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Synthesis, Characterization, *In-vitro* Anticancer and Antimicrobial Properties of Some Metal(II) Complexes of 4-[(2,3-dihydro-1*H*-inden-4-ylimino)methyl] benzene-2,4-diol

A. A. Osowole[1*] and I. Ott[2]

[1]Inorganic Chemistry Unit, Department of Chemistry, University of Ibadan, Ibadan, Nigeria.
[2]Institute of Medicinal and Pharmaceutical Chemistry, Technical University Braunschweig, Beethovenstrasse 55, D-38106 Braunschweig, Germany.

Authors' contributions

This work was carried out in collaboration with all authors. AAO designed the study, wrote the protocol and first draft of the manuscript, while IO managed the analyses, cytotoxic aspect of the study and the final draft of the manuscript. All authors read and approved the final manuscript.

Research Article

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ABSTRACT

Co(II), Ni(II), Cu(II), Zn(II) and Pd(II) complexes of the Schiff base, 4-[(2,3-dihydro-1*H*-inden-4-ylimino)methyl]benzene-2,4-diol are synthesized and characterized by microanalysis, conductance, ^{1}HNMR, infrared and electronic spectral measurements. The ligand coordinates through one of the phenolic *O* and imine *N* atoms to the metal ions as shown by IR measurements, and electronic measurements are corroborative of a four coordinate, tetrahedral /square-planar geometry for the complexes. The metal complexes are hydrated, forming as $[ML_2].aH_2O$ and none is an electrolyte in nitromethane. Cytotoxicity studies reveal that the Pd(II) complex has the best in-vitro anticancer activity against both MCF-7 (human breast adenocarcinoma) and HT-29 (colon carcinoma) cells, with IC_{50} values of 0.94 µM and 1.67 µM respectively, which exceed the activity of Cis-platin. The antimicrobial study shows that Co(II) and Cu(II) complexes have broad-spectrum antimicrobial activity against *Candida albicans*,

**Corresponding author: Email: aderoju30@gmail.com;*

Pseudomonas aeruginosa, *Staphylococcus aureus*, *Bacillus subtilis*, *Escherichia coli* and *Samonella typhi* with inhibitory zones range of 12-24 mm and 12-20 mm respectively.

Keywords: Anticancer activities; antimicrobial activities; broad-spectrum; cis-platin; schiff base.

1. INTRODUCTION

Aminoindane and its derivatives are renowned for their biological activities such as anticonvulsants, antiapoptotic and bronchodilators (Heinzelman et al., 1948; Maruyama et al., 2001; Stewart et al., 1996). Additionally, they are inhibitors of anthocyanin biosynthesis, buckwheat phenylalanine ammonia lyase (PAL) and HIV protease (Zon et al., 2005). Furthermore their catalytic activities include; enantioselective inverse-electron-demand hetero-Diels-Alder reactions of α,β-unsaturated aldehydes, oxidation of alkyl aryl sulfides, and ring opening of mesoaziridines (Bryliakoy et al., 2007; Gademann et al., 2002; Li et al., 1999). Detailed literature search shows that no work has been reported on the Schiff base, 4-[(2,3-dihydro-1*H*-inden-4-ylimino)methyl]benzene-2,4-diol (derived from condensation of 4-aminoindane and 2,4-dihydroxybenzaldehyde) and its Co(II), Ni(II), Cu(II), Zn(II) and Pd(II) complexes (Ahmed and Kassem, 2010; Ceyhan et al., 2011; Craven et al., 2010; Guo et al., 2001; Obaleye et al., 2011; Qiao et al., 2011;Yildiz et al., 2005; Zhao et al., 2005). Thus, our primary aim is to synthesize and characterize the above named Schiff base and its metal(II) complexes in order to investigate their antimicrobial properties for further studies as antiseptics, while the Cu(II), Zn(II) and Pd(II) complexes anticancer activities will be investigated for their potentials as lead compounds in drug research for breast and colon carcinomas. Secondly, the theory that chelation generally improves biologically activities will also be verified (Ajibade and Zulu, 2011; Brandelli et al., 2004; Mittal and Uma., 2010; Nejo et al., 2009; Obaleye et al., 2011; da Silva et al., 2011; Qiao et al., 2011). The ligand used in this study, HL, and its metal(II) complexes are new, being reported for the first time by us as a continuation of our studies on the synthesis, characterization and bioactivities of some metal(II) complexes of various Schiff bases (Osowole and Akpan, 2012; Osowole and Balogun, 2012; Osowole et al., 2008, 2009, 2010, 2011, 2012; Tella et al., 2012).

2. MATERIALS AND METHODS

2.1 Chemicals

Reagent grade 4-aminoindane, 2, 4-dihydroxybenzaldehyde, cobalt(II) nitrate hexahydrate, nickel(II) nitrate hexahydrate, copper(II) nitrate hexahydrate, zinc(II) nitrate hexahydrate and palladium(II) chloride are purchased from Aldrich and BDH chemicals, and are used as received.

2.2 Physical Measurements

Electronic spectra are recorded on a Perkin-Elmer λ25 spectrophotometer while infrared spectra are measured with Thermo Nicolet FTIR 200 spectrophotometer in the range 4000-400 cm^{-1} as KBr discs. The ^{1}H nmr spectra are recorded on a 300 MHz Brucker DRX-400

NMR instrument in $CDCl_3$ at 295K and ^1H chemical shifts are referenced to the residual signals of the protons of $CDCl_3$ and are quoted in ppm. The elemental analyses for C, H and N are recorded on Thermo Quest CE Instruments flash EA1112 analyser, while percentage cobalt, nickel, copper, zinc and palladium in the complexes are determined titrimetrically (Bassett et al., 1978). Electrolytic conductivities in nitromethane are determined using a HANNA HI 991300 conductivity meter and melting points are done with Mel-Temp electro thermal machine.

2.3 Syntheses

2.3.1 Preparation of ligand

The ligand, 4-[(2,3-dihydro-1*H*-inden-4-ylimino)methyl]benzene-2,4-diol, is prepared by adding 11.30 mmol (1.50 g) of 4-aminoindane in 20 mL of ethanol drop wise to a stirring hot 30 mL ethanolic solution of 11.30 mmol (1.56 g) of 2,4-dihydroxybenzaldehyde at 70ºC. The resulting homogeneous yellow solution is then refluxed for 6 h after the addition of 6 drops of acetic acid. The yellow product, formed on cooling in ice, is filtered and recrystallized from ethanol and dried in *vacuo* over anhydrous calcium chloride. The yield of the resulting Schiff base (Fig. 1) is 1.95 g (70%). ^1H NMR (ppm) δ 11.4(s, 1H, $C^{2'}$ OH), 9.7(s, 1H, $C^{4'}$ OH), 8.50(s, 1H, $HC^{7'}N$), 7.3 (m, 3H, $C^{3'}$, $C^{5'}$, $C^{6'}$), 6.40 (m, 3H, C^5, C^6, C^7); 2.98 (t, 2H, C^3), 2.14 (q, 2H, C^2), 3.03 (t, 2H, C^1).

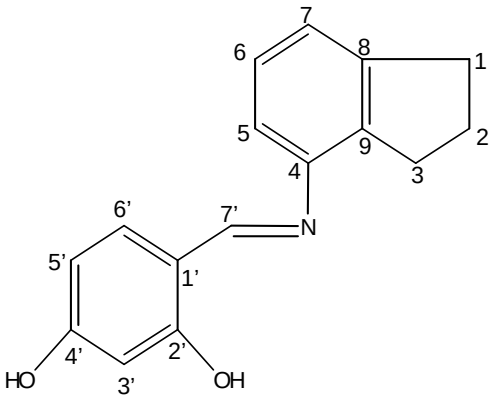

Fig. 1. Proposed structure for the ligand

2.3.2 Preparation of the Metal(II) complexes

The various complexes are prepared by stirring a homogeneous solution of 0.30 mmol (0.05-0.09 g) of hydrated M(II) nitrates (M = Co, Ni, Cu, Zn) and 0.60 mmol (0.15 g) of the ligand in 30 mL of methanol for 5 minutes followed by the addition of 0.06 mmol (0.06 g) of triethylamine. The reaction mixture is then stirred for 24 h at 18ºC. The products formed are filtered, washed with methanol and dried in *vacuo* over anhydrous calcium chloride. The same procedure is used to prepare the Pd(II) complex from its chloride salt.

$[ZnL_2].3H_2O$: ^1H NMR (ppm) δ 10.0(s, 1H, $C^{4'}$ OH), 8.54(s, 1H, $HC^{7'}N$), 7.0 (m, 3H, $C^{3'}$, $C^{5'}$, $C^{6'}$), 6.5 (m, 3H, C^5, C^6, C^7); 3.02 (t, 2H, C^3), 2.15 (q, 2H, C^2), 3.06 (t, 2H, C^1).

$[PdL_2].3H_2O$: ^{1}H NMR (ppm) δ 10.0(s, 1H, $C^{4'}$ OH), 8.56(s, 1H, $HC^{7'}N$), 7.5 (m, 3H, $C^{3'}$, $C^{5'}$, $C^{6'}$), 6.9 (m, 3H, C^5, C^6, C^7); 1.2 (t, 2H, C^3), 3.65 (q, 2H, C^2), 1.26 (t, 2H, C^1).

2.4 Biological Studies

2.4.1 Anticancer studies

The MCF-7 (human breast adenocarcinoma) and HT-29 (colon carcinoma) cells are cultured at the Institute of Medicinal and Pharmaceutical Chemistry, Technical University Braunschweig, Braunschweig, Germany and are maintained in minimum essential medium (MEM) supplemented with 10% of fetal calf serum (FCS) and 50 mg/L gentamycin at 37ºC in a humidified atmosphere with 5% CO_2. Cells are then suspended in cell culture medium (HT-29: 3000 cells/mL, MCF-7: 10000 cells/mL) and 100 µL aliquots thereof are plated in 96 well plates and incubated at 37ºC: 5% CO_2 for 48 h (HT-29) or 72 h (MCF-7). Stock solutions of the metal free ligand and its Cu, Zn and Pd complexes in DMF are freshly prepared and diluted with cell culture medium to the desired concentrations (final DMF concentration: 0.1% v/v). The medium in the plates is replaced with medium containing the compounds in graded concentrations (six replicates, 200 µL per well). After further incubation for 72 h (HT-29) or 96 h (MCF-7) the cell biomass is determined by crystal violet staining, followed by the extraction of the bound dye with ethanol and a photometric measurement at 590 nm. Mean values are calculated and the effects of the compounds are expressed as % $Treated/Control_{corr}$ values according to the following equations:

$$T/C_{corr}\ [\%] = (T\text{-}C_0/C\text{-}C_0).100$$

(C_0 is the biomass of control cells at the time of compound addition; C is the biomass of control cells at the time of the test end; T is the biomass of probes/samples at the time of the test end). The IC_{50} values are determined as those concentrations causing 50% inhibition of cell proliferation (Scheffler et al., 2010; Rubner et al., 2010). Results are represented as means of at least two independent experiments.

2.4.2 Antimicrobial studies

The antimicrobial assay is carried out on the ligand and its metal(II) complexes using the Agar diffusion technique and minimum inhibitory concentrations (MIC) of the complexes against selected microbial strains are determined by agar dilution method. The surface of the Muller Hinton's agar and Potato Dextrose agar (PDA) in a Petri dish is uniformly inoculated with 0.3 mL (10^6 CFU/ mL) of 18 hour old test microbe ({bacteria: *Bacillus subtilis*, *Salmonella typhi*, *Escherichia coli, Staphylococcus aureus* and *Pseudomonas aeuriginosa*} and {fungi: *Candida albicans* and *Penicillum notatum}*) culture. Using a sterile cork borer, 8 mm wells are bored into agar. Thereafter, 10 mg/mL concentration of the ligand and each metal complex in DMSO is then introduced into the wells and the plates are allowed to stand on bench for 30 min before incubation at 37^0C for 24 h, after which inhibitory zones (in mm) are taken as a measure of antimicrobial activity. The minimum inhibitory concentration (MIC) is determined by introduction of six different concentrations (1.0, 2.0, 4.0, 6.0, 8.0 and 10.0 mg/mL) of the compound into six wells bore unto the agar. The lowest concentration of each compound that inhibited growth of the test organism is taken as the minimum inhibitory concentration. The experiments are conducted in duplicates with Gentamycin and Tioconazole as reference drugs for bacteria and fungi respectively.

3. RESULTS AND DISCUSSION

3.1 Analytical Data

All the complexes adopt $[ML_2].aH_2O$ stoichiometry, and the Cu(II) complex is hygroscopic. The generalized equation for the formation of the complexes is:

$$M(NO_3)_2 \cdot 6H_2O + 2HL \rightarrow [ML_2].aH_2O + 2HNO_3 + bH_2O$$

(When M = Zn(II) {a = 3, b= 3}; Co(II) {a = 2, b = 4}; Ni(II) { a = 1, b = 5).

The water molecules associated with the complex formation are outside the coordination sphere; because heating the hydrated complexes in programmed oven in the temperature range 80-100ºC for 1-4 hours leads to dehydration, with corresponding weight loss of 1 – 7½ water molecules. It has been documented that water of coordination is usually eliminated in the temperature range 120–250ºC (Omar et al., 2010).

The purity of the metal complexes is established by the observance of sharp melting points/ decomposition temperature and elemental analyses. The results obtained from the latter are in good agreement with those calculated for the suggested formulae, $[ML_2].aH_2O$. The complexes are soluble in DMSO, DMF, and chloroform but are slightly soluble in ethanol and insoluble in distilled water. The analytical data, colors, percentage yields, melting points and molar conductivities of the complexes are presented in Table 1. Attempts to isolate single crystal for X-ray diffraction measurement have not been successful till now.

3.2 Infrared and Electronic Spectra

The relevant infrared and electronic data are presented in Table 2. The *ν*OH bands are observed as a single broad band at 3426 cm^{-1} in the ligand and the broadness is attributed to intramolecular hydrogen bonding (Osowole et al., 2008). The presence of strong to broad bands in the complexes between 3500-3336 cm^{-1} indicates the presence of phenolic *O*H and ν(OH) of crystallization water. The uncoordinated C=N vibrations in the ligand are observed in the range 1627-1581 cm^{-1} and these bands are bathochromic shifted to 1600-1504 cm^{-1} in the metal complexes, confirming the involvement of the imine *N* atom in coordination to metal(II) ion. The δC—H vibration of the ligand is observed at 976 cm^{-1} and it suffers a bathochromic shift to 854-775 cm^{-1} in the complexes due to the pseudo-aromatic nature of the chelates (Nejo et al., 2009). Further evidence of coordination is the appearance of the bands due to *ν*(M—O) and *ν*(M—N) in the complexes at 496-402 and 599-500 cm^{-1} respectively. These bands are absent in the ligand (Nakamoto, 1997).

Table 1. Analytical data for the compounds

Compound (Empirical formula)	F. m	Color	% Yield	Λ_m^*	M.pt (ºC)	Analysis (Calculated) %C	%H	%N	%M
HL	253.29	Yellow	70	-	190-192	75.89	5.93	5.10	-
($C_{16}H_{15}NO_2$)						(75.87)	(5.97)	(5.53)	
[CoL_2].2H_2O	599.55	Green	50	11.0	198$^+$	64.41	5.80	5.31	9.88
($CoC_{32}H_{32}N_2O_6$)						(64.11)	(5.38)	(4.67)	(9.83)
[NiL_2].H_2O	581.31	Green	80	9.0	170-172	66.12	6.18	4.10	10.32
($NiC_{32}H_{30}N_2O_5$)						(66.12)	(5.20)	(4.82)	(10.10)
#[CuL_2].7½H_2O	703.27	Green	60	15.0	350$^+$	54.82	4.79	3.34	8.98
($CuC_{32}H_{43}N_2O_{11.5}$)						(54.65)	(6.19)	(3.98)	(9.04)
[ZnL_2].3H_2O	624.10	Yellow	70	8.0	220-222	61.88	4.97	4.21	10.35
($ZnC_{32}H_{34}N_2O_7$)						(61.58)	(5.49)	(4.49)	(10.42)
[PdL_2].3H_2O	665.04	Brown	80	20.0	178-180	57.45	5.37	3.50	15.95
($PdC_{32}H_{34}N_2O_7$)						(57.79)	(5.15)	(4.21)	(16.00)

*# = hygroscopic; F. m = formula mass; + = decomposition temperature; *Ω^{-1} cm^2 mol^{-1}*

Table 2. Infrared and electronic (kK) spectral data of the complexes.

Compound	νOH	ν(C=N)	ν(M—N)	ν(M—O)	Electronic transitions (kK)
[HL]	3426b	1627s, 1581s	-	-	24.04, 29.33, 40.65
[CoL_2].3H_2O	3427s	1588s, 1570s,1534s	598s, 515m	443m, 402m	16.13, 23.70, 27.40, 32.60, 40.32
[NiL_2].H_2O	3500b 3423s	1599s, 1579s,1504s	598s, 502s	464m, 428s	13.20, 23.41, 30.03, 36.23.
[CuL_2].7½H_2O	3418b	1597s, 1579s,1550s	570w, 500s	471s, 407s	14.71, 24.57, 27.03, 32.22, 38.91.
[ZnL_2].3H_2O	3500b 3420s	1589s, 1564s,1534s	570s, 515m	485m, 430m	23.81, 30.03, 36.23
[PdL_2].3H_2O	3336b	1600s, 1580s,1543s	599m, 570m	496m, 471m	15.39, 22.73, 30.48, 36.76, 40.0

Key: s = strong, m = medium, b = broad, s = strong; 1 kK = 1000 cm^{-1}

The electronic spectra show ligand bands at 24.04, 29.33 and 40.65 kK and are assigned to $n \rightarrow \pi^*$, $\pi \rightarrow \pi^*$ and CT transitions. These bands are hypsochromic shifted in the complexes to 27.03-30.48, 32.22-38.91 and 40.0-40.32 kK due to coordination (Coombs et al., 2005). The Co(II) complex shows two absorption bands at16.13 and 23.70 kK typical of a 4-coordinate, tetrahedral geometry and are assigned to $^4A_2 \rightarrow {}^4T_1(F)$, ($\nu_2$) and $^4A_2 \rightarrow {}^4T_1(P)$, ($\nu_3$) transitions. Similarly, the Ni(II) complex has absorptions typical of a tetrahedral geometry at 13.20 and 23.41 kK assigned to $^3T_1(F) \rightarrow {}^3T_2$, ($\nu_2$) and $^3T_1(F) \rightarrow {}^3A_2$, ($\nu_3$) transitions (Ajibade and Zulu, 2011; Raman et al., 2004). The observance of two bands at 14.71 and 24.57 kK in the Cu(II) complex supports the assignment of the bands to $^2B_{1g} \rightarrow {}^2A_{1g}$ and $^2B_{1g} \rightarrow {}^2E_{1g}$ transitions in a square planar environment, since tetrahedral and octahedral Cu(II) complexes have single band each below and above 10.0 kK respectively (Nejo et al., 2009). The Zn(II) complex has no d-d bands expectedly, but a $M \rightarrow L$ charge transfer band at 23.81 kK indicative of its tetrahedral geometry (Raman et al., 2004). The spectrum of the Pd(II) complex is typical of square-planar, with absorption bands at 15.39 and 22.73 kK assigned to $^1A_{1g} \rightarrow {}^1B_{1g}$ and $^1A_{1g} \rightarrow {}^1E_{2g}$ transitions (Brandelli et al., 2004).

3.3 ^{1}H NMR and Conductance Measurements

In the metal free ligand the phenolic protons are observed at 11.4 and 9.7 ppm respectively, while the imine proton is seen as a singlet at 8.50 ppm. The protons on $C^{3'}$, $C^{5'}$ and $C^{6'}$ resonate as a multiplet centered at 7.3 ppm while the protons at C^5, C^6 and C^7 in the indane ring are observed as a multiplet centered at 6.40 ppm. The 2H at C^3 is seen as a triplet centered at 2.98 ppm, while those at C^2 resonate as a quintet centered at 2.14 ppm. Finally, the 2H at C^1 resonate as a triplet centered at 3.03 ppm. The Zn(II) complex spectrum shows the absence of phenolic proton at 11.4 ppm, which confirms coordination through the phenol O atom, and the phenolic proton on $C^{4'}$ remains unchanged at 9.7 ppm, thus proving its non-involvement in coordination. The protons at $C^{3'}$, $C^{5'}$, $C^{6'}$ resonate as a multiplet centered at 7.0 ppm and are downfield shifted. The imine proton is observed as a singlet at 8.54 ppm, while the protons on C^5, C^6 and C^7 appear as a multiplet at 6.50 ppm respectively, and are up shifted. Similarly, the 2H protons each on C^3, C^2 and C^1 resonate as a triplet, quintet and triplet centered at 3.02 ppm, 2.15 ppm and 3.06 ppm respectively and are upfield shifted. These shifts are indicative of coordination through the imine N atom (Zhao et al., 2005). Similarly, the spectrum of the Pd complex shows the absence of the phenolic proton on $C^{2'}$ at 11.4 ppm, while the phenolic proton on $C^{4'}$ remains unchanged at 9.7 ppm. These confirm coordination through the former's phenol O atom and non-involvement of the latter's oxygen atom in coordination. The imine proton on $C^{7'}$ is observed as a singlet at 8.56 ppm, while the protons on $C^{3'}$, $C^{5'}$, $C^{6'}$ resonate as a multiplet centered at 7.5 ppm. Similarly, the protons on C^5, C^6 and C^7 resonate as a multiplet centered at 6.90 ppm, and are all upfield shifted. Furthermore, the 2H protons each on C^3, C^2 and C^1 resonate as a triplet, quintet and triplet and are downfield shifted to 1.20 ppm, 3.65 ppm and 1.26 ppm respectively. These shifts are indicative of coordination through the imine N atom (Chang et al., 2002).

The molar conductivities of the complexes in nitromethane are in the range 8.0-20.0 ohm^{-1} cm^2 mol^{-1}, showing that they are non-electrolytes in the solvent. A value of 94-105 ohm^{-1} cm^2 mol^{-1} is expected for a 1:1 electrolyte (Geary, 1971).

3.4 Antiproliferative Effects in Cancer Cells

The results of the anticancer activities are presented in Table 3. The MCF-7 cells are moderately sensitive to the metal free ligand in contrast to HT-29 cells, which are not

affected in their growth at all. The metal complexes displayed activities in the range of 0.92 µM to 86.0 µM. The most active derivative is the Pd complex, which is even more active than the established antitumor agent Cis-platin in the same assay. The Cu and Zn complexes are of moderate activity. In general the antiproliferative activity increased in the order Zn < Cu < Pd. In case of the Pd and Cu derivatives, there is a clear positive effect of metal coordination concerning the cell growth inhibitory activities. However, in the case of the Zn complex a strong increase of bioactivity in relation to the metal free ligand was not noticeable. Thus, the enhanced anticancer activity of most the metal complexes is attributed to the coordinated metal ions, while the better and best anticancer activities of the Cu(II) and Pd(II) complexes against both MCF-7 and HT-29 cells are attributed to their square-planar geometry. It has been documented that complexes with such geometry avoid possible steric hindrance during physiological actions and are consequently more active than complexes of other geometries (Bolos et al., 1998).

Table 3. IC_{50} values of the ligand and its Cu(II), Zn(II), Pd(II) complexes against MCF-7 and HT-29 cells

Compounds	MCF-7(human breast adenocarcinoma) [µM]	HT-29(colon carcinoma cells) [µM]
CDDP(Cis-platin)	2.0	7.0
HL	51.67±0.0	>100
$[CuL_2].7½H_2O$	15.65±0.2	12.97±0.3
$[ZnL_2].3H_2O$	69.53 ± 0.2	86.02 ±0.1
$[PdL_2].3H_2O$	0.92±0.0	1.67±0.1

Results are expressed as means (± error) of at least two independent experiments

3.5 Antimicrobial Activity

The results of the antimicrobial activities are shown in Fig. 2 and presented in Table 4. The ligand is active against just two organisms, *S. typhi* and *P. aeuriginosa* with inhibitory zones range of 10.0 mm and 14.0 mm respectively, while the metal complexes are generally more active than the ligand because of chelation and π-electron delocalisation, which increase the lipophilic character, favouring its permeation into the bacterial membrane, causing the death of the organisms (Mittal and Uma, 2010).

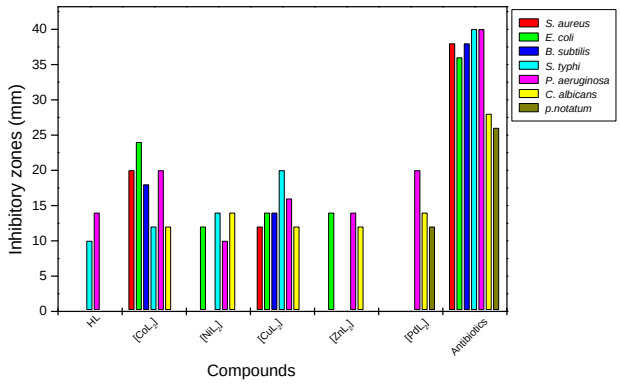

Fig. 2. The comparative activities of the complexes against microbes and standard antibiotics

Table 4. Zones of inhibition and MIC (mm) of the compounds against various microbes

Compounds	*S.aureus*	*B. subtilis*	*E. coli*	*S. typhi*	*P. aeriginosa*	*C. albicans*	*P. notatum*	MIC / organisms
HL	R	R	R	10.0±0.2	14.0±0.2	R	R	10.0 /*S. typhi*
$[CoL_2].3H_2O$	19.0±0.1	18.0±0.4	24.0±0.0	12.0±0.2	20.0±0.3	12.0±0.1	R	4.0 / *P. aeriginosa*
$[NiL_2].H_2O$	R	R	12.0±0.1	14.0±0.1	10.0±0.1	14.0±0.0	R	8.0 /*S. typhi*
$[CuL_2].7½H_2O$	12.0±0.3	14.0±0.2	14.0±0.1	20.0±0.1	16.0±0.0	12.0±0.3	R	6.0 / *B. subtilis*
$[ZnL_2].3H_2O$	R	R	14.0±0.2	R	14.0±0.1	12.0±0.1	R	8.0/ *E. coli*
$[PdL_2].3H_2O$	R	R	R	R	20.0±0.0	14.0±0.1	12.0±0.2	8.0 /*C .albicans*
Gentamycin/ *Tioconazole	38.0±0.0	36.0±0.1	38.0±0.3	40.0±0.2	40.0±0.0	*28.0±0.3	*26.0±0.0	ND

Key: R = Resistance; ND = Not determined; MIC = minimum inhibitory concentration

Furthermore, the better activities of the metal complexes are attributed to the metal ions, since the metal-free ligand has low antibacterial activity and nil anti-fungal activity. e. g. all the metal complexes are active against the fungus *C. albicans* with inhibitory zones range of 12.0-14.0 mm, and are consequently potential anti-fungal agents. Similarly, the Co(II) and Cu(II) complexes exhibit broad-spectrum antimicrobial activity against all the bacteria and the fungus, *C. albicans* with inhibitory zones range of 12.0-24.0 and 12.0-20.0 mm respectively, proving their usefulness as potential broad-spectrum antimicrobial agents (Ajibade and Zulu, 2011; Igbinosa et al., 2009; Nair et al., 2006). In addition, the complexes are more susceptible to the gram negative bacteria due to their thin peptidoglycan layer, which makes it more permeable to the complexes (Sulekh et al., 2009). The minimum inhibitory concentrations confirm that the ligand is not toxic to the organisms as typified in *S. typhi* with an MIC value of 10.0 mg/mL, and it justifies its very weak antimicrobial activities. Similarly, the MIC of the Ni(II), Pd(II) and Zn(II) complexes is 8.0 mg/mL against *S .typhi*, *C. albicans* and *E. coli* respectively. This is indicative of their moderate toxicity to the microbes (Table 4). The Co(II) and Cu(II) complexes with the best antibacterial activities have MIC values of 4.0 mg/mL and 6.0 mg/mL respectively corroborative of their high toxicity. The order of decreasing toxicity is $[CoL_2]$ >$[CuL_2]$> $[NiL_2]$ ~ $[PdL_2]$~ $[ZnL_2]$ > HL.

Gentamycin activities (36.0-40.0 mm) against the various bacterial isolates relative to the metal complexes (10.0-24.0 mm) show that the activities of the metal complexes are much lower, with the optimum activities being 2/3rd, half, and half that of gentamycin in Co(II), Cu(II) and Pd(II) complexes against *E. coli, S. typhi* and *P. aeuriginosa* respectively. Similarly, the Ni(II) and Pd(II) complexes have optimum activities of half (14.0 mm) that of Tioconazole (28.0 mm) against *C. albicans.*

4. CONCLUSION

The ligand coordinates to the Co(II), Ni(II), Cu(II), Zn(II) and Pd(II) ions using the azomethine *N* and one phenol *O* atoms. The assignment of a 4-coordinate, tetrahedral geometry to Co(II), Ni(II) and Zn(II) complexes, and square-planar geometry to the Cu(II) and Pd(II) complexes is corroborated by electronic spectral measurements. The Co(II) and Cu(II) complexes exhibit broad-spectrum antimicrobial activity against the microbes used with the exception of *P. notatum* with inhibitory zones range of 12.0-24.0 mm and 12.0-20.0 mm respectively. The Pd(II) complex has the best in-vitro anticancer activity against both MCF-7(human breast adenocarcinoma) and HT-29 (colon carcinoma) cells, with IC_{50} values of 0.94 µM and 1.67 µM respectively, which exceed the activity of Cis-platin.

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COMPETING INTERESTS

Authors have declared that no competing interests exist.

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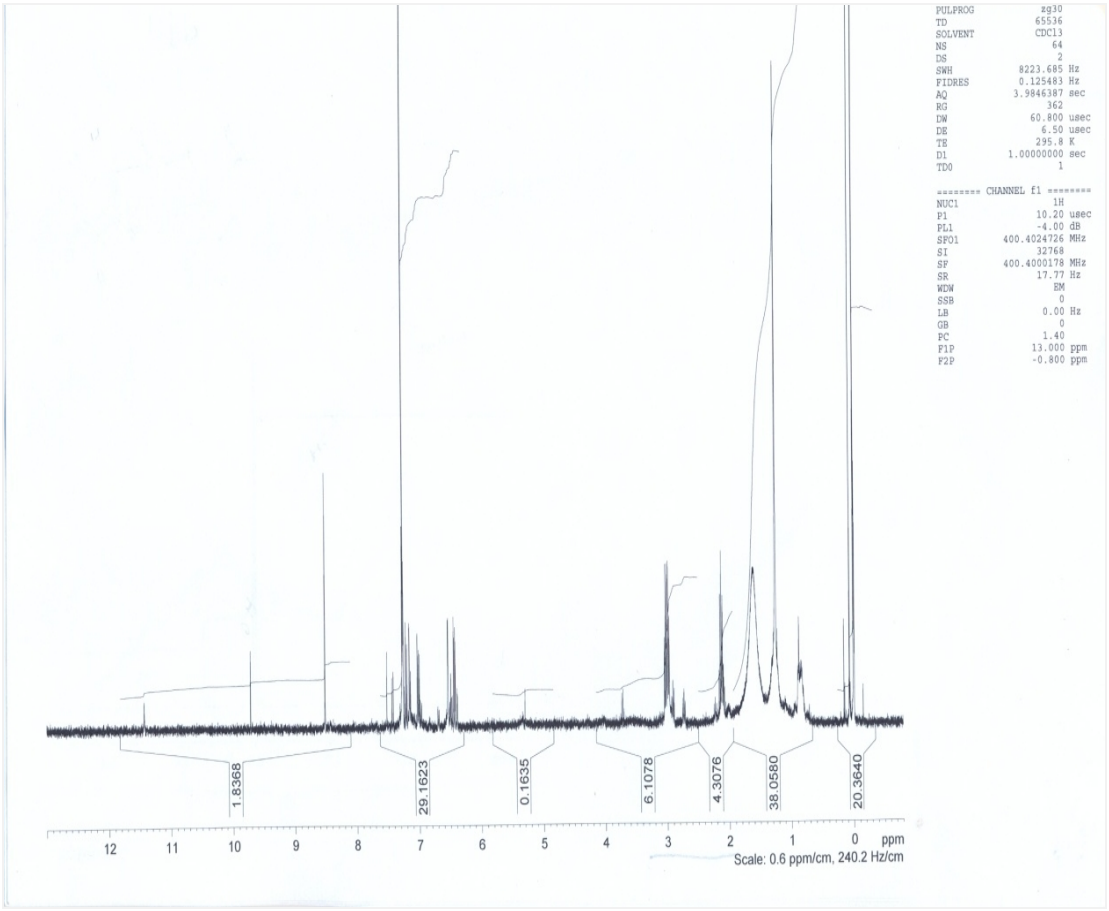
APPENDIX



The ^{1}HNMR spectrum of 4-[(2,3-dihydro-1*H*- inden-4-ylimino)methyl]benzene-2,4-diol.