Synthesis, Spectroscopic Characterisation, In-Vitro Anticancer and Antimicrobial Activities of Some Metal(II) Complexes of 3-{4, 6-Dimethoxy Pyrimidinyl) Iminomethyl Naphthalen-2-ol

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Abstract: The Schiff base, 3-{{[4,6-dimethoxypyrimidin-2-yl]imino}methyl}naphthalen-2-ol and its VO(IV), Mn(II), Co(II), Ni(II), Cu(II), Zn(II) and Pd(II) complexes were synthesised and characterized by IR, electronic and 'Hnmr spectroscopies, elemental analysis and conductance measurements. The ligand coordinated to the metal ions through the azomethine N and phenol O atoms, resulting in a 5-coordinate, square-pyramidal geometry for the VO(IV) complex and a 4-coordinate square planar/ tetrahedral geometry for the Mn(II), Co(II), Ni(II), Cu(II) and Zn(II) complexes. The complexes were non-electrolytes in nitromethane and melted within the temperature range 240-352°C. The in-vitro anticancer studies reveal that the Pd(II) and Cu(II) complexes had the best anticancer activity against MCF-7 (Human breast adenocarcinoma) cells with IC50 values of 3.89 µM and 4.90 µM, which were within the same order of activity as Cis-platin; and the Pd(II) complex activity against HT-29 (Colon carcinoma) cells was the best being about the same order as Cis-platin (7.0 µM) with an IC50 of 6.69 µM. The antimicrobial studies showed that the ligand and the Zn(II) complex exhibited broad-spectrum antibacterial activity against P. mirabilis, B. subtilis, B. cereus and S. typhi with inhibitory zones range of 7.0-21.0 mm and 10.0-19.0 mm respectively.

Key words: Anticancer • Antimicrobial activities • Broad-spectrum • Cis-platin • Schiff base

INTRODUCTION

Pyrimidines are renowned for their various biological activities such as antibiotics, e.g. amino-substituted pyrimidines, which themselves are completely inactive as antibiotics, but when presented on gold nanoparticles (NPs), exhibit antibacterial activities against multidrug-resistant clinical isolates [1] and their isatin analogues are inhibitors of HIV-1 reverse transcriptase [2]. Moreover, triazolo pyrimidine-6-sulfonamide with an incorporated thiazolidinone moiety shows good antitumor activity [3], while 2-mercapto pyrimidine and 2-mercapto-4-amino pyrimidine are able to inhibit the synthesis of t-RNA [4]. In continuation of our studies on synthesis, characterisation and in-vitro anticancer activities of various (substituted) pyrimidinyl Schiff bases and their Cu(II), Pd(II) and Zn(II) complexes against various carcinomas [5-7], we presented the in-vitro anticancer activities of the new Schiff base 3-{{[4,6-dimethoxypyrimidin-2-yl]imino}methyl}naphthalen-2-ol (derived from condensation of 2-amino-4,6-dimethoxy pyrimidine and 2-hydroxy-1-naphthaldehyde) and its Cu(II), Zn(II) and Pd(II) complexes against MCF-7 (human breast adenocarcinoma) and HT-29 (colon carcinoma) cells. Additionally, the antimicrobial activities of all the complexes against Pseudomonas aeruginosa, Proteus mirabilis, Bacillus subtilis, Bacillus cereus, Salmonella typhi and Candida albicans were reported. Thus, the objective of this work was to identify lead metal(II) complexes for further studies in drug development against human breast and colon carcinomas and surface cleaning agents since there is no information in the literature on this Schiff base and its complexes [8-12].

MATERIALS AND METHODS

Materials and Physical Measurements: All the chemicals used were of reagent grade. i.e. 2-amino-4,6-dimethoxy pyrimidine, 2-hydroxy-1-naphthaldehyde, hydrated manganese(II) nitrate, vanadyl sulphate, cobalt(II) nitrate, nickel(II) nitrate, copper(II) nitrate, palladium(II) chloride and zinc(II) nitrate and were used as purchased from Aldrich and solvents were distilled before use.
The elemental analyses for C, H and N were recorded on Thermo Quest CE Instruments flash EA1112 analyser. Percentages of manganese, cobalt, nickel, copper, zinc and palladium were determined titrimetrically, while that of vanadium was determined gravimetrically [13]. The \(^1\)H nmr spectrum was recorded on a 300 MHz Brucker DRX-400 NMR instrument in CDCl\(_3\) at 295K. \(^1\)H chemical shifts were referenced to the residual signals of the protons of CDCl\(_3\) and were quoted in ppm. The reflectance infrared spectra were recorded on Perkin-Elmer A25 spectrophotometer and Perkin-Elmer FTIR spectrum BX spectrophotometer (in the range 400-4000 cm\(^{-1}\)) respectively. Electrolytic conductivities of the compounds in nitromethane were determined using a Hanna HI 991300 conductivity meter and melting points (uncorrected) were recorded on a Mel-Temp electro thermal machine.

**Synthesis**

**Preparation of (3-[[4,6-Dimethoxy Pyrimidin-2-yl]imino][methyl]Naphthalen-2-ol):** The ligand, HL, was prepared by refluxing a mixture of 0.012 mol (1.80 g) of 2-amino-4,6-dimethoxypyrimidine and 0.012 mol (2.01 g) of 2-hydroxy-1-napthaldehyde with 6 drops of acetic acid in 60 mL of ethanol for 6 h. The yellow product, formed on cooling in ice, was filtered and recrystallized from ethanol and dried in vacuo over anhydrous calcium chloride [5]. The yield of the resulting Schiff base (Figure 1) was 2.60 g (70%). Color: Yellow; M.pt(°C) 198-200; IR(cm\(^{-1}\)) vOH (3424s), vC=N(1634s 1606s 1547s); UV(1kK = 1000 cm\(^{-1}\)) 32.26(π-π*), 38.5(π-π*), 40.0(CT), 45.0(CT); \(^1\)Hnmr (300 MHz, CDCl\(_3\), δ in ppm): 13.2 (s, OH), 6.7-9.47 (m, 6H), 8.07(8.10); \(^13\)Cnmr: 29.06(n-π*), 32.0(π-π*), 40.98(CT); Formula mass (702.59); CHN Anal. calcd(found) for Mn(C\(_{44}\)H\(_{34}\)N\(_{4}\)O\(_{9}\)) C, 60.04(59.70); H, 4.36(4.29); N, 12.13(10.68); %Ni calcd(found) 9.10(9.07); %Ni calcd(found) 8.47(8.38); \(\Lambda_w\) 10.0.

**Preparation of the Metal (II) Complexes:** The various complexes were prepared by refluxing a homogeneous solution of 0.30 mmol (0.053-0.089 g) of hydrated M(II) nitrates (M = Co, Ni, Cu, Mn, Zn) and 0.60 mmol (0.19 g) of the ligand, to which 0.06 mmol (0.061 g) of triethylamine was added in 30mL ethanol for 6-24 h. The products formed were filtered, washed with ethanol and dried in vacuo over anhydrous calcium chloride. The oxovanadium(IV) and Pd(II) complexes were prepared from their sulphate and chloride salts using similar procedures [6]. The analytical, IR and electronic data were as follows;

\[
\text{[VOL}_3\text{H}_2\text{O}: \text{% yield 50(0.11 g); Color(green); M.pt(°C)} \text{270-272; IR(cm}^{-1}\text{): vOH (3500 b), vC=N(1599s 1553s 1533s); vM-O(552s 539s), vM-O(452s 420s); VIS/UV(1kK =1000 cm}^{-1}\text{): 12.69[A_A - E_j], 22.62[A_A - A_j], 28.68(n-π*), 35.2(π-π*), 42.0(CT); Formula mass (737.9); CHN Anal. calcd(found) for V(C}_{26}\text{H}_{34}\text{N}_{13}\text{O}_{20}(u)\text{ C}, 55.34(55.83); H, 4.64(4.54); N, 11.39(10.73); %V calcd(found) 6.90(6.85); \(\Lambda_w\) 10.0.]
\]

\[
\text{[MnL}_2\text{]0.5H}_2\text{O}: \text{% yield 70(0.14 g); Color(brown); M.pt(°C) 272-274; IR(cm}^{-1}\text{): vOH (3500 b), vC=N(1599s 1553s 1533s); vM-O(552s 539s), vM-O(452s 420s); VIS/UV(1kK =1000 cm}^{-1}\text{): 12.69[A_A - E_j], 22.62[A_A - A_j], 28.68(n-π*), 35.2(π-π*), 42.0(CT); Formula mass (680.57); CHN Anal. calcd(found) for Mn(C}_{26}\text{H}_{34}\text{N}_{13}\text{O}_{20}(u)\text{ C}, 60.04(59.70); H, 4.30(4.15); N, 12.35(11.70); %Mn calcd(found) 8.07(8.10); \(\Lambda_w\) 35.46.]
\]

\[
\text{[CoL}_2\text{]1.5H}_2\text{O}: \text{% yield 70(0.15 g); Color(red); M.pt(°C) 318-320; IR(cm}^{-1}\text{): vOH (3500 b), vC=N(1600 s 1556 s 1534 s); vM-N(572 s 511 s), vM-O(495 s 448 s); VIS/UV(1kK =1000 cm}^{-1}\text{): 17.86[A_{ij} - T_i(0), 22.88[A_A - A_j; 29.0(n-π*), 32.0(π-π*), 40.98(CT); Formula mass (702.59); CHN Anal. calcd(found) for Co(C}_{26}\text{H}_{34}\text{N}_{13}\text{O}_{20}(u)\text{ C}, 58.14(57.45); H, 4.44(4.22); N, 11.96(11.81); %Co calcd(found) 9.10(9.07); \(\Lambda_w\) 11.01.]
\]

\[
\text{[NiL}_2\text{]H}_2\text{O}: \text{% yield 50(0.10 g); Color(green); M.pt(°C) 337-339; IR(cm}^{-1}\text{): vOH (3500 b), vC=N(1618 s 1600 s 1556 s); vM-N(592 m 500 m), vM-O(448 m 414 m); VIS/UV(1kK =1000 cm}^{-1}\text{): 15.0[T_i(0) - T_j]; 21.93[T_i(0) - A_j], 29.06(n-π*), 32.2(π-π*), 40.63(CT); Formula mass (692.95); CHN Anal. calcd(found) for Ni(C}_{26}\text{H}_{34}\text{N}_{13}\text{O}_{20}(u)\text{ C}, 58.93(58.56); H, 4.36(4.29); N, 12.13(10.68); %Ni calcd(found) 8.47(8.38); \(\Lambda_w\) 7.4.]
\]
[CuL]1.5 H2O: % yield 60 (0.13 g); Color(green); M.pt(°C), 268-270; IR(cm⁻¹): ν OH (3500 b), ν C=N (1621 s 1579 s 1564 s 1536 s), νM-N (550 s 530 m), νM-O (468 s 424 s); VIS/UV(1kK=1000 cm⁻¹): 14.89 [1g A₁g - 1g A₂g], 21.41 [1g B₁g - 1g E₂g], 26.0 (n- π*), 30.0 (π- π*), 41.5 (CT); Formula mass (706.80); CHN Anal. calecd(found) for Cu(C24H20N8O12), C, 57.75(57.76); H, 4.28 (3.59); N, 11.88(5.26); %Cu calecd(found) 8.99(9.02); Λₐₘ 46.43.

[ZnL₃]: % yield 60 (0.12 g); Color (yellow); M.pt(°C), 350-352; IR(cm⁻¹): ν C=N (1600 s 1556 m 1538 m), νM-N (570 m 507 m), νM-O (493 m 444 s); VIS/UV(1kK=1000 cm⁻¹): 22.35 (M – L CT), 28.33 (n- π*), 32.0 (π- π*), 40.98 (CT); Formula mass (681.56); CHN Anal. calecd(found) for Zn(C16H12N6O3) C, 59.92 (61.21); H, 4.14 (4.37); N, 12.33 (12.42); %Zn calecd(found) 9.06 (9.04); Λₐₘ 7.91.

[PdL]12H₂O: % yield 50 (0.14 g); Color (brown); M.pt(°C), 240-242; IR(cm⁻¹): ν OH (3500 b), ν C=N (1599 s, 1558 s 1534 s), νM-N 520 s 514 s, νM-O 471 s 428 s; VIS/UV(1kK=1000 cm⁻¹): 13.05 [1g A₁g - 1g B₁g], 22.08 [1g A₁g - 1g E₂g], 29.10 (n- π*), 31.25 (π- π*), 39.84 (π- π*); 1Hnmr (300 MHz, CDCl₃, 6 in ppm): 6.6-9.5 (m, 6H, CH); 10.6 (s, 1H, CH₉, methine); 5.84 (s, 1H, CH); 4.0 (s, 6H, OCH₃); Formula mass (939.28); CHN Anal. calecd(found) for Pd(C₁₄H₁₀N₆O₅), C, 43.48 (43.43); H, 5.58 (3.52); N, 8.95 (9.20); %Pd calecd (found)11.33 (11.24); Λₐₘ 21.95.

Biological Studies

Anticancer Assay: The MCF-7 (human breast adenocarcinoma) and HT-29 (colon carcinoma) cells were cultured and maintained in minimum essential medium (MEM) supplemented with 10% (V/V) fetal calf serum (FCS) and 50 mg/L of gentamycin at the Institute of Medicinal and Pharmaceutical Chemistry, Technical University Braunschweig, Germany. In 96 well plates, 100 mL of a cell suspension in culture medium at 7500 cells/ml (MCF-7) and 2500 cells/ml (HT-29) were plated into each well and incubated for three days under culture conditions. After the addition of various concentrations of the test compounds, cells were incubated for another 96 and 72 h respectively. Then the medium was removed and the cells were fixed with 1% glutaraldehyde solution and stored under phosphate buffered saline (PBS) at 4°C. Cell biomass was determined by a crystal violet staining, the absence of this band in the complexes indicates the involvement of the phenolic O in bonding to the metal ions. The new broad band at 3500 cm⁻¹ in the hydrated complexes, was assigned to ν(OH) crystallization water. The uncoordinated C=N stretching vibrations in the

RESULTS AND DISCUSSIONS

All complexes were isolated as [MLₓ]xH₂O (VO: {x = 3}; Co, Cu: {x = 1.5}; Ni {x = 1}, Mn{x = 0.5}) with the exceptions of the Zn(II) complex which was anhydrous and the Pd(II) complex which was hygroscopic. Evidence for the formation of the ligand in DMSO was introduced into the wells and the plates were allowed to stand on bench for 30 min before incubation at 37°C for 24 h after which the inhibitory zones (in mm) were taken as a measure of antimicrobial activity. The experiments were conducted in duplicates and gentamycin was used as the reference drug.

All X-ray diffraction measurements could not be done due to the formation of non-suitable crystals.

Infrared Spectra: The νOH band of the ligand was seen at 3424 cm⁻¹ and it was broad as a result of hydrogen bonding which is usually very strong in Schiff bases [15]. The absence of this band in the complexes indicates the involvement of the phenolic O in bonding to the metal ions. The new broad band at 3500 cm⁻¹ in the hydrated complexes, was assigned to ν(OH) crystallization water. The uncoordinated C=N stretching vibrations in the

assay concentrations (0.1% V/V DMF) and Cis-platin was used as the reference drug. The IC₅₀ value was determined as the concentration causing 50% inhibition of cell proliferation and calculated as mean of at least two independent experiments [14].

Antimicrobial Assay: The assay was carried out on the ligand and its metal(II) complexes using agar well diffusion technique [12]. The surface of (Mueller-Hinton) agar in a Petri dish was uniformly inoculated with 0.3 ml of 18 h old culture (10⁸ CFU/mL) of  Bacillus subtilis ATCC 33932, Salmonella typhi, Proteus mirabilis ATCC 21784, Candida albicans MTTC 227, Pseudomonas aeruginosa ATTC 27856 and Bacillus cereus ATTC 14579. Using a sterile cork borer, 6 mm wells were bored into agar. Then 0.06 ml of 10 mg/ml concentration of each metal complex in DMSO was introduced into the wells and the plates were allowed to stand on bench for 30 min before incubation at 37°C for 24 h after which the inhibitory zones (in mm) were taken as a measure of antimicrobial activity. The experiments were conducted in duplicates and gentamycin was used as the reference drug.
These bands suffered bathochromic shifts to 1634-1533 cm$^{-1}$ in the Schiff base complexes and still remained as three bands, with the exception of the Cu(II) complex that had four bands, thus confirming the involvement of the imine $N$ atom in coordination to the metal(II) ion. The $v$(V=O) band of the vanadyl complex appeared strong at 952 cm$^{-1}$, which confirmed its monomeric nature since polymeric complexes have $v$(V=O) in the range 848-860 cm$^{-1}$ [19]. The $\delta$C$^\text{H}$ vibration of the ligand was observed at 839 cm$^{-1}$ and suffered bathochromic shift to 834-745 cm$^{-1}$ in the complexes due to the pseudo-aromatic nature of the heterocyclic conjugated systems. The $\delta$-bands due to $\text{v}(\text{M}=\text{O})$ and $\text{v}(\text{M}^\text{N})$ were observed at 495-410 and 592-500 cm$^{-1}$ respectively in the complexes [18].

**Electronic Spectra:** The oxovanadium(IV) complex, had three absorption bands at 12.92, 16.98 and 23.14 kK which indicates a five coordinate, square-pyramidal geometry with the assignment $b_1 - e_g^*$ band(I), $b_2 - b_1^*$ (bandII) and $b_3 - a_1^*$ band (III) respectively [19]. The spectra of Mn(II) complexes are usually characterized by forbidden transitions from the $^4A_1$ to higher quartet states for all geometries. The Mn(II) complex showed two bands at 12.62 and 22.62 kK, typical of a tetrahedral geometry and were assigned to $^4A_1 - ^4E_1$ ($v_1$) and $^4A_1 - ^4A_1$ ($v_2$) transitions [20]. The Co(II) complex had absorption bands at 17.86 and 22.88 kK typical of a 4-coordinate, tetrahedral geometry and were assigned to $^4A_1 - ^4T_1(F)$, ($v_1$) and $^4A_1 - ^4T_1(P)$, ($v_2$) transitions [21]. The reflectance spectrum of the Ni(II) complex showed absorption bands at 15.00 and 21.93 kK assigned to $^4T_1(F) - ^4T_2^2$ ($v_1$) and $^4T_1(F) - ^4A_2^1$ ($v_2$) transitions, in a tetrahedral environment [22]. The Cu(II) complex had two bands at 14.89 and 21.41 kK which indicates square planar geometry with the bands assigned as $^3B_1g - ^3A_2g$ and $^1B_{2g} - ^1E_{2g}$ transitions, since tetrahedral Cu(II) complexes have a single band below 10.0 kK [16, 22]. The Pd(II) complex showed typical square-planar absorption bands at 13.05 and 22.08 kK, which were assigned to $^1A_{1g} - ^1B_{1g}$ and $^1A_{1g} - ^1E_{2g}$ transitions [23]. The Zn(II) complex expectedly showed only CT transitions from M--L at 22.35 kK, since no d-d transition was expected. This is indicative of tetrahedral geometry [22]. The ligand had two band maxima between 32.26-38.50 and 40.0-45.0 kK in the UV region, which were assigned to $\pi-\pi^*$ and charge transfer transitions. These bands were hypsochromic/bathochromic shifted in the complexes to 31.25-39.84 and 40.63-42.0 kK respectively and an additional band was observed between 26.0-30.57 kK assigned to n-\(\pi^*\) due to coordination [18].

### Biological Studies

**Anticancer Activity:** The results of the anticancer activities are presented in Table 1. The MCF-7 cells weren't sensitive to both the ligand and the Zn(II) complex. The Cu(II) and Pd(II) complexes had IC$_{50}$ values of 4.90 and 3.81 µM respectively against MCF-7 cells which were within the same order as CDDP (2.0 µM). Similarly, the colon carcinoma (HT-29) cells, weren't sensitive to the ligand and the Zn(II) complex, but were sensitive to the Cu(II) complex with an IC$_{50}$ value of 57.50 µM. The Pd(II) complex had the best activity with an IC$_{50}$ value of 6.69 µM which was the same order as Cisplatin (7.0 µM).

The good anticancer activities of the Pd(II) and to a lesser extent Cu(II) complexes against these cell lines may be attributed to their planar structure which has been documented to avoid possible steric hindrance during physiological actions [26]. Thus, coordination enhances anticancer activities with both MCF-7 cells and HT-29 cells expectedly [22], with the exception of the Zn(II) complex which was inactive like the ligand.
Table 2: Zones of inhibition (in mm) of the compounds against various microbes

<table>
<thead>
<tr>
<th>Complexes</th>
<th>P. aeruginosa</th>
<th>P. mirabilis</th>
<th>B. subtilis</th>
<th>B. cereus</th>
<th>S. typhi</th>
<th>C. albicans</th>
</tr>
</thead>
<tbody>
<tr>
<td>HL</td>
<td>21.0±0.1</td>
<td>20.0±0.03</td>
<td>7.0±0.12</td>
<td>20.0±0.2</td>
<td>21.0±0.1</td>
<td>R</td>
</tr>
<tr>
<td>[MnL]0.5H₂O</td>
<td>R</td>
<td>7.0±0</td>
<td>R</td>
<td>R</td>
<td>20.0±0.2</td>
<td>14.0±0.03</td>
</tr>
<tr>
<td>[CoL]1.5H₂O</td>
<td>20.0±0.03</td>
<td>10.0±0.04</td>
<td>7.0±0</td>
<td>15.0±0</td>
<td>R</td>
<td>10.0±0.13</td>
</tr>
<tr>
<td>[NiL]H₂O</td>
<td>R</td>
<td>23.0±0.1</td>
<td>10.0±0.03</td>
<td>10.0±0.4</td>
<td>19.0±0.2</td>
<td>R</td>
</tr>
<tr>
<td>[CuL]1.5H₂O</td>
<td>12.0±0.23</td>
<td>11.0±0</td>
<td>R</td>
<td>R</td>
<td>R</td>
<td>R</td>
</tr>
<tr>
<td>[ZnL]</td>
<td>R</td>
<td>13.0±0.14</td>
<td>10.0±0.03</td>
<td>10.0±0.4</td>
<td>19.0±0.2</td>
<td>R</td>
</tr>
<tr>
<td>[PdL]12H₂O</td>
<td>R</td>
<td>20.0±0</td>
<td>R</td>
<td>R</td>
<td>R</td>
<td>R</td>
</tr>
<tr>
<td>Gentamycin</td>
<td>24.0±0.12</td>
<td>20.0±0.2</td>
<td>20.0±0.2</td>
<td>16.0±0.3</td>
<td>21.0±0.1</td>
<td>18.0±0.03</td>
</tr>
</tbody>
</table>

R = Resistance

Fig. 2: The comparative antimicrobial activities of the complexes and gentamycin against microbes

Antimicrobial Activity: The results of the antimicrobial activities are presented in Table 2 and shown in Figure 2. The ligand was active against the tested organisms; S. typhi, P. mirabilis, B. subtilis, B. cereus and P. aeruginosa with the exception of C. albicans with inhibitory zones range of 7.0-21.0 mm. The Zn(II) complex was active against four organisms namely; S. typhi, P. mirabilis, B. subtilis and B. cereus with inhibitory zones range 10.0-19.0 mm, while the Mn(II) complex was active against three organisms P. mirabilis, S. typhi and C. albicans with inhibitory zone range of 7.0-20.0 mm. The Ni(II) and Cu(II) complexes were both active against two organisms, i.e. B. subtilis and P. mirabilis; and P. aeruginosa and P. mirabilis respectively with inhibitory zones of 7.0, 23.0, 12.0 and 11.0 mm. The Pd(II) complex was active only against Proteus mirabilis with an inhibitory zone of 20.0 mm. The VO(IV) complex wasn’t screened in this study.

The inactivity of the Pd(II) and Cu(II) complexes against most of the microbes occurred because they could not permeate through the cell wall of the microbes [24]. Furthermore, the metal(II) complexes were mostly unexpectedly less effective than the free ligand, with the exceptions of Mn(II) and Co(II) complexes whose activity against C. albicans with inhibitory zones of 14.0 and 10.0 mm respectively was higher than the ligand with nil activity. Similarly, the Ni(II) complex activity of 23.0 mm activity against P. mirabilis was greater than that of the ligand (20.0 mm) and the Zn(II) complex activity of 10.0 mm against B. subtilis was greater than the ligand’s activity of 7.0 mm.

This is contrary to the chelation theory, which states that chelation increases antimicrobial activity, because of partial sharing of its positive charge with donor groups of the ligand and possible $\pi$-electron delocalisation which increased the lipophilic character. This leads to easier penetration of organisms’ cell membrane, leading to the death of the organism [27]. The ligand, Co(II) and Ni(II) complexes had the same activity of 7.0 mm against B. subtilis. The lower activity of the metal complexes is attributed to the lower lipophilicity of the complexes, which decreases the penetration of the complexes through the lipid membrane [28]. Gentamycin activities (16.0-24.0 mm) against the various isolates relative to the metal complexes (7.0-23.0 mm) showed that the activities of the latter are much lower, with the optimum activities being (about) the same as gentamycin in Ni(II), Mn(II) and Co(II) complexes against P. mirabilis, S. typhi and P. aeruginosa. Moreover, the ligand and Zn(II) complex exhibit broad-spectrum antibacterial activity, like gentamycin, against S. typhi, P. mirabilis, B. subtilis, B. cereus, P. aeruginosa and S. typhi, P. mirabilis, B. subtilis and B. cereus with inhibitory zones range of 7.0-21.0 mm and 10.0-19.0 mm respectively. Thus, they provide their usefulness as potential broad-spectrum antibacterial agents.

The Pd(II) and Cu(II) complexes had the best activity against MCF-7 cells with IC₅₀ values of 3.89 µM and 4.90 µM, which were within the same order as Cis-platin (2.0 µM). Similarly, the Pd(II) complex had an IC₅₀ Value of 6.69 µM which was the same order as Cis-platin (7.0 µM) against HT-29 cells. The ligand and the Zn(II) complex exhibited broad-spectrum antibacterial activities like gentamycin.
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