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Design and synthesis of Co(II) and Cu(II) complexes of a dendrimeric chelate: promising anticandidal potential of chelotherapeutic agents

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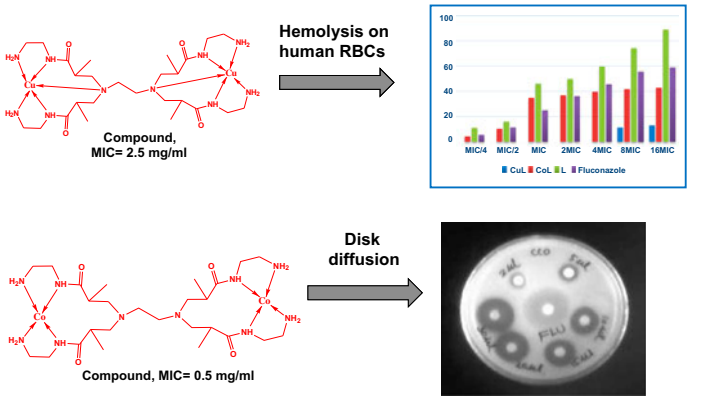

In response to an increasing demand for effective anticandidal agents, a new water-soluble dendrimeric ligand (L) was synthesized by Michael addition of ethylenediamine to methyl methacrylate. The prepared ligand was complexed with Cu(II) and Co(II) ions. Both the ligand and its complexes were characterized by elemental analysis and spectroscopic studies (FT-IR, UV–vis, ^{1}H NMR, and ESI-MS). Square-planar and square-pyramidal geometries were proposed for Cu(II) and Co(II) on the basis of UV–vis spectroscopic data and molar conductance measurements. The ligand and its Cu (II) and Co(II) complexes were screened on *Candida albicans* ATCC 90028 by determining MICs (minimal inhibitory concentrations) and inhibition in solid media (disk diffusion assay). Hemolysis assays on human RBCs indicated that the toxicity of the copper complex was lower as compared to fluconazole. These results taken with limited toxicity make them eligible for further development as antifungals.

Keywords: Dendrimeric ligand; Water soluble; *Candida albicans*; Anticandidal; Hemolysis

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1. Introduction

Fungal infections affect a large fraction of the human population with more adverse effects in immuno-compromised patients [1]. The main causes of the increase in primary and opportunistic fungal infections are the prolonged uses of antibiotics, cancer chemotherapy regimes, and the occurrence of HIV infections [2, 3]. *Candida albicans* has been established as the main agent responsible for most candidal diseases. Some other *Candida* species *viz. Candida glabrata* and *Candida krusei* also pose serious threats [4, 5]. Despite availability of some antifungal drugs, the treatment of invasive candidiasis is still a challenge owing to adverse effects and resistance associated with the widespread use of these drugs [6, 7]. Fluconazole, itraconazole, voriconazole, and posaconazole (figure S1, see online supplemental material at http://dx.doi.org/10.1080/00958972.2015.1040007) are widely used antifungal drugs for the treatment of systemic fungal infections [8, 9].

To overcome this problem of fungal resistance and drug toxicity, development of new active compounds is a matter of urgency. Dendrimers offer several pharmacological advantages as drug carrier candidates. The unique features associated with chemical topologies of dendrimers have led to their widespread use in medicinal chemistry, including diagnostic reagents, protein mimetics, anticancer and antiviral agents, vaccines, drug, and gene delivery systems [10–19]. Metal complexes have been used against several pathogenic microorganisms including fungi and bacteria. A large number of copper(II) and cobalt(II) complexes are reported as antifungal and antibacterial agents, and quite interesting results have been reported in some cases [20–22].

A thorough search of the literature indicated that no report is available on metal complexes of dendrimeric ligands as antifungal agents. Therefore, this report opens a new window for the development of dendrimeric ligands and their complexes as effective antifungal agents. Attempts were made to synthesize a dendrimeric ligand and its metal complexes. The prepared ligand and its complexes were characterized by various physicochemical, analytical, and spectroscopic techniques. Finally, the ligand and its complexes were investigated for their antifungal activities against *C. albicans* ATCC 90028. The synthesized metal complexes can be explored as less resistant and safer alternatives which can be used alone or in combination with existing antifungals.

2. Experimental

2.1. *Materials and methods*

All chemicals were of AR Grades and used without purification. Ethylenediamine and methyl methacrylate were purchased from S.D. Fine Chem. Ltd, Mumbai, India. Metal chlorides (copper(II) chloride dihydrate and cobalt(II) chloride hexahydrate) and methanol were procured from E. Merck, Mumbai, India. Pre-coated aluminum silica gel $60F_{254}$ thin layer plates were purchased from E. Merck, Germany. Stock cultures of the microorganisms were maintained on nutrient agar slants and stored at 4 °C. *C. albicans* ATCC 90028 was grown in YPD media at 37 °C in an orbital shaker at 200 rpm (REMI CIS 24 BL). YPD medium consisted of 2% (w/v) glucose, 2% peptone, and 1% yeast extract (Hi Media, India).

The percentages of C, H, and N were determined by a Vario EL elemental analyzer. Electronic spectra were recorded on a Perkin Elmer Lambda-40 double-beam UV–visible spectrophotometer. FTIR spectra of the compounds were recorded on a Perkin Elmer 1750

FTIR spectrophotometer (CT 06859 USA) using KBr pellets from 4000 to 400 cm^{-1}. ^1H NMR spectra were achieved with a Bruker (DRX-400) spectrometer. Mass spectra were recorded using Model-Q-TOF Micromass ESI source. Molar conductance measurements were carried out on a Decibel Conductivity Meter at room temperature (DB-1038). Melting points were determined on a Veego instrument (REC-2203882).

2.2. *Synthesis of dendrimeric ligand (L)*

Ethylenediamine (0.1 M) and methyl methacrylate (0.4 M) in methanol were mixed together in a round-bottom flask and stirred for 24 h at room temperature. Afterwards, ethylenediamine (0.04 M) was added and refluxed for a further 24 h at 60–65 °C. The golden yellow oily liquid (ligand) was obtained. Yield: 96%, mol. wt. = 572.78, golden yellow oily liquid, Anal. Calcd for $C_{26}H_{56}N_{10}O_4$ (%): C, 54.52; H, 9.9; N, 24.45. Found: C, 54.1; H, 9.2; N, 24.5; IR (KBr pellets, cm^{-1}): 3885 (N–H)str., 1650 (C=O), 1125 (C–N), 3300 (–NH_2)str., 1575 (NH_2)bend.; ^1H NMR (D_2O, ppm): 3.163 (–CH_2, t), 3.459 (–CH_2, t), 3.061 (–CH, t), 0.926 (–CH_3, d), 4.679 (–CH_2, s), 3.380–2.610 (–CH, septet); ESI-MS (*m/z*): 453.4 [M-$C_4N_4H_{14}$ − H^+], 338.5 [M-$C_8N_8H_{28}$ + $2H^+$], 125.2 [M-$C_{18}H_{42}N_9O_4$ + H^+], 108.1 [M-$C_{19}H_{42}N_9O_4$ − $4H^+$], 99.6 [M-$C_{20}H_{42}N_9O_4$ + $3H^+$].

2.3. *Synthesis of metal complexes*

A methanolic solution of L (1 mM) was added to a methanolic solution of copper(II) chloride dihydrate (2 mM) with constant stirring at 40–50 °C. The stirring was continued for 6 h until a green precipitate of the complex formed. The precipitated complex was filtered and washed with methanol and dried under vacuum. Cobalt(II) complex was prepared by a similar procedure using cobalt(II) chloride hexahydrate.

CuL: Yield: 62.3%, mol. wt. = 841.67, m.p. > 300 °C, green solid, Anal. Calcd for $C_{26}H_{56}Cl_4Cu_2N_{10}O_4$: C, 37.1; H, 6.71; N, 16.64. Found: C, 37.5; H, 6.31; N, 15.9; IR (KBr pellets, cm^{-1}): 3420 (NH_2)str., 1590 (C=O)str., 3090 (N–H)str., 1220 (C–N)str., 450, 430, 475 (Cu–N); UV–vis. (H_2O, nm): 219 ($n \rightarrow \sigma^*$), 262 ($\pi \rightarrow \pi^*$), 324 ($n \rightarrow \pi^*$), 709 ($^2B_{1\ g} \rightarrow {}^2B_{2\ g}$); Molar conductance: 600.9 μS cm^{-1}; ESI-MS (*m/z*): 701.8 [M-4Cl + $2H^+$], 350.3 [M-$C_{13}H_{28}N_5O_2Cl_4$ + H^+], 288.2 [M-$C_{13}H_{28}N_5O_2CuCl_4$ + $2H^+$], 257.3 [M-$C_{13}H_{28}N_5O_4CuCl_4$ + $3H^+$], 220.1 [M-$C_{15}H_{34}N_5O_4CuCl_4$ − $4H^+$], 161.2 [{(M-4Cl)/2}–Cu–$C_4H_{13}N_2O_2$ − $4H^+$], 104 [{(M-4Cl)/2}–Cu–$C_6H_{20}N_4O_2$ − $2H^+$].

CoL: Yield: 59.1%, mol. wt. = 832.4, m.p. > 300 °C, violet powder, Anal. Calcd for $C_{26}H_{56}Cl_4Co_2N_{10}O_4$: C, 37.5; H, 6.8; N, 16.8. Found: C, 37.9; H, 7.2; N, 16.1; IR (KBr pellets, cm^{-1}): 3400 (NH_2)str., 3150 (N–H)str., 1650 (C=O)str., 1225, 1300 (C–N)str., 405, 520 (Co–N); UV–vis. (H_2O, nm): 488 ($^2A_{1\ g} \rightarrow {}^2E_g$); Molar conductance: 528 μS cm^{-1}; ESI-MS (*m/z*): 343.3 {(M-4Cl}/2 − $2H^+$], 313.2 {(M-4Cl)/2–2[O]$^+$}, 253 {(M-4Cl)/2–2 [O]–Co − H^+}, 245.2 [(M-4Cl)/2–Co–CH_2O_2 + $5H^+$], 209 [(M-4Cl)/2–Co–$C_3H_9O_2$ − H^+], 172.1 [(M-4Cl)/2–Co–$C_3H_{13}N_2O_2$ − $6H^+$], 101.0 [(M-4Cl)/2–Co–$C_8H_{22}N_3O_2$ + $6H^+$].

2.4. *Solution stability*

A quantitative estimation of the stability of the complexes at physiological pH was obtained by monitoring their UV–vis spectra in aqueous solutions of PBS at pH 7.4 for 24 h. Solutions of the complexes (10^{-4} M) were prepared in aqueous solutions of PBS at pH 7.4. The

hydrolysis profiles of the complexes were assessed by recording their electronic spectra over 24 h at 25 °C [23].

2.5. *Biological screening*

2.5.1. Minimal inhibitory concentration (MIC_{80}). The minimal inhibitory concentration (MIC) is the lowest concentration of the test compound that causes inhibition of visible growth (turbidity). MIC_{80} was determined *in vitro* in liquid medium by the broth microdilution method as per the guidelines of CLSI reference document M27-A3 [24] for fungi. Fluconazole was included as positive control in this study. In addition to this, a drug-free control was also included.

2.5.2. Disk diffusion assay. The assay was performed as discussed previously [25]. Briefly, strains were inoculated into liquid media and grown overnight at 37 °C. Cells were then washed three times with distilled water and approximately 1×10^5 cells mL^{-1} were inoculated into half-strength molten agar media at 42 °C and poured into 100 mm diameter petri plates. After the top layer had solidified, sterile paper disks (4 mm) were impregnated with the test compounds and placed on the agar surface. After incubation at 37 °C for 48 h, the size and pattern of the growth inhibition zone around the disk on agar were evaluated.

2.5.3. Hemolytic assay. Human erythrocytes from healthy individuals were harvested by centrifugation for 10 min at 2000 rpm at 20 °C and washed three times in PBS. To the pellet, PBS was added to yield a 10% (v/v) erythrocytes/PBS suspension. The 10% suspension was then diluted 1 : 10 in PBS. From each suspension, 100 μL was added in triplicate to 100 μL of different dilution series of test agents in the same buffer in Eppendorf tubes. Total hemolysis was achieved with 1% Triton X-100. The tubes were incubated for 1 h at 37 °C and centrifuged for 10 min at 2000 rpm from 20 °C. From the supernatant fluid, 150 μL was transferred to a flat-bottomed microtiter plate (BIO-RAD, iMark, US) and the absorbance was measured spectrophotometrically at 450 nm. The hemolysis percentage was calculated by the following equation:

$$\%\text{Hemolysis} = \left[\frac{\text{Abs}_{415}\text{ of tested compd. treated sample} - \text{Abs}_{415}\text{ of PBS treated sample}}{\text{Abs}_{415}\text{ of Tritou-X treated sample} - \text{Abs}_{415}\text{ of PBS treated sample}}\right] \times 100$$

3. Results and discussion

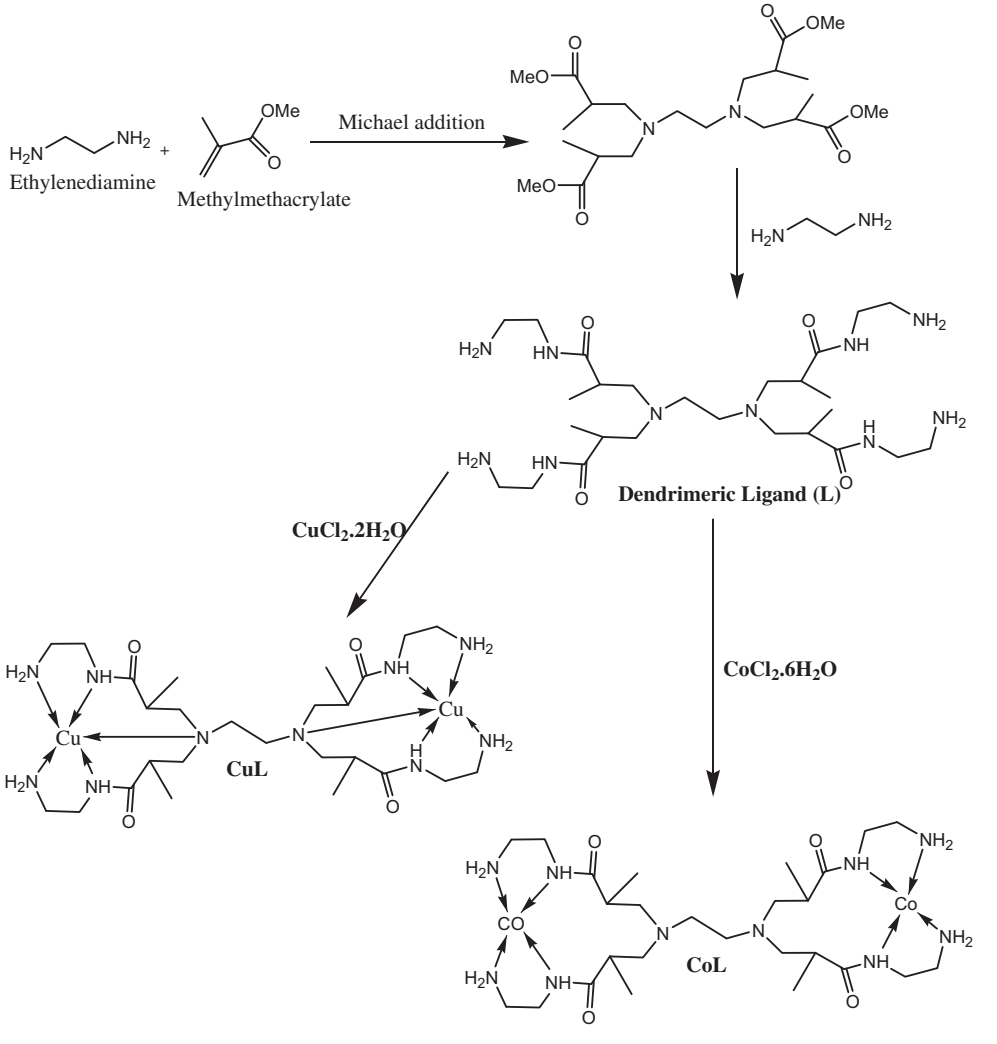
Analytical and spectroscopic data of L, **CuL**, and **CoL** supported their proposed structures. The compounds were hygroscopic, soluble in water, ethanol, and methanol and insoluble in other common organic solvents. Both **CuL** and **CoL** were purified by washing with methanol. All the compounds were characterized by CHNS analysis and UV–vis, FT-IR, ^{1}H NMR, and ES-MS spectroscopic techniques.

The Michael addition of ethylenediamine to methyl methacrylate led to formation of L. The prepared ligand was complexed with Cu(II) and Co(II) metal ions to form **CuL** and

CoL, respectively (scheme 1). High molar conductance values of **CuL** and **CoL** indicated their 1 : 4 electrolytic nature indicative of the fact that the four chlorides existed outside the coordination spheres of these two complexes to balance the four units of positive charge of the two dicationic metal centers in each complex. Finally, it can be assumed that the ligand traps two metal ions at the same time via similar N_4 coordination.

3.1. *Molar conductance*

Molar conductance measurements of the complexes were carried out in double-distilled water at room temperature. Molar conductance values for 10^{-3} M solutions of **CuL** and



Scheme 1. Schematic representation of the synthesis of dendrimeric ligand (L) and its copper(II) and cobalt(II) complexes (proposed structures of L, **CuL**, and **CoL**).

CoL were 600.9 and 528 μS cm^{-1}, respectively. These values are in accord with their 1 : 4 electrolytic nature [26–28]. From the molar conductance data, it can be inferred that four chlorides exist outside the coordination spheres of each complex to balance the four units of positive charges of the two metal ions in each complex. Thus, the chlorides only satisfy the primary valency of the metal ions in these complexes.

3.2. *Solution stability*

Aquation is an important process for the action of a large number of therapeutically active drugs. UV–vis absorption spectroscopy is often used for the solution stability studies of complexes at physiological pH. **CuL** and **CoL** displayed similar spectra in PBS with no shifts in their bands as shown in figure S2 after 24 h and also resisted precipitation over this time period. Water being a polar solvent leads to the decrease in intensity of the band on standing. As the bands do not show any hypsochromic shift or bathochromic shift, the compounds are stable in solution. All these observations indicated the robust nature of the complexes [23].

3.3. *IR spectra*

The structures of L, **CuL**, and **CoL** were confirmed by their FT-IR spectra. The FT-IR spectrum of L showed peaks at 1650, 1125, and 3300 cm^{-1} attributed to vibrations of >C=O, –C–N, and $–NH_2$, respectively. The spectrum of **CuL** showed peaks at 3420, 1590, and 1220 cm^{-1} attributed to $–NH_2$, >C=O, and C–N, respectively. Similarly, the spectrum of **CoL** displayed characteristic peaks at 3400, 1650, and 1225 cm^{-1} attributed to vibrations of $–NH_2$, –C=O, and C–N, respectively. The coordination of the metal ions to the ligands was evident from the shifts of the characteristic group frequencies. The presence of metal nitrogen frequencies in spectra of the complexes further supported their metal coordination with metal ions. **CuL** showed vibrational bands at 430, 450, and 475 cm^{-1} assigned to the three different types of copper–nitrogen vibrational frequencies; **CoL** showed two cobalt–nitrogen frequency bands at 405 and 520 cm^{-1}.

3.4. *NMR spectra*

The structures of L, **CuL**, and **CoL** are well-supported by their ^1H NMR spectra, recorded in D_2O with TMS as internal standard. The signals due to NH and NH_2 protons were absent in the spectra of ligand and its complexes due to their rapid exchange with deuterium of the solvent. The protons in the ligand have been depicted as **A**, **B**, **C**, **D**, **E**, and **F** (figure S3). The signals due to the protons **A**, **B**, and **F** were observed as triplets at 3.163, 3.459, and 3.061 ppm, respectively. Signals due to **E** and **D** were observed as doublets at 0.926 and 4.679 ppm, respectively. Protons due to –CH (**C**) were observed as a multiplet at 3.380–2.610 ppm (figure S4). These signals in the complexes were slightly shifted downfield due to coordination of metal ions (figures S5 and S6) [29, 30].

3.5. *Mass spectra*

ESI-MS in the positive ion mode were recorded for L, **CuL**, and **CoL** and shown in figure S7. The mass spectra of L, **CuL**, and **CoL** supported their proposed structures. Molecular

ion peaks were not observed in spectra of the compounds due to their branching structures. However, several structurally characteristic peaks were observed in the spectra of ligand and its complexes. The mass spectrum of L showed fragment peaks at *m/z* values of 453.4, 338.5, 125.2, 108.1, and 99.6 attributed to [M-$C_4N_4H_{14}$ − H^+], [M-$C_8N_8H_{28}$ + $2H^+$], [{(M-$C_8N_8H_{28}$)/2}–CH_2O_2 + $3H^+$)], and [{(M-$C_8N_8H_{28}$)/2}–$C_3H_2O_2$ + H^+], respectively. The mass spectrum of **CuL** showed peaks at *m/z* values of 701.8, 350.3, 288.2, 257.3, 220.1, 161.2, and 104 assigned to the moieties [M-4Cl + $2H^+$], [(M-4Cl/2) + H^+], [{(M-4Cl)/2}–Cu + $2H^+$], [{(M-4Cl)/2}–Cu–2O + $3H^+$], [{(M-4Cl)/2}–Cu–$C_2H_6O_2$ − $4H^+$], [{(M-4Cl)/2}–Cu–$C_4H_{13}N_2O_2$ − $4H^+$], and [{(M-4Cl)/2}–Cu–$C_6H_{20}N_4O_2$ − $2H^+$], respectively. The mass spectrum of **CoL** exhibited peaks at *m/z* values of 343.3, 313.2, 253, 245.2, 209, 172.1, and 101.0 due to the moieties [{M-4Cl}/2–$2H^+$], [{(M-4Cl)/2}–2O], [{(M-4Cl)/2}–2O–Co − H^+], [{(M-4Cl)/2}–Co–CH_2O_2 + $5H^+$], [{(M-4Cl)/2}–Co–$C_3H_9O_2$ − H^+], [{(M-4Cl)/2}–Co–$C_3H_{13}N_2O_2$ − $6H^+$], and [{(M-4Cl)/2}–Co–$C_8H_{22}N_3O_2$ + $6H^+$], respectively.

3.6. *Electronic spectra*

In order to predict the geometries of **CuL** and **CoL**, their UV–vis absorption spectra were scanned from 200–800 nm in double-distilled water. The absorption spectrum of **CuL** displayed high-energy transitions centered at 215, 255, and 337 nm attributed to $n \rightarrow \sigma^*$, $\pi \rightarrow \pi^*$, and $n \rightarrow \pi^*$ transitions, respectively. The $n \rightarrow \pi^*$ transition might be assigned to the amide carbonyl group. The $\pi \rightarrow \pi^*$ transition might be assigned to the C=O group and $n \rightarrow \sigma^*$ transition might be assigned due to heteroatoms present. It also exhibited a broad low-energy transition at 677 nm corresponding to $^2B_{1g} \rightarrow {}^2B_{2g}$ [31–33]. One of the characteristics of distorted square-pyramidal complexes of Cu(II), as observed from literature, is presence of a broad and intense band in the 550–660 nm range. The UV–vis spectra of the synthesized compound also displays a broad peak at 677 nm, which indicates the possible geometry of the complex to be square pyramidal [34].

The absorption spectrum of **CoL** displayed only one low-energy transition centered at 488 nm, which may be attributed to $^2A_{1g} \rightarrow {}^2E_g$ transition, indicating its square-planar geometry [35–37].

3.7. *Thermogravimetric analysis (TGA/DTA)*

The thermal degradation of the copper complex (figure 1) was done in N_2 at a heating rate of 20 °C min^{-1}. A 5–10 wt% loss occurred at 100 °C due to the evaporation of solvent molecules. The copper complex was degraded mainly by two-stage patterns. The first step shows slight weight loss at 160–180 °C due to loss of chlorides. The second step shows major weight loss from 250–400 °C, attributed to decomposition of the complex.

3.8. *Biological investigation*

3.8.1. Anticandidal susceptibility. The MIC_{80} values obtained for the fungal species are shown in table 1. Both the ligand and its metal complexes were subjected to antifungal activity. The result shows that the ligand and copper complex were less active than the cobalt complex. The ligand showed a high MIC_{80} of 2.8 mg mL^{-1} for *C. albicans* ATCC 90028. The tested fungal pathogen *C. albicans* was more sensitive to the metal complexes

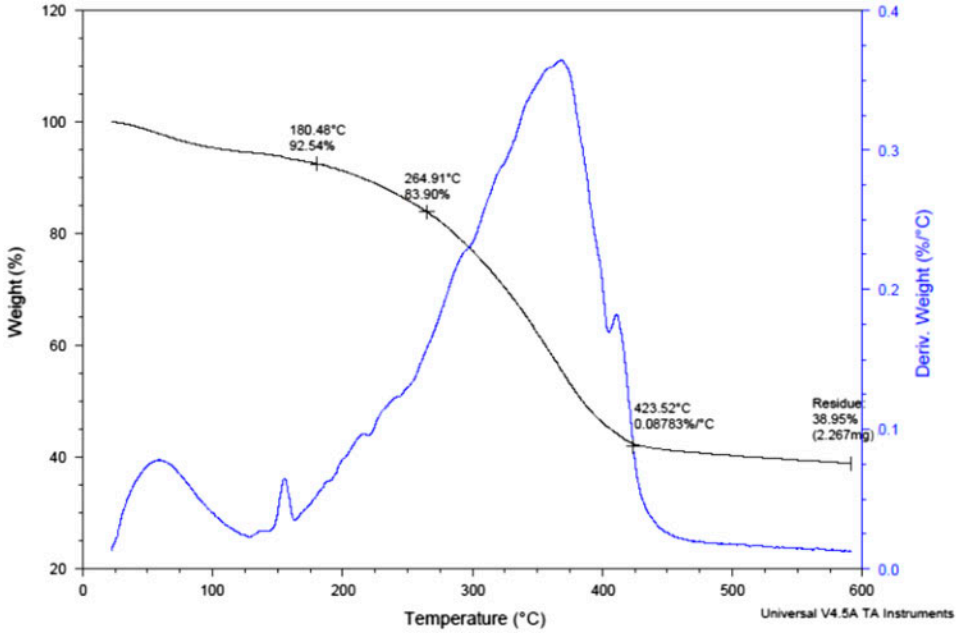


Figure 1. TGA/DTA of the copper complex.

especially **CoL** (MIC_{80} = 0.5 mg mL^{-1}) followed by the **CuL** (MIC_{80} = 2.5 mg mL^{-1}). Respective inhibition by fluconazole was shown at 0.004 mg mL^{-1}. The data are reported as MIC_{80} defined as the lowest concentration required inhibiting 80% growth in comparison to control (absence of any test compound) for each isolate.

Disk diffusion assay was employed to determine sensitivity of *C. albicans* ATCC 90028 as shown in table 2. Antifungal activity on solid media also yielded similar results with the tested yeast more sensitive to metal complexes. The typical disk diffusion plates showing zones of inhibition around disks impregnated with test compounds are shown in figure S8. The concentration of the test compounds ranged from 0.1–1.0 mg per disk. Fluconazole (4 μg mL^{-1}) was used as a positive control. The plates show clear zones of inhibition, indicating the fungicidal nature of the synthesized compounds. Stock solutions of the synthesized compounds were prepared in double-distilled water. The disk impregnated with double-distilled water (negative control) showed no zone of inhibition, and hence, water had no effect on the tested fungal strain used in this study. The obtained results demonstrated that the ability to kill *Candida* species is dependent on the concentration of the test

Table 1. *In vitro* antimicrobial activity of ligand and its metal complexes.

Test agents	MIC (mg mL^{-1}) *C. albicans* ATCC 90028
L (ligand)	2.8
CuL (copper complex)	2.5
CoL (cobalt complex)	0.5
Fluconazole (standard drug)	0.004

Table 2. Disk diffusion assay of *C. albicans* ATCC 90028 showing inhibition in the presence of synthesized ligand and its complexes.

	Zone of inhibition (mm)			
Test concentration (mg mL^{-1})	L	**CuL**	**CoL**	Fluconazole
0.004	*	*	*	22
0.1	*	*	*	*
0.2	*	*	8	*
0.3	*	*	*	*
0.5	6	*	12	*
1.0	*	6	15	*

*No inhibition halo.

compound. The tested *Candida* isolate used in this study showed high sensitivity for metal complexes as evident from the large zones of inhibition.

It was previously reported that dendrimers increase the antifungal activity of antifungal drug, but does not show antifungal activity when used alone [38]. In this study, not only dendrimer (ligand) shows antifungal activity but also M–L complexes possess antifungal activity. These complexes have better antifungal activity than other metal complexes with Schiff bases reported earlier [39, 40]. This result is significant as the conventional drug fluconazole is fungistatic and hence leads to antifungal drug resistance. Complexation of the metal ion has brought about enhancement in activity [41].

3.8.2. Hemolysis. After entry of drugs into animal body, they interact with the blood components, particularly RBCs (oxygen carrying blood cells). One of the complications that the drugs cause is lysis of RBCs called hemolysis. Usually, hemolysis induced by drugs is a rare but serious toxicity. This may be due to direct toxicity of the drug, its metabolite, or an excipient in the formulation. Even in normal adults, high drug concentrations can cause hemolysis. However, individuals who are genetically predisposed to hemolysis are prone to hemolysis even with smaller concentrations of drugs. Thrombocytopenia, neutropenia, hemolytic anaemia, aplastic anaemia, and macrocytic anaemia are some of the complications which occur in some patients treated with drugs [42]. In view of these facts, US FDA has recommended hemolysis screening of newly synthesized drugs as a very important requirement of drug development [43].

The hemolysis results of L, **CuL**, and **CoL** are shown in figure 2. It is clear from the figure that the ligand was the most toxic to RBCs as evident from its high hemolysis percentages at $MIC_{80}/4$, $MIC_{80}/2$, MIC_{80}, $2MIC_{80}$, $4MIC_{80}$, $8MIC_{80}$, and $16MIC_{80}$ concentrations. However, **CoL** was comparatively less toxic than L but more toxic than fluconazole, which was used as a standard. **CoL** exhibited a toxicity of 46.01% at its MIC_{80} value as compared to fluconazole (26.4%). As per figure 2, **CuL** is the safer compound because it induced less hemolysis of the human RBCs. **CuL** is much less toxic to RBCs as compared to L, **CoL**, and fluconazole. **CuL** displayed no toxicity at the concentration range of $MIC_{80}/4$–4 MIC_{80}. However, low values of hemolysis were reported at $8MIC_{80}$ and $16MIC_{80}$ concentrations, respectively.

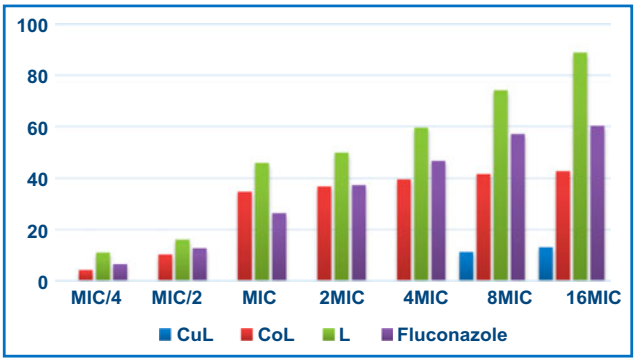


Figure 2. Hemolysis effects of L, **CuL**, and **CoL** with respect to fluconazole at the concentration range of MIC/4–16MIC.

4. Conclusion

The facile synthesis of a dendrimeric ligand and its copper(II) and cobalt(II) complexes has been described. Both ligand and its complexes were obtained in good yields. Copper(II) and cobalt(II) complexes may be attributed to square-pyramidal and square-planar geometries, respectively. Both the ligand and its complexes displayed significant anticandidal activities against *C. albicans* ATCC 90028. The use of total mean $MICs_{80}$ obtained gave a good indication of the overall antimicrobial effectiveness of each test compound. This indicated that the yeast physiology may not be well-equipped to counteract the antifungal properties of these compounds. It was encouraging to see that in solid media, growth was significantly inhibited by metal complexes, and the halo was completely clear, indicating the potential fungicidal activity of the synthesized complexes. Hemolytic results showed that L and **CoL** were toxic to human RBCs whereas **CuL** was non-toxic in comparison with the standard antifungal drug fluconazole. To conclude these results taken together with the limited toxicity of **CuL** towards human red blood cells make them eligible for further development as antifungals. Without understanding of the target, there can be no inspiration for the design of inhibitors, therefore, further studies using animal models are necessary to investigate the mode of action and *in vivo* efficacy of the synthesized compounds.

Supplementary material

Supplementary information contains standard antifungal drugs figure, UV–vis spectra of the complexes, chemical structure of the ligand showing different types of protons, ESI-MS spectrum of L, TGA curves of **CuL**, ^{1}H NMR spectra of ligand and complex, disk diffusion assay of *C. albicans* ATCC 90028 showing zones of inhibition.

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Disclosure statement

No potential conflict of interest was reported by the authors.

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