

# Preparation, Spectral Characterization and Biological Screening of new Azo Schiff base ligand and the Au (Iii) Complex as Anticancer

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## Abstract

A new azo-Schiff base ligand 8-((Z)-(2-(4-hydroxy-3-methylphenyl) imino) ethyl) phenyl diazenyl)-1,3-dimethyl-3,7-dihydro-1H-purine-2,6-dione, has been prepared from reacting (Z)-8-((2-acetylphenyl) diazenyl)-1,3-dimethyl-3,7-dihydro-1H-purine-2,6-dione with 4-amino-2-methyl phenol. A new series of complexes with Co (II), Ni (II), Cu (II), Zn (II), Hg (II), Cd(II), and Au(III) ions were prepared forming chelate complexes. Fourier-transform infrared spectroscopy (FTIR), proton nuclear magnetic resonance (1H-NMR) technique, ultraviolet visible spectroscopy (UV-Vis), mass analysis, molar conductance and magnetic susceptibility were used to characterize the structures of the new ligand and their transition metal complexes. The complexes were found to have the general formula  $[(M)(L)_2]Cl_2$  where M = Co (II), Ni (II), Cu (II), Zn(II), Hg(II), and Cd(II),  $[(M)(L)Cl]Cl_2$  where M = Au(III), The FTIR results showed that the coordination sites were the azomethine nitrogen, imidazole ring nitrogen and azo nitrogen atoms of the azo-Schiff base ligand. The electronic spectral and magnetic measurement data indicated that the complexes exhibited octahedral geometry, except the Au (III) complex suggested a square planar geometry around the central metal ion. The biological activity results showed the highest inhibitory effect for gold the complex. In this study the cytotoxicity of Au (III) complex on human MCF-7 breast cancer and MCF-10A normal cells were MTT assay. The metal complexes showed selective cytotoxicity against breast cancer, this metal complex excelled in halting proliferation of MCF-7 cancer cells with median inhibitory concentration (IC50) values of Au (III) complex. The results indicate undoubtedly the possibility of using them as antitumor drugs in the field of pharmacy breast cancer.

**Keywords:** theophylline; Azo- Schiff base; Transition metal complexes; antitumor (breast cancer).

## 1. Introduction

The organic azo-Schiff base compounds are characterized in that their chemical composition contains two chromophore active groups, namely the azo bridge group (-N=N-) and azomethane group (-CH=N-), long in its discovery and preparation (1). Azo-Schiff base ligand were used in applications various such as biological activity anticancer, antibacterial, antifungal, also they have been used as polymer paper, paint and coating industries as dyeing pigments (2-4). It is noted from the composition of the two groups that both contain a nitrogen atom with a double electron, which gives it many of its chemical and physical properties (5-7). Azo for Theophylline is the trade name and its chemical name is 1,3-dimethylxanthin, Theophylline is present in tea leaves in small amounts (8). It is a commonly used drug for the treatment of asthma, chronic obstructive pulmonary disease and emphysema, and it has antioxidant properties, it has been found that when theophylline is combined with Riboflavin or (vitamin B2), the resulting compound can break down Bilirubin outside the body. Therefore, the compound is considered an "effective treatment" for jaundice in newborns (9).

In this paper, we report the Preparation and Biological Screening of the Gold Complex as Anticancer of New (Azo-Schiff base) Ligand and its metal complexes with Co (II), Ni (II), Cu(II), Zn(II), and Cd(II).

## 2. Measurement

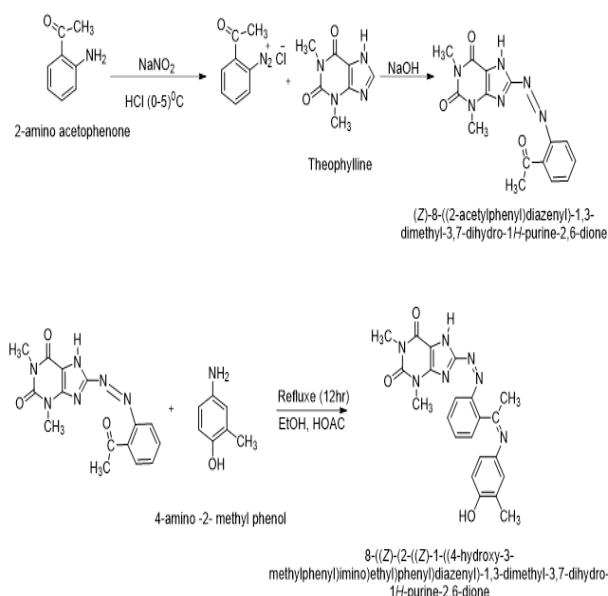
The electrothermal melting point model 9300 was used to measure the melting point of the ligand and its complexes. Elemental analyses were carried out by means of micro analytical unit of 1180 (C.H.N) elemental analyzer. Electronic spectra were recorded on Shimadzu spectrophotometer double beam model 1700 Uv-Vi's spectrophotometer-FTIR spectra were recorded in KBr disc on FTIR Shimadzu spectrophotometer model 8400 in wave number (4000-400)  $cm^{-1}$ . 1H-NMR -spectra in (ppm) unit were operating in DMSO-d<sub>6</sub> as solvent using (Bruker-Ultra Shield 3000 MHz Switzerland). Magnetic susceptibilities were carried out on a balance magnetic (MSB-MKI) using faraday method. The diamagnetic corrections were made by Pascal's constants.

### Preparation of the new Azo-Schiff base ligand

This ligand was prepared in two steps: In the first step, the azo compound was prepared from coupling the diazonium salt of the compound 2-amino acetophenone with Theophylline (the coupling compound), and this was done by adding (0.7g, 0.01mol,) of sodium nitrite dissolved in (15ml) distilled water drop wise. Drop into a solution of (0.01mol, 1.35ml) 2-amino acetophenone dissolved in (30ml) distilled water and (3ml) concentrated

hydrochloric acid in an ice bath with stirring for (15 min), then the mixture was left to settle for (30 min) to complete the process. After that, this solution was added dropwise with continuous stirring to the solution of theophylline compound prepared from dissolving (2.59mol,0.01g) in (30ml) of ethanol and cooled at (0-5°C) in an alkaline medium, where the color of the solution was observed in red. The reaction mixture was left for the next day, after that dilute hydrochloric acid was added dropwise to adjust the hydrogen ion concentration to reach (PH=6), then it was observed that a red precipitate formed, it was left to settle, then filtered and washed several times with distilled water to rid it of the resulting sodium chloride salt. From the chain of chemical reaction, Then it was dried and recrystallized from ethanol and its melting point was measured (113-115 °C).

The second step included the preparation of the final azo-Schiff base ligand by reacting a solution (4.31g, 0.01 mol) of the azo compound prepared in the first step and dissolved in (50ml) of absolute ethanol with a solution (1.23g, 0.01mol) of 4-amino-2-methyl phenol in the same solvent, then (2-3) drops of glacial acetic acid were added and the mixture was refluxed for (12h) with continuous stirring, where it was noticed that the color of the hot mixture solution changed to a dark red colour, it was recrystallized and its melting point was measured and it was (120-127°C). Scheme -1 shows of the preparation of (azo-Schiff base) ligands.



### Preparation of metal complexes

The metal complexes were prepared by mixing of 30ml ethanol solution of (COCl<sub>2</sub>.6H<sub>2</sub>O, NiCl<sub>2</sub>.6H<sub>2</sub>O, CuCl<sub>2</sub>.2H<sub>2</sub>O, ZnCl<sub>2</sub>, CdCl<sub>2</sub>.2H<sub>2</sub>O, and NaAuCl<sub>4</sub>. H<sub>2</sub>O) with 30ml ethanol solution of (Azo-Schiff base) ligand in (1:2) (metal: ligand) ratio, except the Au (III) (1:1). the resulting mixture was refluxed for (1h). The product was isolated after reduced of volume by evaporation. It was filtered

off, washed with ethanol and dried under vacuum. The complexes obtained are listed in table 1.

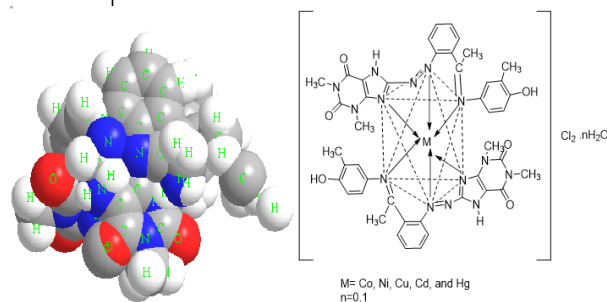


Fig. 1. The Proposed chemical structure of Complexes.

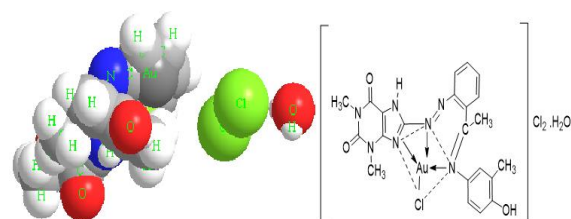


Fig. 2. The Proposed chemical structure of Au(III) Complex.

### 3. Methods

**Cell lines and culture.** MCF7 (a human breast cancer cell line) was purchased from National Cell Bank of Iran (Pasteur Institute, Iran). Cells were grown in RPMI-1640 medium (Gibco) with 10% FBS (Gibco) supplemented with antibiotics (100 U/ml penicillin and 100 µg/ml streptomycin). Cells were maintained at 37°C under humidified air containing 5% CO<sub>2</sub> and were passaged using trypsin/EDTA (Gibco) and phosphate-buffered saline (PBS) solution. Culturing media and conditions used to grow the cells as 3D colonies was the same as monolayer cell culture.

**MTT cell viability assay in MCF7 Cells.** Cell growth and cell viability were quantified using the MTT [3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium Bromide] (Sigma-Aldrich) assay. In brief, for monolayer culture, cells (MCF7) were digested with trypsin, harvested, adjusted to a density of  $1.4 \times 10^4$  cells/well and seeded to 96-well plates filled with 200 µl fresh medium per well for 24 h. When cells formed a monolayer, they were treated with 200-6.25 µg/ml of the compounds for 24 h at 37 °C in 5% CO<sub>2</sub>. At the end of the treatment (24 h), while the monolayer culture was left untouched in the original plate, the supernatant was removed and 200 µl/well of MTT solution (0.5 mg/ml in phosphate-buffered saline [PBS]) was added and the plate was incubated at 37 °C for an additional 4 h. MTT solution (the supernatant of cells was removed, and dimethyl sulfoxide was added (100 µl per well). Cells were incubated on a shaker at 37°C until crystals were completely dissolved. Cell viabilities were quantified by measuring absorbance at 570 nm using an ELISA reader (Model wave xs2, BioTek, USA). The concentration of the compounds that resulted in 50% of cell death (IC<sub>50</sub>) was determined from respective dose-response curves.

## 4. Results and Discussion

All our complexes are Freely soluble in DMF, DMSO, Methanol and Ethanol. Also, they are stable in air. The metal complexes were characterized by elemental analysis, molar conductivities, magnetic susceptibility, IR, UV-Vis, Mass and <sup>1</sup>H, MNR spectra. The analytical data of the complexes agree with the experimental data. The value reveals that the metal to ligand ratio is (1:2). The magnetic susceptibility of the chelate complexes at room temperature were consistent with octahedral geometry, except the Au

(III) complex suggest a square planar geometry around the central metal ion. Most of chelate complexes prepared in this work showed conductivity values of the complexes. This proves that complexes have electrolytic nature.

### Micro analysis

The elemental analysis data of 1:2 [M: L] ratio complexes showed that the theoretical values are in a good agreement with the found data, as listed in [table\(1\)](#). The purity of Azo-Schiff base ligand were tested by TLC technique and C.H.N analysis.

**Table.1: Physical properties and elemental analysis of azo Schiff-base ligand and their metal complexes**

Compound	M.Wt g/mole	Colour	M.p.°C	Yield %	Rf(1:4) (Methanol: Benzen)
C <sub>22</sub> H <sub>21</sub> N <sub>7</sub> O <sub>3</sub>	431	Dark red	(120-127) <sup>o</sup> C	82	0.62
[Co(C <sub>22</sub> H <sub>21</sub> N <sub>7</sub> O <sub>3</sub> ) <sub>2</sub> ] Cl <sub>2</sub>	991.9	Dark purple	>310 <sup>o</sup> C Dec.	85	0.73
[Ni(C <sub>22</sub> H <sub>21</sub> N <sub>7</sub> O <sub>3</sub> ) <sub>2</sub> ] Cl <sub>2</sub> . H <sub>2</sub> O	1009.6	Light purple	>310 <sup>o</sup> C Dec.	78	0.74
[Cu(C <sub>22</sub> H <sub>21</sub> N <sub>7</sub> O <sub>3</sub> ) <sub>2</sub> ] Cl <sub>2</sub>	996.5	Purple	(136-142) <sup>o</sup> C	80	0.67
[Zn(C <sub>22</sub> H <sub>21</sub> N <sub>7</sub> O <sub>3</sub> ) <sub>2</sub> ] Cl <sub>2</sub> . H <sub>2</sub> O	1016.4	Purple	(113-118) <sup>o</sup> C	75	0.52
[Cd(C <sub>22</sub> H <sub>21</sub> N <sub>7</sub> O <sub>3</sub> ) <sub>2</sub> ] Cl <sub>2</sub> . H <sub>2</sub> O	1063.4	Light purple	>310 <sup>o</sup> C Dec.	76	0.68
[Au(C <sub>22</sub> H <sub>21</sub> N <sub>7</sub> O <sub>3</sub> ) Cl] Cl <sub>2</sub> .H <sub>2</sub> O	752.4	Purple	>310 <sup>o</sup> C Dec.	78	0.37

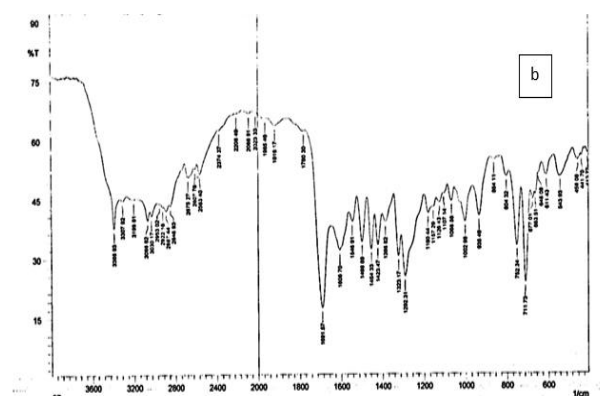
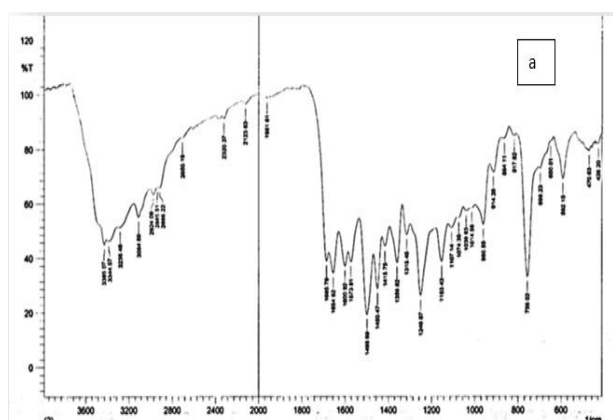
### Infrared spectra studies of the ligand and its complexes

The FTIR spectra provided valuable information regarding the nature of the functional group attached to the metal atom. The most important infrared spectral bands that provided conclusive structural evidence for the coordination of the ligand to the central metal ions are given in [Table 2](#). The FTIR spectrum of the ligand showed characteristic bands at (3388, 1600 and 1450) cm<sup>-1</sup> due to the O-H, C=N and N=N functional groups, respectively (10). The IR spectra of the ligand exhibited appropriate shifts due to the formation of all complexes prepared in this study. The C=N and

N=N bands in the free ligand shifted from 1600 cm<sup>-1</sup>, 1450 cm<sup>-1</sup> to (1625-1546) cm<sup>-1</sup> and (1458 -1423) cm<sup>-1</sup>, respectively for the complexes. These shifts confirmed the coordination of the ligand via the nitrogen of azo methine group and the azo group to metal ions (11). The absorption band in free ligand observed at 3388 cm<sup>-1</sup> was attributed to the  $\nu$ (OH) of hydroxyl group (12). This band remained unchanged in the spectra of their complexes, which suggested that the hydroxyl group was not taking part in coordination (13). New bands were attributed to  $\nu$ (M-N) vibrations appearance in all complexes at (599- 540) cm<sup>-1</sup> respectively (14). Representative example for their spectra is given in [Fig. 3](#).

**Table. 2: Characteristic IR absorption bands of the ligand and its complexes**

Compounds Formula	$\nu$ (H <sub>2</sub> O) OH	$\nu$ (NH) Imida	$\nu$ (C=O)	$\nu$ (C=N) Imida.	$\nu$ (C=N) Schiff	$\nu$ (N=N)	$\nu$ (M-N)
L= C <sub>22</sub> H <sub>21</sub> N <sub>7</sub> O <sub>3</sub>	3388	3300	1685	1654	1600	1450	-----
[Co(L) <sub>2</sub> ] Cl <sub>2</sub>	3402	3300	1685	1625	1625	1438	565
[Ni (L) <sub>2</sub> ] Cl <sub>2</sub> .H <sub>2</sub> O	3518	3379	1685	1654	1625	1454	599
[Cu (L) <sub>2</sub> ] Cl <sub>2</sub>	3385	3344	1685	1608	1581	1456	540
[Zn (L) <sub>2</sub> ] Cl <sub>2</sub> .H <sub>2</sub> O	3388	3307	1691	1606	1546	1423	543
[Cd(L) <sub>2</sub> ] Cl <sub>2</sub> .H <sub>2</sub> O	3520	3371	1685	1597	1597	1454	559
[Au(L)Cl] Cl <sub>2</sub> .H <sub>2</sub> O	3361	3059	1683	1649	1606	1458	559



**Fig. 3 FTIR spectra of (a) azo Schiff-base ligand and (b) Co (II) complex.**

## Electronic spectra

Electronic spectra provided the most detailed information about the electronic structure. The UV-Vis spectrum of the azo-Schiff base ligand exhibited two charge transfer (C.T) bands at (204nm, 49019cm<sup>-1</sup>), (253nm, 39525cm<sup>-1</sup>) and (311nm, 32154cm<sup>-1</sup>), which was attributed to ( $\pi-\pi^*$ ,  $n-\pi^*$ ,  $\pi-\pi^*$ ) transitions in the azo Schiff-base ligand (15). In the spectrum of the complexes, the (C.T) bands at (204nm, 253, nm) remained as such, in agreement with the transition of the azo Schiff-base ligand. The

band observed at 311 nm in the spectrum of the free ligand was red-shifted to in the complexes due to ligand to metal charge transfer (LMCT) transition (16), suggesting an octahedral geometry around metal (II) in the complexes (17), except the Au (III) complex suggest a square planar geometry around the central metal ion(18). The electronic spectra of the ligand and the Co (II) complex are shown in Fig.4. The electronic transitions, magnetic properties and conductivity values of the ligand and its complexes are listed in Table 4.

Table 3. Electronic spectra, conductivity and magnetic moment of complexes

CompoundS	Absorption Bands (nm)	Absorption Bands (/cm)	Transition	$\mu_{\text{eff}}$ (BM)	Conductivity (S cm <sup>2</sup> /mol)	Geometry	Hybridization
L= C <sub>22</sub> H <sub>21</sub> N <sub>7</sub> O <sub>3</sub>	204nm 253nm 311nm	49019cm <sup>-1</sup> 39525cm <sup>-1</sup> 32154cm <sup>-1</sup>	$\pi-\pi^*$ $n-\pi^*$ $\pi-\pi^*$	-----	-----	-----	-----
[Co(L) <sub>2</sub> ] Cl <sub>2</sub>	263nm 574nm 656nm	38022cm <sup>-1</sup> 17421cm <sup>-1</sup> 15243cm <sup>-1</sup>	M → L, CT 4T <sub>1g</sub> (4F) →4T <sub>1g</sub> (P) 4T <sub>1g</sub> (4F) →4A <sub>2g</sub> (F)	4.9	77	Octahedral (regular)	sp <sup>3</sup> d <sup>2</sup>
[Ni(L) <sub>2</sub> ] Cl <sub>2</sub> .H <sub>2</sub> O	255nm 546nm 678nm	39215cm <sup>-1</sup> 18315cm <sup>-1</sup> 14749cm <sup>-1</sup>	M → L, CT <sup>3</sup> A <sub>2g</sub> → <sup>3</sup> T <sub>2g</sub> (F) <sup>3</sup> A <sub>2g</sub> → <sup>3</sup> T <sub>1g</sub> (F)	3.2	72	Octahedral (regular)	sp <sup>3</sup> d <sup>2</sup>
[Cu(L) <sub>2</sub> ] Cl <sub>2</sub>	888nm	11261cm <sup>-1</sup>	<sup>2</sup> E <sub>g</sub> → <sup>2</sup> T <sub>2g</sub>	1.71	76	Octahedral (distorted)	sp <sup>3</sup> d <sup>2</sup>
[Zn(L) <sub>2</sub> ] Cl <sub>2</sub> .H <sub>2</sub> O	480nm	20833cm <sup>-1</sup>	M → L, CT	Dia	78	Octahedral (distorted)	sp <sup>3</sup> d <sup>2</sup>
[Cd(L) <sub>2</sub> ] Cl <sub>2</sub> .H <sub>2</sub> O	395nm	25316cm <sup>-1</sup>	M → L, CT	Dia	78	Octahedral (regular)	sp <sup>3</sup> d <sup>2</sup>
[Au(L)Cl] Cl <sub>2</sub> .H <sub>2</sub> O	493nm	20283cm <sup>-1</sup>	M → L, CT	Dia	74	Square-planar	dsp <sup>2</sup>

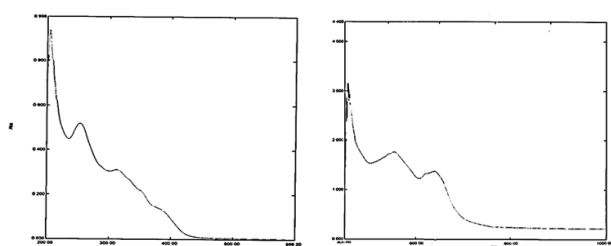


Fig. 5 Electronic spectrum of (a) ligand and (b) Co(II) complex.

## Magnetic measurements

The Co (II) complex had a magnetic moment of 4.9 BM, which agreed with the reported value for octahedral Co (II) complexes (19). The present Ni (II) complex showed a magnetic moment value of 3.1 within the range of 2.9-3.3 BM (20), suggesting an octahedral environment. The Cu (II) complex showed a magnetic moment value of 1.71 BM, which was monomeric and consistent with a distorted octahedral geometry (21). The Zn (II), Cd (II), and Au (III) were diamagnetic and according to the empirical formulae of complexes. An octahedral geometry was proposed (22), except the Au (III) complex suggested

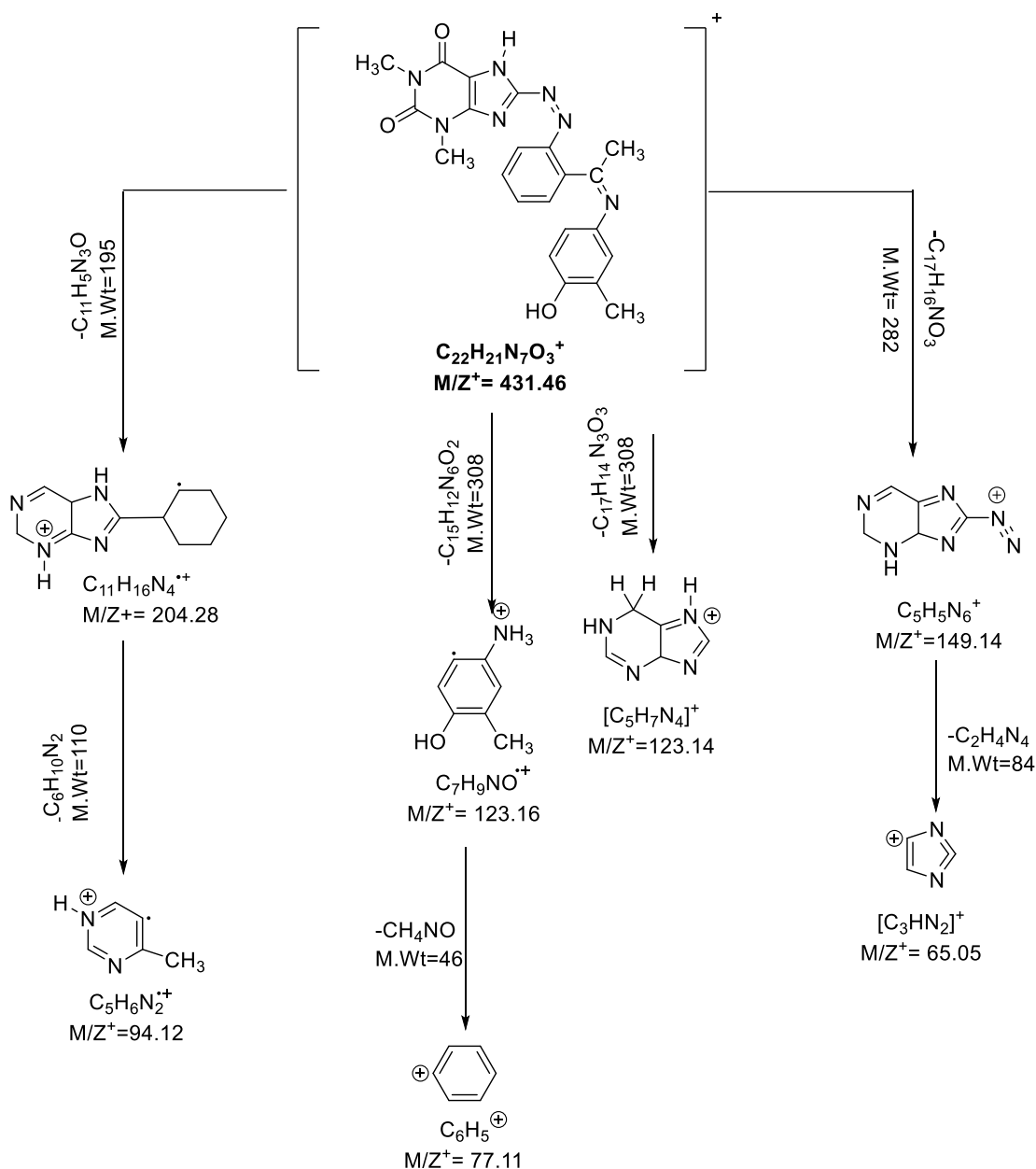
a square planar geometry around the central metal ion (23). Based on the above results, we could deduce the probable.

## Mass spectrum of azo- Schiff base ligand

Mass spectrum of azo-Schiff base ligand is given in Fig (5). The mass spectrum pattern gives the expected molecular ion peak at (m/z+ 431), confirming the proposed formula for preparation ligand and in good agreement with their formula as expressed from micro analytical data. The mass spectral data fragmentation of the ligand shown in Scheme 2 and Fig. 5.

Table. 4: Mass fractionation products of Azo-Schiff base

Fraq	M/Z <sup>+</sup> Exacs Mass	Relative Abundance
[C <sub>22</sub> H <sub>21</sub> N <sub>7</sub> O <sub>3</sub> ] +	431.46	1
[C <sub>11</sub> H <sub>16</sub> N <sub>4</sub> ] •+	204.28	12.43
[C <sub>7</sub> H <sub>9</sub> NO] •+	123.16	29.72
[C <sub>3</sub> HN <sub>2</sub> ] +	65.05	8.10
[C <sub>5</sub> H <sub>7</sub> N <sub>4</sub> ] +	123.14	29.72
[C <sub>6</sub> H <sub>5</sub> ] +	77.11	43.24
[C <sub>5</sub> H <sub>6</sub> N <sub>2</sub> ] •+	94.12	100



Scheme 2 Mass spectrum fragmentation of azo-Schiff base ligand.

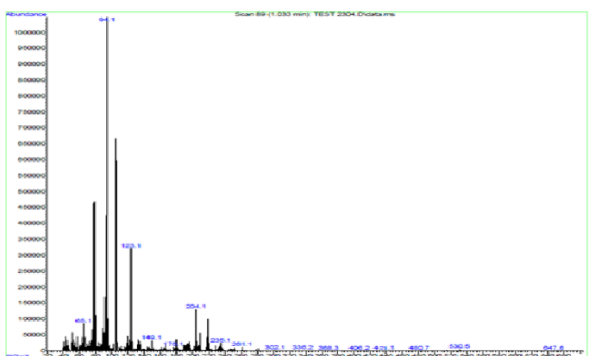


Fig. 5 Mass spectrum of (a) azo-Schiff base ligand.

### $^1H$ -NMR spectra

$^1H$ -NMR spectrum of azo-schiff base and complex is given in (Fig 6) was measured in DMSO- $d_6$  solvent with TMS as an internal reference. The  $^1H$ -NMR spectrum of the ligand showed the following signals: Phenyl multiples at 6.5–8.0 ppm, =C-CH<sub>3</sub> at 2.7 ppm, -N-CH<sub>3</sub> at 4.3 ppm, and -OH at 10.8 ppm (24). This peak was noted in the spectra of complex indicated that the -OH proton did not contribute to the complexity (25).

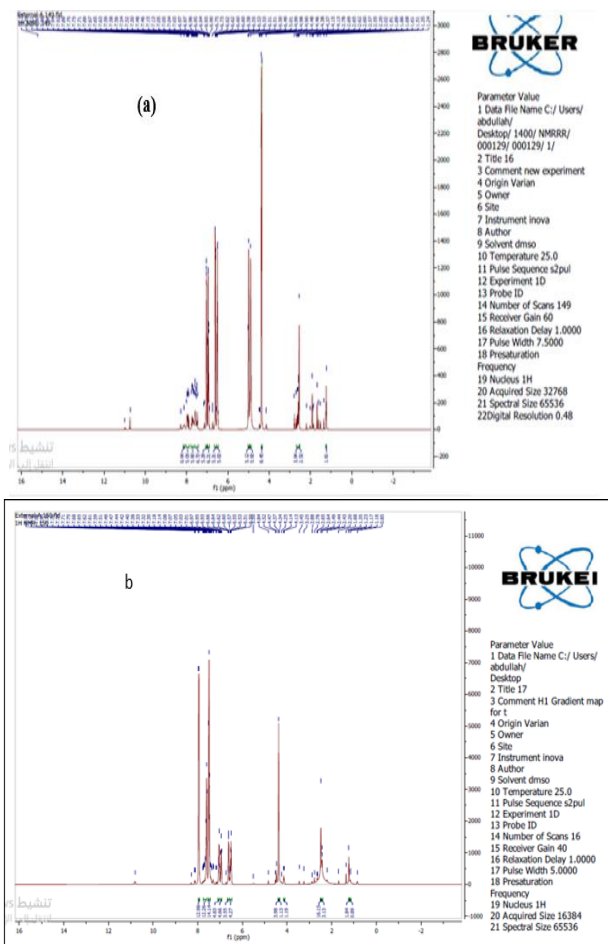


Fig. 6 <sup>1</sup>H-NMR spectrum of (a) azo Schiff-base ligand and (b) Au (III) complex.

### Conductivity measurement

Most of the chelate complexes prepared in this work

showed the conductivity values ranged between (72-78) S cm<sup>2</sup>/mol in DMSO at room temperature, which were very low values (26). This could support the electrolytic nature of the metal complexes. According to these results, the structural formulae of these ligand and complexes may be proposed in Fig. 6.

### Anticancer activity

Evaluation of newly preparation complexes in cancer therapy were studied. In this study the antitumor activities of the preparation azo-Schiff base and Au (III) complex were tested against a human breast cancer MCF7 cell line. The results showed that the highest inhibitory effect was reported for azo-Schiff base ligand and Au (III) complex, giving the IC<sub>50</sub> value as of azo-Schiff base ligand is 67.59 and Au (III) complex is 46.59.

The cell cytotoxic effect of the tested azo-Schiff base ligand and Au (III) complex was calculated. The optical density was measured with the micro plate reader to determine the number of viable cells, and the percentage of viability was calculated as

$$\text{Cytotoxicity} = \frac{A-B}{A} * 100$$

Where A and B are the optical density of control and the optical density of test.

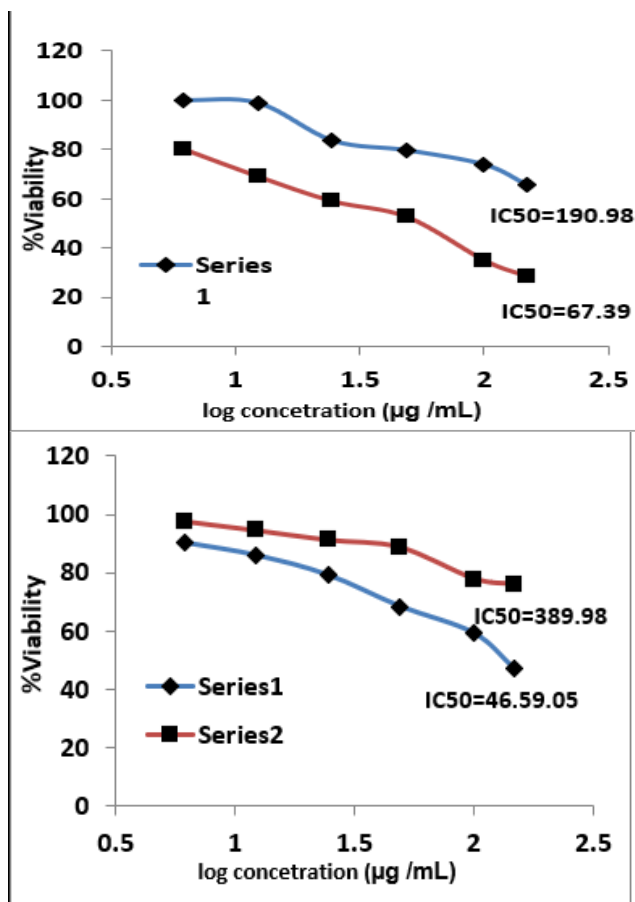
The relation between surviving cells and drug concentration was plotted to get the survival curve of each tumor cell line after treatment with the specified compounds. The anticancer activity of azo-Schiff base ligand and Au (III) complex was determined against an breast cancer MCF7 cell line using different concentrations.

Table 4: The percentage of inhibition for the azo-Schiff base.

Con. (µg. mL <sup>-1</sup> )	Mean Percentage (%) for each cell line			
	MCF7		MCF10A	
	Cancerous line cells of (MCF-7)		Normal line cells of MCF10A	
	Cell Viability	Cell Inhibition	Cell Viability	Cell Inhibition
6.25	80.1	19.9	99.92	0.08
12.5	69.01	30.99	98.76	1.24
25	59.06	40.94	83.41	16.59
50	52.68	47.32	79.48	20.52
100	35.2	64.8	73.65	26.35
200	28.83	71.17	65.45	34.55

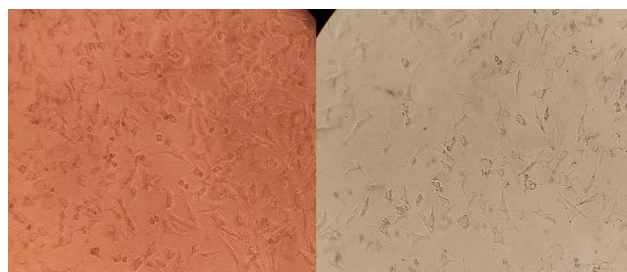
Table 5: The percentage of inhibition for the Au(III) complex.

Con.(µg/mL)	Mean Percentage (%) for each cell line			
	MCF-7)(		MCF10A	
	Cancerous line cells of (MCF-7)		Normal line cells of (MCF10A	
	Cell Viability	Cell Inhibition	Cell Viability	Cell Inhibition
6.25	90.13	9.87	97.67	2.33
12.5	85.84	14.16	94.54	5.46
25	79.08	20.92	91.23	8.77
50	68.37	31.63	88.76	11.24
100	59.18	40.82	77.88	22.12
200	46.94	53.06	75.87	24.13

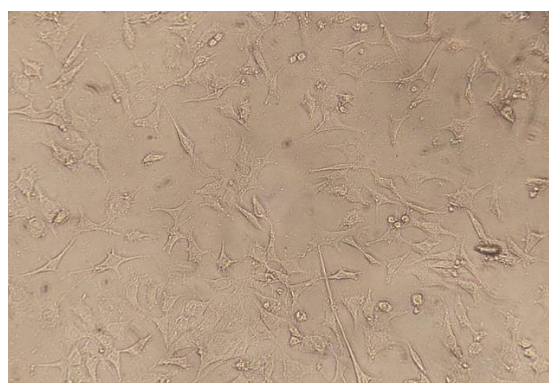


(b)

Fig. 7 Curve with plotting of IC<sub>50</sub> of (a) Azo-Schiff base ligand and (b) Au(III) complex



Control cells Au(III) complex.



Azo-Schiff base ligand

Fig. 8. Anti-proliferative activity of metal complex in MCF-7 cell.

## 5. Conclusions

This work described the preparation and identification of a new series of cobalt (II), nickel (II),

copper (II), zinc (II) and cadmium (II) Azo-Schiff base ligand derived from theophylline. These chelate complexes with ligand were characterized by using different physicochemical techniques. The spectrum revealed that ligand behaves as neutral tridentate ligand coordinated to the metal ions through imidazole-N, Azo-N, Schiff base-N donor atoms. The spectral and magnetic studies of the prepared metal complexes of Azo-Schiff base ligand reveals that all ligands chelate complexes are having octahedral geometry. except the Au (III) complex suggested a square planar geometry around the central metal ion, also from the above studies it can be concluded that the preparation ligand and Au (III) complex has been appeared Anti proliferative activity of MCF-7 cell.

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