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WILEY Applied Organometallic Chemistry

# Synthesis, spectroscopic characterization and biological evaluation of a novel chemosensor with different metal ions

M. Gaber<sup>1</sup>  $\square$  | Tarek A. Fayed<sup>1</sup>  $\square$  | Marwa N. El-Nahass<sup>1</sup>  $\square$  | H.A. Diab<sup>1</sup> | Mohammed M. El-Gamil<sup>2</sup>  $\square$ 

<sup>1</sup>Department of Chemistry, Faculty of Science, Tanta University, 31527 Tanta, Egypt

<sup>2</sup> Department of Toxic and Narcotic Drug, Forensic Medicine, Mansoura Laboratory, Medico Legal Organization, Ministry of Justice, Egypt

#### Correspondence

Tarek A. Fayed, M. Gaber and Marwa N. El-Nahass, Department of Chemistry, Faculty of Science, Tanta University, 31527, Tanta, Egypt. Email: tfayed2013@science.tanta.edu.eg; mabuelazm@science.tanta.edu.eg; marwa.elnahas@science.tanta.edu.eg A novel chemosensor, namely 3-(4-chlorophenyl)-1-(pyridin-2-yl)prop-2-en-1one, CPPEO, and its metal complexes have been synthesized and characterized by using sets of chemical and spectroscopic techniques, such as elemental analysis, mass, Fourier transform-infrared and UV-Vis spectral analysis. The thermal properties of the metal complexes have been investigated by thermogravimetric techniques. The decomposition mechanism of the titled complexes was suggested. The results showed that the  $Co^{2+}$  and  $Mn^{2+}$  complexes have an octahedral geometry, while Zn<sup>2+</sup> and Cd<sup>2+</sup> complexes have tetrahedral geometry. The kinetic and thermodynamic parameters of the thermal decomposition stages have been evaluated using the Coats-Redfern method. The optical sensing response of the investigated chemosensor to the different metal ions was investigated. It responds well to the tested metal ions as reflected from the significant change in both absorption and emission spectra upon adding different concentrations of the metal salts, confirming the intramolecular charge transfer of the chemosensor upon effective coordination with the used metal ions. This leads to enhancing ICT interaction, causing a significant shift in the presence of strongly complexing metal ions. This was fully reversible, where the solution of dye-metal ion complex was decomplexed by adding an EDTA solution to revert the original spectrum of the dye. The stability constants, K, for the complexes of the investigated chemosensor with the mentioned metal ions were calculated, indicating that  $Co^{2+}$  is the most effectively detected, and the potential of the novel dye was highly efficient switchers for Co<sup>2+</sup> ions. Additionally, the molecular modeling was carried out for the chemosensor and its metal complexes. Finally, the solid complexes have been tested for their in vitro antimicrobial activities against some bacterial strains (Gram +ve and Gram -ve bacteria), as well as antifungal strains.

#### KEYWORDS

antimicrobial activities, chemosensor, molecular modeling, optical sensing

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### **1** | INTRODUCTION

Fluorescent push-pull dyes have received considerable attention owing to a growing interest in different fields.<sup>[1,2]</sup> They are known as effective photosensitive materials, and have exhibited considerable photophysical and photochemical properties.<sup>[3]</sup> They are extensively used as non-linear optical materials,<sup>[4]</sup> photorefractive polymers,<sup>[5]</sup> and in the study of the photo-alignment layer of liquid crystal displays.<sup>[6]</sup> Also, they can be used as chemosensor probes for toxic metal ion detection. Among these metal ions, Co (II), Mn (II), Zn (II) and Cd (II) were the most commonly found ones in wastewater. Their high degree of toxicity rank among the priority metals that are of public health significance, so their removal from wastewater has become a major task for many scientists.<sup>[7-11]</sup> Additionally, chalcones are of interest chemotypes for both chemists and physicists, due to the high natural abundance of them and their easy synthesis. Also, they are well known for biological activities, such as antitumor, anti-inflammatory, immunomodulatory, antibacterial, antimalarial, anti-leishmanial, trypanocidal and nitric oxide inhibitory activity.<sup>[12,13]</sup> Diverse chalcone-like compounds have been found to be potent anticancer agents against human cancer cell lines with different mechanisms of actions.<sup>[14]</sup> All the synthesized chalcones were screened for in vitro anti-proliferative activities.<sup>[15]</sup> Chalcones are interesting chemical entities from a medicinal chemistry perspective with a wide variety of applications, although their ease of isomerization and Michael-acceptor potential may hamper some of these applications.<sup>[16]</sup> The development of new chalcone-based therapeutics against ADs are promising lead compounds for future research in anti-AD drugs discovery and development.<sup>[17]</sup> The results suggest that chalcones could represent good strategies for the control of acute and chronic pain, without significant sideeffects.<sup>[18]</sup>

In light of these considerations, our work aimed at synthesis, structural characterization and optical studies of a novel chemosensor, namely 3-(4-chlorophenyl)-1-(pyridin-2-yl)prop-2-en-1-one, CPPEO, and its metal complexes. Their structures were elucidated by using sets of chemical and spectroscopic techniques. The thermal properties of the metal complexes have been investigated using thermogravimetric (TG) techniques. The optical sensing responses of the investigated chemosensors to different metal ions such as  $Co^{2+}$ ,  $Mn^{2+}$ ,  $Zn^{2+}$  and  $Cd^{2+}$  have been investigated. Also, the reversibility of the chemosensor response has been elucidated using EDTA solution. Additionally, molecular modeling was carried out. Finally, the solid complexes have been tested for their *in vitro* antimicrobial activities against some

bacterial strains, also their biological activities were screened against Gram-positive, Gram-negative bacteria and antifungal strains.

### 2 | EXPERIMENTAL

### 2.1 | Materials

All the chemicals used in the present study were of pure grade available from BDH, Aldrich or Sigma. They include 2-acetyl pyridine, 4-chlorobenzaldehyde and metal chlorides (CoCl<sub>2</sub>·6H<sub>2</sub>O, MnCl<sub>2</sub>.4H<sub>2</sub>O, ZnCl<sub>2</sub>.4H<sub>2</sub>O and CdCl<sub>2</sub>.H<sub>2</sub>O). The solvents used for the spectral study were spectroscopic grade from Aldrich.

### 2.2 | Physical measurements

Perkin-Elmer 2400 CHN Elemental Analyzer was used for the elemental microanalysis of the prepared compounds. The Perkin-Elmer 1430 IR spectrophotometer was used for recording the infrared (IR) spectra (as KBr discs) within the range 4000–200  $\text{cm}^{-1}$ . The magnetic susceptibility of the solid complexes was carried out at room temperature by the Gouy's technique for the magnetic susceptibility instrument. Mass spectra of metal complexes were carried out on a Varian Mat 311 with startend (m/z) (40-1000) and ionization mode (EI). The Schimadzu TG-50 TG analyzer was used for the TG analysis (TGA) of the solid complexes with a heating rate of 10°C/min under nitrogen atmosphere, in the range 25-800°C. Electron spin resonance (ESR) spectra of solid manganese complex at room temperature were obtained on a JEOL EPR spectrometer working in the X-band (9.435 GHz) with a modulation frequency of 100 kHz, and the microwave power was adjusted to 5 mW. Steady-state absorption and emission spectral measurements were carried out using a Shimadzu UV-3101PC scanning spectrophotometer and an Agilent Cary Eclipse Fluorescence Spectrophotometer using matched quartz cuvettes, respectively. In all experiments,  $2 \times 10^{-5}$  M solutions were used, and were handled under dim light at room temperature. The samples were excited at 430 nm, while recording the fluorescence spectra.

### 2.3 | Synthesis of the chemosensor, CPPEO

The chemosensor (Figure 1), was prepared and characterized as previously described.<sup>[19]</sup> The purity of the prepared compound was checked by melting point, Fourier transform (FT)-IR and UV–Vis spectral measurements.



FIGURE 1 The structure of the investigated chemosensor, CPPEO

### 2.4 | Synthesis of the metal complexes

To a hot methanolic solution of CPPEO (0.01 mol in 20 ml), a hot methanolic solution (0.01 mol in 20 ml) of the hydrated metal chlorides  $[Co^{2+}, Mn^{2+}, Zn^{2+}]$  and  $Cd^{2+}$  ions] was added. The resulting solutions were refluxed under stirring for 4 hr. The solid products were thus separated out, filtered off, washed several times with methanol and finally dried in a vacuum desiccator over anhydrous calcium (II) chloride. The analytical data are collected in Table 1.

### 2.5 | Quantum chemical computations

The density functional theory (DFT) computations with periodic boundary environments were accomplished utilizing the well-known DMol<sup>3</sup> code,<sup>[20]</sup> by means of Materials Studio set.<sup>[21]</sup> The tasks were utilized as part of a combination together with the specific dual mathematical and polarization premise set DNP that is precisely Gaussian basis sets.<sup>[22-24]</sup> The RPBE (GGA) functions<sup>[25]</sup> is up to now the greatest exchange-correlation function,<sup>[26]</sup> and is applied to consider the exchange properties of the electrons.

### 2.6 | Antimicrobial activity

For screening the antimicrobial activity of organic ligand and its metal complexes, the agar diffusion technique was used.<sup>[27]</sup> The tested organisms are Gram-negative bacteria (*Escherichia coli*, *Pseudomonas aeruginosa*, *Klebsiella pneumoniae*, *Proteus vulgaris* and *Acinetobacter*), Gram-WILEY-Organometallic 3 of 16

positive bacteria (Staphylococcus aureus, Enterobacter cloacae) and fungi (Candida albicans, Candida dubliniensis, Candida glabrata, Candida krusei, Candida tropicalis and Trichophyton mentagrophytes). Freshly prepared spore suspension of different test microorganisms (0.5 ml of about 106 cells/ml) was mixed with 9.5 ml of melting sterile Sabouraud's dextrose medium (for fungi) or nutrient agar medium (for bacteria) at 45°C, poured on sterile Petri dishes, and left to solidify at room temperature. Regular cellulose filter paper discs of 6 mm diameter were prepared under aseptic conditions. Each disc was saturated with 20 mg of each tested suspended material. For each test three replicas were made. All plates were incubated at 27°C for 48 hr for fungi, and at 32°C for 24 hr for bacteria. The average diameters of inhibition zones were recorded in millimeters. All experiments were carried out in triplicate and the mean results were evaluated.

### **3** | **RESULTS AND DISCUSSION**

The structures of the investigated chemosensor and its metal complexes were elucidated by means of their elemental, molar conductivity and IR spectral data. The results of elemental analysis and molar conductance are collected in Table 1. The isolated solid complexes are stable in air, and soluble in DMF and DMSO. The melting points of the metal complexes were found to be over  $300^{\circ}$ C The low molar conductance values of Zn<sup>2+</sup> and Cd<sup>2+</sup> complexes revealed that these complexes are nonelectrolytes in DMF. The presence of Cl<sup>-</sup> ions outside the coordination sphere was confirmed by the chemical reaction with AgNO<sub>3</sub>, where the white precipitate of AgCl was observed. The molar conductance values were 77 and 88 ohm<sup>-1</sup> cm<sup>2</sup> mol<sup>-1</sup> for Co<sup>2+</sup> and Mn<sup>2+</sup> complexes, respectively, indicating the electrolyte nature of these complexes and the presence of the anion outside the coordination sphere.<sup>[28]</sup>

TABLE 1 Elemental analysis and molar conductance of the investigated chemosensor, CPPEO, and its metal complexes

|         |  |                          |         | Melting | Elemental analysis % (found) |             |             |               |    |
|---------|--|--------------------------|---------|---------|------------------------------|-------------|-------------|---------------|----|
| Complex |  | Color yield              | Mol. Wt | point   | С                            | н           | Ν           | Metal content | Λm |
| C1      | $\begin{array}{l} [CoL_{2} \cdot (H_{2}O)_{2}](Cl)_{2.} \ (H_{2}O) \\ \textbf{C_{28}H_{26}Cl_{4}Co} \ \textbf{N_{2}O_{5}} \end{array}$ | Dark brown<br><b>78%</b> | 671.19  | > 300°C | 50.14 (50.10)                | 4.13 (3.87) | 4.14 (4.17) | 8.06 (8.78)   | 77 |
| C2      | $[MnL \cdot (H_2O)_4](Cl)_{2.}2(H_2O) \\ C_{14}H_{22}Cl_3Mn \ NO_7$  | Dark brown<br><b>83%</b> | 477.52  | >300°C  | 35.82 (35.21)                | 4.41 (4.63) | 3.17 (2.93) | 11.60 (11.50) | 88 |
| C3      | [ZnL·(Cl) <sub>2</sub> ]·(C <sub>2</sub> H <sub>5</sub> OH)<br>C <sub>16</sub> H <sub>16</sub> Cl <sub>3</sub> Zn NO <sub>2</sub>      | Dark brown<br><b>77%</b> | 426.108 | >300°C  | 45.39 (45.099)               | 4.66 (3.78) | 2.9 (3.28)  | 14.87 (15.35) | 7  |
| C4      | $[CdL \cdot (Cl)_2] \cdot (C_2H_5OH)$<br>C <sub>16</sub> H <sub>16</sub> Cl <sub>3</sub> CdNO <sub>2</sub>                             | Dark brown<br><b>72%</b> | 473.129 | >300°C  | 40.71 (40.61)                | 4.20 (3.40) | 3.25 (2.95) | 24.22 (23.75) | 13 |

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### 3.1 | FT-IR analysis

Assignment of the IR diagnostic bands is depicted in Table 2. The IR spectrum of the free chemosensor showed that the vC=O band at 1675 cm<sup>-1</sup> is shifted to a lower frequency (48–85  $\text{cm}^{-1}$ ) in all complexes, indicating the participation of the oxygen atom of the carbonyl group in all complex formation. The stretching vibration of the vC=N linkage of the pyridine ring, which appeared at 1496  $\text{cm}^{-1}$  in free chemosensor, was shifted to a lower or higher frequency  $(8-60 \text{ cm}^{-1})$ , indicating the involvement of C=N in the coordination process, confirming the participation of the carbonyl oxygen and pyridine nitrogen atom in complexation with the appearance of new bands in the spectra of the complexes within the range 525–550 and 442–487  $cm^{-1}$  for  $\upsilon M$   $\rightarrow$   $O^{[29]}$  and  $vM \rightarrow N^{[30]}$  stretching vibrations, respectively. A very broad band in the range 3417-3441 cm<sup>-1</sup> in the spectra of the complexes is associated with coordinated and/or hvdrated water molecules.<sup>[31]</sup> The presence of coordination water molecules has been confirmed on the basis of a medium intensity band at 693-780 cm  $^{-1}$  (vOHrocking).<sup>[32]</sup>

### 3.2 | Mass analysis

Figures S1–S4 show the mass spectra of the investigated metal complexes. As can be seen, the mass spectrum of C1 provided good evidence for its molecular formula:  $[CoL_2(H_2O)_2](Cl)_2 \cdot (H_2O)$  (MW 671.19), indicating that the ligand coordinates with Co<sup>2+</sup> ion with M:L ratio

(1:2). The molecular ion peak for C1 at m/z = 670.72 (20.22%) corresponding to ( $C_{28}H_{26}C_{14}CoN_2O_5$ ). Furthermore, the mass spectrum of C2, C3 and C4 exhibited a good indication for the proposed molecular formula of C2, C3 and C4 (MW 477.52, 426.108 and 473.129, respectively), indicating that the ligand coordinates with metal ions with a M:L ratio of (1:1). Moreover, the molecular ion peaks for C2 [m/z = 477.51 36.41%)], C3 [m/z = 426.48 (15.58%)] and C4 [m/z = 473.36 (57.49%)] correspond to ( $C_{14}H_{22}Cl_3MnNO_7$ ), ( $C_{16}H_{16}Cl_3ZnNO_2$ ) and ( $C_{16}H_{16}Cl_3CdNO_2$ ), respectively.

### 3.3 | Magnetic and electronic absorption measurements

The electronic spectra of ligands and isolated chelates were illustrated in Table 3. The values of the observed magnetic moment of the Co<sup>2+</sup> complex ( $\mu_{eff} = 5.66$  BM) show the presence of three unpaired electrons in the d-orbital. On the other hand, the observed magnetic moment of the Mn<sup>2+</sup> complex ( $\mu_{eff} = 6.94$  BM) shows the presence of five unpaired electrons in the d-orbital. It was found that complexes C1 and C2 have octahedral geometry with sp<sup>3</sup>d<sup>2</sup> hybridization.<sup>[33-35]</sup>

The absorption spectra of Co (II) complex show bands at 16 420 and 19 230 cm<sup>-1</sup>, corresponding to  ${}^{4}T_{1g} \rightarrow {}^{4}A_{2g}$ ,  ${}^{4}T_{1g} \rightarrow {}^{4}T_{1g}$  (P) transition, indicating the octahedral structure. The spectra of Mn (II) complex show bands at 27 855 and 21 645 cm<sup>-1</sup>, corresponding to  ${}^{6}A_{1g} \rightarrow {}^{4}T_{2g}$  and  ${}^{6}A_{1g} \rightarrow {}^{4}E_{g}$  transition, also indicating the octahedral structure.<sup>[36]</sup>

TABLE 2 The important bands in the IR spectra of the investigated chemosensor, CPPEO, and its metal complexes

|              | Wave number (cm <sup>-1</sup> ) |      |                    |                    |      |  |  |  |  |
|--------------|---------------------------------|------|--------------------|--------------------|------|--|--|--|--|
| No.          | vHOH crystalline                | υC=0 | $\upsilon M \to N$ | $\upsilon M \to 0$ | υC=Ν |  |  |  |  |
| Ligand CPPEO | -                               | 1675 | -                  | -                  | 1496 |  |  |  |  |
| C1           | 3418–779                        | 1590 | 444                | 534                | 1556 |  |  |  |  |
| C2           | 3425, 779                       | 1627 | 482                | 525                | 1518 |  |  |  |  |
| C3           | 3424, 780                       | 1605 | 442                | 532                | 1519 |  |  |  |  |
| C4           | 3417, 774                       | 1595 | 477                | 533                | 1504 |  |  |  |  |

TABLE 3 The electronic absorption spectral data and magnetic moment of the investigated metal complexes

| No. | $\mu_{\mathrm{found}}$ BM | CT band (cm <sup>-1</sup> )    | d-d spectral ban | ud (cm <sup>-1</sup> ) | g <sub>eff</sub> |
|-----|---------------------------|--------------------------------|------------------|------------------------|------------------|
| C1  | 5.66                      | 28 011, 26 246                 | 19 230           | 16420,15082,13192      | _                |
| C2  | 6.94                      | 30 864, 27 855, 26 315         | 21 645           | 17857, 14492,13157     | 1.909            |
| C3  | _                         | 35 971, 29 239, 26 881         | _                | -                      | _                |
| C4  | -                         | 33 003, 30 581, 28 409, 26 595 | -                | -                      | -                |

### 3.4 | ESR spectra

The X-band ESR spectra of the powdered Mn (II) complex (C2) were recorded at room temperature (25°C). The ESR spectra of  $Mn^{2+}$  complex showed a negative deviation from the  $g_{eff}$  values of the free electron (2.0023). This may be due to the partial ionic character of the covalent bond between the Mn (II) ion and the ligand molecules.<sup>[37]</sup> The spectra of  $Mn^{2+}$  complex showed a broad signal that indicates an octahedral geometry around the  $Mn^{2+}$  ion. The g-value of  $Mn^{2+}$ complex is shown in Table 3 and Figure 2.



FIGURE 2 X-band electron spin resonance (ESR) spectra of complex C2

### 3.5 | Thermal analysis

The thermal behavior of metal complexes was studied by means of TGA techniques. The data, including the stages of decomposition, temperature ranges, peak temperatures, decomposition product loss, found and the calculated mass loss percentages are listed in Table 4 and Figure 3.

The obtained data indicated that all the metal complexes underwent thermal decomposition within three or four steps. Complexes C1 went through four stages of decomposition processes. The first step of decomposition appeared within the temperature range 17–120°C and



FIGURE 3 Thermogravimetric analysis (TGA) curves of the investigated metal complexes

**TABLE 4** Thermal decomposition data of the investigated metal complexes

|       |  |                              | Mass loss %                      |                                  |   |
|-------|--|------------------------------|----------------------------------|----------------------------------|---|
| Compl | ex   | Temp. °C                     | Estimate                         | Calcd                            | Assignment  |
| C1    | $\begin{array}{l} [CoL_2 \cdot (H_2O)_2](Cl)_{2.} \ (H2O) \\ C_{28}H_{26}Cl_4Co \ N_2O_5 \end{array}$  | 17–120<br>120–299<br>299–735 | 7.24<br>20.97<br>60.76<br>11.00  | 8.04<br>21.12<br>59.66<br>11.16  | Loss of 3H <sub>2</sub> O molecules<br>Loss of 4Cl<br>Dissociation of the organic ligand in two steps<br>CoO  |
| C2    | $[MnL\cdot(H_2O)_4](Cl)_{2.}2(H2O) \\ C_{14}H_{22}Cl_3Mn \ NO_7$   | 23–199<br>199–444<br>444–730 | 22.61<br>13.99<br>29.15<br>35.27 | 21.58<br>14.84<br>27.52<br>34.95 | Loss of 6 H <sub>2</sub> O molecules in two steps<br>Loss of 2Cl ions<br>Dissociation of the organic ligand with formation of<br>MnO + 8C as final products |
| C3    | $\begin{array}{l} [\text{ZnL} \cdot (\text{Cl})_2] (\text{C}_2\text{H}_5\text{OH}) \\ \text{C}_{16}\text{H}_{16}\text{Cl}_3\text{Zn NO}_2 \end{array}$ | 24–159<br>159–392<br>392–718 | 9.83<br>17.46<br>55.46<br>17.01  | 10.79<br>16.63<br>53.46<br>19.1  | Loss of ethanol molecule<br>Loss of coordinated 2Cl ion<br>Dissociation of the organic ligand<br>ZnO  |
| C4    | $\begin{array}{l} [CdL\cdot(Cl)_2]_{\cdot}\left(C_2H_5OH\right)\\ C_{16}H_{16}Cl_3CdNO_2 \end{array}$  | 26–149<br>149–436<br>436–663 | 8.79<br>21.70<br>41.82<br>27.67  | 9.72<br>22.47<br>40.62<br>27.14  | Loss of ethanol molecule<br>Loss of 3Cl<br>Dissociation of the organic ligand<br>CdO  |

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was assigned to the loss of water molecules. The second step appeared within the temperature ranges 120–299°C, corresponding to the loss of four chlorides atoms for C1. The third and fourth steps of decomposition appeared at temperature ranges 299–735°C for complex C1 corresponding to the loss of the organic ligand, and the final product of decomposition left behind was assigned as the thermally stable CoO.

Complex C2 decomposed in four successive decomposition steps. The first and second steps appeared within the temperature range 23–199°C, which were assigned to the loss of six water molecules. The third step of decomposition appeared within the ranges 199–444°C, corresponding to the loss of two chloride anion. The last step of decomposition (444–730°C) corresponded to further decomposition of the organic ligand. The final product of decomposition left behind was assigned as the thermally stable MnO + 8C.

Complexes C3 and C4 gave three stages of decomposition processes. The first step of decomposition appeared within the temperature ranges 24–159 and 26–149°C, respectively, and was assigned to the loss of ethanol molecule. The second step appeared within the temperature ranges 159–392 and 149–436°C for complexes C3 and C4, respectively, corresponding to the loss of three chloride atoms for C4. The last step of decomposition was at 392–718 and 436–663°C for complexes C3 and C4, respectively, corresponding to the further decomposition of the organic ligand. The final product of decomposition left behind was assigned as the thermally stable ZnO and CdO.

## 3.6 | The kinetic parameters of the decomposition processes of the complexes

The activation energy  $(E^*)$ , enthalpy  $(\Delta H^*)$ , entropy  $(\Delta S^*)$ and free energy of the decomposition  $(\Delta G^*)$  as well as the order (n) is evaluated graphically by using the Coats– Redfern<sup>[38]</sup> equation:

$$\ln\left[\frac{1 - [1 - \alpha]^{1 - n}}{[1 - n]T^2}\right] = \frac{M}{T} + B \text{ for } n \neq 1$$
 (1)

$$\ln\left[\frac{-\ln[1-\alpha]}{T^2}\right] = \frac{M}{T} + B \text{ for } n = 1$$
(2)

where M = -E/R and  $B = \ln (ZR/\varphi E)$ , where *E*, *R*, *Z* and  $\varphi$  are the activation energy, gas constant, pre-exponential factor and heating rate, respectively, n = 0, 0.33, 0.5, 0.66, 1. The order (*n*) and thermokinetic parameters of the decomposition steps for the chosen complexes are listed in Table 5. From the obtained data, the following observations were made.

- 1. The  $\Delta S^*$  values for complexes were found to be positive. This indicates that the activated complex is less ordered than the reactants and/or the reactions are fast.<sup>[39]</sup>
- 2. The values of  $\Delta G^*$  increase and decrease significantly for subsequent decomposition stages due to increasing or decreasing the values of  $T\Delta S^*$  from one step to another, which override the values of

|         |       |              | Coats- | Redfern    |           |              |               |              |
|---------|-------|--------------|--------|------------|-----------|--------------|---------------|--------------|
| Complex | Steps | <i>T</i> (K) | n      | r          | $E^*$     | $\Delta H^*$ | $-\Delta S^*$ | $\Delta G^*$ |
| C1      | 1     | 353          | 1      | -0.9917824 | 9.6045809 | 6.6697389    | 0.0873084     | 37.48962     |
|         | 2     | 498.5        | 1      | -0.9918643 | 14.404004 | 10.259475    | 0.0922166     | 56.22945     |
|         | 3     | 674.25       | 1      | -0.9999019 | 31.218162 | 25.612447    | 0.1111245     | 100.5381     |
|         | 4     | 794.75       | 1      | -0.9816343 | 73.226897 | 66.619345    | 0.1405206     | 178.2981     |
| C2      | 1     | 329          | 1      | -0.9913327 | 45.974145 | 43.238839    | 0.2019277     | 109.673      |
|         | 2     | 415.75       | 1      | -0.9902433 | 24.6492   | 21.192655    | 0.1170319     | 69.84867     |
|         | 3     | 612          | 0      | -0.9949615 | 14.026481 | 8.9383133    | 0.0857255     | 61.402323    |
|         | 4     | 901.75       | 1      | -0.9925623 | 115.89734 | 108.40019    | 0.0773851     | 178.1822     |
| C3      | 1     | 371.25       | 1      | -0.9958815 | 2.9269016 | 0.1596709    | 0.0847936     | 31.63929     |
|         | 2     | 546.25       | 1      | -0.9905973 | 19.216575 | 14.675053    | 0.0972558     | 67.80103     |
|         | 3     | 908.75       | 1      | -0.9964788 | 211.04678 | 203.49143    | 0.1958555     | 381.4751     |
| C4      | 1     | 364.75       | 1      | -0.9754141 | 15.050419 | 12.017887    | 0.0940093     | 46.3078      |
|         | 2     | 578          | 1      | -0.9805662 | 13.690393 | 8.8849015    | 0.0821868     | 56.38887     |
|         | 3     | 868.25       | 0      | -0.99972   | 42.56595  | 35.347323    | 0.100569      | 122.6661     |

TABLE 5 Temperatures of decomposition and activation parameters (kJ/mol) of decomposition for the investigated metal complexes

 $\Delta H^*$ . This increase or decrease reflects that the rate of removal of the subsequent chemosensor will be lower/higher than that of the precedent chemosensor.<sup>[40]</sup> This may be attributed to the structural rigidity of the remaining complex after the expulsion of one or more ligands, as compared with the preceding complex, which requires more energy for its rearrangement before undergoing any compositional change.

The positive values of ΔH<sup>\*</sup> mean that the decomposition processes are endothermic<sup>[41]</sup> (data shown in Table 5 and Figures S5a–d).



**FIGURE 4** Comparison of experimental and theoretical infrared (IR) spectra of ligand



FIGURE 5 Computational structure of the ligand

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### 3.7 | Molecular modeling

### 3.7.1 | IR analysis

The theoretical IR spectrum was estimated to produce the spectroscopic signs of the ligand, and exhibits the vC=O band (measured: 1675 cm<sup>-1</sup>; predicted: 1628 cm<sup>-1</sup>) and vC=N band (measured: 1496 cm<sup>-1</sup>; predicted: 1474 cm<sup>-1</sup>). The small differences between the predicted and measured frequencies are illustrated in Figure 4. The fundamental purpose behind the distinction is that the count was performed in a vacuum, while the measurements were refined for solid state. The lower symmetry is the main reason for the complexity of the vibrational modes of the investigated chemosensor. All plane modes are difficult to assign, due to the ring modes besides the imitative, especially torsion. Regardless, the presence of some supportive vibrations is in a good agreement with the obtained graph.

### 3.7.2 | Geometry optimization and chemical reactivity

The optimized structural models are shown in Figures 5–9. Inspection of the bond distances and angles is shown in Tables S1 and S2, and the subsequent observations were made.

- 1. The active groups (C=O and C=N) are elongated upon coordination with the metal ion. This refers to the formation of M-N and M-O bonds,<sup>[42]</sup> which enable the C=N and C=O bonds to become weaker.
- 2. The M-N and M-O band distances are in agreement with the sum of covalent radii for M and N or O atoms, and are similar to values reported earlier.<sup>[43]</sup>
- 3. In C3 and C4, the two axial positions are occupied by chloride ions, exhibiting that the bond distances of M-Cl are longer than M-N and M-O.
- The bond angles are similar to those reported for octahedral C1 and C2 complexes with d<sup>2</sup>sp<sup>3</sup> or sp<sup>3</sup>d<sup>2</sup>



FIGURE 6 Computational structure of complex C1



FIGURE 7 Computational structure of complex C2



FIGURE 8 Computational structure of complex C3



FIGURE 9 Computational structure of complex C4

hybrid orbitals; while C3 and C4 exhibit tetrahedral geometry with sp<sup>3</sup> hybrid orbitals.

The highest occupied molecular orbital (HOMO) level is defined as the one that essentially shows electron donation behavior. And the lowest unoccupied molecular orbital (LUMO) is the one that significantly acts as an electron acceptor. Both named frontier molecular orbitals (FMOs; Figures S6–S10) estimate electric optical properties, electronic transitions and kinetic stability.<sup>[44]</sup> The FMOs hypothesis anticipates sites of coordination (electrophilic attack) on an aromatic compound. The interaction between the HOMO of one moiety with the LUMO on another is a major reason in most of the reactions. We can demonstrate from computation that the oxygen of the C=O group has the largest values of molecular orbital coefficients, showing that it is a suitable site of complexation.

The energy gap ( $\Delta E = E_{\text{HOMO}} - E_{\text{LUMO}}$ ), chemical descriptors such as softness (*S*), hardness ( $\eta$ ), electronegativity ( $\chi$ ), chemical potential ( $\mu$ ) and electrophilicity ( $\omega$ ) and softness ( $\sigma$ ) for the isolated compounds were shown in Table S3. These descriptors can be estimated using the following equations:<sup>[45–48]</sup>

$$\chi$$
 (electronegativity) =  $-1/2 (E_{\text{LUMO}} + E_{\text{HOMO}})$  (3)

$$\mu \text{ (potential)} = -\chi = 1/2 \left( E_{\text{LUMO}} + E_{\text{HOMO}} \right) \quad (4)$$

$$\eta \text{ (hardness)} = 1/2 \left( E_{\text{LUMO}} - E_{\text{HOMO}} \right) \tag{5}$$

$$S (\text{softness}) = 1/2\eta$$
 (6)

$$\omega \text{ (electrophilicity)} = \mu^2 / 2\eta \tag{7}$$

The inverse value of the global hardness is designed as the softness  $\sigma$  as follows:

$$\sigma = 1/\eta \tag{8}$$

According to calculation results in Table S3, the following were shown.

- i. The  $E_{\text{HOMO}}$  and  $E_{\text{LUMO}}$  are almost negative, showing the stability of the isolated compounds.<sup>[49,50]</sup>
- ii. Gutmann's variation rules, "the bond strength increases as the neighboring bonds become weaker", such as found by Linert and Taha.<sup>[51]</sup> This interpretation agrees well with the result, as the increase of the  $E_{\text{HOMO}}$  is conveyed by a weakness (elongation) of the metal–ligand bond, which prompts a reinforcing (shortness) of the sites next to the metal–ligand centers.
- iii. A hard molecule is represented by a large HOMO LUMO difference, while a soft and more active framework has a small energy difference. The chemical potential ' $\mu$ ' that estimates the escaping capability of electrons from its equilibrium framework diminishes as follows: C2 (-3.248) > C1 (-3.499) > ligand (-4576) > C3 (-4.895) = C4 (-4.895).
- iv. The importance of  $\eta$  and  $\sigma$  are to measure the molecular stability and reactivity. In a complex formation system, metal ions are Lewis acids (soft acids), and

thus Lewis base (soft base) ligands are most effective for complex formation. Accordingly, it is concluded that the investigated ligand with a proper  $\sigma$  value has a good tendency to chelate metal ions effectively.<sup>[52]</sup>

The calculations of the total energy (Table 6) revealed that the increase in the value of the calculated binding energy of complexes compared with that of the ligand indicates that the stability of the formed metal complexes is higher than that of the ligand. The dipole moment values of the complexes are larger than the ligand value, except the dipole moment of  $\text{Co}^{2+}$  complex (C1) has a lower value than that of the ligand. The lowest value of the dipole moment of  $\text{Co}^{2+}$  complex may be due to the trans-isomer of both ligand moieties, which are equal and opposite.<sup>[53]</sup>

The structure-activity relationship studies were investigated to correlate the antimicrobial properties of the studied compounds related to physicochemical properties. The dipole moments are the property of interest that gives some insight into the degree of hydrophobicity/hydrophilicity of the compounds. As the dipole moment decreases, the polarity decreases. Thus, the lipophilic nature of the compound increases, which favors its permeation through the lipid layer of the microorganism, then destroying them.

### 3.7.3 | Molecular electrostatic potential (MEP)

Molecular electrostatic potential is graphed based on the electron density surface. It is additionally exceptionally valuable in the research of sub-atomic structure with its physiochemical property association and hydrogen bonding interactions.<sup>[54–56]</sup> The electrostatic potential V(r) at a given point r(x, y, z) is characterized as a function of the

interaction energy between the electrical charge produced from the electrons, nuclei and protons placed at r.<sup>[57]</sup> Calculation of the electrostatic potential is feasible for atoms utilizing the  $\Gamma$ -point and various k-points. In the current investigation, 3D plots of MEPs of ligands and their metal complexes (Figures S11–S15) have been produced. The largest negative part, which is the desired



SCHEME 1 The structure of the formed complexes

TABLE 6 Some energy of the investigated chemosensor, CPPEO, calculated by D-Mol<sup>3</sup> method using DFT-calculation

| Compound                               | Free chemosensor       | C1                     | C2                     | C3                     | C4                     |
|--|------------------------|------------------------|------------------------|------------------------|------------------------|
| Sum of atomic energies (kcal/mol)      | $-7.06 \times 10^{05}$ | $-1.61 \times 10^{06}$ | $-9.73 \times 10^{05}$ | $-1.44 \times 10^{06}$ | $-1.34 \times 10^{06}$ |
| Kinetic energy (kcal/mol)              | $-4.99 \times 10^{03}$ | $-8.69 \times 10^{03}$ | $-4.19 \times 10^{03}$ | $-5.88 \times 10^{03}$ | $-4.97 \times 10^{03}$ |
| Electrostatic energy (kcal/mol)        | $-4.82 \times 10^{02}$ | $-3.51 \times 10^{03}$ | $-3.38 \times 10^{03}$ | $9.74 \times 10^{01}$  | $-7.52 \times 10^{02}$ |
| Exchange-correlation energy (kcal/mol) | $1.18 \times 10^{03}$  | $2.69 \times 10^{03}$  | $1.65 \times 1003$     | $1.27 \times 10^{03}$  | $1.24 \times 10^{03}$  |
| Spin polarization (kcal/mol)           | $9.12 \times 10^{02}$  | $2.03 \times 10^{03}$  | $1.38 \times 10^{03}$  | $9.29 \times 10^{02}$  | $9.08 \times 10^{02}$  |
| Total energy (kcal/mol)                | $-7.09 \times 10^{05}$ | $-1.62 \times 10^{06}$ | $-9.78 \times 10^{05}$ | $-1.45 \times 10^{06}$ | $-1.34 \times 10^{06}$ |
| Binding energy (kcal/mol)              | $-3.37 \times 10^{03}$ | $-7.48 \times 10^{03}$ | $-4.54 \times 10^{03}$ | $-3.59 \times 10^{03}$ | $-3.58 \times 10^{03}$ |
| Dipole moment (Debye)                  | 3.4128                 | 1.3896                 | 11.2473                | 5.3146                 | 7.8108                 |

site for electrophilic attack, is indicated by red shading; the largest positive region, which is the desired site for nucleophilic attack, is indicated by the blue color. The potential decreases as follows: red < green < blue, where blue demonstrates the most preferred site for the attraction and red reveals the best site for the repulsion. The areas with negative potential are over the electronegative molecules, while the districts with positive potential are over the hydrogen atoms.

### 3.7.4 | Mulliken atomic charges

Mulliken atomic charge estimation of ligands and their complexes (Figure S16; Tables S4–S8) shows a significant role in the procedure of theoretical approximation of the molecular framework. Figure S16 elucidates the charge distribution of ligand. Both nitrogen and oxygen atoms have negative values due to their donating ability. On the other hand, hydrogen atoms and most of the carbon atoms displayed positive values because of their accepting ability. Based on the above results, the structures of the mentioned complexes were shown in Scheme 1.

### 3.8 | Optical sensing of metal ions using the investigated chemosensor, CPPEO

In order to evaluate the metal-binding potential, the optical properties of the investigated 3-(4-chlorophenyl)-1-(pyridin-2-yl)prop-2-en-1-one (CPPEO) were investigated using absorption and emission techniques in the presence of metal ions such as  $Mn^{2+}$ ,  $Cd^{2+}$ ,  $Zn^{2+}$  and  $Co^{2+}$ . As can be seen in Figure 10, the investigated CPPEO exhibited a broad band at  $\lambda_{max} = 321$  nm with an extinction coefficient  $\varepsilon \approx 3.9 \times 10^4 \text{ M}^{-1} \text{ cm}^{-1}$  in MeOH. Addition of  $Mn^{2+}$  and  $Co^{2+}$  ions resulted in marked changes both in the energy and the shape of the absorption spectra of the investigated CPPEO. More dramatic changes occurred within the ranges  $4-28 \times 10^{-4}$  M, which produced intense new bands at 357 and 367 nm, respectively. However, for the interaction of the investigated CPPEO with Cd<sup>2+</sup> and Zn<sup>2+</sup> ions in MeOH, the band shifts only to a small extent. Additionally, well-defined isosbestic points appear at 337, 338, 341 and 345 nm for Mn<sup>2+</sup>, Cd<sup>2+</sup>, Zn<sup>2+</sup> and Co<sup>2+</sup>, respectively. These results confirm the existence of two species in equilibrium, and imply the presence of ground-state complexation between the investigated CPPEO and the studied metal ions via the nitrogen of the pyridine moiety and the oxygen of the carbonyl



**FIGURE 10** Absorption spectra of  $2 \times 10^{-5}$  M CPPEO in the absence and presence of different concentrations of the used metal ions in MeOH

group. This leads to enhancing the ICT interaction, which causes a significant shift in the presence of strongly complexing metal ions.

For the synthesized chemosensor, recognition reversibility is an important requirement for continuous recyclability and reusability. Its optical response to  $Mn^{2+}$ ,  $Cd^{2+}$ ,  $Zn^{2+}$  and  $Co^{2+}$  ions was found to be fully reversible on adding EDTA to the formed complex (Figure 11),



**FIGURE 11** The absorption spectra of the reversible interaction of dye/metal ions complexes in the presence of EDTA



**FIGURE 12** Benesi-Hildebrand plots for the binding of CPPEO with the used metal ions

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where the metal ion chelator restored the original absorbance and the nano-sensor exists largely in the switched-off state.

The ground-state binding constants of  $Mn^{2+}$ ,  $Cd^{2+}$ ,  $Zn^{2+}$  and  $Co^{2+}$  complexes with the investigated dye were determined by employing the Benesi Hildebrand equation<sup>[58]</sup> as follows:

$$\frac{[\text{Lo}]}{A - A_{\text{o}}} = \frac{1}{\varepsilon_{\text{ML}} - \varepsilon_{\text{L}}} + \frac{1}{(\varepsilon_{\text{ML}} - \varepsilon_{\text{L}})K[\text{M}]}$$
(9)

where  $A_0$  and A are the absorbance values of the free dye solution and with the metal complex at a given wavelength;  $\varepsilon_{\rm L}$  and  $\varepsilon_{\rm ML}$  are the molar extinction coefficients of the investigated dye and its metal complex, [M] is the concentration of the studied metal ions,  $[L_0]$  is the initial concentration of the investigated dye, and K is the binding constant for the interaction, which is determined from the plots of  $\frac{[\text{Lo}]}{A - A_0}$  against 1/[M] (Figure 12). The binding constants, K, for the complexes of the investigated dyes with the mentioned metal ions were calculated, and are summarized in Table 7. The obtained data indicate that  $Co^{2+}$  is the strongest binding metal ion with the investigated chemosensor compared with the other tested metal ions, indicating that Co<sup>2+</sup> is the most effectively detected and the potential of the novel dye as highly efficient switchers for  $Co^{2+}$  ions.

A much greater effect has been observed on recording the emission spectra of the investigated CPPEO in the presence of methanolic solutions of Zn<sup>2+</sup>, Cd<sup>2+</sup>, Co<sup>2+</sup> and Mn<sup>2+</sup>, as shown in Figure 13. The fluorescence of the investigated CPPEO appears as a broad and structureless band with a maximum at about 456 nm in MeOH. Upon adding different concentrations of  $Zn^{2+}$ ,  $Cd^{2+}$ ,  $Co^{2+}$  and  $Mn^{2+}$  ions within the ranges  $(0.2-35) \times 10^{-4}$  M, the fluorescence intensities of the chemosensor increase gradually pronounced with hypsochromic shifted bands. The continuous

**TABLE 7** Spectroscopic parameters, absorption (<sup>a</sup>) and fluorescence (<sup>f</sup>) maxima, the binding constants,  $K(M^{-1})$ , in the ground and excited states for the studied metal ions with the investigated chemosensor, CPPEO

| Metal ion        | $\lambda_{\max}^{a}$ , nm | Isosbestic point | $\lambda_{\max}^{f}$ , nm | $K_{b1 (M)}^{-1}$ | $K_{b2}^{*} (M^{-1})$ |
|------------------|---------------------------|------------------|---------------------------|-------------------|-----------------------|
| Cd <sup>2+</sup> | 321*, 328                 | 338              | 457*, 450                 | 123.46            | 115.05                |
| Zn <sup>2+</sup> | 329                       | 341              | 463                       | 306.32            | 359.47                |
| Co <sup>2+</sup> | 367                       | 345              | 402                       | 534.80            | 901.87                |
| Mn <sup>2+</sup> | 357                       | 337              | 402, 446                  | 169.3             | 249.48                |

<sup>a</sup>absorption.

fluorescence.

\*the binding constant calculated in the excited state.



FIGURE 13 Fluorescence spectra of CPPEO upon addition of different metal ions in MeOH

Wavelength (nm)

600

enhancement in the fluorescence intensities suggests the optical chemosensor as a potential design for the off-on sensitive sensing of metal ions and confirming their role in the semi-quantitative detection of these metal ions.

400

The binding constants of the formed complexes between the investigated chemosensor and the used metal ions were also calculated from the emission spectra using the Benesi–Hildebrand equation:<sup>[58]</sup>

$$\frac{1}{\Delta F} = \frac{1}{\Delta F \max} + \left(\frac{1}{K[M]^{n+}}\right) \left(\frac{1}{\Delta F \max}\right)$$
(10)

where  $\Delta F = F_x - F_o$  and  $\Delta F_{max} = F_{\infty} - F_o$ , and where  $F_{\rm o}$ ,  $F_{\rm x}$  and  $F_{\infty}$  are the emission intensities of the nano-sensors, considered in the absence of metal ions, at certain metal ions concentrations, and at the concentration of complete interaction, respectively.  $[M]^{n+}$  is the concentration of the metal ions and K is the binding constant for the interaction, which is determined from the plots of  $1/\Delta F$  against  $1/[M]^{n+}$ . Typical linear reciprocal plots were obtained. The binding constants, K, were calculated from the intercept and the slope ratio (Table 7). As can be seen in Figure 14, the binding constant values increase in the order  $Co^{2+} > Zn^{2+} >$  $Mn^{2+} > Cd^{2+}$  complexes.

#### | Docking analysis 3.9

The free energy of binding, inhibition constant  $(K_i)$ , total estimated energy of  $vd_W + H_{bond} + de_{solv}$  (EVHD),



Wavelength (nm)

FIGURE 14 Benesi-Hildebrand plots for the binding of CPPEO with the used metal ions

electrostatic energy, the total intermolecular energy, frequency of binding, and interacting surface area parameters were evaluated to estimate the favorable binding of the ligand to the protein. Table S9 shows the complete profile of these parameters of the ligand for its interaction with receptor of P. vulgaris (4mcx-toxin) and secreted from C. albicans (5kbk- oxidoreductase).

One of the most favorable bindings of the ligand was its binding with 5kbk protein with the estimated free energy of binding -4.78 kcal/mol, and total intermolecular energy of -5.63 kcal/mol. The ligand showed the inhibition constant ( $K_i$ ) of 314.91 mM. Figure S17 shows the binding of the ligand to the protein 5kbk. The ligand

was bound with 4mcx protein with an estimated free energy of binding -4.93 kcal/mol, and the total intermolecular energy was -5.80 kcal/mol. The ligand showed the inhibition constant  $(K_i)$  of 241.43 mM. Figure S18 shows the binding of the ligand to the protein 4mcx. A HB plot<sup>[42,59]</sup> was generated to mention interactions with different amino acids of the proteins (Figures S19 and S20). A 2D plot was generated where ligand bond, nonligand bond and hydrogen bonds along with their length were mentioned (Figures S21 and S22). Table S9 exhibited the clustering results obtained from the docking of the ligand into 5kbk and 4mcx proteins. Based on the results of docking studies, it has been clearly expressed that the ligand possibly showed favorable binding with 5kbk and 4mcx. Hence, the ligand can be a potential inhibitor to the pathogenic microorganisms like bacteria and fungi. This interaction could deactivate or kill the microorganisms. The characteristic feature of the ligand was represented in the presence of several active sites available for hydrogen bonding interaction. This theoretical analysis proposes the high biological activity of the organic ligand towards different bacteria or fungi.

### 3.10 | Biological screening

### 3.10.1 | Antimicrobial activity

The screening results of antimicrobial activity for metal complexes in comparison with the free chemosensor are summarized in Table 8 and represented in Figure 15. The chemosensor showed activity towards *P. vulgaris* only. Generally, the investigated chemosensor has lower activity than the complexes, and complexes showed the highest activity towards Gram-positive bacteria and Gram-negative bacteria.



FIGURE 15 Antimicrobial assay for the investigated metal complexes

In the present case, the activity is dependent on the central metal ion and its ability to diffuse into the cell membrane of the organism.

The variation in the activity of different complexes against different microorganisms depends either on the impermeability of the cells of the microbes or differences in ribosomes in microbial cells.<sup>[60]</sup> The data listed in Table 8 indicated that all the tested compounds showed a moderate to good antimicrobial activity against the tested microorganisms when compared with the standard drugs, except for *Acinetobacter*.

Co (II) complex was more active against Gram-positive than other complexes, while Mn (II) complex was inactive against Gram-negative bacteria such as *E. coli* only. It may be concluded that the antimicrobial activity of the compounds is related to the cell wall structure of the bacteria. It is possible because the cell wall is essential to the survival of bacteria and some antibiotics are able to kill bacteria by inhibiting a step in the synthesis of peptidoglycan. Gram-positive bacteria possess a thick cell wall containing many layers of peptidoglycan and teichoic

|        | Inhibition zone diameter (mm/mg sample) |                         |                     |                           |                          |                     |               |                |  |  |
|--------|---|-------------------------|---------------------|---------------------------|--------------------------|---------------------|---------------|----------------|--|--|
|        | Gram (+)-bacteria                       |                         | Gram (–)-bacteria   |                           |                          |                     |               | Fungus         |  |  |
|        | Staphylococcus<br>aureus                | Enterococcus<br>cloacae | Escherichia<br>coli | Pseudomonas<br>aeruginosa | Klebsiella<br>pneumoniae | Proteus<br>vulgaris | Acinetobacter | Trichophyton   |  |  |
| Sample | 1                                       | 2                       | 3                   | 4                         | 5                        | 6                   | 7             | mentagrophytes |  |  |
| C1     | 14.33 ± 1.25                            | $13.66 \pm 0.76$        | 14.83 ± 1.04        | 14.5 ± 1                  | 14.66 ± 0.76             | 14.33 ± 1.15        | 0             | $13 \pm 1$     |  |  |
| C2     | $21 \pm 1$                              | 0                       | 0                   | 12                        | 9.33 ± 1.25              | 9.5 ± 1             | 0             | 0              |  |  |
| C3     | $23.83 \pm 0.76$                        | 0                       | 15.33 ± 1.25        | 15                        | 10.5 ± 1                 | $10 \pm 1$          | 0             | $13 \pm 1.25$  |  |  |
| C4     | 22.66 ± 0.76                            | 0                       | 12.33 ± 1.25        | 13                        | 9.33 ± 1.15              | 9.5 ± 1             | 0             | $12 \pm 0.76$  |  |  |

TABLE 8 Antimicrobial activity data of the investigated metal complexes

Mean  $\pm$  SD = standard deviation.

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TABLE 9 Diameters of inhibition zones (mm) of the metal complexes against different test Candida types

| Types of Candida |       |                                       |    |                |                    |  |  |  |  |
|------------------|-------|---------------------------------------|----|----------------|--------------------|--|--|--|--|
| Candida albicans |       | Candida dubliniensis Candida glabrata |    | Candida krusei | Candida tropicalis |  |  |  |  |
| N.O.             | 1     | 2                                     | 3  | 4              | 5                  |  |  |  |  |
| Free chemosensor | 11.66 | 13                                    | 10 | 12             | 14                 |  |  |  |  |
| C1               | 11    | 10                                    | 0  | 10             | 11                 |  |  |  |  |
| C2               | 13    | 13                                    | 10 | 10             | 13                 |  |  |  |  |
| C3               | 11    | 11                                    | 13 | 11             | 12                 |  |  |  |  |
| C4               | 11    | 11                                    | 14 | 14             | 12                 |  |  |  |  |



FIGURE 16 Antifungal assay for the investigated metal complexes

acids but, in contrast, Gram-negative bacteria have a relatively thin cell wall consisting of a few layers of peptidoglycan surrounded by a second lipid membrane containing lipopolysaccharides and lipoproteins. These differences in cell wall structure can produce differences in antibacterial susceptibility, and some antibiotics can kill only Gram-positive bacteria and are infective against Gram-negative pathogens.<sup>[61]</sup>

### 3.10.2 | Antifungal activity (different *Candida* types)

For the sensitive organisms *C. albicans*, *C. dubliniensis*, *C. glabrata*, *C. krusei* and *C. tropicalis*, the diameter of the inhibition zone (mm) was used to compare the antifungal activity of the complexes with that of the free chemosensor (Table 9; Figure 16).

The free chemosensor and its complexes were biologically active against all *Candida* types, except Co (II) was inactive towards *C. glabrata*. In addition to chemosensor, Cu (II) and Mn (II) complexes were biologically inactive against *T. mentagrophytes*.

### 4 | CONCLUSION

Co (II), Mn (II), Zn (II) and Cd (II) complexes of the titled chemosensor have been synthesized and characterized by analytical and spectral methods. The data indicated that the investigated ligand acts as a bidentate ligand coordinated to the metal ions via the O and N atoms of the C=O and C=N groups, respectively. The spectral and magnetic data revealed the formation of octahedral complexes for Co (II), Mn (II), Zn (II) and Cd (II) complexes, while Cu (II) complex has a tetrahedral geometry. The thermal properties of the metal complexes have been investigated using the TG technique. The kinetic and thermodynamic parameters of the decomposition steps have been calculated. The optical sensing responses of the investigated chemosensor to the different metal ions were investigated. It responds well to the tested metal ions as reflected from the significant change in both absorption and emission spectra upon adding different concentrations of the metal salts, confirming the intramolecular charge transfer of the chemosensor upon effective coordination with the used metal ions. This leads to enhancing ICT interaction, causing a significant shift in the presence of strongly complexing metal ions. They were fully reversible on adding EDTA to the formed complexes. Also, the solution of dye-metal ion complex was decomplexed by adding a solution of EDTA to revert the original spectrum of the dye, thus demonstrating the reversibility of the sensing. Molecular orbital calculations have been performed for the ligand and its complexes. Finally, the antibacterial and antifungal activities of the ligand and its complexes have been tested.

### ORCID

*M. Gaber* <sup>(D)</sup> https://orcid.org/0000-0003-2315-5710 *Tarek A. Fayed* <sup>(D)</sup> https://orcid.org/0000-0001-6353-6978 *Marwa N. El-Nahass* <sup>(D)</sup> https://orcid.org/0000-0002-7464-404X Mohammed M. El-Gamil https://orcid.org/0000-0001-5605-2844

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### SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section at the end of the article.

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