, Ahmed Bari, and Alexander Villinger. Synthesis and evaluation of new coumarin derivatives as antioxidant, antimicrobial, and anti-inflammatory agents. Mol. 2020,25, 3251. https://doi.org/10.3390/molecules25143251 .

[32] 32)Marie, M. M., A. A. Salem, and E. M. R. El Zairy. A novel printing method to enhance the fixation of reactive dyes on wool–polyamide fabrics." Journal of the Textile Institute 102, no. 9 (2011): 790-800.

[33] 33)Ferrero, Franco, and Monica Periolatto. Ultrasound for low temperature dyeing of wool with acid dye. Ultrason. Sonochem. 2012,19, 601-606. https://doi.org/10.1016/j.ultsonch.2011.10.006 . Zozulya, G., Kuntyi, O., Mnykh, R., & Sozanskyi, M. SYNTHESIS OF ANTIBACTERIALLY ACTIVE SILVER NANOPARTICLES BY GALVANIC REPLACEMENT ON MAGNESIUM IN SOLUTIONS OF SODIUM POLYACRYLATE IN AN ULTRASOUND. Chem. Chem. Technol. 202115, 493-499. http://dx.doi.org/10.23939/chcht15.04.493 .

[34] 34)Ali, W. A., Mihsen, H. H., & Guzar, S. H. Synthesis, Characterization and Antibacterial Activity of Sn (II) and Sn (IV) Ions Complexes Containing N-Alkyl-N-Phenyl Dithiocarbamate Ligands. Chem.

Chem. Technol, 2023, 17(4), 729-739. https://doi.org/10.23939/chcht17.04.729 .

[35] 35)Ahmed, Ameen Haider, and Fakhri Ahmed. Identification of MRSA (methicillin resistant Staphylococcus aureus) by mecA gene. AJMS. 2022,1, 25-30. https://doi.org/10.55145/ajbms.2022.1.2.004 .

[36] 36)AL-FATLAWI, HAWRAA YOUSIF, and Saher Mahmood Jwad. Assessing the level of a trial natriuretic peptide and some biochemical parameters in men with type 2 diabetic nephropathy. Utt. Prad. J. 2022, 1-13. https://doi.org/10.56557/upjoz/2022/v43i93018 .

[37] 37)Ahmed, Fakhri S., and Ameen Haider Ahmed. Isolation of ferric Yersinia bactin A (fyuA) as virulence gene and biofilm forming in Escherichia coli was Collected from patient with UTI. AJMS. 2023,2, 6-11. https://doi.org/10.55145/ajbms.2022.1.2.005.

[38] 38)Chaudhary, Narendra Kumar, and Parashuram Mishra. "Metal complexes of a novel Schiff base based on penicillin: characterization, molecular modeling, and antibacterial activity study. Bioinorg. Chem.2017,2017. https://doi.org/10.1155/2017/6927675 .

[39] 39)Mohamad, M. Some transition metal complexes with new Schiff base ligand hexa dentate.Acta chimica. Pharm. Indica .2013,3,140-148.

[40] 40)MOHAMMED, LAYLA ALI, RAHEEM TAHIR MEHDI, and ABID ALLAH MOHAMMED ALI. Synthesis, identification and structural of some transition metal complexes with New heterocyclic azoschiff base ligand derived from 4-amino antipyrine. Int. J. Pharm. Res. 2020,12. https://doi.org/10.31838/ijpr/2020.12.04.121 .

[41] 41)Hassan, Mohammad, Karan Malhotra, and Mohd Firdaus. Application of artificial intelligence in IoT security for crop yield prediction. JIST. 2022,2,136-157. https://orcid.org/0009-0002-2232-2855 .

[42] 42)Tello, A.B. et.al., Application of Artificial Intelligence and IOT for Increasing Productivity of Agricultural Sector, IJET .2022,4, 39-45. https://doi.org/10.1016/j.cpb.2022.100263 .

[43] 43)Jawad, Aseel Mahmood, Nagham Mahmood Aljamali, Saher Mahmood Jwad, Aseel MJ, and Saher MJ. Development and preparation of ciprofloxacin drug derivatives for treatment of microbial contamination in hospitals and environment. Indian J Med Forensic Med Toxicol. 2020,14, 1115-1122. https://doi.org/10.37506/ijfmt.v14i2.3067 .

[44] 44)Mahmoud, Ghyath Salih, and Wael Adil Obaid. Experimental studies on the effect of Chlorpyrifos on rats. VI. Population of intestinal mast cells and hypersensitivity reactions. AJMS. 2022,1 6-11. https://doi.org/10.55145/ajbms.2022.1.1.002 .

[45] 45)Mkhaiber, Ahmed, and Naz Jarallah. Study The Relationship Between Bremsstrahlung Dose Rate and the Energy of Beta Ray for Different Types of Shield: Nuclear Physics. Malays. J. Sci. 2022, 47-54. https://doi.org/10.22452/mjs.vol41no2.4 .

[46] **46)**Bagheri, Mitra, Majid Validi, Abolfazl Gholipour, Pooyan Makvandi, and Esmaeel Sharifi. Chitosan nanofiber biocomposites for potential wound healing applications: Antioxidant activity with synergic antibacterial effect. Bioeng. transl. med. 2022,7, e10254. https://doi.org/10.1002/btm2.10254