European Journal of Applied Sciences 4 (1): 14-20, 2012
ISSN 2079-2077

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 ^{1}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 IC_{50} 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 IC_{50} 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-napthaldehyde) 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*, *Samonella 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-napthaldehyde, 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.

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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 and infrared spectra were recorded on Perkin-Elmer λ25 spectrophotometer and Perkin-Elmer FTIR spectrum BX spectrophotometer (in the range 4000-400 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-hydoxy-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}): *ν*OH (3424s), *ν*C=N (1635s 1606s 1547s); UV(1kK= 1000cm^{-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, C_9H_6); 10.82 (s, 1H, $CH_{pyrimidine}$); 5.82 (s, 1H, CH); 3.9(s, 6H, OCH_3); Formula mass (309.11); CHN Anal. calcd(found) for $C_{17}H_{15}N_3O_3$: C, 66.01(65.92); H, 4.89(4.85); N, 13.58(13.59).

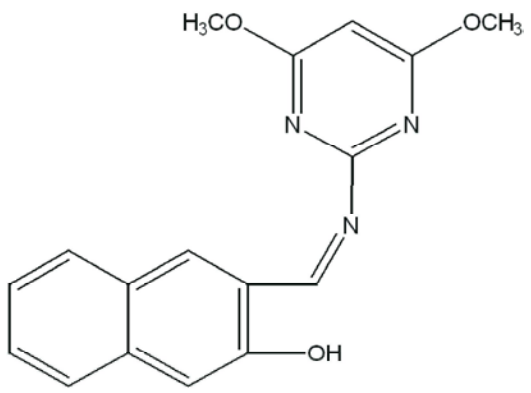

Fig. 1: 3 - { [(4 , 6 - d i m e t h o x y p y r i m i d i n - 2 - yl)imino]methyl}naphthalen-2-ol

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;

$[VOL_2]3H_2O$: % yield 50(0.11 g); Color(green); M.pt(°C), 270-272; IR(cm^{-1}): *ν*OH (3500 b), *ν*C=N(1634 s 1605 s 1544 s), *ν*M-N (542s 500s), *ν*M-O (437s 410s); VIS/UV(1kK= 1000 cm^{-1}): 12.92[$b_2 \rightarrow e_1$*], 16.98[$b_2 \rightarrow b_1$*], 23.14[$b_2 \rightarrow a_1$*], 30.57(π -π*), 33.2(π- π*), 41.7(CT); Formula mass (737.9); CHN Anal. calcd(found) for $V(C_{34}H_{34}N_6O_{10})$ C, 55.34(55.83); H, 4.64(4.54); N, 11.39(10.73); %V calcd(found) 6.90(6.85); Λ_m, 10.0.

$[MnL_2]0.5H_2O$: % yield 70(0.14 g); Color(brown); M.pt(°C), 272-274; IR(cm^{-1}): *ν*OH (3500 b), *ν*C=N (1599s 1553s 1533s); *ν*M-N (552s 539s), *ν*M-O (452s 420s); VIS/UV(1kK =1000 cm^{-1}): 12.69[$^6A_1 \rightarrow {}^4E_1$], 22.62[$^6A_1 \rightarrow {}^4A_1$], 28.68(n -π*), 35.2(π- π*), 42.0(CT); Formula mass (680.57); CHN Anal. calcd(found) for $Mn(C_{34}H_{29}N_6O_{6.5})$ C, 60.04(59.70); H, 4.30(4.15); N, 12.35(11.70); %Mn calcd(found) 8.07(8.10); Λ_m, 35.46.

$[CoL_2]1.5H_2O$: % yield 70(0.15 g); Color(red); M.pt(°C), 318-320; IR(cm^{-1}): *ν*OH (3500 b), *ν*C=N (1600 s 1556 s 1534 s); *ν*M-N (572 s 511 s), *ν*M-O (495 s 448 s); VIS/UV(1kK =1000 cm^{-1}): 17.86[$^4A_2 \rightarrow {}^4T_1$(F)], 22.88[$^4A_2 \rightarrow {}^4T_1$ (P)], 29.0(n -π*), 32.0(π- π*), 40.98(CT); Formula mass (702.59); CHN Anal. calcd(found) for $Co(C_{34}H_{31}N_6O_{7.5})$ C, 58.14(57.45); H, 4.44 (4.22); N, 11.96(11.81); %Co calcd(found) 9.10(9.07); Λ_m, 11.01.

$[NiL_2]H_2O$: % yield 50(0. 10 g); Color(green); M.pt(°C), 337-339; IR(cm^{-1}): *ν*OH (3500 b), *ν*C=N (1618 s 1600 s, 1556 s); *ν*M-N (592 m 500 m), *ν*M-O (448 m 414 m); VIS/UV(1kK=1000 cm^{-1}): 15.0[$^3T_1$(F) → $^3T_2$], 21.93[$^3T_1$(F) → $^4A_2$], 29.06(n -π*), 32.2(π- π*), 40.63(CT); Formula mass (692.95); CHN Anal. calcd(found) for $Ni(C_{34}H_{30}N_6O_7)$ C, 58.93(58.56); H, 4.36 (4.29); N, 12.13(10.68); %Ni calcd(found) 8.47(8.38); Λ_m, 7.4.

$[CuL_2]1.5\ H_2O$: % yield 60(0.13 g); Color(green); M.pt(°C), 268-270; IR(cm^{-1}): νOH (3500 b), νC=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[$^2B_{1g} \rightarrow {}^2A_{1g}$], 21.41[$^2B_{1g} \rightarrow {}^2E_{1g}$], 26.0 (n- π^*), 30.0(π- π^*), 41.5(CT); Formula mass (706.80); CHN Anal. calcd(found) for $Cu(C_{34}H_{31}N_6O_{7.5})$ C, 57.75(57.76); H, 4.28 (3.59); N, 11.88(5.26); %Cu calcd(found)8.99(9.02); Λ_m, 46.43.

$[ZnL_2]$: % yield 60(0.12g); Color (yellow); M.pt(°C), 350-352; IR(cm^{-1}): νC=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); Formular mass (681.56); CHN Anal. calcd(found) for $Zn(C_{34}H_{28}N_6O_6)$ C, 59.92(61.21); H, 4.14 (4.37); N, 12.33(12.42); %Zn calcd(found) 9.06(9.04); Λ_m, 7.91.

$[PdL_2]12H_2O$: %yield 50(0.14 g); Color(brown); M.pt(°C), 240-242; IR(cm^{-1}): νOH (3500 b), νC=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[$^1A_{1g} \rightarrow {}^1B_{1g}$], 22.08[$^1A_{1g} \rightarrow {}^1E_{2g}$], 29.10(n- π^*), 31.25(π- π^*), 39.84(π- π^*); ^{1}Hnmr (300 MHz, $CDCl_3$, δ in ppm): 6.6-9.5 (m, 6H, C_9H_6); 10.6 (s, 1H, $CH_{pyrimidine}$); 5.84 (s, 1H, CH); 4.0(s, 6H, OCH_3); Formular mass (939.28); CHN Anal. calcd(found) for $Pd(C_{34}H_{52}N_6O_{20})$ C, 43.48(43.43); H, 5.58 (3.52); N, 8.95(9.20); %Pd calcd (found)11.33 (11.24); Λ_m, 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) of 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% glutardialdehyde solution and stored under phosphate buffered saline (PBS) at 4°C. Cell biomass was determined by a crystal violet staining, followed by extracting of the bound dye with ethanol and a photometric measurement at 590 nm. The test compounds were prepared fresh as stock solutions in DMF and diluted with the cell culture medium to the final assay concentrations (0.1% V/V DMF) and Cis-platin was used as the reference drug. The IC_{50} 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 (10^6 CFU/mL)of *Bacillus subtilis* ATTC 33932, *Salmonella typhi*, *Proteus mirabilis* ATTC 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.

RESULTS AND DISCUSSIONS

All complexes were isolated as $[ML_2]xH_2O$ (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 pure form was from microanalyses and ^{1}Hnmr. The ligand melted at 198-200°C while the complexes melted at 240-352°C, an evidence of coordination. The generalised equation for the formation of the complex is:

$M(NO_3)_2.2H_2O + 2HL \rightarrow [ML_2]xH_2O + 2HNO_3 + bH_2O$ (when M = Co, Cu (x = 1.5, b = 0.5); Ni(x =1, b =1); Mn(x = 0.5, b = 1.5).

Single 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

ligand were seen as three bands at 1635-1547 cm^{-1} [16-18]. 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 *ν*(V=O) band of the vanadyl complex appeared strong at 952 cm^{-1}, which confirmed its monomeric nature since polymeric complexes have *ν*(V=O) in the range 848-860 cm^{-1} [19]. The δC¯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 chelates. The bands due to ν(M¯O) and ν(M¯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 $b_2 \rightarrow e_p^*$ band(I), b2 → b1*(bandII) and $b_2 \rightarrow a_1^*$ band (III) respectively [19]. The spectra of Mn(II) complexes are usually characterized by forbidden transitions from the $^6A_1$ 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 was assigned to $^6A_1 \rightarrow {}^4E_1$ (ν_1) and $^6A_1 \rightarrow {}^4A_1$ (ν_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 $^4A_2 \rightarrow {}^4T_1(F)$, ($\nu_2$) and $^4A_2 \rightarrow {}^4T_1(P)$, ($\nu_3$) transitions [21]. The reflectance spectrum of the Ni(II) complex showed absorption bands at 15.00 and 21.93 kK assigned to $^3T_1(F) \rightarrow {}^3T_2$, ($\nu_2$) and $^3T_1(F) \rightarrow {}^3A_2$, ($\nu_3$) 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 $^2B_{1g} \rightarrow {}^2A_{1g}$ and $^2B_{1g} \rightarrow {}^2E_{1g}$ 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 $^1A_{1g} \rightarrow {}^1B_{1g}$ and $^1A_{1g} \rightarrow {}^1E_{2g}$ 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 π-π* 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-π* due to coordination [18].

^{1}Hnmr Spectra and Conductance Measurements: The napthyl ring protons resonated as a multiplet at δ 6.70-9.47 ppm (m, 6H, $C_{10}H_6$). The phenolic proton was observed as a singlet at 13.2 ppm(s, 1H, OH) and the imine proton resonated at δ 10.82 ppm (s,1H, H=CN), while CH of the pyrimidine ring resonated as a singlet at δ 5.82 ppm(s, 1H, $CH_{pyrimidine}$). The two methoxy substituents of pyrimidine resonated as 6H singlet at 3.90 ppm (s, 6H, OCH_3).

The Zn(II) complex spectrum showed that the napthyl ring protons were deshielded and resonated as a multiplet at δ 6.6-9.5 ppm (m, 6H, $C_{10}H_6$). The phenolic proton was conspicuously absent, indicating the involvement of phenol O atom in coordination. The HC=N proton signal appeared at δ 10.6 ppm. The downfield shift indicated deshielding due to coordination of the imine nitrogen atom, while the up field shifts of the CH of the pyrimidine and methoxy substituents of the pyrimidine to δ 5.84 and δ 4.0 ppm respectively further corroborated coordination through the imine nitrogen of the pyrimidine moiety [7]. The ^{1}Hnmr measurement could not be done on the Pd(II) complex due to its hygroscopic nature.

The molar conductances of the complexes were in the range 7.40-46.43 Ω^{-1} cm^2 mol^{-1} in nitromethane, proving their covalent nature. A value of 94-105 ohm^{-1} cm^2 mol^{-1} was expected for a 1:1 electrolyte [25].

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 Cis-platin (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 atttibuted 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

Complexes	*P. aeriginosa*	*P. mirabilis*	*B. subtilis*	*B. cereus*	*S. typhi*	*C. albicans*
HL	21.0±0.1	20.0±0.03	7.0±0.12	20.0±0.2	21.0±0.1	R
$[MnL_2]0.5H_2O$	R	7.0±0	R	R	20.0±0.2	14.0±0.03
$[CoL_2]1.5H_2O$	20.0±0.03	10.0±0.04	7.0±0	15.0±0	R	10.0±0.13
$[NiL_2]H_2O$	R	23.0±0.1	7.0±0.03	R	R	R
$[CuL_2]1.5H_2O$	12.0±0.23	11.0±0	R	R	R	R
$[ZnL_2]$	R	13.0±0.14	10.0±0.03	10.0±0.4	19.0±0.2	R
$[PdL_2]12H_2O$	R	20.0±0	R	R	R	R
Gentamycin	24.0±0.12	20.0±0.2	20.0±0.2	16.0±0.3	21.0±0.1	18.0±0.03

R = Resistance

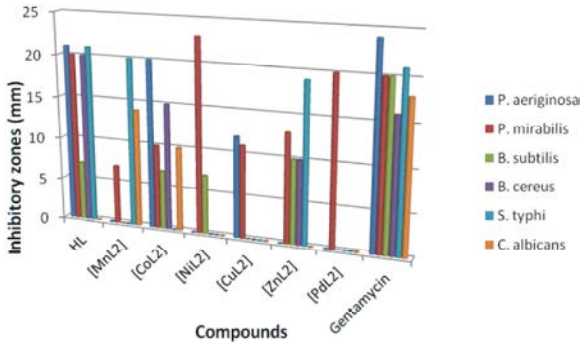

Fig. 2: The comparative antimicrobial activities of the complexes and gentamycin against microbes

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 7.0mm.

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 π-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 IC_{50} 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 IC_{50} 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.

ACKNOWLEDGEMENTS

AAO thanks TWAS (The Academy of Sciences for The Developing World) and DFG (Deutsche Forschungsgemeinschaft) for the award of a Fellowship; The Abdus Salam International Centre for Theoretical Physics (ICTP) for financial support and Prof Ingo Ott of Institute for Medicinal and Pharmaceutical Chemistry, Technical University Braunschweig, Beethoven Strasse 55, D-38106 Braunschweig, Germany is thanked for the collaboration on cell line studies.

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