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Synthesis, Spectral and Theoretical Characterization and Antimicrobial and Cytotoxic Studies of Some Transition Metal Complexes of 4-[(2*E*)-2-Benzylidenehydrazinyl]-7*H*-pyrrolo[2,3-*d*]pyrimidine

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Present work describes the synthesis and characterization of complexes of 4-[(2*E*)-2-benzylidenehydrazinyl]-7*H*-pyrrolo[2,3-*d*]pyrimidine with Fe(II), Mn(II), Co(II), Ni(II), Pd(II), Zn(II), Cu(II), Cd(II) and Hg(II). The results of the elemental and spectroscopic analyses suggest a 1:2 metal-ligand ratio, [ML_2]. The electronic spectra and magnetic moments of the metal(II) complexes suggest that Fe(II), Mn(II), Co(II) and Ni(II) complexes are in an octahedral geometry, while Pd(II) in a square planar ligand geometry. In contrast, the Cu(II), Zn(II), Cd(II) and Hg(II) are in tetrahedral geometry. The conductance measurements in nitrobenzene suggest the non-electrolytic nature of all the metal-coordination compounds. The tested biological species *viz*. *Staphylococcus aureus*, *Pseudomonas aeruginosa*, *Escherichia coli*, *Bacillus cereus*, *Proteus mirabilis*, *Klebsiella oxytoca*, *Aspergillus niger*, *A. flavus* and *Rhizopus stolonifer* exhibited the moderate to strong antimicrobial activity. At 10 mg/mL concentration in nitrobenzene, cobalt(II) complex is observed to be a more promising antimicrobial than any other metal(II) complexes synthesized. The antioxidant potential of the synthesized metal(II) compounds was also evaluated using 1,1-diphenyl-2-picrylhydrazyl (DPPH) radical scavenging assay and shows the high DPPH radical scavenging activity. The nickel complex had the highest DPPH radical scavenging activity compared to the other metal(II) complexes.

Keywords: Pyrrolopyrimidine, Electronic spectra, Antimicrobial activities, Transition metal(II) complexes.

INTRODUCTION

Inorganic coordination and medicinal chemistry have been greatly benefited from introducing organic ligands containing chalcogenide and nitrogen donor atoms [1]. These are widely used to create active metal-based medicines, nanoparticle stabilizers, *etc.* [2,3]. These ligands constitute excellent therapeutic agents because they interact with many biomolecules (proteins, enzymes, DNA, *etc.*) *via* dipole-dipole interactions and coordinative hydrogen bonds [4]. Additionally, these classes of compounds have the exceptional catalytic ability, biomimetic modelling applications, building molecular magnets and liquid crystals [5] because of their ability to ligate towards metal ions at low concentrations. Due to their interesting physiological activities, pyrimidine derivatives are of significant interest [6,7]. The antibacterial [8], antitumor [9], anticancer [10], antioxidant [11], antiviral [12] and anti-inflammatory [13] activities of this class of chemicals are significant. As antimetabolites in purine metabolic processes, they are advantageous [14]. Their harmful effects as dihydrofolate reductase inhibitors and antifolates entail several mechanisms. Additionally, these class of compounds function as significant pharmacophores in several medications, including iclaprim (a dihydrofolate inhibitor), sulfamethomidine (an antibacterial agent), zalcitabine (an antiviral agent), voriconazole (an antifungal agent), nilotinib and capecitabine (an anticancer agent) [15].

There has been a considerable increase in the number of studies devoted to the synthesis of pyrrolopyrimidines, pyrrolopyridazines and pyrrolopyrazines over the past 15 years [16].

Schiff bases with *bis*-pyrimidine moiety are recently found to have antibacterial and anticancer properties [17]. Among the many heterocyclic systems, pyrrolopyrimidine derivatives

are significant since they contain substances with various biological activities. These bicyclic compounds also function as structural mimics of biogenic purines, making them potential antimetabolites in the metabolism of nucleic acids [18]. These findings have been and will continue to be the foundation for synthesizing a wide range of pyrrolopyrimidine derivatives to identify physiologically active compounds among them [19]. Compared to the reference medication, 5-fluorouracil, the pyrimidine derivatives were more effective against the human colorectal carcinoma cell line [20]. Copper(II) and cobalt (II) complexes are the most effective compounds against cancer cell lines [21]. Considering the biological properties of pyrimidine derivatives, it is essential to investigate the biological potential of other pyrimidine derivatives and their metal complexes to develop novel antimicrobial molecules with novel modes of action that may provide additional options for treating various resistant, antimicrobial infections [22]. In recent years, several drugs developed using the pyrrolopyrimidine scaffold proved effective as kinase inhibitors. This research aimed to synthesize metal(II) complexes of a new pyrimidine derivative, 24-[(2*E*)-2-benzylidenehydrazinyl]-7*H*-pyrrolo[2,3-*d*]pyrimidine (HPPHBA). An in-depth density functional theory (DFT) calculation was also performed on the proposed compounds' structures to obtain electronic and spectral properties [23-25]. Bioactivity as an antibacterial, antifungal and cytotoxic agent of the synthesized HPPHBA ligand and its transition metal(II) complexes will be studied.

EXPERIMENTAL

Metal(II) salts *viz*. ferrous sulphate hexahydrate ($FeSO_4 \cdot 7H_2O$), manganese chloride hexahydrate ($MnCl_2 \cdot 4H_2O$), cobalt chloride hexahydrate ($CoCl_2 \cdot 4H_2O$), nickel(II) chloride heptahydrate ($NiCl_2 \cdot 7H_2O$), palladium(II) chloride ($PdCl_2$), cupric chloride dihydrate ($CuCl_2 \cdot 2H_2O$), zinc chloride heptahydrate ($ZnCl_2 \cdot 2H_2O$), cadmium chloride ($CdCl_2$), mercuric chloride ($HgCl_2$) were purchased from Research Lab Co., India and used as received. The organic compounds as well as solvents *e.g*. benzaldehyde, hydrazine hydrate, pyrralopyrimidine, ethanol, methanol, *etc*. were also procured from Research Lab Co., India.

Physical measurements: The ligand and metal(II) complexes were investigated for their structure and properties using (^{1}H and ^{13}C) nuclear magnetic resonance (NMR) spectra were recorded on a BRUKER AVANCE III HD NMR 500 MHz spectrophotometer in dimethylsulfoxide (DMSO). A Carlo-Erba LA-118 micro-dosimeter was used to determine the elemental (C,H,N) compositions. The volumetric titration was used to determine the percentage metal content of metal(II) complexes. UV-Vis spectral measurements were measured with a JASCO V 650 UV-Vis spectrophotometer and Fourier-transform infrared (FTIR) spectra were taken with BRUKER FT-IR spectrophotometer, magnetic susceptibility measurements were made using a Gouy balance. The melting/decomposition temperature of the compounds was determined using an Electrothermal Temp-Mel melting point apparatus in open glass capillary tubes and are uncorrected. The molar conductance measurements were carried out using a HANNA HI 991300 conductivity cell meter with a dip-type cell calibrated in KCl solution.

Synthesis of 4-[(2*E*)-2-benzylidenehydrazinyl]-7*H*-pyrrolo-[2,3-*d*]pyrimidine (HPPHBA): 4-[(2*E*)-2-benzylidenehydrazinyl]-7*H*-pyrrolo[2,3-*d*]pyrimidine was synthesized as per reported method [25,26]. In brief, 14.92 g (0.1 mol) of 4-hydrazinyl-7*H*-pyrrolo[2,3-*d*]pyrimidine dissolved in 100 mL methanol was added gradually to 10.60 g (0.1 mol) of benzaldehyde and refluxed for 3 h, on cooling the resultant solution in an ice bath a product precipitated. The product was separated at suction filtration, rinsed with methanol and recrystallized in a warm ethanol solution. Yield: 78.92%, m.p.: 176 ºC, IR (KBr, ν_{max}, cm^{-1}): 3420 (-NH- arom.), 3120 (-NH- aliph.), 3077 (-CH=), 1544/1460 (>C=C<), 1625 (>C=NN-), 746 (mono sub-benzene ring). ^{1}H NMR (DMSO-d_6) δ ppm: 13.96 (s, 1H, -NH- aliph.), 12.56 (s, 1H, NH, arom.), 8.58 (s, 1H, -CH=), 8.40 (s, 1H, pyrimidine-H), 7.55-7.91 (6H, 7.55 (1H, d, *J* = 3.86), 7.723 (2H, tt, *J* = 1.47, 1.14), 7.86 (2H, dddd, *J* = 7.85, 7.47, 1.91, 0.44), 7.88 (2H, dtd, *J* = 7.85, 1.39, 0.44), 7.91 (1H, d, *J* = 3.88). Anal. calcd. (found) % for $C_{13}H_{11}N_5$ (*m.w.* 237.26): C, 65.81 (64.88); H, 4.67 (4.63); N, 29.52 (29.10).

Synthesis of metal(II) complexes: A weighed mass of 2.37 g (0.01 mol) of 4-[(2*E*)-2-benzylidenehydrazinyl]-7*H*-pyrrolo[2,3-*d*]pyrimidine dissolved in 25 mL ethanol was added gradually to each metal(II) solution (0.005 mol/L) separately followed by the addition of 3 mL of NaOH (0.1 M) and then refluxed the solution for 3-5 h. The collected solid precipitate was washed with thoroughly with ethanol, recrystallized with hot methanol solution and then stored in decissator containing anhydrous $CaCl_2$.

[Fe(PPHBA)$_2$]: Yield: 81.19%, m.p.: 207 ºC. IR (KBr, ν_{max}, cm^{-1}): 3119 (-NH- aliph.), 3081 (-CH=), 1543/1462 (>C=C<), 1594 (>C=NN-), 749 (mono sub-benzene ring). Anal. calcd. (found) % of $C_{26}H_{20}N_{10}Fe$ (*m.w.* 528.36): C, 59.05 (58.88); H, 3.79 (3.63); N, 26.50 (26.19); Fe, 10.60 (10.25).

[Co(PPHBA)$_2$]: Yield: 72.97%, m.p.: 206 ºC. IR (KBr, ν_{max}, cm^{-1}): 3116 (-NH- aliph.), 3073 (-CH=), 1590 (>C=NN-), 1539 and 1459 (>C=C<), 747 (mono sub benzene ring). Anal. calcd. (found) % of $C_{26}H_{20}N_{10}Co$ (*m.w.* 528.36): C, 58.48 (57.89); H, 3.75 (3.63); N, 26.24 (26.19); Co, 11.10 (10.96).

[Ni(PPHBA)$_2$]: Yield: 77.09%, m.p.: 209 ºC. IR (KBr, ν_{max}, cm^{-1}): 3122 (-NH- aliph.), 3072 (-CH=), 1598 (>C=NN-), 1542 and 1465 (>C=C<), 750 (mono sub benzene ring). Anal. calcd. (found) % of $C_{26}H_{20}N_{10}Ni$ (*m.w.* 528.21): C, 58.51 (58.00); H, 3.75 (3.66); N, 26.26 (26.20); Ni, 11.00 (10.78).

[Pd(PPHBA)$_2$]: Yield: 83.39%, m.p.: 215 ºC. IR (KBr, ν_{max}, cm^{-1}): 3123 (-NH- aliph.), 3068 (-CH=), 1599 (>C=NN-), 1542 and 1465 (>C=C<), 746 (mono sub-benzene ring). ^{1}H NMR (DMSO-d_6) δ ppm: 12.59 (s, 2H, NH, arom.), 8.62 (s, 2H, -CH=), 8.38 (s, 2H, pyrimidine-H), 7.59-7.90 (m, 12H, arom.-H). Anal. calcd. (found) % for $C_{26}H_{20}N_{10}Pd$ (*m.w.* 580.52): C, 53.74 (53.66); H, 3.45 (3.36); N, 24.12 (24.09); Pd, 18.26 (17.96).

[Cu(PPHBA)$_2$]: Yield: 80.12%, m.p.: 203 ºC. IR (KBr, ν_{max}, cm^{-1}): 3109 (-NH- aliph.), 3066 (-CH=), 1590 (>C=NN-), 1540 and 1469 (>C=C<), 747 (mono sub-benzene ring). Anal. calcd. (found) % for $C_{26}H_{20}N_{10}Cu$ (*m.w.* 538.07): C, 57.99 (58.00); H, 3.72 (3.66); N, 26.02 (26.20); Cu, 11.80 (11.55).

[Zn(PPHBA)$_2$]: Yield: 79.62%, m.p.: 203 ºC, IR (KBr, ν_{max}, cm^{-1}): 3122 (-NH- aliph.), 3069 (-CH=), 1593 (>C=NN-), 1544 and 1462 (>C=C<), 748 (mono sub-benzene ring). ^{1}H NMR (DMSO-d_6) δ ppm: 12.55 (s, 2H, NH, arom.), 8.66 (s, 2H, -CH=), 8.39 (s, 2H, pyrimidine-H), 7.66-7.95 (m, 12H, arom.-H). Anal. calcd. (found) % for $C_{26}H_{20}N_{10}Zn$ (*m.w.* 539.91): C, 57.79 (57.68); H, 3.70 (3.66); N, 25.93 (25.92); Zn, 12.11 (11.99).

[Cd(PPHBA)$_2$]: Yield: 80.12%, m.p.: 207 ºC, IR (KBr, ν_{max}, cm^{-1}): 3123 (-NH- aliph.), 3068 (-CH=), 1599 (>C=NN-), 1542 and 1465 (>C=C<), 746 (mono sub-benzene ring). ^{1}H NMR (DMSO-d_6) δ ppm: 12.59 (s, 2H, NH, arom.), 8.62 (s, 2H, -CH=), 8.38 (s, 2H, pyrimidine-H), 7.59-7.90 (m, 12H, arom.-H). Anal. calcd. (found) % for $C_{26}H_{20}N_{10}Cd$ (*m.w.* 586.93): C, 53.16 (53.01); H, 3.41 (3.35); N, 23.85 (23.78); Cd, 19.15 (18.97).

[Hg(PPHBA)$_2$]: Yield: 82.21%, m.p.: 214 ºC, IR (KBr, ν_{max}, cm^{-1}): 3126 (-NH- aliph.), 3076 (-CH=), 1593 (>C=NN-), 1542 and 1465 (>C=C<), 748 (mono sub-benzene ring). ^{1}H NMR (DMSO-d_6) δ: 12.55 (s, 2H, NH, arom.), 8.62 (s, 2H, -CH=), 8.38 (s, 2H, pyrimidine-H), 7.59-7.90 (m, 12H, arom.-H). Anal. calcd. (found) % for $C_{26}H_{20}N_{10}Hg$ (*m.w.* 674.52): C, 46.26 (46.02); H, 2.97 (2.89); N, 20.76 (20.34); Hg, 29.74 (29.18).

[Mn(PPHBA)$_2$]: Yield: 78.35%, m.p.: 204 ºC, IR (KBr, ν_{max}, cm^{-1}): 3109 (-NH- aliph.), 3066 (-CH=), 1590 (>C=NN-), 1540 and 1469 (>C=C<), 747 (mono sub-benzene ring). Anal. calcd. (found) % for $C_{26}H_{20}N_{10}Mn$ (*m.w.* 527.46): C, 59.15 (58.89); H, 3.79 (3.63); N, 26.54 (26.44); Mn, 10.40 (10.25).

Antimicrobial studies: According to established procedures [25-27], the antimicrobial potential of HPPHBA ligand and its Fe(II), Mn(II), Co(II), Ni(II), Pd(II), Zn(II), Cu(II), Cd(II) and Hg(II) complexes were evaluated against Gram-positive bacteria species (*Bacillus subtilis* and *Staphylococcus aureus*) and Gram-negative bacteria species (*Escherichia coli*). Sterilized Petri dishes were prepared using 25 mL of sterile Muller-Hinton agar and potato dextrose agar (PDA) well-diffusion procedure was adopted to investigate the antimicrobial potential [28,29]. After applying a 24 h test McFarland culture to the Petri dish's surface, it was let dry for roughly 15 min, then 12.5 mg/mL of each compound, produced at 250 mg/mL in DMSO, was injected into 6 mm wells and drilled into the agar using a cork borer. Ciprofloxacin for bacterial strains and fluconazole for fungal strains served as positive controls. The zone of inhibition in millimetres was calculated as the average of three replicates.

RESULTS AND DISCUSSION

The conductivity measurements of Fe(II), Co(II) and Ni(II) complexes in a 10^{-3} M nitrobenzene solution were observed to be in the range of (Λ_m) 0.21 to 5.29 ohm^{-1} cm^2 mol^{-1}, the low values suggests non-electrolytic nature of these complexes [30]. Additionally, the quantitative and elemental (CHN) analysis data, in which anions were not found, substantially supported the molar conductance values.

NMR spectra; studies: A signal at δ 12.56 ppm in the spectrum of HPPHBA ligand can be attributed to the aromatic N–H proton [31]. The disappearance of this signal in Pd(II), Zn(II), Cd(II) and Hg(II) complexes suggests deprotonation and ligation of the ligand, HPPHBA to the metal ion *via* the deprotonated pyrrole group. In the spectra of HPPHBA ligand, signals at δ 8.57-8.63 and δ 8.40-8.52 ppm may be attributed to -CH= and aliphatic N–H protons, respectively. The HPPHBA ligand and its metal(II) complexes contain around δ 7.55 to 7.95 ppm of aromatic protons [32,33].

Electronic spectra and magnetic moment: The UV-visible spectra were used to observe the electronic transitions of the ligand (n→π*, π→π*) and its metal(II) complexes (*d-d* transitions, L→M charge-transfer transitions). Two absorption peaks at 345 and 267 nm in the ligand's UV spectra were attributed to the n→p* and π→π* electronic transitions, respectively. Due to the chelation of ligand to the metal(II) ions, these peaks were discovered to be displaced to a lower wavelength in the complex spectra [25].

Two bands at 275 and 208 nm in [Fe(PPHBA)$_2$] complex's electronic spectrum are attributed to π→π* and charge-transfer (CT) transitions. One high-spin permitted transition, $^5E \rightarrow {}^5T_2$, is linked to four-coordinate tetrahedral [Fe(PPHBA)$_2$] complexes. This transition is typically intense and broad due to the allowed electronic wavefunction and Jahn-Teller processes [33]. Square planar iron complexes, primarily [Fe(PPHBA)$_2$] complexes with nitrogen donor atom ligands, are linked to spin crossover processes involving the $^5T_{2g}$ ($t_2^4\, e^2$) and $^1A_{1g}$ (t_2^6) states [34,35]. One single absorption band, corresponding to the $^5E \rightarrow {}^5T_2$ transition, was detected in the [Co(PPHBA)$_2$] complex's visible spectra at 490 nm [35]. The observed band's broadness may be attributed to the Jahn-Teller effect in the excited state, which corroborates the tetrahedral geometry of this transition [36,37]. The tetrahedral geometry is suggested by the reported magnetic moment of 4.97 B.M. [38,39].

The visible spectrum of [Co(PPHBA)$_2$] complex exhibited characteristic absorption bands at 503 and 830 nm, which were attributed to the $^4A_2 \rightarrow {}^4T_1(t_2)$ and $^4A_2 \rightarrow {}^4T_1(P)$ (t_3) transitions, respectively. This aligns with a cobalt complex's four-coordinate tetrahedral structure [40]. Since a moment of 4.20-4.60, B.M. is predicted for tetrahedral Co(II) complexes, the magnetic moment the value of 3.40 B.M. supported the assignment of such a high-spin tetrahedral geometry to the cobalt(II) complex [41].

The ultraviolet spectra of [Ni(PPHBA)$_2$] complex revealed three distinct absorptions at 210, 285 and 400 nm attributed to charge transfer, n→p* and p→p* electronic transitions, respectively. To support an octahedral geometry, the visible spectra of the [Ni(PPHBA)$_2$] complex showed characteristic absorption bands at about 712, 515 and 770 nm caused by $^3A_{2g} \rightarrow {}^3T_{2g}(P)$, $^3A_{2g} \rightarrow {}^3T_{1g}(F)$ and $^3A_{2g} \rightarrow {}^3T_{1g}(F)$ transitions [42,43]. While $3d^8$ tetrahedral nickel complexes are anticipated to have a magnetic moment in the 3.4-4.2 B.M., square planar [Ni(PPHBA)$_2$] complexes are typically diamagnetic. The magnetic moment of [Ni(PPHBA)$_2$] complex in the six-coordinate field ranges at 3.13 B.M. Due to [Ni(PPHBA)$_2$]'s B.M. magnetic moment, an octahedral geometry was assigned to that as well [44,45].

Bands appeared at 641 nm in copper(II) complex of the HPPHBA ligand can be attributed to the $^2B_{1g} \rightarrow {}^2A_{1g}$ (ν_1) transition, which indicate a distinctive square planar geometry band [44].

A magnetic moment value of 1.87 B.M. at ambient temperature is within the expected range for square planar complexes [45]. Strong absorption bands in the range of 426 and 519 nm were observed in the electronic spectra of homo-binuclear [Mn(PPHBA)$_2$] complex. These bands were identified as $^6A_{1g} \rightarrow {}^4E_g(^4D)$ and $^6A_{1g} \rightarrow {}^4T_{1g}(^4P)$ transitions, respectively, which is consistent with the octahedral geometry of the metal complexes [46]. The measured magnetic moment value (6.08 BM) also corroborated the [Mn(PPHBA)$_2$] complex's high spin octahedral shape [47,48].

The intra-ligands charged transfer transition observed at region 400-429, 349-374 and 220-297 nm are attributed to the strong bands in the electronic spectra of Pd(II), Zn(II), Cd(II) and Hg(II) complexes, respectively. These spectral characteristics indicate a connection between HPPHBA and the metal(II) *via* a nitrogen atom [49,50].

FT-IR spectral studies: The secondary amine group's asymmetric and symmetric stretching vibrations and the N-H group's bending vibration at 1455 cm^{-1} were attributed to the bands in the ligand's spectra at 3489 and 3325 cm^{-1} [51]. The azomethine group was observed at 1625 cm^{-1} in the synthesized ligand. This band is shifted to lower frequencies in all metal(II) complexes, indicating that ligand bonded to the metal(II) ion through azomethine nitrogen. These bands were entirely missing from the complexes' spectra, showing that the metal(II) complexes were coordinated to the metal ions *via* the nitrogen atom of the deprotonated amine group. The stretching vibration of the C=N group in the pyrimidine ring and the C=C group in the Schiff base was attributed to the sharp bands at 1575 and 1549 cm^{-1}. Due to the pseudo-aromatic character of metal(II) complexes, the ν(C-H) vibration at 975 cm^{-1} that the ligand exhibits were also seen at 990-985 cm^{-1} [6]. The bands in the complexes' spectra were attributed to the ν(M-N) vibrations, respectively, in the ranges 567-525 and 515-503 cm^{-1} [52]. These findings indicated that the Schiff base functions as a bidentate ligand, coordinating with the metal ion *via* nitrogen atom of the deprotonated secondary amine group and the carbonyl group at position C_{10}.

Antimicrobial studies: The antibacterial properties of 4-[(2*E*)-2-benzylidenehydrazinyl]-7*H*-pyrrolo[2,3-*d*]pyrimidine and its metal(II) complexes were investigated *in vitro*. Broad-spectrum antibiotic activity against pathogenic bacteria has been reported for heterocyclic ligands containing N, O and S atoms [53-55]. However, they become more active when combined with metal ions [54]. According to the findings, ligand HPPHBA is effective against all of the tested microorganisms, with inhibitory zones ranging from 9.0 to 19.0 mm however, it was ineffective against *S. aureus*. As predicted, all metal(II) complexes out performed ligand HPPHBA in terms of antibacterial activity against the studied pathogens. The chelation effect, which boosts the antibacterial activity primarily because of the partial sharing of the positive charge on the metal ion with the donor groups of the ligand and potential electron delocalization on the aromatic rings, is responsible for the improved activity of the metal(II) complexes.

According to a critical analysis of the antibacterial results, Fe(II), Co(II) and Ni(II) complexes were more effective against Gram-negative *K. oxytoca* and *E. coli*, except Ni(II), which the latter was not susceptible. This was expected since the metal(II) complexes have a far easier time penetrating the thin peptidoglycan covering of Gram-negative bacteria [56]. Furthermore, Fe(II) complex is the most effective against the pathogenic organisms tested, with inhibitory zones ranging from 14 to 25 mm (Table-1), but ineffective against *P. aeruginosa* and *S. aureus*. *K. oxytoca* was the only bacterium that Ni(II) complex (9.5 mm) was able to suppress. A low degree of permeability of the microbial cells can be the cause of the lower antibacterial activities displayed by Fe(II) and Ni(II) complexes relative to the ligand against *P. mirabilis* (11.0 mm), *K. oxytoca* (14.0 mm), *K. oxytoca* (9.5 mm), *B. cereus* (12.0 mm) and *P. aeruginosa* (14.5 mm) [57]. In comparison to the standard ciprofloxacin, the Fe(II) and Co(II) complexes showed superior antibacterial activity against *P. mirabilis* (25 mm), *P. aeruginosa* (29 mm) and *P. mirabilis* (20 mm), however Co(II) complex demonstrated the highest antibacterial activity against all of the microbial species tested.

Most of the compounds exihibited the good to moderate antifungal activity against *A. niger*, *A. flavus* and *R. stolonifer*. The inhibitory zones of ligand HPPHBA were in the range of 15-40 mm. Meanwhile, Fe(II) complex was only effective against *A. flavus*, whereas Co(II) complex was effective against all the studied bacterial strains (14 mm). The Ni(II) complex did not affect the fungal strains tested, however the ligand is potent against *A. flavus* (39 mm) and *R. stolonifer* than the

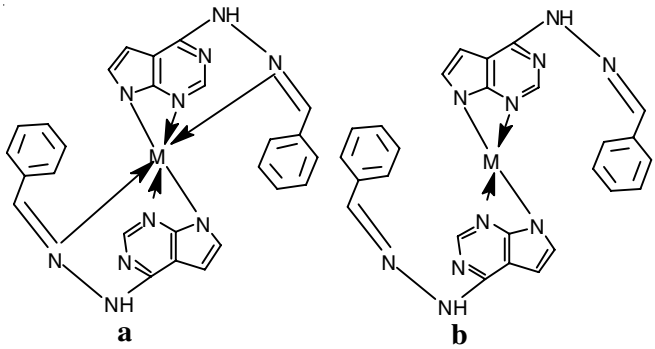
TABLE-1
ANTIBACTERIAL AND ANTIFUNGAL ACTIVITIES OF HPPHBA LIGAND AND ITS METAL COMPLEXES

Compound	Zone of inhibition (mm)									
	Antibacterial activity							Antifungal activity		
	S. aureus	*P. aeruginosa*	*B. subtilis*	*E. coli*	*P. mirabilis*	*K. oxytoca*	*B. cereus*	*A. niger*	*A. flavus*	*R. stolonifer*
HPPHBA	9.5	10.0	9.5	9.0	8.0	7.5	10.0	10.5	10.0	9.5
Fe(PPHBA)$_2$	14.0	11.5	13.5	14.0	13.0	10.5	14.0	17.0	11.5	13.5
Co(PPHBA)$_2$	22.5	29.0	21.0	19.5	25.0	18.0	17.5	25.0	22.0	23.0
Ni(PPHBA)$_2$	10.5	14.5	11.0	11.5	20.0	9.5	12.0	17.5	39	40
Pd(PPHBA)$_2$	17.0	11.5	12.0	9.5	10.0	0	0	17.0	22.5	0
Cu(PPHBA)$_2$	0	12.5	10.5	13.0	0	16.0	0	14.5	12.5	20
Zn(PPHBA)$_2$	0	0	11.5	0	12.0	14.0	0	17.5	9.5	13.5
Cd(PPHBA)$_2$	12.0	13.5	0	12.5	12.5	11.5	0	20.0	13.5	0
Hg(PPHBA)$_2$	19.5	17.5	0	10.5	11.0	12.0	0	29.5	16.0	0
Mn(PPHBA)$_2$	20.5	19.5	20.5	19.0	17.5	0	0	20.5	29.0	21.0

standard fluconazole (40 mm). The outstanding antifungal potential of the HPPHBA ligand compared to the metal(II) complexes against the tested organisms may be explained by the ligand's chelating capacity to the biomolecules of fungal organisms caused by the heteroatoms and C=N- moiety in the ligand [58].

Conclusion

A novel synthesized pyrimidine Schiff base analogue ligand *viz*. 4-[(2*E*)-2-benzylidenehydrazinyl]-7*H*-pyrrolo[2,3-*d*]-pyrimidine was successfully coordinated with several transition metal(II) complexes. The antibacterial and antifungal activities of all the metal(II) compounds were examined. According to the experimental findings, Fe(II), Co(II), Ni(II), Mn(II) and Cu(II) complexes presumably have octahedral structures. However, Pd(II) complex appears to have a square planar structure and whereas Hg(II), Zn(II) and Cd(II) complexes suggested the tetrahedral geometry. The metal chelation using bihybrid organic ligand enhanced the synergy of all the synthesized metal(II) complexes, resulting in the remarkable antibacterial activity. Based on the findings, the suggested geometry of the synthesized complexes are shown below:



where M = **(a)** Fe(II), Co(II), Ni(II), Cu(II) and Mn(II), (**b**) Pd(II), Zn(II), Cd(II) and Hg(II)

CONFLICT OF INTEREST

The authors declare that there is no conflict of interests regarding the publication of this article.

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