



Novel Schiff Base Metal Complexes and Their Biological Applications

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Abstract

Cr(III), Zn(II), Ni(II) and Cu(II) complexes of a symmetric Schiff base ligand (L), (Z)-N'-((1E,2E)-1-(2-(p-tolyl)hydrazineylidene)propan-2-ylidene)-2-((E)-1-(2-(p-tolyl)hydrazineylidene)propan-2-ylidene)hydrazine-1-carbohydrazide has been synthesized. Elemental analysis, UV-Visible, FT-IR, mass spectra and conductometric techniques were used to characterize the ligand and its metal complexes. The microorganisms utilized in this study involve *Streptococcus mutans*, *Staphylococcus Aureus* (as Gram-positive bacteria), *Escherichia Coli* and *Klebsiella pneumonia* (as Gram-negative bacteria) and *Aspergillus Nigar* and *Candida albicans* (as fungi). Comparing all the studied species, the Cu(II) complex exhibits the highest activity versus tested fungi. The Zn- and Ni-complexes were found to have promising anticancer activity.

Keywords: Schiff base; UV-Visible; FT-IR; Mass Spectra; Conductometric techniques; Antimicrobial activity; Anticancer activity

1. Introduction

The scientific community has evaluated many metal complexes using different Schiff-bases, Schiff bases are generally bi-, tri-, or tetra-dentate chelate ligands and form very stable complexes with transition metal ions [1, 2]. They are usually very good activators of small molecules [3], have good redox capability [4], present interesting optical properties [5], are good corrosion inhibitors [6, 7], and have shown attractive thermal and electrical properties [8]. It is observed that the complexes of poly dentate Schiff bases which are very stable complexes have been used in catalysis [9], medicine [10], crystal engineering [11], and corrosion protection [12]. In this paper we are considered with Schiff bases derived from the condensation of diamine with carbonyl compounds which represent an important class of chelating agents. They can be obtained by condensing diamines with carbonyl compounds in 1:2 M ratio [13–17]. Several such symmetrical Schiff bases of 1,2- and 1,3- diamines, where one and the same type of simple aldehydes or ketones are condensed on both nitrogen atoms and their complexes are reported [18–27]. These metal complexes exhibit interesting structures and geometries. Therefore, these complexes have numerous applications in biological field as anti-bacterial, antifungal and as anti-cancer agents [28–33], analytical- [34] and industrial fields [35–39].

1. Experimental

2. In this study, high-purity chemicals were used. They included hydrazinecarbohydrazide (Sigma-Aldrich), 1-(2-(p-tolyl)hydrazineylidene)propan-2-one (Merck), $\text{CuCl}_2 \cdot 2\text{H}_2\text{O}$ (Sigma Aldrich), $\text{NiCl}_2 \cdot 6\text{H}_2\text{O}$ and $\text{ZnSO}_4 \cdot 7\text{H}_2\text{O}$ (BDH), $\text{CrCl}_3 \cdot 6\text{H}_2\text{O}$ (Alpha Chemika), Absolute Ethanol as an organic solvent, was spectroscopic pure, from BDH. Bidistilled water collected from all glass equipment was usually used in all preparations. Human tumour cell line breast cell (MCF-7) was obtained frozen in liquid nitrogen (-180°C) from American Type Culture Collection. The tumour cell line (MCF-7) was maintained in the National Cancer Institute, Cairo, Egypt, by serial sub-culturing.

Solutions

Metal complexes were dissolved in ethanol in precisely weighed amounts to prepare stock solutions of 1×10^{-3} M. By diluting the previously prepared stock solutions, solutions of the Schiff base ligand and its metal complexes (1×10^{-5} M) were prepared for evaluating their UV-Vis spectra.

2.1.1. Instrumentation

Microanalyses of carbon, hydrogen and nitrogen were carried out at the Microanalytical Center, Cairo University, Egypt, using a CHNS-932 (LECO) Vario elemental analyzer. Melting point measured by triforce XMTD-3000. The metal content was measured at the Egyptian Petroleum Research Institute's using inductively coupled plasma (ICP). Fourier-transform infrared spectroscopy (FT-IR) spectra were recorded on a Perkin-Elmer 1650 spectrometer ($4000\text{--}400\text{ cm}^{-1}$) using KBr as measured at the Egyptian Petroleum Research Institute's using inductively coupled plasma (ICP). Fourier-transform infrared spectroscopy (FT-IR) spectra were recorded on a Perkin-Elmer 1650 spectrometer ($4000\text{--}400\text{ cm}^{-1}$) using KBr disks. Molar

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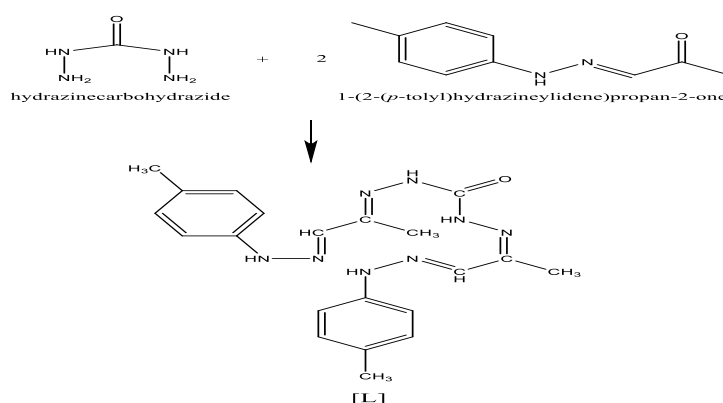
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conductivities of 10⁻³ M solutions of the solid complexes in ethanol were measured using a Jenway 4010 conductivity meter. As solutions in DMSO-d₆, ¹H NMR spectra were reported using tetramethylsilane as an internal standard with a 300 MHz Varian-Oxford Mercury at room temperature. Mass spectra were recorded using the electron ionization technique at 70 eV with an MS-5988 GS-MS Hewlett-Packard instrument at the Microanalytical Centre, Egypt. Thermogravimetric (TG) and differential thermogravimetric (DTG) measurements of the Schiff base ligand and metal complexes were done using a Shimadzu TG-50H thermal analyzer from room temperature to 1000 °C. The spectrophotometric measurements in solution were carried out using automated spectrophotometer UV-Vis PerkinElmer Model Lambda 20 ranged from 200 to 700 nm. Anticancer activity experiments were performed at the National Cancer Institute, Cancer Biology Department, Pharmacology Department, Cairo University, Egypt. Antimicrobial measurements were carried out at the Microanalytical Centre, Cairo University, Egypt.

2.2. Procedures

2.2.1. Synthesis of the Schiff base ligand [L]

The new Schiff base ligand (L) was synthesized from the condensation of hydrazinecarbohydrazide (3.998 mmol, 0.36 g) dissolved in water (25 °C) and 1-(2-(*p*-tolyl)hydrazineylidene)propan-2-one (8.001 mmol, 1.41 g) dissolved in absolute ethanol (25 °C) in 1:2 molar ratio and the reaction mixture were left under reflux for 4 h. The reaction was shown in (Scheme 1). The orange product obtained was separated after evaporation then filtered off and recrystallized from water-ethanol mixture to give pure Schiff base ligand with 96.23% yield. The structure of the Schiff base ligand as well as its general formation reaction are shown in Scheme (1).



Scheme. 1: Synthesis pathway of the Schiff base ligand (L).

2.2.2. Synthesis of the metal complexes

The metal chelates were prepared by mixing hot solution of absolute ethanol (20 ml) (70°C) of the Schiff base ligand (0.739 mmol, 0.3 g) with metal chloride and sulphate salts (0.739 mmol, 0.127 g CuCl₂·2H₂O, 0.197 g CrCl₃·6H₂O) dissolved in hot absolute ethanol (30 mL) (60°C), while (0.176 g NiCl₂·6H₂O, 0.212 g ZnSO₄·7H₂O) dissolved in hot water (30 mL) (60°C). The resulting mixture was stirred under reflux for 1 h whereupon the complexes precipitated. It was collected by filtration and purified by washing with ethanol/water several times and dried under vacuum over anhydrous CaCl₂.

2.3. Antimicrobial activity

The in-vitro antibacterial and antifungal activities of the ligand and its complexes were studied along with ampicillin as a standard antiseptic drug, gentamycin as a standard antibiotic drug and nystatin as a standard antifungal drug. The microorganisms utilized in this study involve *Streptococcus mutans*, *Staphylococcus Aureus* (as Gram-positive bacteria), *Escherichia Col* and *Klebsiella pneumonia* (as Gram-negative bacteria) and *Aspergillus Nigar* and *Candida albicans* (as fungi). The ligand's antimicrobial activity and its metal complexes were tested using diffusion agar technique [40-43].

3. Results and Discussion

3.1. Characterization of tetra dentate Schiff base ligand (L)

Orange solid Schiff base ligand (L) dissolves in typical organic solvents. All the metal complexes and the ligand were soluble in ethanol and stable at room temperature. The hypothesized structure was discovered to be consistent with CHNO analyses, IR spectra, and NMR data. Table 1 provides a summary of the information on the elemental analysis, colour, solubility M.P., and molecular formula. The data for LS's content in C, H, N, and O were found to be accurate when compared to the value estimated using the synthetic and suggested structures.

The existence of an apparent IR band at 1563 cm⁻¹ caused by ν (C=N), rather than bands corresponding to ν(C=O) or ν(NH₂), confirmed the formation of the Schiff base ligand (table 2). The proton of the NH group was detected in the Schiff base ligand's ¹H NMR spectrum at 10.45 and 11.20 ppm, along with azomethine protons at 7.55 ppm and aromatic protons between 6.93 and 7.21 ppm (see Table 3). The synthesis of Schiff base ligand L is confirmed by the absence of any evidence for the NH₂ group. The hypothesized formula [C₂₁H₂₆N₈O]⁺ with an atomic mass of 406 amu was validated by the mass spectrum of the ligand, which showed a molecular ion peak at m/z = 406 amu matching to [M]⁺. These investigations led to the structural resolving of the symmetric tetra-dentate Schiff base ligand (L).

3.2. Characterization of metal complexes

The response of ligands to metal salts was taken into consideration for the effective production of the metal complexes. Under reflux conditions, a colour shift was seen when a ligand in ethanol was combined with metal(II) salts in ethanol (1:1). The estimated values and the experimental elemental analysis of complexes agreed more closely. According to (Table 1), the complexes exhibit a 1:1 ML-type metal-ligand stoichiometry. The complexes have very high melting points and purity.

Table 1: Physical and analytical data of Schiff base ligand (L) and its metal complexes

Compound (chemical formula)	Colour	M.P. (°C)	Found (Calcd)					A_m ($\Omega^{-1} \text{ mol}^{-1} \text{ cm}^2$)
			C (%)	H (%)	N (%)	O (%)	M (%)	
L(C ₂₁ H ₂₆ N ₈ O)	Orange	110 -113	62.04 (63.11)	6.40 (6.51)	20.68 (20.72)	3.94 (4.01)	-----	-----
[CrLCl ₂]Cl.2H ₂ O	Brick Red	>300	41.95 (42.06)	4.33 (4.47)	13.98 (14.15)	2.66 (2.81)	8.66 (8.95)	78
[ZnL(H ₂ O) ₂]SO ₄	Pale Orange	>300	37.52 (37.61)	3.87 (4.26)	12.51 (12.86)	2.38 (2.51)	9.73 (9.98)	67
[NiL(H ₂ O) ₂]Cl ₂ .2H ₂ O	Brown	>300	41.45 (41.67)	4.28 (4.51)	13.82 (14.29)	2.63 (2.80)	9.65 (9.88)	108
[CuL(H ₂ O) ₂]Cl ₂	Reddish Brown	102 -105	43.69 (43.90)	4.51 (4.73)	14.56 (15.12)	2.77 (3.01)	11.02 (11.18)	105

3.2.1. IR spectral studies

The Schiff base ligand and its chelates were characterized by FT-IR spectroscopy and the data are shown in (Table 2). IR spectra of Schiff base and its complexes is used to find the coordination sites of ligand with metal ion. A band at 1563 cm⁻¹ in the ligand is due to C=N stretching vibration. On complexation, this band is displaced to a lower frequency. The negative shift of this band is an obvious indication of the participation of the azomethine nitrogen atoms in complex formation [44,45]. The movement of electrons from nitrogen to the metal's unoccupied d-orbitals can attest to this alteration [46]. In addition, in all cases two new bands appeared between 407 and 425 cm⁻¹ (assigned to metal nitrogen bond $\nu(\text{M-N})$) and between 508 and 524 cm⁻¹ (corresponding to metal oxygen bond $\nu(\text{M-O})$) [47]. In all cases there is a sharp band present around 3587 cm⁻¹ this band due to presence of water.

Table 2: Prominent infrared frequencies (4000–400 cm⁻¹) of L and its metal complexes (sh = sharp, m = medium, s = small, w = weak and br = broad).

Compound	$\nu(\text{C=N})$	$\nu(\text{C=O})$	$\nu(\text{M-O})$	$\nu(\text{M-N})$
L	1563sh	1636sh	-----	-----
[CrLCl ₂]Cl.2H ₂ O	1512sh	1635sh	-----	425w
[ZnL(H ₂ O) ₂]SO ₄	1519s	1635sh	524w	407w
[NiL(H ₂ O) ₂]Cl ₂ .2H ₂ O	1519sh	1635sh	517w	424w
[CuL(H ₂ O) ₂]Cl ₂	1527m	1635sh	508w	425w

3.2.2. ¹H NMR spectrum

¹H NMR spectrum of the free ligand, dissolved in DMSO-d₆ and D₂O, showed two signals at 11.20 and 10.45 ppm, which may be assigned to NH of (E)-1-(2-(p-tolyl)hydrazinylidene)propan-2-one and hydrazine carbohydrazide, respectively. The signal observed at 7.55 ppm may be assigned to CH protons of the azomethine group. Another signal observed at 2.32 may be assigned to methyl protons attached to phenyl and another signal observed at 2.07 ppm may be assigned to methyl protons attached to azomethine group. The aromatic protons were observed in the range of 6.93-7.21 ppm. For Zn-complex there were slight changes happening on ¹H NMR spectrum of the free ligand.

Table 3: ¹H NMR spectral data of the Schiff base ligand (L).

Compound	Chemical shift, (δ) ppm	Assignment
L	11.203	(s, 2H, NH)
	10.455	(s, 2H, NH)
	7.550	(s, 2H, azomethine CH)
	6.929-7.208	(m, Phenyl)
	2.320	(s, 6H, Phenyl CH ₃)
	2.070	(s, 6H, CH ₃)
Zn-complex	11.200	(s, 2H, NH)
	10.441	(s, 2H, NH)
	7.547	(s, 2H, azomethine CH)
	6.921-7.205	(m, Phenyl)
	2.312	(s, 6H, Phenyl CH ₃)
	2.065	(s, 6H, CH ₃)

3.2.3. Mass spectral studies

The Schiff base ($C_{21}H_{26}N_8O$) and its complex's mass spectra revealed the molecular ion peaks shown in (table 4). The mass spectra data established the metal complex's stoichiometric composition as ML. Additionally, the results of these examinations were entirely consistent with estimated molecular formulae, which are also corroborated by elemental analysis data. A strong indicator of the complexation process is the presence of the ligand moiety at 406 m/z in all complex spectra.

Table 4: Mass spectral data of L Schiff base ligand and its complexes.

Compound	m/z value		Interpretation
	Calculated	Found	
L ($C_{21}H_{26}N_8O$)	406.5	406	$[M]^+$
$[CrLCl_2]Cl \cdot 2H_2O$	600.7	601	$[M+1]^+$
$[ZnL(H_2O)_2]SO_4$	604	603	$[M]^+$
$[NiL(H_2O)_2]Cl_2 \cdot 2H_2O$	607.9	608	$[M+1]^+$
$[CuL(H_2O)_2]Cl_2$	576.8	575	$[M]^+$

3.2.4. Molar conductance

The new Schiff base ligand and metal complexes were prepared in 1:1 molar ratio. The elemental analysis results obtained for Schiff base ligand and its complexes were in good agreement with those calculated for the proposed formula. The molar conductivity (Λ_m) of 10^{-3} M solutions for each complex at 25 °C could be determined because some of the complexes were soluble in ethanol and the others soluble in water. The results showed that Cr(III), Zn(II), Cu(II) and Ni(II) complexes were electrolytes and ionic in nature, with molar conductance values ranging from 67 to $108 \Omega^{-1} \text{ mol}^{-1} \text{ cm}^2$. (Table 1) contains a list of the data.

3.2.5. UV-Visible spectroscopy

The electronic spectral data for the free Schiff base ligand and its complexes were studied in DMF solvent at room temperature in the range of 200–700 nm using the same solvent as blank. Three bands at 240, 303 and 349 nm appeared in the spectrum of the Schiff base ligand. The first band might be congruent to $\pi-\pi^*$ transition. The second and third higher absorption bands were attributed to the $n-\pi^*$ transition of the azomethine group ($C=N$) and charge transfer. In complexation, these transitions shifted in the spectra of complexes indicated the coordination of the ligand with metal ions (table 5). In addition, in Cr(III) complex, a weak band appeared at 626 nm, which could be assigned to d-d transition.

Table 5: electronic spectral data for the ligand and its complexes

Compound	Wavelength (nm)	Type of transition
L	240, 303, 349	$\pi \rightarrow \pi^*$, $n \rightarrow \pi^*$
$[CrLCl_2]Cl \cdot 2H_2O$	238, 346, 626	$\pi \rightarrow \pi^*$, $n \rightarrow \pi^*$, d-d
$[ZnL(H_2O)_2]SO_4$	240, 302, 356	$\pi \rightarrow \pi^*$, $n \rightarrow \pi^*$
$[NiL(H_2O)_2]Cl_2 \cdot 2H_2O$	240, 303, 357	$\pi \rightarrow \pi^*$, $n \rightarrow \pi^*$
$[CuL(H_2O)_2]Cl_2$	240, 348	$\pi \rightarrow \pi^*$, $n \rightarrow \pi^*$

3.2.6. Thermal gravimetric analysis (TGA & DTG)

Thermal gravimetric analysis (TGA) is used in this study to evaluate the thermal stability along with to confirm and identify the types of water (hydrated or coordinated) molecules in the structure of the prepared metal-complexes [18,23]. Schiff base ligand and metal complexes were characterized using TG and DTG analyses within the temperature range from room temperature to 1000 °C. The thermogram of $[CrLCl_2]Cl \cdot 2H_2O$ complex showed its decomposition in four successive steps. The first, second and third decomposition steps corresponds to the loss of hydrated water molecule, three molecules of Cl and $C_4H_{10}N_2$ molecule. Accordingly, the fourth and fifth steps could be attributed to degradation of the remaining ligand molecule, leaving $\frac{1}{2}Cr_2O_3$ as a residue. The TG curve of $[NiL(H_2O)_2]Cl_2 \cdot 2H_2O$ complex showed six decomposition steps. The first three steps were associated with the loss of hydrated water molecules, coordinated water molecules, Cl_2 gas and $C_5H_8N_4$ molecule. The fourth step corresponds to the elimination of $C_2H_4N_4$ molecule. The last two steps indicated to the loss of the rest of the ligand, leaving $NiO+2C$ as a residue. The thermal analysis curve of $[ZnL(H_2O)_2]SO_4$ complex reported that decomposition occurred in five steps. The first two decomposition steps indicate the loss of two coordinated water molecules with SO_2 . The third step represented the loss of $C_{14}H_{16}N_4$ molecules. The last two steps of decomposition correspond to the loss of $C_2H_{10}N_4O$ molecules, leaving $ZnO+5C$ as a residue. The thermogram of $[CuL(H_2O)_2]Cl_2$ complex represents three decomposition steps. The first step attributed to the loss of two coordinated water molecules, Cl_2 gas and $C_5H_8N_4$ molecule. The second and third steps correspond to the removal of remaining ligand, leaving CuO as a residue.

3.2.7. Antimicrobial activity

The in-vitro antibacterial and antifungal activities of the ligand and its complexes were studied along with ampicillin as a standard antiseptic drug, gentamycin as a standard antibiotic drug and nystatin as a standard antifungal drug. The microorganisms utilized in this study involve *Streptococcus mutans*, *Staphylococcus Aureus* (as Gram-positive bacteria), *Escherichia Col* and *Klebsiella pneumonia* (as Gram-negative bacteria) and *Aspergillus Nigar* and *Candida albicans* (as

fungi). The results are presented in (Table 6). Comparing the biological activity of the ligand, metal (II) complexes and standard drug, indicate that all complexes exhibit more inhibitory effects on bacterial growth than the parent ligand. It can be inferred from the antibacterial test data that:

- 1.) On Chelation, the polarity of M(II) decreases by neutralizing positive metal ion charge with ligand-donor groups. As a result of chelation, the hydrophobic and lipophilicity nature of the ligand increases, making it easier to permeate through lipid layers of cells membrane causing deactivation of enzymes responsible for the respiratory process and blocking of protein synthesis, in another words, limiting the growth of the organism.
- 2.) All the synthesized compounds have no antifungal activity versus *Aspergillus Nigar* except Cu- complex which is very effective even more than Nystatin.
- 3.) Cu-complex is more toxic for *Staphylococcus aureus* than ampicillin.
- 4.) The antifungal activity of compounds against *Candida albicans* obeyed this order: (Cu-complex) > Nystatin > (Ni-complex) > (Zn-complex) > (Cr-complex).

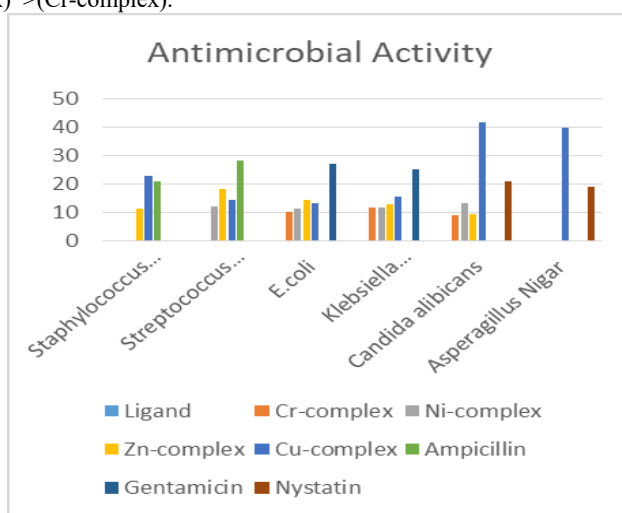


Figure 1: Graphical representation for Antimicrobial Activity.

There are additional criteria for antibacterial action besides chelation. The antimicrobial activity is greatly influenced by many significant parameters, including the nature of the metal ion, the nature of the ligand, coordinating sites, and geometry of the complex, concentration, hydrophobicity, lipophilicity, and the presence of co-ligands. The hazardous substance cannot penetrate the bacterial cell wall if the geometry and charge distribution around the molecule is incompatible with the geometry and charge distribution surrounding the pores of the bacterial cell wall. This prevents the toxic reaction from occurring inside the pores. This might help to explain why some complexes have weak activity [48-53].

Table 6: Biological Activity of Ligand [L] and Its Metal Complexes, (NA: no activity).

Sample	Inhibition zone diameter (mm / mg sample)						
	Gram positive bacterial species		Gram negative bacterial species		Fungi		
	Staphylococcus aureus	Streptococcus mutans	E.coli	Klebsiella pneumoniae	Candida albicans	Asperagillus Nigar	
L	NA	NA	NA	NA	NA	NA	
[CrLCl ₂]Cl ₂ .2H ₂ O	NA	NA	10.0±1.0	11.6±0.50	9.0±1.0	NA	
[NiL(H ₂ O) ₂]Cl ₂ .2H ₂ O	NA	12.0±1.0	11.3±0.50	11.6±0.50	13.3±0.50	NA	
[ZnL(H ₂ O) ₂]SO ₄	11.3±0.5	18.3±0.6	14.3±0.50	12.6±0.50	9.3±0.50	NA	
[CuL(H ₂ O) ₂]Cl ₂	22.6±0.6	14.3±0.5	13.3±0.50	15.3±0.50	41.6±0.60	39.6±0.60	
Standard	Ampicillin	21±0.10	28±0.50	-----	-----	-----	-----
	Gentamicin	-----	-----	27±0.50	25±0.50	-----	-----
	Nystatin	-----	-----	-----	-----	21±0.50	19±0.50

3.2.8. Anticancer Activity

In vitro potential cytotoxicity of the ligand and its complexes were checked against MCF-7 (Breast carcinoma) and BHK (Baby Hamster Kidney Cell). The relation between relative viability of the cells and medication concentration is graphed to obtain the survival graph of tumour and normal cell lines. IC₅₀ values are shown in (Table 7). Cytotoxicity of the studied compounds against MCF-7 (Breast carcinoma) cells indicates that:

- a) The Zn(II) and Ni(II) complexes show significant activity against cancer cells with IC₅₀ values of 8 and 8.5 µg.mL⁻¹, respectively, and their activities against BHK were relatively low comparing with those against MCF-7, especially the activity of Zn(II) complex. That indicates to chemotherapeutic importance of Zn(II) and Ni(II) complexes where IC₅₀ is the concentration that make by 50% inhibition for the growth of cancer cells.
- b) The rank order of potency as a function of chelated metal ion with ligand follows the order Cu(II) < Cr(III) < L < Ni(II) < Zn(II) against MCF-7.

- c) Comparing of the antitumor activities of the free ligand and its metal complexes indicate that the Zn-complex has a higher antitumor activity than ligand and its other metal complexes (Table 7).
- d) There is no correlation between antitumor activities and antimicrobial activities i.e., Cu-complex have a higher antifungal activity against investigated fungal species than the free ligand and its other metal complexes but the antitumor activities of them > Cu-complexes.
- e) Complexes that have antibacterial activity do not necessarily have antitumor activity.

Table 7: Cytotoxic activity of the synthesized compounds against human tumour cells (IC_{50} ($\mu\text{g/ml}$) = cytotoxic dose at 50%, i.e. the drug concentration to inhibit the growth of the cancer cells by 50%, IC_{50} ($\mu\text{g/ml}$): = 1-10 (very strong), 11-20 (strong), 21-50 (moderate), 51-100 (weak) and above 100 (non-cytotoxic), MCF-7 (Breast carcinoma) and BHK (Baby Hamster Kidney Cell).)

Compounds	In vitro Cytotoxicity IC_{50} ($\mu\text{g/ml}$)	
	MCF-7	BHK
L	9	9
Cr	10	10
Zn	8	32
Ni	8.5	12
Cu	15	10

4. Conclusions

In this study, the tetradentate Schiff base ligand and its metal (II)/(III) complexes are studied using elemental analysis, molar conductance, mass spectroscopy, IR, and UV-visible spectroscopy. The outcomes of these investigations led to coordination compounds containing octahedral-shaped Cr(III), Ni(II), Cu(II) and Zn(II) complexes. Antimicrobial investigation proved that Cu-complex has the highest antifungal activity against *Staphylococcus aureus* even more than Ampicillin and the Anticancer Activity of Zn(II) complex is very promising.

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