Research Article

Synthesis and Biological Evaluation of Novel Zn(II) and Cd(II) Schiff Base Complexes as Antimicrobial, Antifungal, and Antioxidant Agents

Mutlaq S. Aljahdali¹ and Ahmed A. El-Sherif²

¹Department of Chemistry, Faculty of Science, King Abdulaziz University, Jeddah 21589, Saudi Arabia

²Department of Chemistry, Faculty of Science, Cairo University, Cairo, Egypt

Correspondence should be addressed to Ahmed A. El-Sherif; aelsherif72@yahoo.com

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(E)-N,N-Dimethyl-2-((E)-1-(2-(p-tolyl)hydrazono)propan-2-ylidene)hydrazine-1-carbothioamide (DMPHP) and their Zn(II) and Cd(II) complexes have been synthesized and characterized. Different tools of analysis such as elemental analyses, IR, mass spectra, and ¹H-NMR measurements were used to elucidate the structure of the synthesized compounds. According to these spectral results, the DMPHP ligand behaved as a mononegatively charged tridentate anion. Modeling and docking studies were investigated and discussed. Novel Schiff base (DMPHP) ligand protonation constants and their formation constants with Cd(II) and Zn(II) ions were measured in 50% DMSO solution at 15°C, 25°C, and 35°C at $I = 0.1 \text{ mol} \cdot \text{dm}^{-3} \text{ NaNO}_3$. The solution speciation of different species was measured in accordance with pH. Calculation and discussion of the thermodynamic parameters were achieved. Both $\log K_1$ and $-\Delta H_1$, for M(II)-thiosemicarbazone complexes were found to be somewhat larger than $\log K_2$ and $-\Delta H_2$, demonstrating a shift in the dentate character of DMPHP from tridentate in 1 : 1 chelates to bidentate in 1 : 2; M : L chelates and steric hindrance were generated by addition of the 2nd molecule. The compounds prepared have significant activity as antioxidants, similar to ascorbic acid. It is hoped that the results will be beneficial to antimicrobial agent chemistry. The formed compounds acted as a potent antibacterial agent. Molecular docking studies were investigated and have proved that DMPHP as antibacterial agents act on highly resistant strains of *E. coli* and also as an anticancer agent.

1. Introduction

Lately, there has been a very successful interaction between inorganic chemistry and biology. Schiff bases and their complexes in medicinal chemistry are an essential class of compounds [1, 2]. Schiff bases play a crucial role in coordination chemistry, since they form stable metal complexes [3–12].

The role of coordination compounds in detoxification of heavy metals is a complex subject that involves cooperation between numerous scientific branches. The primary contribution of chemistry to this subject is to produce both models of coordination and complex formation constants between chelating agents and metal ions, in a parliamentary procedure to compare the power of the formed complexes

with their properties. Column 12 metal complexes are typically attractive in view of their marked differences in chemical and biological behaviors.

Zn is the human body's second most abundant trace metal [13] and can catalyze over 300 enzymes, such as those responsible for the synthesis of DNA and RNA [14]. It is also physiologically essential for bone metabolism, collagen synthesis, the integrity of the immune system, anti-inflammatory actions, and defense versus free radicals [15]. Therefore, Zn(II) is better removed by novel methods away from classical coordination methods used in vivo.

Nevertheless, cadmium is a very toxic metal ion that poses both human and animal health hazards. Its toxicity is done by its easy localization inside the liver and then by the binding of metallothionein, which eventually forms a

complex and is transmitted into the blood stream to be lodged in the kidney.

The cause of Cd toxicity is the negative effect on cell enzyme systems that are the consequences of metallic ion substitution (mainly Zn^{2+} , Cu^{2+} , and Ca^{2+}) into metalloenzymes and its strong interaction with thiol groups [16]. Zinc (II) replacement with Cd(II) ion usually causes apo-protein catalysis to break down [17, 18]. Thus, substances that can form stable chelates with Cd may be produced in a significant research field as they can be used as detoxifying compounds. Referable to the broad scope of pharmacological properties of thiosemicarbazone ligands and their compounds, these compounds can also very well fit for this role. With this in mind and in the perpetuation of our studies in the subject area of bioactive compounds [19–22], it seems of great interest to synthesize and identify novel compounds involving both thiosemicarbazone and hydrazo moieties. In addition, our goal is comparison of M complexes strength with DMPTHP in quantitative terms in order to evaluate the capability of that ligand to extract Cd and also to explore the biological activities of the identified compounds.

2. Experimental

2.1. Chemicals Used. All the chemicals used were of A.R. grade quality. Metallic ion solutions were formed by the dissolution of metal ion salts in deionized H_2O , and EDTA titrations were used to calculate their concentrations. NaOH solution was accurately standardized by the standard KH phthalate solution.

2.2. Synthesis

2.2.1. 1-(p-Tolylhydrazono)-propan-2-one (PTHP) Compound. We have synthesized 1-(p-tolylhydrazono)-propan-2-one (PTHP) compound using the reported method [23, 24].

2.2.2. Synthesis of (E)-N,N-Dimethyl-2-((E)-1-(2-(p-tolyl)hydrazono)propan-2-ylidene)hydrazine-1-carbothioamide (DMPTHP) Thiosemicarbazone Compound. PTHP (from Sigma–Aldrich) (0.1760 g, 1 mmol) in 30 ml ethanol was combined with N,N-dimethylthiosemicarbazide (from Sigma–Aldrich) in ethanol solution (30 ml) (0.120 g, 1 mmol) and refluxed for 3–4 hours into a hot plate. The isolated precipitate was washed with Et_2O and dried overnight under silica gel.

Yield, 76%. Anal. Calc. for $\text{C}_{13}\text{H}_{19}\text{N}_5\text{S}$: C, 56.29; H, 6.90; N, 25.26; and S, 11.56. Found: C, 56.18; H, 6.94; N, 25.19; and S, 11.66%. IR (KBr, cm^{-1}): 3352 (N_2H), 1499, 1250, 1080, and 798 (bands I, II, III, and IV of thiomide, respectively), 1082 (N–N), 1615 (C=N), 1548 (C=C), 3434 (N_5H), and 3012 (C–H). MS (m/z): 279 ($\text{M}^+ + 2$, 4.87%), 278 ($\text{M}^+ + 1$, 14.92%), 277 (M^+ , 100%), 247 (2.51%), 11.39 (s, 1H, NH), 10.77 (s, H, NH), 6.91–7.11 (m, 4H, –Ar), 7.36 (s, H, CH=N), 2.02 (s, 3H, $-\text{CH}_3$), and 2.23 (s, 6H, $-\text{CH}_3$). ^{13}C -NMR (DMSO): 178.4, 178.2, 148.6, 142.4, 135, 130, 120, 112.8, 40.1, 38.2, and 21.4.

2.2.3. Synthesis of M(II) Complexes. In presence of triethylamine, ethanol solution (2 mmol, DMPTHP) was gradually added with stirring to the warm aqueous metal solution (2 mmol) and refluxed for 5 hours into a hot plate. The solid product was filtered out, washed with $\text{C}_2\text{H}_5\text{OH}$ followed by Et_2O , and vacuum-dried over P_4O_{10} .

(1) Zn(II)-DMPTHP Complex. Yield, 65%. Anal. Calc. for $\text{C}_{13}\text{H}_{18}\text{N}_5\text{SZnCl}$: C, 41.39; H, 4.81; N, 18.57; Cl, 9.40; and S, 8.50. Found: C, 41.28; H, 4.72; N, 18.45; Cl, 9.35; and S, 7.49%. IR (KBr, cm^{-1}): 1496, 1247, 1075, and 770 (bands of thiomide, I, II, III, and IV, respectively), 1092 (N–N), 1582 (C=N), 1522 (C=C), 3418 (N_5H), 276 (Zn–Cl), 440 (Zn–N), and 318 (Zn–S). MS (m/z): 377 ($\text{M}^+ + 2$, 58%), 375 (M^+ , 100%), 11.61 (s, 1H, NH), 6.70–7.01 (m, 4H, –Ar), 7.11 (s, H, CH=N), 1.95 (s, 3H, $-\text{CH}_3$), and 2.08 (s, 6H, $-\text{CH}_3$).

(2) Cd(II)-DMPTHP Complex. Yield, 66%. Anal. Calc. for $\text{C}_{13}\text{H}_{18}\text{N}_5\text{SCdCl}$: C, 36.81; H, 4.28; N, 16.51; Cl, 8.36; and S, 7.56. Found: C, 36.78; H, 4.22; N, 16.45; Cl, 8.28; and S, 7.49%. IR (KBr, cm^{-1}): 1499, 1243, 1079, and 768 (bands of thiomide, I, II, III, and IV, respectively), 1090 (N–N), 1586 (C=N), 1525 (C=C), 3418 (N_5H), 252 (Cd–Cl), 411 (Cd–N), and 298 (Cd–S). MS (m/z): 425 (M^+ , 100%), 11.53 (s, 1H, NH), 6.68–7.05 (m, 4H, –Ar), 7.08 (s, H, CH=N), 1.96 (s, 3H, $-\text{CH}_3$), and 2.05 (s, 6H, $-\text{CH}_3$).

2.3. Instruments. All the ingredients used have been supplied by Aldrich. A CHNS automatic analyzer, Vario EII-Elementar, was used to conduct elemental microanalysis for C, H, N, and S. In a Perkins Elmer FTIR, spectrophotometer type 1650 with KBr disk and IR was registered. A Perkin Elmer FTIR, type 1650 spectrophotometer with the potassium bromide disc was used to monitor IR spectra. On a spectrophotometer of Shimadzu 3101 pc, electronic spectra are recorded. A Bruker ARX-300 instrument was applied to monitor the ^1H -NMR spectra using deuterated dimethylsulphoxide (d_6 -DMSO) as solvent relative to TMS. Mass spectrometry analyses have been carried out using Shimadzu GCMS-QP1000EX. A Metrohm 848 Titrino supplied with a Dosimat unit (Switzerland-Herisau) has been utilized for potentiometric titrations. Inside the cell, a constant temperature was maintained through the circulating waterbath. Based on low solutions for the DMPTHP synthesized compound and the potential aqueous solution hydrolysis, all potentiometric measurements were performed in 50% water-DMSO mixture.

2.4. Potentiometric Titrations. Through potentiometric technique, using the method depicted above in the literature, the constant ligand protonation and formation of complexes were estimated [25]. The standard buffer solutions are used for accurately calibrating the glass electrode to NBS standards using KH phthalate and mixture of $\text{KH}_2\text{PO}_4 + \text{Na}_2\text{HPO}_4$ as buffer solutions [26]. The standard solution of 0.05 mol/dm³ NaOH, free of CO_2 , is used to titrate all samples in the N_2 atmosphere. Sample solution was developed to avoid hydrolysis of the DMPTHP compound

during titration by mixing equal volumes of DMSO and water. In addition, the ionic strength was kept constant during titration using a mixture of NaNO_3 as supporting electrolyte.

As known, the calculated formation constants using a potentiometric method have been carried out using a concentration of hydrogen ion expressed in molarity. Nevertheless, the concentration in a pH meter has been expressed in activity coefficient $-\log a_{\text{H}^+}$ (pH). Thus, this equation of Van Uiter and Hass (equation (1)) was used to convert the pH meter readings (B) to $[\text{H}^+]$ [27, 28].

$$-\log 10 [\text{H}^+] = B + \log 10 U_H, \quad (1)$$

where $\log_{10} U_H$ is the solvent composition correction factor and the ionic strength read by B . pK_w for titrated samples was estimated as previously described [29]. All measurements and procedures comply with literature requirements [30–32].

Titration (40 cm^3) ($1.25 \times 10^{-3} \text{ mol/dm}^3$) DMPHP thiosemicarbazone solution with standard sodium hydroxide solution estimated the protonation constants of the compound thiosemicarbazone. Metal (II) complex formation constants were determined by titration (40 cm^3) of ($\text{MCl}_2 \cdot n\text{H}_2\text{O}$) ($1.25 \times 10^{-3} \text{ mol/dm}^3$) + (DMPHP) ($1.25 \times 10^{-3} \text{ mol/dm}^3 / 2.5 \times 10^{-3} \text{ mol/dm}^3$). The following equations have described the equilibrium constants from the titration data in which M, L, and H represent M(II), DMPHP, and H^+ , respectively.

$$p(\text{M}) + q(\text{L}) + r(\text{H}) = [\text{M}_p(\text{L})_q(\text{H})_r] \quad (2)$$

$$\beta_{pqr} = \frac{[\text{M}_p(\text{L})_q(\text{H})_r]}{[\text{M}]^p [\text{L}]^q [\text{H}]^r}. \quad (3)$$

2.5. Processing of Data. MINIQUAD-75 computer program has been applied to calculate ca. 100 readings for each titration [33]. Species distribution diagrams for the studied samples were given by the SPECIES program [34].

2.6. Molecular Modeling Studies. In the Materials Studio package [35], DFT calculations were carried using DMOL³ software [36–38]. Different calculations were carried out using double numerical base and functional polarization sets (DNP) [39] for DFT semicore pseudopods. The numerical RPBE functional is dependent on the generalized gradient approximation as the best correlation function [40, 41].

2.7. Molecular Docking. Docking is used to predict compound conformation and orientation in the binding pocket of the receptor. In this study, the molecular interaction of compound and its poses were studied against the three-dimensional structure of PDB ID: 1NEK in *E. Coli* and PDB ID: 3HB5 in breast cancer to get information correlated to their correct binding orientation and to realize the interaction nature between them. Crystal structure of the protein receptor 1NEK in *E. Coli* and 3HB5 in breast cancer were downloaded from the RCSB Protein Data Bank [42]. Docking of the compounds in the active site of the protein receptors is performed by MOE software [43]. Energy minimizations were performed with an RMSD (root of mean square deviation) gradient of $0.05 \text{ kcal} \cdot \text{mol}^{-1} \cdot \text{\AA}^{-1}$ using the GBVI/WSADG force field, and the partial charges were calculated.

2.8. Biological Activity

2.8.1. In Vitro Antibacterial Activity. The ability thiosemicarbazone compounds to suppress the bacterial growth were checked by the disc diffusion method [44]. Aerobic Gram-positive bacteria, *Staphylococcus aureus* and *Bacillus subtilis*, and Gram-negative aerobic bacteria, *Escherichia coli* and *Neisseria gonorrhoeae*, are among the bacterial strains that were used in this study in addition to two fungal strains including *Aspergillus flavus* and *Candida albicans*. Novel synthesized compounds were prepared in DMSO. $100 \mu\text{l}$ of each of the synthesized thiosemicarbazone compounds was inserted into discs (0.8 cm), and then, they were allowed to dry. The discs were completely saturated with the synthesized compounds. The discs were then placed at least 25 mm from the edge into the upper layer of the medium. The disks were then gently placed on the same plate's surface. At 37°C for 72 hours, the plate was then incubated, and the clear area of inhibition was examined. The inhibition zone (an area where there is no growth around the disc's) was eventually determined by the ruler millimeter.

2.8.2. In Vitro Antioxidant Activity. Free radical scavenging action of the synthesized DMPHP thiosemicarbazone compound was analyzed by 1,1-diphenyl-2-picrylhydrazyl assay [45] using ascorbic acid as a reference standard material. Using Thermo Scientific Evolution 201 UV-Visible Spectrometer, the absorbance of the sample, blank, and control were measured in the dark at 517 nm . The experimental test was performed three times. Antioxidant activity percentage was measured as follows:

$$\text{Antioxidant activity percentage} = 100 - \left[\frac{(\text{Abs}_{\text{sample}} - \text{Abs}_{\text{blank}}) \times 100}{\text{Abs}_{\text{control}}} \right]. \quad (4)$$

3. Results and Discussion

3.1. Characterization of DMPHP Thiosemicarbazone Compounds. Condensation of the 1-(p-tolylhydrazono)-

propan-2-one compound with N,N-dimethylthiosemicarbazide readily gives rise to the corresponding DMPHP thiosemicarbazone compound. The isolated compounds are air stable and insoluble in H_2O , yet easily

soluble in solvents such as DMF or DMSO. Cd-DMPHP and Zn-DMPHP complexes have a higher m.p. than the parent DMPHP ligand. Different analytical tools were employed to identify the structure of prepared thiosemicarbazone compounds. The results from the basic analysis are well in line with the calculated results for the proposed formula.

3.2. IR Spectrum. The preliminary allocations of the major IR bands of DMPHP and its M(II) complexes show the following characteristics:

- (1) New band of ν (C=N) stretching vibration [46] at 1615 cm^{-1} with disappearance of the ν (>C=O) confirming the condensation reaction and formation of the DMPHP compound
- (2) Presence of -NH-C=S linkage support thione $\leftrightarrow$ thiol tautomerism of thiosemicarbazone compounds [47], but ν (S-H) absorption band at $2500\text{--}2600\text{ cm}^{-1}$ was absent with an appearance of ν (C=S) band at 798 cm^{-1} indicating the presence of the DMPHP compound in the solid state as a thione form
- (3) For the DMPHP thiosemicarbazone compound, vibrational bands with the wave numbers of 3012 cm^{-1} ($\nu_{\text{C-H}}$ and Ar-H), 1615 cm^{-1} ($\nu_{\text{C=N}}$), 1548 cm^{-1} ($\nu_{\text{C=C}}$), and 1082 cm^{-1} ($\nu_{\text{N-N}}$) were detected
- (4) In the DMPHP thiosemicarbazone compound spectra, the bands observed in the range 1499 , 1250 , 1080 , and 798 cm^{-1} are attributed to the bands of thiomide I, II, III, and IV, consecutively [48]
- (5) The far IR spectra of the Cd(II)-DMPHP complex showed a band at 411 cm^{-1} and 298 cm^{-1} referring to the ν (Cd-N) and ν (Cd-S) vibrations, respectively [49], while the Zn(II)-DMPHP spectrum displays a band at 440 cm^{-1} and 318 cm^{-1} corresponding to the ν (Zn-N) and ν (Zn-S) vibrations, respectively [50]. Such new nonligand bands due to M-N and M-S vibrations in DMPHP complexes are in the predictable order of increasing energy, (M-N) > (M-S), as expected due to the greater dipole moment change in the M-N vibration, greater electronegativity of the N atom, and shorter M-N bond length than the M-S bond length.
- (6) According to literature, the ranges from 160 cm^{-1} to 300 cm^{-1} are allocated to the M-Cl and M-Br vibration bonds where M is the metal [51, 52]. The ν (M-Cl) that appeared in our work between 252 cm^{-1} and 276 cm^{-1} are well in line with the literature values. According to these spectral results, the DMPHP ligand is asserted to have lost the N2-H proton and bonded to M^{n+} as a mononegatively charged tridentate anion after deprotonation via the thiolate sulfur atom and the two azomethine N atoms.

3.3. NMR Spectrum. $^1\text{H-NMR}$ spectra of DMPHP in DMSO- d_6 show no resonance at approximately 4.0 ppm due

to -SH proton [48], whereas the presence of a peak at 10.77 ppm (signal field of existence of the NH group next to C=S) suggests that they remain in the thione form even in a polar solvent like DMSO. Methine proton of the characteristic azomethine group (CH=N) for the DMPHP compound was observed at $\delta = 7.36\text{ ppm}$. Signals of the aromatic protons appear at $6.91\text{--}7.11\text{ ppm}$. Methyl group was observed as a singlet signal at $\delta = 2.02\text{--}2.21$. As common [53], the interaction with the d^{10} Cd(II) ion moves the complex $^1\text{H-NMR}$ signals downfield from those of free DMPHP ($\Delta\delta = 0.0\text{--}0.2\text{ ppm}$) as a result of coordination via the N-atom [54] (α 11.39 ppm in DMPHP and 11.53 in the complex).

3.4. UV-Vis Spectrum. Electronic DMPHP ligand spectrum shows two absorption bands. The first band at about 33020 cm^{-1} was assigned to $\pi \rightarrow \pi^*$ and the second one at 26830 cm^{-1} region is due to the $n \rightarrow \pi^*$ transition. Always, $n \rightarrow \pi^*$ transitions often take place at lower energy than $\pi \rightarrow \pi^*$ transitions [55].

3.5. Mass Spectrum. The proposed formulas can be further proven by mass spectroscopy. In addition to a number of peaks that are attributive to the different fragments of the DMPHP compound, the electron mass impact spectrum of DMPHP support the anticipated formulation by displaying a peak at 277 , which corresponds to the compound moiety ($\text{C}_{13}\text{H}_{19}\text{N}_5\text{S}$). These data suggest that a ketone PTHP group is condensed with the N-dimethylthiosemicarbazide NH_2 group. The M(II) complex mass spectra have been studied. Comparing the molecular formula weights with m/z values confirm the suggested molecular formula for these complexes. Molecular ion peaks for Zn-DMPHP and Cd-DMPHP complexes were observed at $m/z = 375$ and 425 , respectively. These data agree very well with the molecular formulation proposed for (Zn(DMPHP)Cl) (1) and (Cd(DMPHP)Cl) (2) complexes.

3.6. Conductivity Measurements and Magnetism. Conductivity measurements provide an insight into the degree of complexes ionization, i.e., the ionized complexes have a higher molar conductivity than nonionized ones. The molar conductance is calculated by this relationship:

$$\Lambda_M = \frac{K}{C} \times 1000, \quad (5)$$

where C (mol/l) represents the concentration of the solution, and K is the specific conductivity. The obtained lower values ($\Lambda_M = 8.9\text{--}10.2\text{ }\Omega^{-1}\cdot\text{cm}^2\cdot\text{mol}^{-1}$) for conductivity measurements agree with the fact that nonelectrolytes have $\Lambda_M < 50\text{ }\Omega^{-1}\cdot\text{cm}^2\cdot\text{mol}^{-1}$ in DMSO solutions [56]. This observation was also confirmed by a chemical analysis in which the addition of the AgNO_3 solution does not precipitate Cl^- ion.

3.7. Molecular Modeling. The following parameters such as dipole moment, total energy, binding energy, HOMO, and

LUMO energies have been measured and provided in Table 1 after geometric optimizations of the free DMPHP compound structures and their M(II) complexes using DFT semicore pseudopotential calculations using DMOL³ software [35–38] in the Materials Studio package.

The DMPHP compound's molecular structure and zinc (II) complex along with the atom numbering scheme are shown in Figures 1 and 2.

3.7.1. Bond Length and Bond Angles. Tables 1S–4S list the bond angles and lengths of the DMPHP ligand and Zn(II)-DMPHP complex, while the selected bond lengths of the metal (II) complexes compared to the free DMPHP thiosemicarbazone compound are given in Table 2.

The bond length of the free DMPHP compound is modified slightly as a result of coordination [57].

In a DMPHP system of both complexes, metal-azomethine and metal-S bond formation leads to an increase for the distances N(6)–C(7), N(3)–C(2), and N(4)–C(1) (Table 1) when compared with free DMPHP structure.

In complexes, the metal (II) is bound to the Cl atom (Cd–Cl = 2.413 Å; Zn–Cl = 2.255 Å) and to the sulfur atom of the DMPHP ligand (Cd–S = 2.538 Å; Zn–S = 2.379 Å). The bond angles around the center of both Zn(II) (~108.1–123.1) and Cd(II) (~109.9–120.5) suggest that the geometric form is distorted tetrahedral as suggested by the various analytical tools mentioned above.

C–S bond length increases from 1.697 Å in DMPHP to 1.755 Å and 1.765 Å in the Cd-DMPHP and Zn-DMPHP complexes, respectively. Likewise, the N–C(S) bond is substantially increased from 1.354 Å in the free DMPHP ligand to 1.393 Å and 1.369 Å in Cd-DMPHP and Zn-DMPHP complexes, respectively. Such modifications mean that deprotonated sulfur is coordinated after enethiolization. Thus, the single bond character of C–S distances (Table 1) being some of the largest found for DMPHP complexes (typical bond lengths being C(sp²)-S 1.706 Å in (CH₃)₂C=C(SCH₃)₂) [58, 59].

3.7.2. Molecular Parameters. Quantum chemical parameters such as E_{HOMO} and E_{LUMO} in addition to the separation energy (ΔE), absolute electronegativity (χ), ionization energy (IE), absolute hardness (η), electron affinity (EA), electrophilicity (w), electron accepting power (w^+), electron donating power (w^-), and additional electronic charge (ΔN_{max}) have been computed according to the following equations [60–65]. Softness (σ) is the global hardness inverse [66].

$$\chi = -\frac{1}{2}(E_{\text{LUMO}} + E_{\text{HOMO}}), \quad (6)$$

$$\text{IP} = -E_{\text{HOMO}}, \quad (7)$$

$$\eta = \frac{1}{2}(E_{\text{LUMO}} - E_{\text{HOMO}}), \quad (8)$$

$$S = \frac{1}{2\eta}, \quad (9)$$

$$\Delta N_{\text{max}} = -\frac{\text{IE}}{\eta}, \quad (10)$$

$$\sigma = \frac{1}{\eta}, \quad (11)$$

$$\text{EA} = -E_{\text{LUMO}}, \quad (12)$$

$$\omega = \frac{\text{IE}^2}{2\eta}, \quad (13)$$

$$\omega^- = \frac{(3 * \text{IE} + \text{EA})^2}{16(\text{IE} - \text{EA})}, \quad (14)$$

$$\omega^- = \frac{(\text{IE} + 3 * \text{EA})^2}{16(\text{IE} - \text{EA})}. \quad (15)$$

We can infer the following from the data obtained in Tables 1 and 3:

- The calculated negative energy values of HOMO (electron-rich) and LUMO (electron-poor) indicating the stability of M(II) complexes [63]
- Absolute hardness (μ) and softness (μ) are important characteristics in calculation of molecular stability and reactivity. The hard molecules have a large energy space with less reactivity ($E_{\text{HOMO}} - E_{\text{LUMO}}$), whereas the soft molecules have a smaller energy space and a greater reactivity, meaning that the energy gap is an index of stability to measure the chemical reactivity and kinetic stability of the molecule [67, 68]. Chemical hardness values of the complexes have been observed to adopt this order: (Cd(DMPHP)Cl) ($\eta = 1.39$) > (Zn(DMPHP)Cl) ($\eta = 1.22$).
- When HOMO energy decreases, the molecule's ability to donate electron decreases, while high HOMO energy means that the molecule is an efficient donor of electrons. A significant parameter for the formation of a charging transfer complex between the compound and its biological target is the greater donation function of the compound.
- The energies of HOMO metal (II) systems have been found to be closely spaced (E_{HOMO} , (Cd(DMPHP)Cl) -4.75 eV; E_{HOMO} , (Zn(DMPHP)Cl) -4.61 eV)
- The energy gap ($E_{\text{HOMO}} - E_{\text{LUMO}}$) for the synthesized DMPHP compound is 2.20. For the title compound, this large HOMO-LUMO distance automatically assumed high excitation strength, good stability, and great chemical hardness.
- The energy separation values for the synthesized metal (II) complexes between the HOMO and

TABLE 1: The calculated quantum chemical parameters of the DMPTHP ligand and M(II)-DMPTHP complexes.

Compound	E_H	E_L	ΔE	IE	EA	α	η	S	$\Delta N_{\max}$	ω	ω^-	ω^+
DMPTHP	-8.50	-2.19	6.31	8.50	2.19	5.35	3.16	0.32	-2.69	4.53	7.59	2.25
Zn-L	-4.61	-2.17	2.44	4.61	2.17	3.39	1.22	0.82	-3.78	4.71	6.56	3.17
Cd-L	-4.75	-1.98	2.77	4.75	1.98	3.37	1.39	0.72	-3.43	4.09	5.94	2.58

FIGURE 1: The molecular structure of the DMPTHP thiosemicarbazone compound along with the atom numbering scheme.

FIGURE 2: The molecular structure of the (Zn(DMPTHP)Cl) complex along with the atom numbering scheme.

TABLE 2: Selected bond length of the DMPTHP ligand and M(II)-DMPTHP complexes.

Bond	DMPTHP	Cd(II)-DMPTHP	Zn(II)-DMPTHP
C(7)-N(6)	1.354	1.393	1.369
C(2)-N(3)	1.317	1.322	1.319
C(1)-N(3)	1.304	1.310	1.322
C(7)-S(8)	1.697	1.755	1.765
M-S	—	2.538	2.379
M-N(3)	—	2.350	2.075
M-N(4)	—	2.595	2.230
M-Cl	—	2.413	2.255

LUMO are 2.44–2.77 eV. This energy gap conforms to the values for stable metal transition complexes [69].

- (g) Based on binding energy calculations, the binding energy value of complexes (-72725.7 to $-72869.8 \text{ kcal}\cdot\text{mol}^{-1}$) is improved compared to that of free DMPTHP ($-65204.4 \text{ kcal}\cdot\text{mol}^{-1}$), meaning that its stability exceeds that of the free DMPTHP ligand.
- (h) As is known, the electrical dipole moment measures electrical charging separation of a system. Thus, the (Zn(DMPTHP)Cl) complex with 2.76 dipole moment is more polar than the (Cd(DMPTHP)Cl) complex with the smallest dipole moment (2.63).

3.8. Structure of the Complexes. From various analytical instruments used, it is inferred that the DMPTHP ligand was bound to metal as a monobasic tridentate (NNS-

TABLE 3: Some energetic properties of the DMPHP ligand and M(II)-DMPHP complexes.

Ligand/ complex	Total energy (kcal/mol)	Binding energy (kcal/mol)	Electronic energy (kcal/mol)	Nuclear energy (kcal/mol)	Dipole moment (debye)
DMPHP	-65204.4	-3726.1	-447505.9	382301.5	3.55
Zn-L	-72869.8	-3792.7	-515891.3	443021.4	2.76
Cd-L	-72725.7	-3762.4	-498546.9	425821.2	2.63

donor) ligand, and the chlorine atom behaves as a monobasic monodentate ligand. The dipositively charged metals' neutrality comes from deprotonation of the DMPHP ligand SH group and the negatively charged Cl⁻ group. The nonelectrolytic character of complexes is demonstrated by the obtained low molar conductance values.

3.9. Biological Activity

3.9.1. Antimicrobial Activity. Biological activity of the synthesized compounds was tested for the DMPHP ligand and its M(II) complexes. We have used more than one research organism to assess the antimicrobial efficiency of these substances to estimate the possibility that antibiotic principles have been detected in the sample. The DMPHP ligand's antimicrobial activity and its metal complexes were tested using diffusion agar technique [48, 70, 71]. The tool used for population growth was nutrient agar. Table 4 and Figures 3 and 4 show the results of the antimicrobial behavior of free DMPHP and its complexes. It can be inferred from the antibacterial test data that

- (i) The N and S system of DMPHP ligand donors is designed to inhibit enzyme development because these enzymes are particularly likely to inactivation by metal ions of complexes
- (ii) DMPHP ligand and its complexes have antibacterial activity due to the presence of toxophorically essential imine groups ($-C=N$) where the mode of action of these compounds could include formation of H-bonds via the azomethine group with an active center of cell constituents causing interference with normal cell processes [72]
- (iii) In vitro biocidal ligand experiments on coordination with M(II) ion with all strains of microorganisms under similar test conditions were significantly improved. Chelation that decreases polarity of M(II) by neutralizing positive metal ion charge with ligand-donor groups can explain antibacterial growth [73]. As a result of chelation, the lipophilicity and hydrophobic nature of the ligand increases, making it more easier to permeate through lipid layers of cells membrane causing deactivation of enzymes responsible for the respiratory process and blocking of protein synthesis, thereby limiting the growth of the organism.

- (iv) The data show that the complexes were more toxic to G⁺ than G⁻ strains due to the difference in bacterial cell wall structure [74]
- (v) Most substances may have a standard drug activity similar to ampicillin. The antibacterial activity of compounds against selected bacterial forms can be ordered as (Cd(DMPHP)Cl) > (Zn(DMPHP)) > DMPHP, thereby indicating an improvement in lipophilic behavior.
- (vi) DMPHP's biological function is based on their ability to chelate metal ions because of the presence of hydrazo, imine, and thione groups
- (vii) The synthesized compounds have no antifungal activity versus *Aspergillus flavus*
- (viii) The antifungal activity of compounds against *Candida albicans* obeyed this order: (Cd(DMPHP)Cl) > ampicillin > (Zn(DMPHP)) > DMPHP

3.9.2. Bioactivity and Physicochemical Properties of Synthesized Compounds. Dipolar moment can provide a description of the substances hydrophobicity/hydrophilicity. Studies of SAR have shown that complex dipole moment is inversely related to their bioactivity versus the tested bacterial strains. As the dipole moment decreases, polarity increases through lipophilicity that enhances its permeation more effectively through the microorganism's lipid layer [59], thus more violently destroying them. As tabulated in Table 1, (Cd (DMPHP) Cl) has a lower dipole moment ($\mu = 2.63$). It therefore has greater biological activity and lipophilic nature than the other compounds.

Therefore, this sequence of synthesized compounds (Cd(DMPHP)Cl) > (Zn(DMPHP)) > DMPHP represents the order of lipophilicity, which in turn facilitates cytoplasmic membrane penetration and disables the essential enzymes of the microorganisms tested for respiration processes. Lower values of the dipole moment thus help increasing the antibacterial activity.

(Cd(DMPHP)Cl) complex with the lowest energy values of HOMO ($E_H = -3.47$) and the highest energy values of LUMO ($E_L = -1.98$) among the synthesized compounds showed high activity vs. the investigated bacterial strains. This corresponds to the values provided in the literature [75].

3.9.3. Antioxidant Activity. Recently, antioxidants have a great interest in medical purposes. DPPH• is a stable, free radical used in chemical analysis to detect radical scavenge behaviors [76] in contrast to other methods in a relatively

TABLE 4: Antibacterial and antifungal activities of the synthesized compounds.

Compound	Gram positive		Gram negative		Fungi	
	<i>Staphylococcus aureus</i>	<i>Bacillus subtilis</i>	<i>Escherichia coli</i>	<i>Neisseria gonorrhoeae</i>	<i>Aspergillus flavus</i>	<i>Candida albicans</i>
DMPTHP	16	10	13	9	—	15
Cd-DMPTHP	20	18	19	17	—	22
Zn-DMPTHP	18	14	15	13	—	18
Ampicillin	21	26	25	28	—	—
Amphotericin B	—	—	—	—	17	21

Ampicillin, standard antibacterial agent; amphotericin B, standard antifungal agent.

FIGURE 3: Antibacterial activity of the synthesized compounds.

FIGURE 4: Antifungal activity of the synthesized compounds.

short time [77]. The compounds antioxidant activity is related to their electron or radical hydrogen release ability to DPPH leading to the formation of stable diamagnetic molecules [77]. Thus, absorbance of DPPH[•] diminishes by its interaction with antioxidants as the color changes from purple to yellow. Therefore, DPPH[•] is usually used for assessing the antioxidant activity as a substrate [78]. The maximum absorption of a stable DPPH[•] was at 517 nm in EtOH. The decrease in absorption of radicals of DPPH at 517 nm may therefore be calculated as a consequence of its reduction [77]. The antioxidant activity of the synthesized compounds can be evidenced by decreasing the initial concentration of DPPH[•] radical in solution. The synthesized compounds showed an enhanced behavior as a radical scavenger compared to the standard ascorbic acid scavenging capacity.

Such findings suggest that the antioxidant function of ligands is enhanced by complexity like previous studies in literature [79, 80]. In addition, with the rise in their concentrations, the free radical activity of the free DMPTHP ligand and their M(II) complexes is increasing. These compounds are free radical inhibitors based on the results of this research (Table 5). This can limit the human body's free radical harm. The antioxidant activity of the studied compounds referred to the presence (C = N)_{azomethine}, SH, and hydrazo groups [81].

3.9.4. Antioxidant Activity and Physicochemical Properties of Synthesized Compounds. The orbital energies of HOMO and LUMO are closely linked to antioxidants' free radical scavenging activities [82, 83]. The HOMO energy is directly linked to the ionization potential, which suggests the molecule's sensitivity to electrophilic attack, while the LUMO energy is related to the electron affinity, which indicates the molecule's susceptibility to nucleophilic attack [84]. Nucleophiles and electrophiles, respectively, have high-energy HOMO and low-energy LUMO. Electron donating atoms have high HOMO with a loose hold of valence electron, which makes them oxidable [85]. Electrons can quickly be lost by low-ionizing energy compounds and are thus likely to be involved in chemical reactions. Compounds with high E_{HOMO} and low E_{LUMO} values and a lower energy gap (EG) are known as good species releasing electron. In this study, the powerful antioxidants of M(II) complexes have the lowest ΔE values ($\Delta E = 2.63\text{--}2.76$) compared to ($\Delta E = 3.55$)

TABLE 5: DPPH activity.

Compound	Concentration ($\mu\text{g/ml}$)	DPPH scavenging activity (%)
DMPTHP	50	86.11
	100	87.32
	150	90.51
	200	92.67
Zn-DMPTHP	50	88.11
	100	89.32
	150	91.51
	200	92.52
Cd-DMPTHP	50	93.8
	100	94.9
	150	95.4
	200	95.7
Ascorbic acid	50	96.8
	100	97.09
	150	97.6
	200	97.8

DPPH, 1,1-diphenyl-2-picrylhydrazyl.

for the free DMPTHP ligand under consideration, reflecting their high electron release affinities [86]. The synthesized antioxidant compounds are in the following order: $(\text{Cd}(\text{DMPTHP})\text{Cl}) > (\text{Zn}(\text{DMPTHP})) > \text{DMPTHP}$.

3.10. Docking Studies. In drug development, docking plays a significant role in determining the appropriate molecular scaffolding and in deciding the target protein selectivity. The obtained docking results of interaction for DMPTHP as a representative example with the specific protein of the target organism are represented graphically in Figures 5–7. The protein was prepared for docking studies by assigning of H-bond state of the receptors and removal of H_2O molecules. The MOE alpha site finder was used for the active sites search in the enzyme.

Docking protocol was verified by redocking of the cocrystallized ligand in the vicinity of the active site of the protein with the energy score (S).

The extent of interaction between the DMPTHP ligand and different protein can be measured by the value of the docking S-score in kcal/mol with active sites residue as follows:

(i) For inhibitor binding to *E. coli*

For inhibitor binding to INEK protein of *E. coli*

Pose (I) $(-8.5665 \text{ kcal/mol}) > \text{pose (II)}$
 $(-7.9073 \text{ kcal/mol}) > \text{pose (III)} (-7.7547 \text{ kcal/mol})$
 $> \text{pose (IV)} (-7.5662 \text{ kcal/mol})$

(ii) For inhibitor binding to 3HB5 protein of breast cancer

Pose (I) $(-6.5507 \text{ kcal/mol}) > \text{pose (II)}$
 $(-6.2346 \text{ kcal/mol}) > \text{pose (III)} (-6.1535 \text{ kcal/mol})$
 $> \text{pose (IV)} (-6.1066 \text{ kcal/mol})$

Lead to optimization of newly synthesized DMPTHP as antibacterial agents selection acts on highly resistant strains of *E. coli* and also as an anticancer agent had been confirmed and clarified via the molecular modeling as follows:

(1) Careful studying of the structural activity relationship (SAR) of the biologically tested compound and its chemical structure as an antibacterial and anti-tumor agent

(2) Compound DMPTHP has the following essential features necessary for high biological activities

(a) DMPTHP directed to bind target enzymes

(b) Nonplanar structures as confirmed using the DFT method via different many hydrogen bonding centers that allow careful fitting, while the nonplanar structure allows the molecule to introduce itself between building blocks of target enzymes causing conformational changes and inhibition to enzymes

3.11. Equilibrium Studies. Protonation constants of the DMPTHP ligand are calculated. This DMPTHP ligand behaves as a tetraprotic as shown in equations (16)–(19). All results are given in Tables 6–9.

The 1st protonation constant correspond to the thiolate group protonation, while the 2nd and 3rd protonation constants correspond to the protonation of the two *N*-imino sites in the DMPTHP ligand.

The $\log K_{N\text{-imino}}$ values (Table 6) ranges from 3.20 to 3.77 are similar to those found in the literature for the imino group (4.40) [87]. The $\log K_{SH}$ value ranges from 8.11 to 8.51 are similar to those described in the literature for hydrazo moiety (5.5–5.90) [88].

The ligand titration curves (DMPTHP) were measured in the presence and absence of Zn^{2+} or Cd^{2+} ions and compared. The titration curves are located below the ligand curve due to the H^+ release by displacement of M^{n+} during complex formation. Table 7 shows that $\log K_1$ – $\log K_2$ typically has some positive values because metal ion coordination sites are free to bind the 1st ligand than the 2nd ligand. The Cd(II) compounds have greater stability constants with DMPTHP than those with Zn(II) compounds. This is because the softer Cd(II) interacts more than harder Zn(II) with relatively soft sulfur atoms [87, 89].

Figure 8 shows a concentration distribution diagram for the complex Zn(II)-DMPTHP. The 110 complex species of DMPTHP with Zn(II) begins to form in acidic pH range and

FIGURE 7: (a) 3D molecular interaction of DMPTHP for inhibition to 3HB5 protein of *Homo sapiens*. (b) 3D molecular interaction of DMPTHP for inhibition to 3HB5 of *Homo sapiens* inside the core on the protein surface.

TABLE 6: Protonation constants for the DMPTHP ligand and stability constants for the Zn(II) and Cd(II) complexes with the DMPTHP ligand at 0.1 mol·L⁻¹ NaNO₃ at different temperatures.

Reaction	<i>p</i>	<i>q</i>	<i>r</i>	log β ($\pm\sigma$) ^a		
				15°C	25°C	35°C
L + H = HL ^a	0	1	1	8.51 (0.02)	8.31 (0.09)	8.11 (0.04)
L + 2H = H ₂ L	0	1	2	11.88 (0.04)	11.58 (0.05)	11.31 (0.04)
L + 3H = H ₃ L	0	1	3	15.65 (0.05)	15.24 (0.03)	14.88 (0.03)
Zn + L = ZnL	1	1	0	8.82 (0.06)	8.73 (0.07)	8.632 (0.04)
Zn + 2L = ZnL ₂	1	2	0	11.24 (0.06)	11.09 (0.04)	10.94 (0.09)
Cd + L = CdL	1	1	0	10.19 (0.08)	10.03 (0.04)	9.92 (0.05)
Cd + 2L = CdL ₂	1	2	0	13.41 (0.05)	13.18 (0.04)	13.01 (0.06)

^a(σ) is the standard deviation; definitions of stability constants: $\beta_{0110} = ([ML]/[M][L])$; $\beta_{120} = ([ML_2]/[M][L]^2)$; L = thiosemicarbazone ligand. Charges are omitted for clarity.

TABLE 7: Stepwise stability for the complexes of DMPTHP with Zn(II) and Cd(II) metal ions in 50% DMSO-H₂O (V/V) solution at I = 0.1 mol·dm⁻³ NaNO₃.

Temperature (°C)	log K_1 ($\pm\sigma$) ^a		log K_2 ($\pm\sigma$)		log $K_1 - \log K_2$	
	ZnL	CdL	ZnL ₂	CdL ₂	Zn(II) complex	Cd(II) complex
15	8.82 (0.06)	10.19 (0.05)	2.42 (0.08)	3.22 (0.05)	6.40	6.97
25	8.73 (0.07)	10.03 (0.03)	2.36 (0.05)	3.15 (0.04)	6.37	6.88
35	8.63 (0.04)	9.92 (0.06)	2.31 (0.07)	3.09 (0.06)	6.32	6.83

^a(σ) is the standard deviation; definitions of stability constants: $K_1 = [ML]/[M][L]$; $K_2 = [ML_2]/[ML][L]$; L = DMPTHP. Charges are omitted for simplicity.

FIGURE 8: Concentration distribution of various species as a function of pH in the Zn-DMPHP system (at concentrations of $1.25 \text{ mol}\cdot\text{dm}^{-3}$ for Zn(II) and $1.25 \text{ mol}\cdot\text{dm}^{-3}$ for DMPHP) at 25°C and $I = 0.1 \text{ mol}\cdot\text{dm}^{-3} \text{ NaNO}_3$.

FIGURE 9: Effect of temperature on the protonation constant of DMPHP.

FIGURE 10: Effect of temperature on the formation constant of Zn(II)-DMPHP complexes.

TABLE 8: Thermodynamic parameters for the protonation of the ligand (DMPHP) in 50% DMSO- H_2O (V/V) solution at $I = 0.1 \text{ mol}\cdot\text{dm}^{-3} \text{ NaNO}_3$.

Parameter ^a	L + H = HL ^a			Reaction L + 2H = H ₂ L			L + 3H = H ₃ L		
	288	293	298	288	293	298	288	293	298
$-\Delta G$	46.95	47.44	47.85	20.88	20.89	21.06	18.59	18.67	18.88
$-\Delta H$		33.99			17.01			14.47	
ΔS		44.99			13.09			14.16	

ΔG , Gibbs energy/ $\text{kJ}\cdot\text{mol}^{-1}$; ΔH , enthalpy/ $\text{kJ}\cdot\text{mol}^{-1}$; ΔS , entropy/ $\text{J}\cdot\text{mol}^{-1}\cdot\text{K}^{-1}$.

TABLE 9: Thermodynamic parameters for Zn(II) and Cd(II) complexes in 50% DMSO- H_2O (V/V) solution at $I = 0.1 \text{ mol}\cdot\text{dm}^{-3} \text{ NaNO}_3$.

Parameter ^a	Zn + L = ZnL			Reaction Zn + 2L = ZnL ₂			Cd + L = CdL			Cd + 2L = CdL ₂		
	288	293	298	288	293	298	288	293	298	288	293	298
$-\Delta G$	48.66	49.84	50.92	13.35	13.47	13.63	56.22	57.26	58.53	17.77	17.98	18.23
$-\Delta H$		16.14			9.36			22.99			11.06	
ΔS		112.77			13.84			115.19			23.26	

ΔG , Gibbs energy/ $\text{kJ}\cdot\text{mol}^{-1}$; ΔH , enthalpy/ $\text{kJ}\cdot\text{mol}^{-1}$; ΔS , entropy/ $\text{J}\cdot\text{mol}^{-1}\cdot\text{K}^{-1}$.

reaches a steady concentration of 99.9% at pH = 5.8, whereas Zn(DMPHP)₂ complex species reaches a maximum concentration of 17% at pH 9.6.

3.12. Thermodynamics. The data derived for ΔH° , ΔS° , and ΔG° associated with protonation of DMPHP and its complex formation with Zn(II) and Cd(II) metal ions were calculated from the given data in Tables 6 and 7. Enthalpy change (ΔH) for ligand protonation or the complexation process was determined from plot slope ($\log K$ vs. $1/T$) (Figures 9 and 10) through the graphical representation of the van't Hoff equation.

$$-2.303RT \log 10 K = \Delta H^\circ - T\Delta S^\circ, \quad (20)$$

or

$$\log K_{10} = -\left(\frac{\Delta H^\circ}{2.303R}\right)\left(\frac{1}{T}\right) + \frac{\Delta S^\circ}{R}. \quad (21)$$

With the well-known relations (20) and (21), from the values of free energy change (ΔG) and enthalpy change (ΔH), one can deduce the entropy change (ΔS):

$$\Delta G^\circ = -2.303RT \log 10 K, \quad (22)$$

$$\Delta S^\circ = \frac{(\Delta H^\circ - \Delta G^\circ)}{T}.$$

The main reasons for the protonation constant determination can be explained as follows:

- (1) Protonation constants can be used in determination of the pH and ratio of the various forms of a substance
- (2) A newly synthesized compound can also supply structural details. The suggested structure can be reliable where protonation constants are theoretically well calculated according to the experimental values.
- (3) Because different types of substances have different UV spectra, quantitative spectrophotometric analysis can be performed by choosing the appropriate pH value. To choose the pH values, the known protonation constants are required.
- (4) Protonation constants are required for buffer solutions preparation at different pH values [48, 90]
- (5) Therefore, the measurements of the stability constants for the complicated formation of bioactive ion compounds include protonation constants to be determined

Additionally, their protonation constants are used for calculating the stability constants of the dynamic formation of bioactive compounds with metal ions [91]

- (6) The equilibrium constants of certain compounds must be understood to measure the concentration of each ionized species at pH to understand their

physiochemical behavior [92]. The protonation constants of the newly synthesized compounds were thus calculated by this study. Table 8 describes the thermodynamic functions measured and can be interpreted as follows:

- (1) The corresponding thermodynamic processes for the protonation reactions are as follows:
 - (i) Neutralization reaction is an exothermic process
 - (ii) Ions desolvation is an endothermic process
 - (iii) Structure alteration and H-bonds alignment in free and protonated ligands
- (2) When the temperature rises, the value of pK^H decreases and its acidity rises
- (3) Negative ΔH° for DMPHP protonation means its interaction is followed by release of heat
- (4) DMPHP's protonation reaction has a positive entropy, which could be due to increased disorder due to desolvation processes and breakdown of H-bonds

Table 7 includes the step-by-step stability constants of the complexes formed at various temperatures. Such values decrease and confirm that the complexation is preferred at low temperature. These results provide the following findings:

- (1) Negative ΔG° for complexation (Table 9), indicating the spontaneity of the coordination process
- (2) The coordinating process is exothermic with $-\Delta H^\circ$, i.e., the complexation reaction is preferred at low temperatures
- (3) It is commonly found that ΔG° and ΔH° values for the 1:1 complexes are more negative than that of 1:2 complexes, indicating a change in this ligand's dentate character from tridentate in 1:1 chelates to bidentate in 1:2. M:L chelates and steric hindrance are generated by addition of the 2nd molecule.
- (4) The electrostatic attraction in the 1:1 complex is greater than in the 1:2 complex due to the 1:1 complex being formed by the interaction between the dipositively charged metal ion and the mononegatively charged ligand anion. While the 1:2 complex is generated by the monopositively charged 1:1 complex and mononegatively charged ligand anion interactions.
- (5) The ΔS° values for all investigated complexes are positive due to the release of bound solvent molecules on coordination is greater than the decrease results from the coordination process itself.

4. Conclusion

The condensation reaction of 1-(p-tolylhydrazono)-propan-2-one (PThP) with N,N-dimethylthiosemicarbazide in the molar ratio (1:1) provided the corresponding (E)-N,N-dimethyl-2-((E)-1-(2-(p-tolyl)hydrazono)-propan-2-ylidene)

hydrazine-1-carbothioamide (DMPHP) compound. The IR spectra showed that, after deprotonation via the two azomethine nitrogen atoms and the thiolate sulfur atom, the DMPHP compound presents in the thione form in the solid state and coordinated to the metal(II) ion as a tridentate anion. M(II) complexes are nonelectrolytes with a distorted tetrahedral structure. The antibacterial and antimicrobial testing data show that a newly generated compound is a moderately to highly antimicrobial agent. Inverse correlation exists between dipole moment and synthesized compounds' behavior against the studied bacterial and fungal organisms, as stated by SAR studies. The relationship between morphological and biological characteristics has been studied, which can assist in the production of more effective antibacterial agents. Potentiometric studies have shown that DMPHP forms complexes 1 : 1 or 1 : 2 with ions Zn(II) and Cd(II). Comparison of Zn(II) and Cd(II) stability constants with DMPHP shows that DMPHP stability constants with Cd(II) are higher than Zn(II) constants. The $\log K_1$ and $-\Delta H_1$, for M(II) DMPHP complexes are larger than $\log K_2$ and $-\Delta H_2$, demonstrating alteration of the DMPHP dentate character from tridentate in 1 : 1 chelates to bidentate in 1 : 2; M : DMPHP chelates and steric hindrance is generated by addition of 2nd molecule. DMPHP may be viewed from the biological perspective, as it constitutes a highly stable compound, as a possible antidote to Cd^{2+} ion.

Data Availability

The data used to support the findings of this study are available in the microanalytical center, Cairo University, Egypt. The telephone number of this center is 00201001010194.

Conflicts of Interest

The authors declare that they have no conflicts of interest.

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Supplementary Materials

The bond length (Å) and bond angles (°) of DMPHP were calculated using the DFT method. Selected bond length (Å) and bond angles of (Zn(DMPHP)Cl) were also calculated. Data are given in Tables S1–S4. (*Supplementary Materials*)

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