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2-(4-nitrophenyl)iminomethyl phenol Schiff base metal complexes: Synthesis, spectroscopic characterization, anticancer and antimicrobial studies

E. Vijaya Sekhar^a, Javarappa Rangaswamy^b, Mahesh Bhat^a, and Nagaraja Naik^b

^aPost graduate Department of Chemistry, JSS College for Women, Mysuru, Karnataka, India; ^bDepartment of Studies in Chemistry, University of Mysore, Mysuru, Karnataka, India

ABSTRACT

An imine-based molecule, 2-(4-nitrophenyl)iminomethyl phenol Schiff base (**NPIMP**) ligand was synthesized by microwave and conventional methods by reaction between 4-nitroaniline (**1**) and salicylaldehyde (**2**). The metal complexes of La(III), Co(II), Ni(II) and Cu(II) (**3a-d**) with **NPIMP** were synthesized as potential anticancer and antimicrobial drug candidates. The synthesized ligand and metal complexes were structurally characterized by spectral (NMR, FT-IR, LC-MS and UV-Vis), scanning electron microscopy, elemental analysis, powder X-ray diffraction and thermo gravimetric (TG) data. Spectroscopic studies suggested a distorted octahedral structure for all the complexes. The systems were evaluated for their anticancer and antimicrobial activities. The anticancer activity studies revealed that all the complexes exhibited promising activity against MCF-7 breast and HeLa cell lines. Antimicrobial activity has shown that all the complexes were showed certain degree of activity. As for the antimicrobial activity, La(III) and Co(II) complexes displayed potential antibacterial and antifungal activity against the tested microbes.

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KEYWORDS

Schiff base; metal complexes; 2-hydroxybenzaldehyde; *in-vitro* anticancer activity; antimicrobial activity

Introduction

The vital role of Schiff base is one of the interesting areas in coordination chemistry because of their synthesis and biological applications.^[1,2] Schiff bases and their metal complexes form an important class of compounds in chemistry owing to their synthetic flexibility and varied applications.^[3–5] Most of the Schiff bases are easily synthesized following a simple procedure and they can be obtained with widely varied substitution by selection of appropriate reactants. A lot of Schiff bases can act as ligands.^[6,7] By changing the nature and the position of donor atoms or groups, it is possible to control the size of chelate rings formed and to exploit them for various uses. These factors make Schiff bases, with appropriate structure, chelating agents of great potential in analytical chemistry.^[8–10] Metal complexes with tailor-made Schiff base ligands find use in pigments & dyes and polymer industries.^[11,12]

The large classes of Schiff base ligand containing metal complexes are predominantly tested for their biological and pharmaceutical applications including antibacterial,^[13–15] antifungal,^[16] anticancer,^[17,18] antioxidant,^[19,20] anti-inflammatory,^[21] antimalarial,^[22] antiviral^[23] agents.

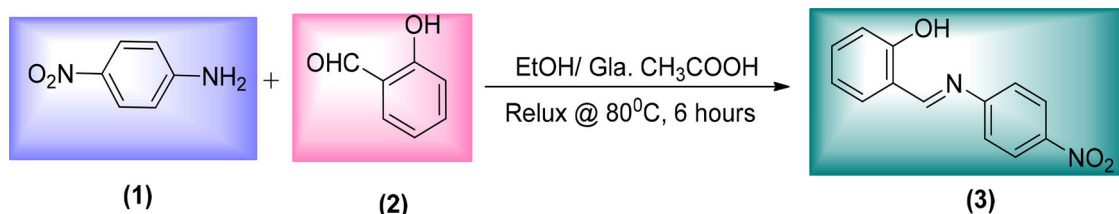
Considering these facts and in continuation of our research interest in the synthesis of bioactive metal complexes, we undertake the present study comprising of the synthesis of a Schiff base ligand: 2-(4-nitrophenyl)iminomethyl phenol (**NPIMP**) (Scheme 1) and its complexes with

biologically active metals as La(III) (**3a**), Co(II) (**3b**), Ni(II) (**3c**) and Cu(II) (**3d**), their spectroscopic and analytical characterization and biological evaluation.

Experimental

Materials and methods

Analytical grade reagents and solvents from Merck Chemicals and Sigma-Aldrich (India) were used without further purification. Elemental (C, H, N) analysis data for ligand (**NPIMP**) and its complexes were procured from CDRI, Lucknow. Conductance measurements (Molar Conductance $\Omega^{-1} \text{ cm}^2 \text{ mol}^{-1}$) on the complexes were done in DMF at 10^{-3} M concentration using a Digisun digital conductivity meter while the Gouy balance calibrated with $\text{Hg}[\text{Co}(\text{NCS})_4]$ was used to measure magnetic susceptibility. The Fourier transform infrared (FT-IR) spectra of ligand as well as complexes were recorded in KBr (IR grade) between $4000\text{--}450 \text{ cm}^{-1}$ on Perkin-Elmer FTIR spectrophotometer. Electronic spectra were obtained on Perkin-Elmer UV-Vis spectrophotometer. ^1H NMR (400 MHz) and ^{13}C NMR (100 MHz) spectra in DMSO were obtained employing an AC Bruker spectrometer. Mass spectra were obtained on an Electron Impact mass spectrometer at 70 eV ionizing beam and using a direct insertion probe. WIN-EPR (Bruker) spectrophotometer was used to record the electron spin resonance (ESR) spectrum of Cu (II) (**3d**) complex between



Scheme 1. Synthetic route for the preparation of 2-(4-nitrophenyl)iminomethyl phenol Schiff base (NPIMP).

8.8–9.6 giga-Hertz (GHz) in DMF at liquid nitrogen temperature (LNT). The powder X-ray diffraction (PXRD) analysis was carried out at SJCE, Mysuru on a Proto X-ray diffractometer at 30 kV and 20 mA. Thermogravimetric analysis was performed on (TAI) SDT Q 600 between 0–700 °C. The morphology and size of particles recorded Scanning electron microscopy (SEM) technique was carried out at SJCE, Mysuru.

Synthesis protocol for 2-(4-nitrophenyl)iminomethyl phenol [NPIMP]^[24]

Conventional method

The ligand (NPIMP) was prepared as illustrated in (Scheme 1) by the condensation of an equimolar solutions of 4-nitroaniline (1) and salicylaldehyde (2) in ethanol with a catalytic amount of glacial acetic acid and refluxed at 75 °C for 6 hrs. TLC was used to monitor the progress of the reaction in n-hexane: ethyl acetate (7:3) as eluent. On standing the reaction mixture overnight at room temperature (25 °C), the yellow precipitate obtained was filtered and washed with cold ethanol. The product was recrystallized from ethanol. Yield = 80%.

Microwave method

The ligand (NPIMP) was also synthesized by microwave method; ethanolic mixture of 4-nitroaniline (0.1 M) and salicylaldehyde (0.1 M) in a flask was irradiated in a microwave oven for 6–8 min. TLC monitored the completion of the reaction and the reaction mixture was allowed to attain room temperature (25 °C). The yellow crystals were obtained after recrystallization from ethanol (Scheme 1).

Yield = 86% Yellow, M.P.: 180–182 °C. Mol. formula: $\text{C}_{13}\text{H}_{10}\text{N}_2\text{O}_3$, *Anal.* (%) for Calc, C, 64.46%; H, 4.16%; N, 11.56%, found: C, 62.20%; H, 3.70%; N, 10.26%. Mass (m/z%): 242.07 (M^+). FT-IR (KBr, cm^{-1}): 1655 (C=N), 3050 (O-H). ^1H NMR (300 MHz) (DMSO- d_6) δ (ppm): 8.70 (s, 1H, HC=N), 8.17–8.15 (d, J = 8 Hz, 2H, Ar-H), 7.89–7.87 (d, J = 8 Hz, 1H), 7.76–7.74 (d, J = 8 Hz, 1H), 7.66–7.49 (m, 2H, Ar-H), 7.21–7.19 (d, J = 8 Hz, 2H). ^{13}C NMR (DMSO- d_6 100 MHz) δ ppm: 161.9, 158.3, 145.0, 134.0, 133.0, 131.8, 130.2, 127.5, 126.2, 122.4, 122.0, 121.6, 115.5.

Synthesis of Schiff base metal complexes (3a–3d)

The ligand (NPIMP) (2 mmol) was dissolved in ethanol by heating and intensive stirring. To the warm suspension, a warm ethanol solution of metal salts $\text{La}(\text{NO}_3)_3 \cdot 6\text{H}_2\text{O}$ /

$\text{CoCl}_2 \cdot 6\text{H}_2\text{O}$ / $\text{Ni}(\text{OAc})_2 \cdot 4\text{H}_2\text{O}$ / $\text{CuCl}_2 \cdot 2\text{H}_2\text{O}$ (1 mmol) (3a–3d) was added drop wise. The resulting mixture was kept under reflux over a water bath for 4 hrs at 80 °C. The solvent was evaporated in vacuum, and the obtained solid was directly used for further processing.

[La-(NPIMP)₂(NO₃)₂]₂NO₃ (3a)

Yield (80%). Color, M.P. >300 °C. Mol. Formula $[\text{La}(\text{C}_{13}\text{H}_9\text{N}_2\text{O}_3)_2]$. *Anal.* (%) for Calc, 62.86%; H, 4.01%; N, 10.36%, Found: C, 60.20%; H, 3.70%; N, 10.2%. FT-IR (KBr, cm^{-1}): 1151 (C-O), 1561 (C=N, azomethine), 684 (M-N), 595 (M-O). Mass (m/z%): 781.0 (M^+).

[Co(NPIMP)₂Cl₂] (3b)

Yield (75%). Dark Brown, M.P. >300 °C. Mol. Formula $[\text{Co}(\text{C}_{13}\text{H}_9\text{N}_2\text{O}_3)_2\text{Cl}_2]$. *Anal.* (%) for Calc: C, 59.00%; H, 4.22%; N, 10.5%, Found: C, 58.20%; H, 3.99%; N, 10.16%. FT-IR (KBr, cm^{-1}): 1270 (C-O), 1550 (C=N, azomethine), 763 (M-N), 515 (M-O). Mass (m/z%): 647.0 (M^+).

[Ni-(NPIMP)₂OAc₂] (3c)

Yield (70%), Light green, M.P. >300 °C, Mol. Formula $[\text{Ni}(\text{C}_{13}\text{H}_{10}\text{N}_2\text{O}_3)(\text{OAc})_2]$. *Anal.* (%) for Calc, C, 54.28%; H, 3.68%; N, 9.28%, Found: C, 54.02%; H, 3.44%; N, 9.01%. FT-IR (KBr, cm^{-1}): 1269 (C-O), 1599 (C=N, azomethine), 684 (M-N), 525 (M-O). Mass (m/z%): 699.0 (M^+).

[Cu-(NPIMP)₂Cl₂] (3d)

Yield (65%), Bottle Green, M.P. 285–287 °C Mol. Formula $[\text{Cu}(\text{C}_{13}\text{H}_{10}\text{N}_2\text{O}_3)_2\text{Cl}_2]$. *Anal.* (%) for Calc, C, 59.28%; H, 3.28%; N, 10.02%, obtained: C, 59.00%; H, 3.04%; N, 9.91%. FT-IR (KBr, cm^{-1}): 1269 (C-O), 1561 (C=N, azomethine), 754 (M-N), 530 (M-O). Mass (m/z%): 653.0 (M^+).

Biological evaluation

Antimicrobial activity

The newly synthesized ligand (NPIMP) and its metal complexes (3a–3d) were screened for their antibacterial activity using Muller-Hilton (MH) method.

The pathogenic bacterial strains Gram (+) *Bacillus subtilis* (MTCC-441), Gram (–) *Escherichia coli* (MTCC 40), *Staphylococcus aureus* (MTCC 7443) and two fungal strains

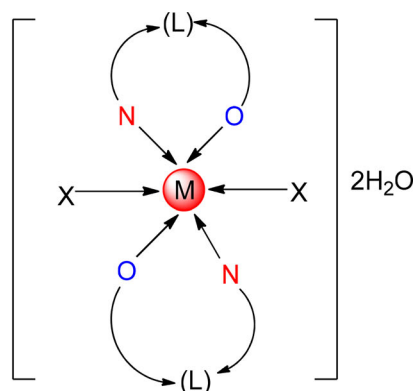
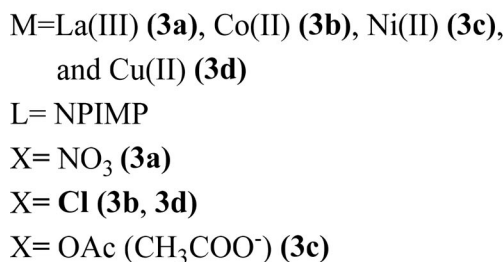


Figure 1. General structure of Schiff base (NPIMP) metal complexes (3a-3d).

Aspergillusniger (MTCC-1344) and *Penicilliumrubrum* (MTCC-1663) were used for screening of antimicrobial activity of synthesized ligand and its metal complexes.^[25]

Antibacterial activity

20 mL of sterilized agar media were poured into pre-sterilized petri-plates. Excess of suspension was decanted and plates were dried in an incubator at 37 °C for 1 h. 20 mL of bacterial suspension (in sterilized MH agar media) was poured into, swabbed neatly and allowed to solidify. Wells were made on each petri-plate using 6 mm sterile cork-borer. 100 µL of test compounds (5 mg/mL in DMSO) were added to each of them. The plates were incubated at 37 °C for 24 hrs and zone of inhibition (ZI) was measured in millimeter (mm) using digital micrometer and compared with reference standard chloramphenicol (5 mg/mL). Each experiment was performed in triplicate.^[26]

Antifungal activity

Antifungal screening of ligand (NPIMP) and its metal complexes were carried out by well diffusion method against *Aspergillusniger* (MTCC-1344) and *Penicilliumrubrum* (MTCC-1663) in sterilized Asthana and Hawker's agar media as reported earlier.^[27,28] The fungal suspension (in 3 mL of saline solution) mixed with 20 mL sterile agar media was poured into petri plates and allowed to solidify. Later, the plates were dried at 37 °C for 1 hr in incubator. Wells were made using 6 mm sterile cork borer to which 100 µL of test compounds (5 mg/mL in DMSO) were added. The petri-plates were prepared in triplicate and incubated at 25 °C for 72 hrs. Zone of inhibition (in mm) was measured and compared with reference fluconazole.^[17,29]

Anticancer assay

The inhibition of cell growth by Schiff base ligand (NPIMP) and its metal complexes (3a-3d) was evaluated using 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyl tetrazolium bromide (MTT) cleavage assay with MCF-7 and HeLa cell lines.^[30] The cells were seeded at 1×10^4 cells/well in 96 well plates

in RPMI medium supplemented with 10% Fetal Bovine Serum (FBS). After 20 hrs of culture, transition metals (3a-3d) and uncoordinated ligand (NPIMP) at 10 µM concentration were added in triplicate and the cells were further cultured for 72 hrs. The cells were then exposed to 5 mg/mL MTT in Phosphate buffer saline (PBS) at a final concentration of 1 mg/mL in culture for 5 hrs. Formazan crystals formed during the incubation period were dissolved overnight at 37 °C by adding 10% SDS containing 20 mM HCl. The absorbance was measured at 570 nm.

Results and discussion

The ligand (NPIMP) was synthesized by two ways where microwave assisted synthesis is more accessible, convenient, have short reaction time and higher yield, Scheme 1.

The reaction of ligand with $\text{MX}_2 \cdot n\text{H}_2\text{O}$ in (2:1) molar ratio led to the formation of Schiff base metal complexes (3a-3d), Figure 1. The analytical, spectral and thermal data are presented in Tables 1, 2.

All the complexes are stable, non-hygroscopic, partially soluble in most organic solvents such as ethanol, methanol, acetone, chloroform, benzene and completely soluble in DMSO and DMF. The molar conductivity measurements for all the complexes (1×10^{-3} M) in DMF solution at 25 °C are found within the range of non-electrolytic nature except La (3a) complex ($65 \Omega^{-1} \text{ cm}^2 \text{ mol}^{-1}$) where it corresponds to 1:1 electrolytic type. The molar conductance values of all the complexes are presented in Table 1.^[10] The magnetic studies reveal that Co(II) and Cu(II) complexes are paramagnetic to extent of respectively three and one unpaired electrons, while other La(III) and Ni(II) complexes are diamagnetic.

IR spectral analysis

The formation of ligand and its complexes were confirmed by comparing the IR spectra of Schiff base ligand and their metal complexes (3a-3d). The IR stretching frequencies of the free ligand and its complexes are given in Table 1. A medium intensity band at 3345 cm^{-1} for -OH stretching was observed in FTIR spectrum of NPIMP and found missing in all complexes indicating deprotonation of the hydroxyl group during the reaction and involvement in complex

Table 1. FTIR spectral data molar conductance and magnetic moments of NPIMP and its metal complexes (3a–3d).

Code	Compound	γ C–O	γ NO ₂	γ C = N (Azomethane)	γ M–N	γ M–O	Molar conductance ($\Omega^{-1} \text{ cm}^2 \text{ mol}^{-1}$)	μ_{eff} B.M.
L	NPIMP	1269	1599	1624	–	–	–	–
3a	[La(NPIMP) ₂ (NO ₃) ₂]NO ₃	1151	1599	1601	684	595	65	–
3b	[Co(NPIMP) ₂ Cl ₂]	1270	1599	1596	763	515	12	3.92
3c	[Ni-(NPIMP) ₂ OAc ₂]	1262	1600	1598	754	525	09	–
3d	[Cu-(NPIMP) ₂ Cl ₂]	1063	1670	1602	700	530	11	1.83

Table 2. Thermogravimetric characteristics of metal complexes (3a–3d).

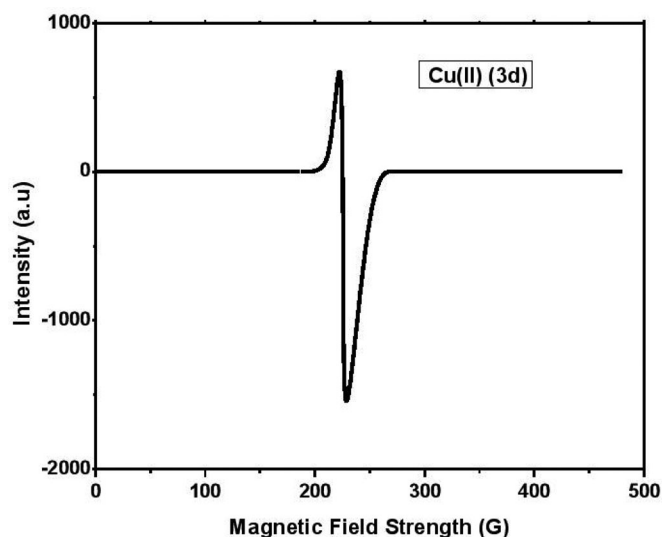
Complexes (3a–3d)	Process of degradation	Temp range (°C)	Product degraded	No. of moles	Weight		Residue (MO)
					Cal	Expt	
[La(NPIMP) ₂ (NO ₃) ₂]	Dehydration	92–115	H ₂ O	2	7.95	8.01	LaO
	Decomposition of NPIMP	190–340	NPIMP	2	45.50	45.50	
	Decomposition of X	340–620	NO ₃ [–]	2	62.54	62.25	
[Co(NPIMP) ₂ Cl ₂]	Dehydration	95–112	H ₂ O	2	10.30	10.25	CoO
	Decomposition of NPIMP	185–350	NPIMP	2	47.53	47.00	
	Decomposition of X	350–590	Cl [–]	2	75.13	75.90	
[Ni-(NPIMP) ₂ OAc ₂]	Dehydration	96–110	H ₂ O	2	6.35	6.25	NiO
	Decomposition of NPIMP	190–345	NPIMP	2	41.5	42.00	
	Decomposition of X	345–620	OAc	2	71.20	71.20	
[Cu-(NPIMP) ₂ Cl ₂]	Dehydration	95–119	H ₂ O	2	9.10	9.15	CuO
	Decomposition of NPIMP	184–350	NPIMP	2	48.30	47.90	
	Decomposition of X	350–630	Cl [–]	2	70.14	70.00	

formation. A small band at 1269 cm^{-1} is assignable to C–O group in the ligand. The sharp band at 1624 cm^{-1} in the ligand represents imine linkage of azomethine which was found to be lower shifted by $20\text{--}25 \text{ cm}^{-1}$ in the complexes, indicating involvement of azomethine nitrogen in complex formation. Moreover, the involvement of phenolic oxygen in coordination was confirmed by shift in stretching frequency of (C–O) from 1269 cm^{-1} to lower value. In addition, new bands appeared at lower frequency region around 700 and $515\text{--}595 \text{ cm}^{-1}$ due to stretching frequency of (M–N) and (M–O). These observations suggest that the ligand acts as a mono negative bidentate one coordinating through phenolic oxygen and nitrogen of C = N group.^[31,32] The mass spectra of the complexes are shown in Figures S1–S5.

UV-visible spectra

The electronic spectra of NPIMP and its metal complexes were recorded in DMF solution (200–800 nm) at room temperature as shown in supplementary file, Figure S6.

In free ligand, two bands observed at 305 and 315 nm are attributed to $\pi\text{--}\pi^*$ and $n\text{--}\pi^*$ transition of aromatic moiety and azomethane functional group of ligand.^[33] In the metal complexes $\pi\text{--}\pi^*$ and $n\text{--}\pi^*$ transitions were shifted to longer wavelength as a consequence of coordination to metal ion.^[34] Besides, a moderate broad band observed at 390–418 nm with absorption maxima (λ_{max}) at 410 nm (3a), 390–415 nm (3b), 390 nm (3c) and 418 nm (3d), were attributed to the metal ligand charge transition (MLCT) in complexes. The spectra further display a broad band in the region 460–580 nm, which may be due to metal-centered d–d transitions of a distorted octahedral geometry (Figure S6). The absorption maxima of d–d transition bands of the complexes are depicted in Table S1.

**Figure 2.** ESR spectrum of Cu(II) complex (3d).

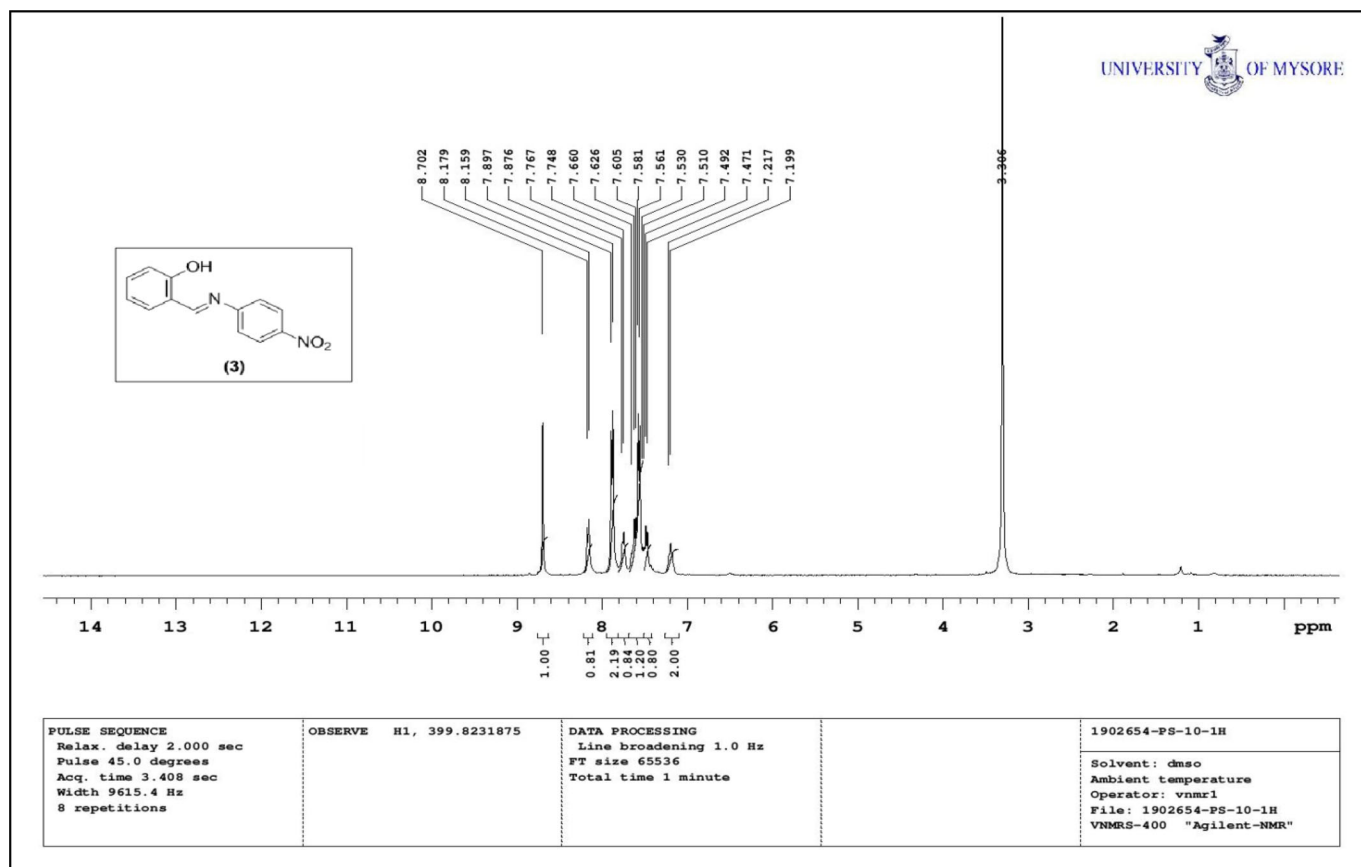
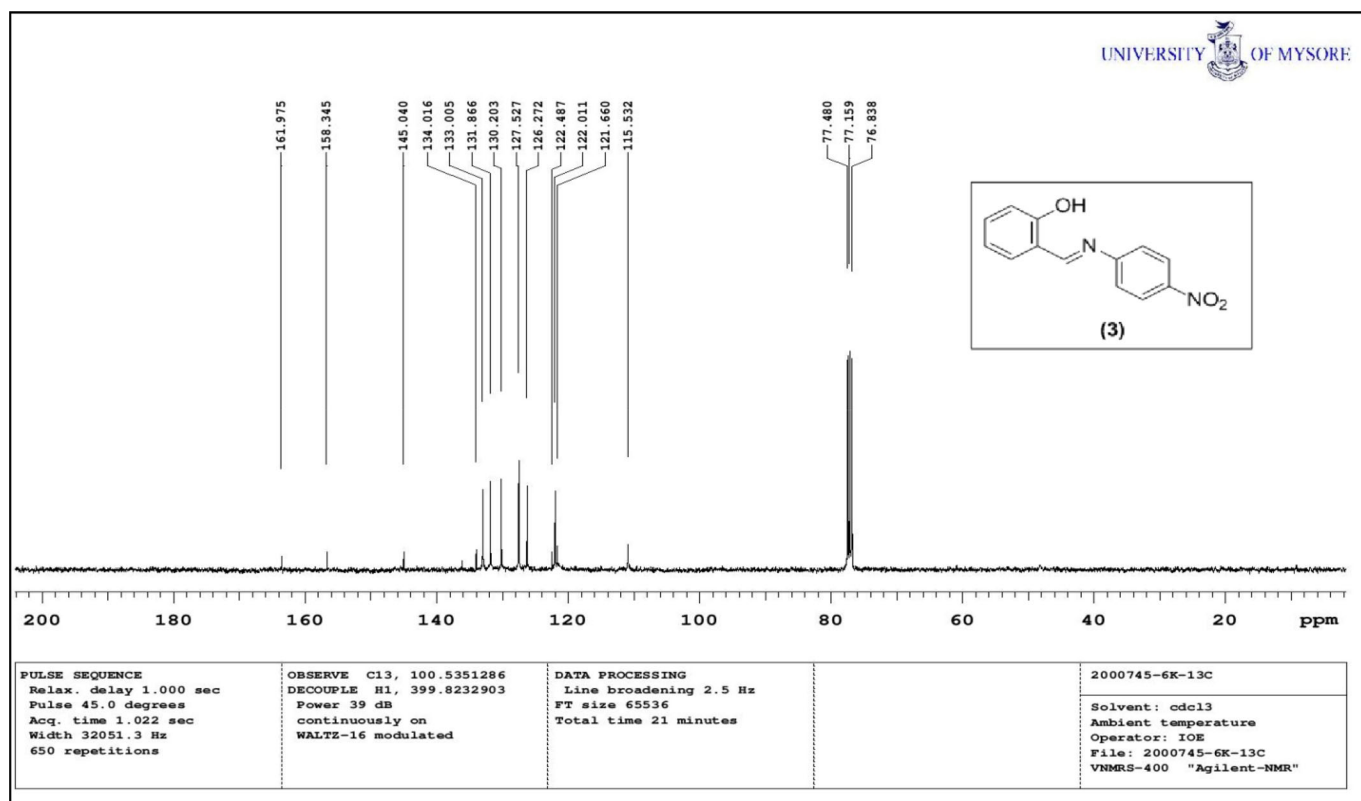
Electron spin resonance spectra

The ESR spectrum of Cu(II) complex is of isotropic nature in that it shows a single well defined peak corresponding to g 2.22, Figure 2.^[35,36]

NMR spectroscopy

¹H and ¹³C NMR spectra of ligand (NPIMP) were recorded in DMSO-*d*₆ and are given in Figures 3 and 4.

The resonance of CH = N group of hydrogen was attributed singlet peak at 8.60 ppm. The signals of Ar–H were observed in the δ 6.91–8.10 ppm. The resonance of the phenolic OH was not observed for ligand. It may be due to hydrogen reseating by deuterium atom.

Figure 3. ¹H NMR spectrum of ligand (NPIMP).Figure 4. ¹³C NMR spectrum of ligand (NPIMP).

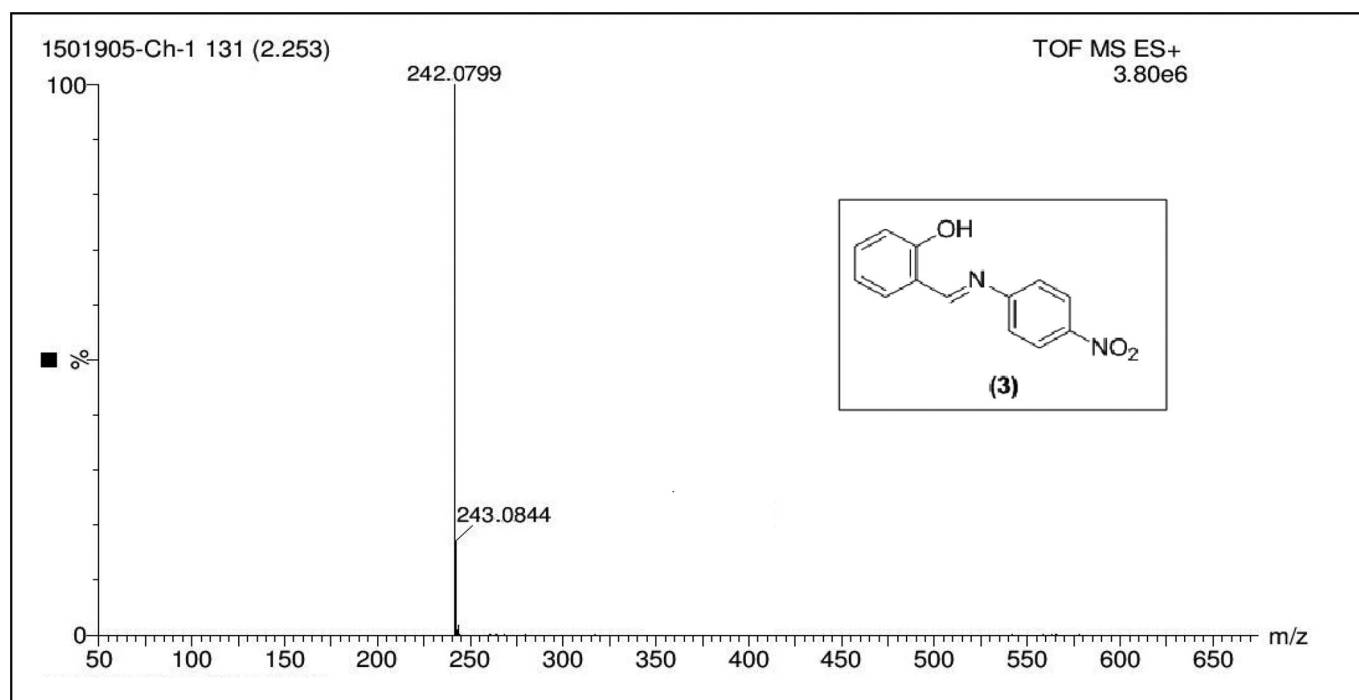


Figure 5. Mass spectrum of ligand (NPIMP).

The structure of the **NPIMP** was evaluated further using ^{13}C NMR. The signal resonate at = 161.5 ppm was attributed to carbon of ($\text{CH}=\text{N}$). The peaks of other aromatic ring carbons were observed at 117.0–154.0 ppm. The peak of 159.5 ppm corresponds to $-\text{COH}$ group.

Mass spectroscopy

The formation of the ligand and its metal complexes (**3a–3d**) was confirmed through MS techniques. Mass spectrum of ligand (**NPIMP**) is depicted in Figure 5. The molecular ion peak was observed at $m/z = 242.07$ consistent with the molecular mass of ligand. The mass spectra of complexes (**3a–3d**) with the molecular ion peaks at $m/z = 781$, 647, 699, 653, 700 give evidence for the coordination of La(III) (**3a**), Co(II) (**3b**), Ni(II) (**3c**) and Cu(II) (**3d**) with the ligand (**NPIMP**). The mass spectra of the complexes are shown in Figures S7–S10.

Thermal analysis The TG curves of the complexes are shown in Figure 6. All the curves show weight loss in three stages corresponding to dehydration, decomposition of organic moiety and of inorganic ligand in the ranges 92–119 °C, 184–350 °C and 350–630 °C, respectively. The final product corresponds to respective metal oxide (Table 2).

Powder XRD

The synthesized Schiff base ligand and metal complexes, their crystalline size and structure were determined by powder X-ray diffraction analysis. The powdered X-ray patterns of $[\text{Ni}(\text{C}_{13}\text{H}_{10}\text{N}_2\text{O}_3)(\text{OAc})_2]$ and $[\text{La}(\text{C}_{13}\text{H}_{10}\text{N}_2\text{O}_3)_2]$ complexes are shown in Figure 7, respectively. The XRD patterns were possessing sharp peaks and it is confirmed that

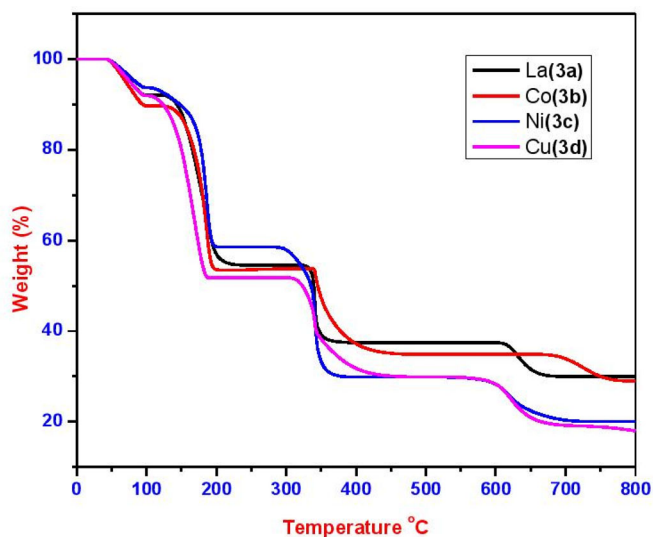


Figure 6. TGC curves of complexes (**3a–3d**).

the prepared samples were highly crystalline and single-phase materials without amorphous nature. Moreover, it indicates that the synthesized complexes are pure without any impurities. The average crystallite size was determined by using Scherrer-Debye formula

$$D = 0.9\lambda / \beta \cos \theta$$

where θ is the Bragg diffraction angle for hkl plane, β is full width half maximum of the characteristic peak, 0.9 is the morphology constant and λ (1.5406 Å) wavelength of X-ray source used in XRD. From these diffraction peaks it was found that La (III) complex has an average crystal size 40 nm and Ni(II) complex 36 nm suggesting the complexes to be nano-crystalline.^[37]

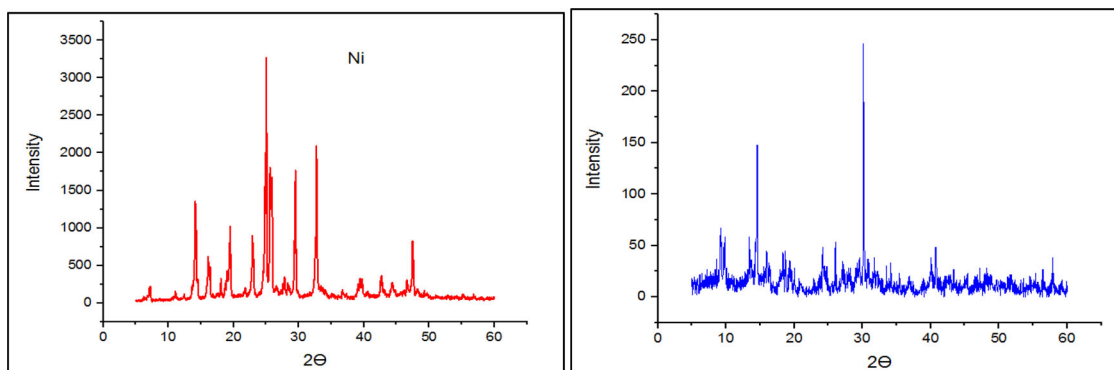


Figure 7. Powdered XRD of La (3a) and Ni (3d) complexes.

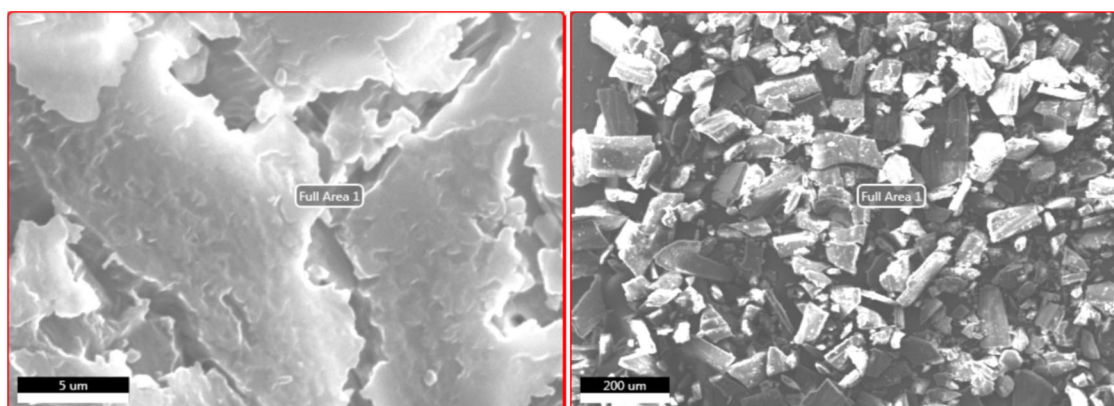


Figure 8. SEM and EDAX images of La (3a) and Ni (3d) complexes.

SEM and EDAX

The surface morphology of the Schiff base complexes La (3a) and Ni (3c) was analyzed by using scanning electron microscopy (SEM). The metal complexes of the elements analyzed by energy dispersive X-ray analysis (EDAX). The SEM micrographs show the agglomerate particles of the complexes. In case of La(III) (3a) some agglomerates appear to be of spherical plates, while the Ni(II) (3c) Complex agglomerates appear to have tiny needles like morphologies (Figure 8). The XRD data suggest that these complexes are polycrystalline with nano sized grains.^[38]

Biological studies

Antimicrobial activity

The antimicrobial activity of ligand (NPIMP) and its metal complexes were studied against *Bacillus subtilis* (Gram + ve), *Escherichia coli* (Gram – ve) and fungal strains *Penicillium rubrum*, *Aspergillus niger*. The results were measured in ZI and represented in Figures 9 and 10 and Table S2. The literature review suggests that cobalt, nickel and zinc complexes with Schiff base ligands have showed widely antimicrobial activities^[39,40] and in addition, La(III) and inner transition metal complexes showed antimicrobial activity against various pathogenic bacterial and fungal strains.^[41] Among the synthesized complexes, La (3a) and Co (3b) complexes showed better antimicrobial activity

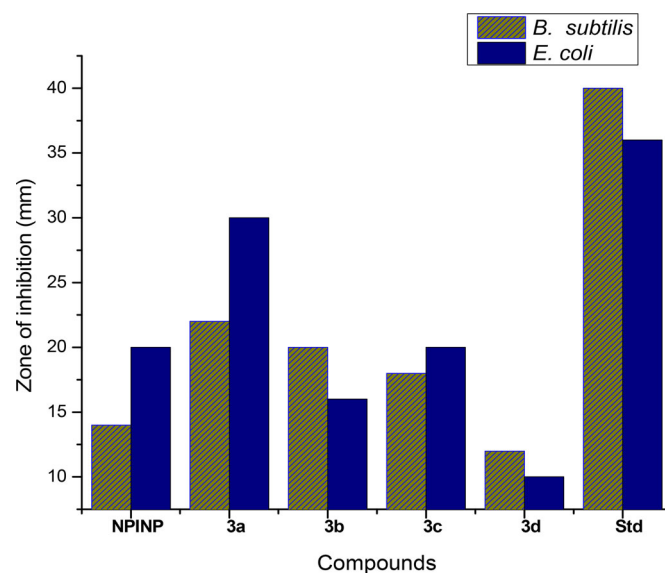


Figure 9. Graphical representation of antibacterial activity of complexes (3a-3d).

against tested bacterial strains as well as fungal strains. The complexes 3c and 3d exhibited moderate to good activity, when compared to the reference drug Chloramphenicol (36–40 mm ZI) and fluconazole (40–46 mm ZI). The higher activity of the synthesized complexes compared to free ligand may be attributed to chelation which reduces polarity of

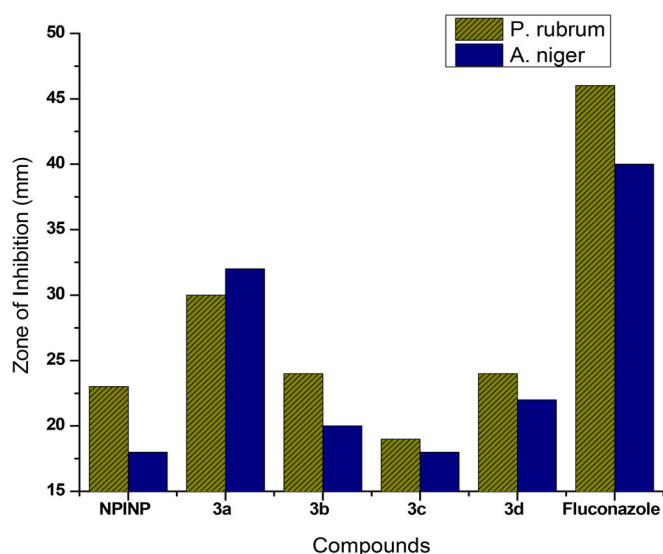


Figure 10. Graphical representation of antifungal activity of complexes (3a-3d).

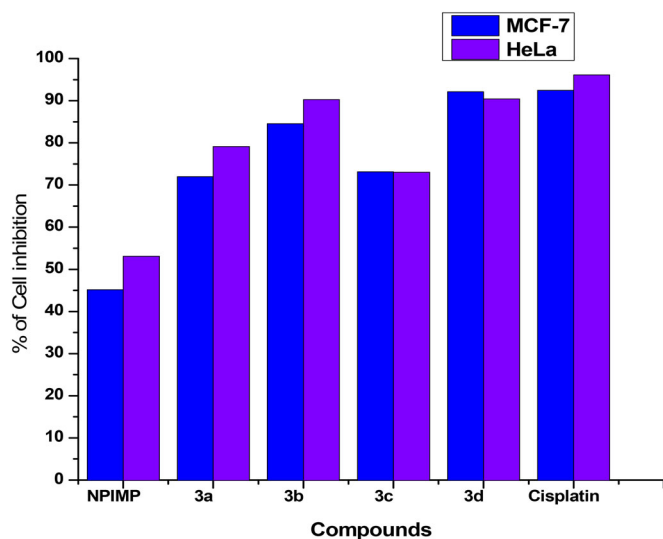


Figure 11. Graphical representation anticancer activity of complexes (3a-3d).

the metal ion by partial sharing of the positive charge with donor atoms of the ligand.^[42]

Anticancer activity

All synthesized complexes (3a-3d) and the corresponding uncoordinated ligand (NPIMP) were examined for *in vitro* anticancer activity against MCF-7 breast and HeLa cell lines. Anticancer activity included measurement of % of the *in vitro* cell inhibition by using MTT colorimetric assay at concentration 10 μ M. The results of anticancer activity was shown in Figure 11 and Table S3, indicated that these complexes revealed much higher activity when compared to the uncoordinated ligand. Interestingly, a variety of research found that the anti-cancer activity of Schiff bases copper complexes was higher than that of the free ligands.^[43-45] This further showed that which indicate that the coordination of the chelate ligand around the metal atom enhances

the anticancer activity. Among the synthesized complexes, Cu (3d) and Co (3b) complexes exhibit highest activity against tested cell lines very close to standard drug. Whereas, complexes of La (3a) and Ni (3c) revealed moderate activity compared to Cu (3d) and Co (3b) complexes.

Conclusion

To sum up, we have synthesized 2-(4-nitrophenyl)imino-methyl phenol Schiff base (NPIMP) ligand and its new La(III) (3a), Co(II) (3b), Ni(II) (3c) and Cu(II) (3d) metal complexes. The analytical and spectral data supported the structure and geometry of complexes. The Schiff base ligand and its metal complexes (3a-3d) were assessed for their *in vitro* antimicrobial activity against two bacterial and fungal strains. The complexes exhibited higher antibacterial and antifungal effect than the uncoordinated ligand. Among the complexes La (3a) and Co (3b) were found to be potential antimicrobial agents. The evaluation of anticancer activity against MCF-7 and HeLa cell lines proved that the complexes are more promising than the free ligand as anticancer active agents. Of all the complexes, Cu (3d) and Co (3b) complexes showed higher anticancer activity. Further studies on variation in organic substituted moiety and transition metal type to furnish these classes of bioactive complexes are currently underway.

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Disclosure statement

All authors declare that they have no conflict of interest.

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