



Synthesis and characterization of a novel schiff base of 1,2-diaminopropane with substituted salicylaldehyde and its transition metal complexes: Single crystal structures and biological activities



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ABSTRACT

A novel schiff base H2L derived from simple condensation of 2-hydroxy-6-isopropyl-3-methyl benzaldehyde and 1,2-diaminopropane in 2:1 M ratio and its [MnL], [CoL] and [NiL]₂ complexes have been prepared and characterized by spectroscopic technique, elemental analysis, SEM-EDX analysis, and cyclic voltammetry. Additionally, single crystal X-ray diffraction technique has been applied to the schiff base ligand H2L and its nickel complex. The structure of nickel complex exhibited dimeric form with formula [NiL]₂ with distorted square planar geometry around each nickel center. Furthermore, all the synthesized compounds were screened for their antimicrobial and antioxidant and DNA cleavage activities.

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1. Introduction

Compounds with azomethine functional group ($-\text{HC}=\text{N}$), typically known as schiff bases have been synthesized by the condensation of primary amines with active carbonyls (aldehyde or ketone) [1]. The presence of a lone pair of electrons in the sp^2 hybridized orbital of nitrogen atom of the azomethine group presents good chelating ability on schiff bases especially when combined with one or more donor atoms close to the azomethine group. This chelating ability of the Schiff base combined with the ease of separation and flexibility in varying the chemical environment about the $\text{C}=\text{N}$ group, makes Schiff base interesting ligands in coordination chemistry [2]. Metal complexes of schiff bases derived from salicylaldehyde and diamine can increase the dimensionality of the system and can form supramolecular architectures through $\text{O}-\text{H}\cdots\text{N}$ and $\text{N}-\text{H}\cdots\text{O}$ type of hydrogen bonds [3]. Moreover, these complexes have remained an important and popular area of research due to their simple synthesis, versatility and diverse range of applications [4–10]. Tetradentate schiff bases with a N_2O_2 donor

atom set are well known to coordinate with various metal ions, and have many applications in the organic and inorganic fields [11–16]. Their metal complexes possess effective antibacterial, antifungal [17], antioxidant [18], anticancer [19,20], anti-inflammatory [21], DNA cleavage [22] and catalytic [23–27] properties, phosphorescence and electroluminescence [28]. Because of their wide applications area, schiff bases have been the focus of attention of scientists and hence the literature relating to schiff bases is extremely rich [16–28]. To contribute to search area of schiff base we report synthesis of a new type of tetradentate schiff base ligand formed by the simple condensation of 1,2-diamino propane with 2-hydroxy-6-isopropyl-3-methyl benzaldehyde and its Mn(III), Co(II), and Ni(II) complexes. The synthesized ligand and its complexes were characterized using elemental analysis, FT-IR, UV-visible, NMR, LC-MS and single crystal X-ray crystallography, magnetic susceptibility, cyclic voltammetry and further screened for antimicrobial and antioxidant activities.

2. Experimental

All the solvents and chemicals were of commercial reagent grade and used as received without further purification. FT-IR spectra were recorded as KBr pellets on a SHIMADZU FT-IR-8400

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spectrometer. The electronic spectra were recorded as DMF solutions on the UV 2400 series spectrophotometer. ^1H and ^{13}C -NMR spectra were precise with a BRUKER AVANCE III (400 MHz) spectrometer and proton chemical shifts are recorded in ppm relative to tetramethylsilane as an internal standard using CDCl_3 as solvent and the LC-MS spectra of compounds have been carried out with Waters Micromass Q-ToF Micro instrument. The elemental analyses were carried out with a Thermo Finnigan elemental analyzer. Magnetic susceptibilities are measured at room temperature on a guoy balance using $\text{Hg}[\text{Co}(\text{NCS})_4]$ as reference. SEM-EDX analyses were performed on SEM JEOL JSM 6360 and JEOL JSM 5400, Japan. Molar conductance of metal complexes was measured on Systronic Conductivity Bridge. The electrochemical characterization is carried out using electrochemical analyzer supplied by CH Instruments, USA in 0.1 M tetrabutyl ammonium perchlorate (TBAP) electrolyte with Ag/AgCl as reference electrode at scan rate 100 mVs^{-1} .

2.1. Synthesis of schiff base ligand H2L

The ligand was prepared by dropwise addition of methanolic solution of propane-1,2-diamine (0.074 gm, 1 mmol) to a constantly stirring warm solution of 2-hydroxy-6-isopropyl-3-methyl benzaldehyde (0.356 gm, 2 mmol) in methanol. The resulting solution was refluxed for 2 h, the yellow solution, obtained was filtered, and allowed to cool. The yellow crystals formed were collected and washed with water at room temperature.

Yield: 80%. Colour: Yellow solid. Anal. Calcd for $\text{C}_{25}\text{H}_{34}\text{N}_2\text{O}_2$ (%): C 76.10, H 8.69, N 7.10; Found: C 77.20, H 8.45, N 7.51. UV-vis (DMF) λ_{max} (nm): 269, 333. FT-IR (KBr pellet, cm^{-1}) ν_{max} : 2965 (OH), 1612 (C=N), 1450 (C=C), 1249 (C-O). ^1H -NMR (CDCl_3 , 400 MHz) (δ , ppm): 13.87 (brs, 2H, OH), 8.68 (d, 2H, $J = 16 \text{ Hz}$, $-\text{HC}=\text{N}$), 7.08 (d, 2H, Ar, $J = 8 \text{ Hz}$), 6.60–6.58 (dd, 2H, Ar, $J = 4, 8 \text{ Hz}$), 4.01–3.97 (m, 1H, $-\text{CH}$), 4.72–3.68 (m, 1H, $-\text{CH}$), 4.61–3.56 (m, 1H, $-\text{CH}$), 3.25–3.18 (m, 1H, $-\text{CH}_2$), 2.18 (d, 6H, $J = 8 \text{ Hz}$, 2CH_3), 1.45 (d, 3H, $J = 8 \text{ Hz}$, CH_3), 1.18 (d, 6H, $J = 8 \text{ Hz}$, 2CH_3), 1.02 (d, 6H, $J = 4 \text{ Hz}$, 2CH_3). ^{13}C -NMR (CDCl_3 , 400 MHz) (δ , ppm): 162.53, 160.34, 147.33, 133.74, 123.53, 114.24, 65.92, 65.29, 27.76, 23.52, 20.48, 15.52. LC-MS (m/z): calcd 394.26; obsv 395.41.

2.2. General procedure for the synthesis of metal complexes

The complexes were prepared by dropwise addition of methanolic solution of the corresponding metal salts such as manganese acetate tetrahydrate, cobalt acetate tetrahydrate and nickel chloride hexahydrate (1 mmol) to the methanolic solution of schiff base ligand (1 mmol) with constant stirring and the product was collected and washed with plenty of water and dried at room temperature.

[MnL] complex: Yield: 78%. Colour: Brown. Anal. Calcd for $\text{C}_{27}\text{H}_{35}\text{MnN}_2\text{O}_4$ (%): C 64.02, H 6.96, N, 5.53; Found: C 64.08, H 6.49, N 5.80. UV-Vis (DMF) λ_{max} (nm): 270, 331, 471. FT-IR (KBr, pellet cm^{-1}) ν_{max} : 1598 (C=N), 1286 (C-O), 1382 (C=C), 524 (M-O), 474 (M-N). LC-MS (m/z): calcd 447.47; obsv 447.47. μ_{eff} : 4.21 B M. Conductance (Λ_{M} , $\Omega^{-1} \text{ cm}^2 \text{ mol}^{-1}$) in DMF: 20.0.

[CoL] complex: Yield: 71%. Colour: Shining reddish brown. Anal. Calcd for $\text{C}_{25}\text{H}_{32}\text{CoN}_2\text{O}_2$ (%): C 66.51, H 7.14, N 6.20; Found: C 66.38, H 7.33, N 6.06. UV-Vis (DMF) λ_{max} (nm): 264, 357, 420, 507. FT-IR (KBr pellet, cm^{-1}) ν_{max} : 1556 (C=N), 1224 (C-O), 1458 (C=C), 536 (M-O), 450 (M-N). LC-MS (m/z): calcd 451.47; obsv 451.2. μ_{eff} : 1.33 B M. Conductance (Λ_{M} , $\Omega^{-1} \text{ cm}^2 \text{ mol}^{-1}$) in DMF: 5.5.

[NiL]2 complex: Yield: 79%. Colour: Orange. Anal. Calcd for $\text{C}_{50}\text{H}_{64}\text{N}_4\text{Ni}_2\text{O}_4$ (%): C 66.54, H 7.14, N 6.20; Found: C 66.20, H 7.56, N 6.35. UV-Vis (DMF) λ_{max} (nm): 264, 354, 426, 549. FT-IR (KBr pellet, cm^{-1}) ν_{max} : 1558 (C=N), 1226 (C-O), 1456 (C=C), 523 (M-O), 433 (M-N). ^1H -NMR (CDCl_3 , 400 MHz) (δ , ppm): 7.936 (s, 2H), 7.0435

(d, 2H, $J = 7.6 \text{ Hz}$), 6.371 (d, 2H, $J = 7.6 \text{ Hz}$), 3.758 (dd, 1H, $J = 6 \text{ Hz}$), 3.486 (t, 1H, $J = 6 \text{ Hz}$), 3.054–3.128 (m, 2H), 2.975 (m, 1H), 2.196 (s, 6H), 1.471 (d, 3H, $J = 6.4 \text{ Hz}$), 1.225 (d, 12H, $J = 6.8 \text{ Hz}$). LC-MS (m/z): calcd 451.23; obsv 451.28. Conductance (Λ_{M} , $\Omega^{-1} \text{ cm}^2 \text{ mol}^{-1}$) in DMF: 12.0.

3. Biological activities

3.1. Protocol for antibacterial activity

The antibacterial activity of the compounds was performed by colony count method [29]. The test organisms on which the antibacterial activity was performed were *E. coli*, *P. aeruginosa*, *B. subtilis*, and *S. aureus*. Ciprofloxacin and Ampicillin were used as standard drugs. In this method, the cells of test organisms were grown in nutrient broth till mid log phase and used as an inoculum for carrying out antimicrobial test. An approximately, 1×10^6 cells/mL test organisms were each inoculated with 0–500 $\mu\text{g}/\text{mL}$ concentration of dissimilar compounds, separately, and each incubated for 16–18 h at 37°C . During this incubation, cells tend to grow and multiply in number. However, if the compounds interfere with growth of cells, the number of cells decreases. After 16–18 h, workable number of cells was recorded by spreading an aliquot from the broth inoculated with test organisms and compounds as colony forming units per milliliter [30].

3.2. Protocol for antifungal activity

The antifungal activity of compounds was investigated against different fungal strains such as *C. albicans*, *A. flavus*, *A. niger* and *C. neoformans*. In this procedure, the medium yeast nitrogen base was dissolved in Phosphate buffer pH 7 and it was autoclaved at 110°C for 10 min. The suitable concentration of standard was incorporated in the medium. With each set a growth control without the antifungal agent and solvent control DMSO were included.

The fungal strains were freshly subcultured on to Sabouraud dextrose agar (SDA) and incubated at 25°C for 72 h. The fungal cells were suspended in sterile distilled water and diluted to get $n 10^5$ cells/mL. Ten microlitre of standardized suspension was inoculated onto the control plates and the media were incorporated with the antifungal agents. The inoculated plates were incubated at 25°C for 48 h. The readings were taken at the end of 48 h and 72 h. Minimum inhibitory concentration (MIC) values were determined using standard agar method as per CLSI guidelines. Micanazole and Fluconazole were used as standard antifungal drugs [31].

3.3. Free radical scavenging activity (DPPH method)

DPPH (2,2-diphenyl-1-picrylhydrazyl) radical scavenging activity was evaluated according to the reported method [32,33]. In these methods, The 100 ppm solution of DPPH in methanol was prepared and 1.0 mL of this solution was added to dilutions of compound solution in water at different concentrations (10 ppm, 20 ppm, 40 ppm, 60 ppm, 80 ppm, 100 ppm). Thirty minutes later, the absorbance was measured at 517 nm. Ascorbic acid was used as standard. Scavenging activity versus concentration in ppm were plotted to estimate a 50% reduction of its initial value (EC_{50}).

Lower absorbance of the reaction mixture indicates higher free radical scavenging activity.

The capability to scavenge the DPPH radical was calculated using the following equation:

$$\text{DPPH radical scavenging activity (\%)} = \frac{\text{Absorbance}_{(\text{control})} - \text{Absorbance}_{(\text{standard})}}{\text{Absorbance}_{(\text{control})}} \times 100.$$

Where, Absorbance (control): Absorbance of DPPH radical + methanol. Absorbance (standard): Absorbance of DPPH radical + extract/standard.

3.4. DNA cleavage activity

DNA cleavage potential of the ligand and its complexes has been studied in the presence of oxidant H_2O_2 by agarose gel electrophoresis method. The test samples for the study of DNA cleavage potential of the compounds were prepared in 0.5 mL transparent Eppendorf microcentrifuge tubes containing pBR 322 DNA and total sample volume 10 μL made for the gel-electrophoresis. Supercoiled pBR322 DNA was treated with the samples (10, 20, 50, 100, 150 and 200 μM) and the mixtures were incubated in the dark for 30 min at 37 °C. The reaction was quenched by adding 2 μL DNA loading dye (two dye mixture containing bromophenol blue and xylene cyanol) and the samples were loaded in the wells prepared by 1% agarose gel (Tris-boric acid-EDTA (TBE) buffer, pH = 8.2) for 3 h at 40 V. The pBR 322 DNA bands were stained by Ethidium bromide and the level of cleavage of pBR 322 DNA was determined by measuring the intensities of the bands using a UVITECH Gel Documentation System [34].

4. Results and discussion

The N_2O_2 donor symmetrical schiff base was prepared by simply condensation of 2-hydroxy-6-isopropyl-3-methyl-benzaldehyde [35] with propane-1,2-diamine in 2:1 M ratio in methanolic solution. The $[\text{MnL}]$, $[\text{CoL}]$ and $[\text{NiL}]_2$ complexes were synthesized by the direct reaction of ligand with an equimolar amount of metal (II) acetate/chloride salts in same solvent in 1:1 M ratio (Fig. 1). All the compounds are soluble in polar solvents. The spectral analyses agree well with the proposed structure of the complexes.

4.1. X-ray crystallographic analysis

The ORTEP diagrams and packing diagram are shown in Figs. 2–5. The crystallographic parameters, data collection and refinement for the schiff base ligand H2L and its dimeric $[\text{NiL}]_2$ complex are as shown in Table 1. The selected bond lengths and bond angles are given in Tables 2 and 3 While, the hydrogen bonding parameters are given in Tables 4 and 5. The crystal structure of the schiff base ligand represented, the N1–C8 distance as

1.271 (6) for C=N double bond. The molecule adopts E-configuration in connection with C=N bond with C9i–C9–N1–C8 and C22i–C22–N2–C21 torsion angle found as 151 (5)°, –150.7 (18)°. The bond distance 1.350 (5) for C7–O1 illustrated the C–O phenolic single bond. In the ligand structure, molecule is associated with intramolecular hydrogen bonding, where the H atom of phenolic hydroxyl group forms a strong O–H ...N intramolecular hydrogen bond with O ...N distance 2.53 Å [36–38].

In the present nickel's dimeric crystal structure the bond lengths of Ni–O and Ni–N are in the range of 1.824–1.832 Å and 1.820–1.877 Å respectively. The N2–Ni–O1 and O2–Ni–O1 bond angles have been found to be 178.51° (16) and 170.9° (3) respectively; and from these trans values of each metal ions, it can be concluded that complex has distorted square planar geometry. The bond angles around the metal ion N2–Ni–O2, O1–Ni–O2, N2–Ni–N1, and O1–Ni–N1 exhibit the values viz. 93.95° (15), 87.47° (12), 85.7° (3) and 92.8° (3) respectively. All these mentioned values are nearly same as related reported nickel complexes [39–41]. In addition the packing diagram shows intramolecular C–H...O interaction between one methyl H atoms of benzene ring and neighboring oxygen atoms. Another intramolecular C–H...N interaction is observed in diamine bridge where methyl's one H atom is in vicinity of one imine nitrogen.

5. Spectral characterization

5.1. UV–vis spectra

The electronic spectra in DMF solution showing absorption of high energy 265–280 nm and 340–490 nm are assigned to the intraligand $\pi \rightarrow \pi^*$ and $n \rightarrow \pi^*$ transitions respectively [42]. For cobalt (II) and nickel (II) complexes, d-d transition appeared below 600 nm, which is the characteristic feature of square planar structure [43].

5.2. IR spectra

In the IR spectra of the ligands the band at 3417 cm^{-1} is assigned to the phenolic OH group and its frequency was found to disappear

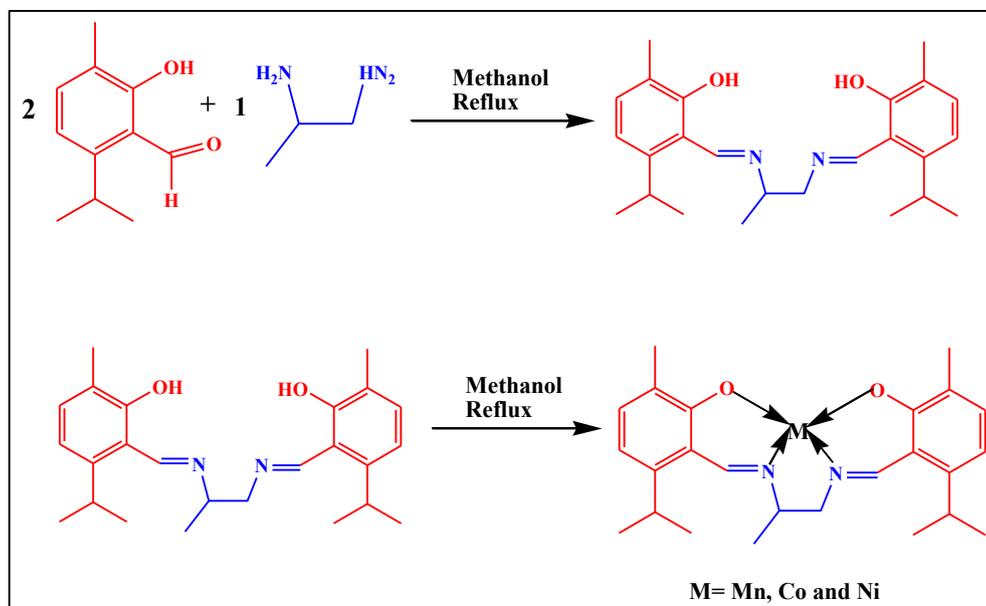


Fig. 1. Synthesis route for the schiff base ligand H2L and its metal complexes.

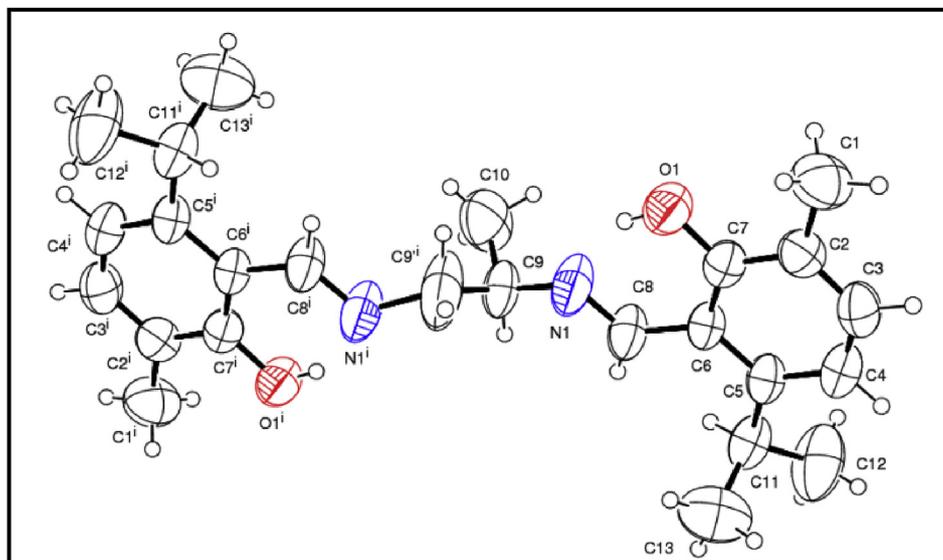


Fig. 2. ORTEP diagram of schiff base ligand H2L.

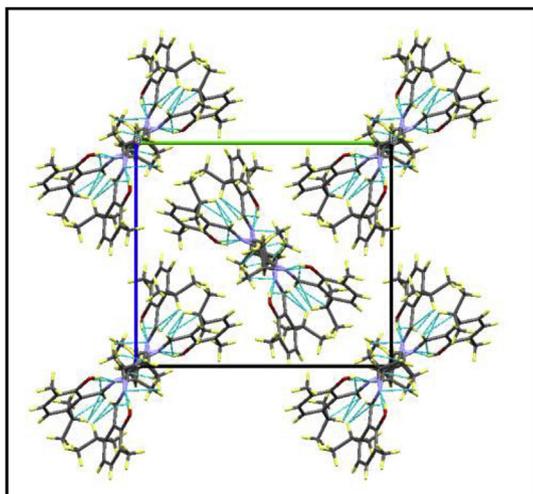


Fig. 3. The crystal packing of the ligand H2L viewed along an axis. The intramolecular C–H...O and C–H...N hydrogen bonds are shown as a light blue dashed line, and all atomic labels have been omitted for clarity. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

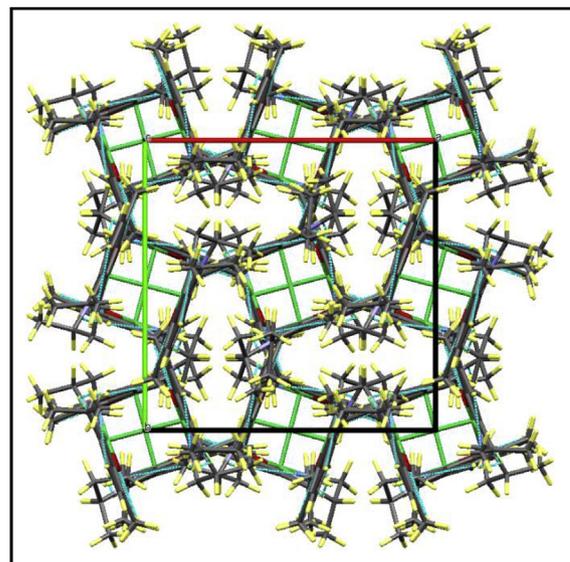


Fig. 5. The crystal packing of the dimeric nickel [NiL]₂ complex viewed along the c axis with 101 plane. The intramolecular C–H...O and C–H...N hydrogen bond is shown as a light blue dashed line, and all atomic labels have been omitted for clarity. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

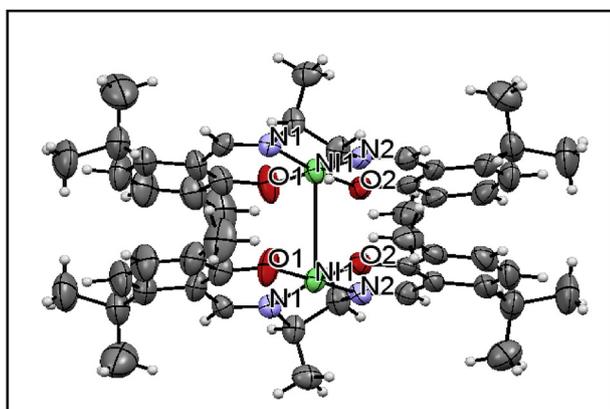


Fig. 4. ORTEP diagram of dimeric [NiL]₂ complex.

in the complexes. A band at 1612 cm^{-1} region is assigned to C=N absorption, this band of ligand undergoes small shifts to lower frequencies in the spectra of the complexes $1598\text{--}1566\text{ cm}^{-1}$ indicating coordination of the imine nitrogen [44,45]. Additional evidence for coordination of oxygen (M–O) and nitrogen (M–N) is the presence of the bands in the range $523\text{--}673$ and $433\text{--}487\text{ cm}^{-1}$ respectively which is in agreement with the literature [46].

5.3. Mass spectra

In the present investigation, the mass spectrum of H2L shows molecular ion peak at $m/z = 395$ [M^{+1}] corresponding to [$C_{25}H_{34}N_2O_2$] ion. The spectrum also exhibits peaks for the fragment at m/z 235 corresponding to [$C_{14}H_{22}N_2O$] $^{+1}$. The spectra of

Table 1
Crystallographic parameters, data collection and refinement for ligand H2L and its dimeric [NiL]2 complex.

Compounds	H2L	[NiL]2 Complex
Empirical formula	C25H34 N2 O2	C25H32 N2 Ni O2
Formula weight	394.54	451.23
Temperature	296 (2) K	296 (2) K
Wavelength	0.71073 Å	0.71073 Å
Crystal system	Monoclinic	Tetragonal
Space group	P2 ₁ /n	I-42 d
Unit cell dimensions	a = 10.2052 (7) Å α = 90° b = 16.5306 (11) Å β = 100.699 (2)° c = 14.7520 (8) Å γ = 90°	a = 12.3870 (3) Å α = 90° b = 12.3870 (3) Å β = 90° c = 60.928 (2) Å γ = 90°
Volume	2445.4 (3) Å ³	9348.7 (6) Å ³
Z	4	16
Density (calculated)	1.072 Mg/m ³	1.282 Mg/m ³
Absorption coefficient	0.068 mm ⁻¹	0.853 mm ⁻¹
F (000)	856	3840
Crystal size	0.350 × 0.300 × 0.250 mm ³	0.300 × 0.250 × 0.200 mm ³
Theta range for data collection	2.245–25.000°	1.678–24.996°
Index ranges	−12 ≤ h <= 12, −19 ≤ k <= 19, −17 ≤ l <= 14	−14 ≤ h <= 14, −14 ≤ k <= 14, −72 ≤ l <= 72
Reflections collected	33069	106989
Independent reflections	4307 [R (int) = 0.0505]	4120 [R (int) = 0.0635]
Completeness to theta = 25.000°	99.9%	99.9%
Absorption correction	Semi-empirical from Equivalents	Semi-empirical from equivalents
Max. and min. Transmission	0.995 and 0.967	0.85 and 0.71
Refinement method	Full-matrix least-squares on F ²	Full-matrix least-squares on F ²
Data/restraints/parameters	4307/64/300	4120/111/317
Goodness-of-fit on F ²	1.081	1.154
Final R indices [I > 2sigma(I)]	R1 = 0.0819, wR2 = 0.1996	R1 = 0.0311, wR2 = 0.0795
R indices (all data)	R1 = 0.1667, wR2 = 0.2912	R1 = 0.0401, wR2 = 0.0848
Largest diff. Peak and hole	0.247 and −0.167 e.Å ⁻³	0.254 and −0.179 e.Å ⁻³

Table 2
Selected bond lengths (Å) and bond angles (°) for schiff base ligand H2L.

Bond Lengths		Bond Angles	
C (6)–C (8)	1.457 (6)	C (7)–C (6)–C (8)	120.1 (4)
C (7)–O (1)	1.350 (5)	C (5)–C (6)–C (8)	120.3 (4)
C (8)–N (1)	1.271 (6)	O (1)–C (7)–C (6)	121.0 (4)
C (9)–N (1)	1.474 (10)	N (1)–C (9)–C (10)	114.8 (10)
C (9)–C (10)	1.481 (13)	N (1)–C (8)–H (8)	119.2
C (9)–H (9)	0.9800	C (10)–C (9)–H (9)	108.7

Table 3
Selected bond lengths (Å) and bond angles (°) for dimeric [NiL]2 complex.

Bond Lengths		Bond angles	
C (13)–N (2)	1.487 (12)	N (2)–Ni(1)–O (2)	93.95 (15)
C (10)–N (1)	1.288 (11)	O (1)–Ni(1)–O (2)	87.47 (12)
N (1)–Ni(1)	1.877 (9)	N (2)–Ni(1)–N (1)	85.7 (3)
N (2)–Ni(1)	1.820 (3)	O (1)–Ni(1)–N (1)	92.8 (3)
O (1)–Ni(1)	1.824 (3)	O (2)–Ni(1)–N (1)	170.9 (3)
O (2)–Ni(1)	1.832 (3)	N (2)–Ni(1)–O (1)	178.51 (16)

Table 4
Hydrogen bonding for schiff base ligand H2L.

D–H ... A	d (D–H)	d (H ... A)	d (D ... A)	<(DHA)
C (8)–H (8) ... O (2)#3	0.93	2.66	3.520 (6)	154.7
C (9)–H (9) ... O (2)#3	0.98	2.65	3.580 (19)	157.4
C (21)–H (21) ... O (1)	0.93	2.63	3.467 (6)	149.4
C (22')–H (22 B) ... O (1)	0.97	2.60	3.51 (3)	155.8
O (1)–H (1) ... N (1)	0.82	1.79	2.530 (5)	148.7
O (2)–H (2) ... N (2)	0.82	1.78	2.519 (5)	148.7

Symmetry transformations used to generate equivalent atoms: #1 -x+1,-y+2,-z #2 -x,-y+2,-z #3 x+1,y,z.

[MnL], [CoL] and [NiL]2 complexes show molecular ion peaks at m/z 447 [M^{OAc}], 451 [M⁺] and 451 [M⁺] respectively that are

Table 5
Hydrogen bonding for dimeric [NiL]2 complex.

D–H ... A	d (D–H)	d (H ... A)	d (D ... A)	<(DHA)
C (13')–H (13C) ... O (1)#1	0.97	2.64	3.260 (14)	122.0
C (13')–H (13C) ... O (1)#1	0.97	2.64	3.260 (14)	122.0

Symmetry transformations used to generate equivalent atoms: #1 -x+2,-y,z.

equivalent to their molecular weights. The manganese complex gave a fragment ion peak at m/z 287 [M⁻¹] corresponding to C₁₄H₂₁MnN₂O and nickel complex shows molecular ion peak at m/z 453 [M⁺²]. The m/z of all the fragments of schiff base ligand H2L and their metal complexes confirm the [ML] stoichiometry of the complexes.

5.4. Conductivity measurement

The complexes were dissolved in DMF and the molar conductivities of their 10⁻³ M solutions were measured at room temperature. The molar conductivity values of the complexes were in the range 4–28 Ω⁻¹ cm⁻¹ mol⁻¹. This value indicated that the complexes have non-electrolytic in nature [47].

5.5. Magnetic susceptibility

The [MnL] complex shows the magnetic moment 4.85 B M. which corresponds for Mn(III) d⁴ configuration [48]. The magnetic moment 1.33 B. M. of the [CoL] complex is consistent with square-planar [49]. The [NiL]2 complex is square planar and diamagnetic in nature.

5.6. SEM

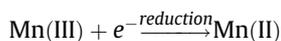
Scanning electron micrograph (SEM) has been currently used to determine the morphology and the particle or grain size of the metal complexes. The SEM photographs of all the metal complexes

are illustrated in Fig. 6. The SEM photographs were taken in the different scale range from 2 μm to 20 μm . From the SEM photograph it was noted that there is a uniform matrix in all the metal complexes with homogeneous phase material. The single phase formation in [MnL], [CoL], and [NiL]2 complexes having morphologies with particle size 1 μm –10 μm .

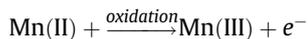
5.7. Cyclic voltammetry

The electrochemical behavior of schiff base ligand and metal complexes was examined in DMF and TBAP as supporting electrolyte. Fig. 7 shows the electrochemical cyclic voltammograms of curves of ligand, [MnL], [CoL] and [NiL]2 complexes in DMF at 10^{-3} M concentration of compounds containing 0.1 M tetrabutyl ammonium perchlorate (TBAP) as electrolyte with Ag/AgCl as reference electrode at scan rate 100 mVs^{-1} . The electrochemical data is summarized in Table 6.

For the schiff base ligand H2L, a cyclic sweep in the -1.5 to $+0.50$ V range shows a cathodic peak at -0.999 V and an anodic peak at -1.141 V. The electrochemical properties of manganese complex show the one-electron reduction peak (Epc), corresponding to the Mn(III/II) which occurs at -0.242 V and during the reverse scan the oxidation peak (Epa) is observed at -1.138 V. During the forward scan the Mn(III) gets reduced as:



Similarly during the reverse potential the oxidation of the Mn(II) takes place to Mn(III) which can be shown as:



The redox reaction therefore, can be used as an indication of major analytical tool for the determination of the trace elements which are electro active in nature.

The electrochemical data of cobalt and nickel complexes have similar reduction peaks (Epc) in the potential range given in Table 6, attributed to the Co(II/I) and Ni(II/I), the sweep potential shows the oxidation peak (Epa) for both the complexes at the potential value -1.123 V and -1.129 V respectively, as shown in Fig. 7 [40].

6. Biological activities studies

6.1. Antibacterial activity

The Minimal Inhibitory Concentration (MIC) of schiff base ligand and their metal complexes against bacteria were compared with the MIC values of standard drugs Ciprofloxacin and Ampicillin. The MIC values of the ligand H2L was observed to be $91 \mu\text{g/mL}$, $91 \mu\text{g/mL}$ and $111 \mu\text{g/mL}$ against *E. coli*, *B. subtilis* and *S. aureus*

respectively, the values exhibit better activities as compared to the standard drug Ampicillin and lower activities than Ciprofloxacin. In case of the MIC values of metal complex, [MnL] complex possesses MIC values ($90 \mu\text{g/mL}$) and ($65 \mu\text{g/mL}$) which are better than the MIC value of Ampicillin against *E. coli* and *B. subtilis*. The [CoL] complex exhibited super MIC values as ($165 \mu\text{g/mL}$) and ($176 \mu\text{g/mL}$) against *B. subtilis* and *S. aureus* respectively, while the MIC values against *E. coli* and *P. aeruginosa* were very high ($500 \mu\text{g/mL}$) and ($209 \mu\text{g/mL}$) as compared to standards. The [NiL]2 complex acquired excellent MIC values as ($49 \mu\text{g/mL}$), ($55 \mu\text{g/mL}$) and ($42 \mu\text{g/mL}$) against *P. aeruginosa*, *B. subtilis* and *S. aureus* respectively as compared to standard drugs Ampicillin and Ciprofloxacin, while its MIC ($125 \mu\text{g/mL}$) value against *E. coli* shows negligible activity.

The enhanced activity of the complexes can be explained on the basis of Overton's concept and Tweedy's Chelation theory [50,51]. The Chelation considerably decreases the polarity of the metal ion because of partial sharing of its positive charge with donor groups and possible pi-electron delocalization over the whole chelate ring. Such a chelation could enhance the lipophilic character of the central metal atom, which subsequently favors its permeation through the lipid layer of the cell membrane.

6.2. Antifungal activity

The MIC values of the ligand H2L and its four metal complexes [MnL], [CoL] and [NiL]2 show very poor activity as compared to standard drugs Miconazole and Fluconazole except [CoL] complex which possesses equal antifungal activity against the fungi *C. neoformans* as compared to the standard drug Miconazole. The low activity of the compounds might be visualized because low cell permeability, fitness of the particles size of the metal ion and the presence of the bulkier organic moieties [52].

6.3. Antioxidant activity

DPPH radical form absorbs at 517 nm. When a hydrogen atom or electron is transferred to the odd electron in DPPH radical, the absorbance at 517 nm decreases proportionally to the increase of nonradical forms of DPPH. As a consequence, DPPH radical is usually used as a substrate to estimate the anti-oxidative activity of antioxidants. Hence, if the absorbance decreases more rapidly, the more potent is the antioxidant activity of the compound. It is also visually noticeable as a change in colour from purple to yellow [53,54].

The results of percentage of free radical scavenging activity for the ligand H2L and its metal complexes are presented in supporting data. The synthesized ligand possesses better antioxidant property with ($\text{EC}_{50} = 0.1157$) as compared to ascorbic acid as a standard. The ligand upon complexation with the metals [MnL], [CoL] and [NiL]2 demonstrated a broad spectrum of results. The [NiL]2, [MnL] and

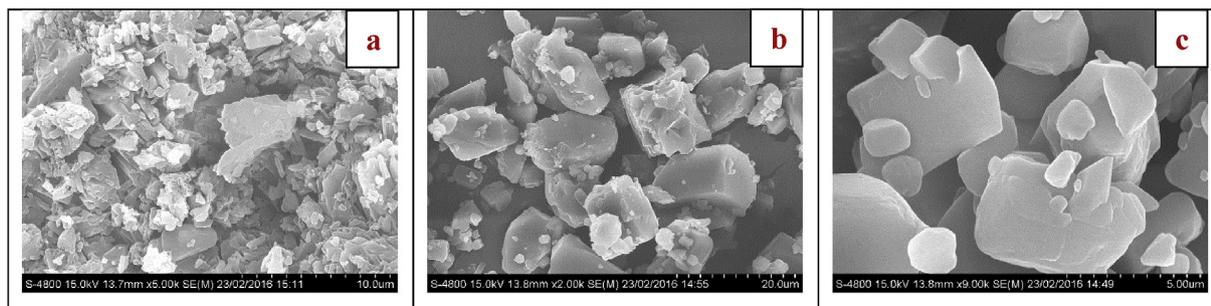


Fig. 6. SEM photographs of a) [MnL], b) [CoL] and c) [NiL]2 complexes.

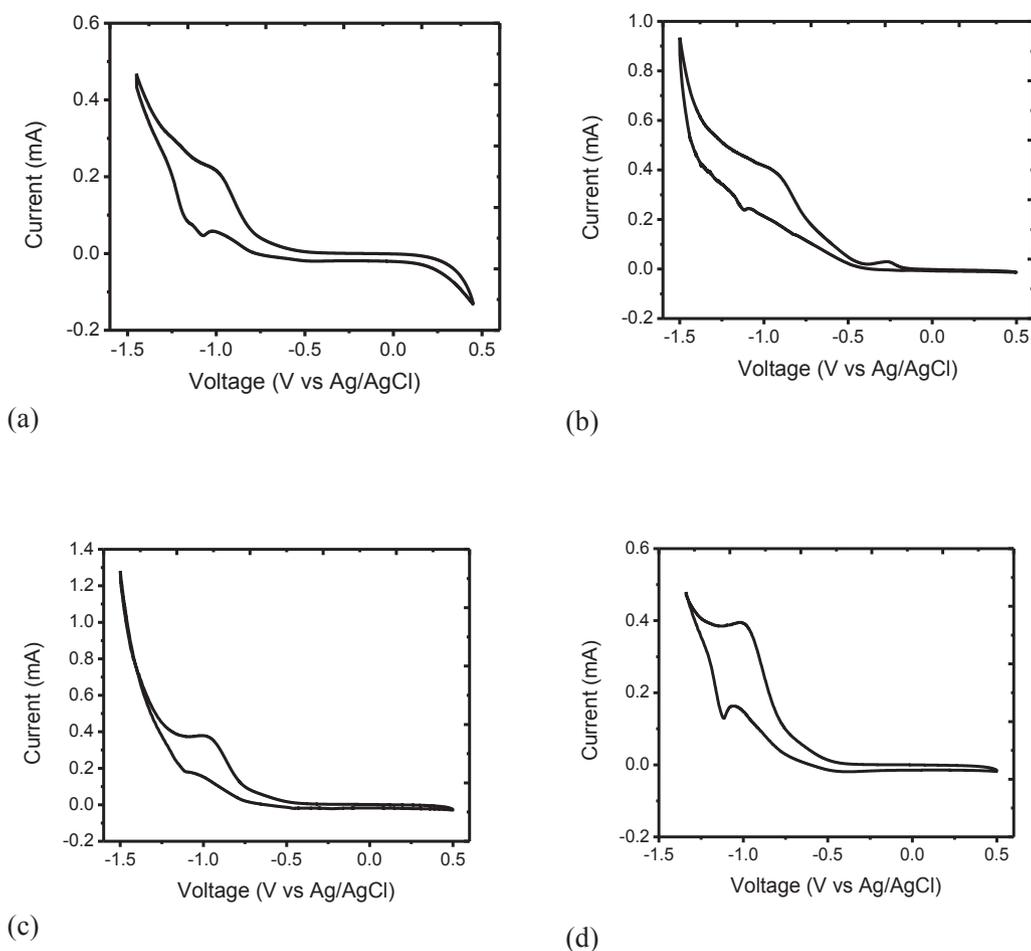


Fig. 7. Cyclic voltammograms of (a) schiff base ligand H2L; (b) [MnL]; (c) [CoL] and (d) [NiL]2 complexes respectively at room temperature in DMF solution containing 0.1 M TBAP as electrolyte at scan rate of 100 mVs^{-1} .

Table 6

Electrochemical cyclic voltammetry data of metal complexes in DMF solution containing 0.1 M TBAP as electrolyte at scan rate of 100 mVs^{-1} .

Compounds	Epa (II→I) (V)	Epc (I→II) (V)	ΔE (V)
H2L	-1.141	-0.999	0.142
[MnL]	-1.138	-0.242	0.896
[CoL]	-1.123	-0.935	0.188
[NiL]2	-1.129	-0.98	0.149

[CoL] complexes showed a super activity. In general, all other complexes exhibited higher scavenging activity than the schiff base ligand. These results clarify that, the synthesized compounds scavenged the DPPH radical in a concentration dependent approach.

6.4. DNA cleavage activity

The chemical nuclease activity of all the compounds has been investigated by agarose gel electrophoresis using pBR 322 DNA as a substrate. When circular plasmid DNA is subjected to electrophoresis, relatively fast migration is observed for the supercoiled form (SC form I). If scission occurs on one strand (nicking), the supercoil will relax to generate a slower moving open circular form (NC form II). If both strands are cleaved, a linear form (form III) that migrates between form I and form II is generated. The plasmid pBR 322 DNA (200 ng) were mixed with different concentrations of compounds

in the presence of oxidant H_2O_2 . In presence of H_2O_2 , pBR 322 DNA was converted from SC (form I) to NC (form II). The ligand H2L and [MnL] and [NiL]2 complexes showed the cleavage of the SC form (form I) to NC (form II), while, the [CoL] complex showed the complete conversion of SC form I to nicked DNA form (II) as the concentration increases from $20 \mu\text{M}$ to $200 \mu\text{M}$ [55,56].

7. Conclusion

In this study, the transition metal complexes of manganese, cobalt and nickel have been prepared from a new salen type ligand (H2L) and characterized through elemental, spectral, magnetic measurements, molar conductivity, electrochemical measurements and single crystal structures, from this data structures of the ligand and complexes have been confirmed. The antibacterial activity of the compounds was performed against *E. coli*, *P. aeruginosa*, *B. subtilis*, and *S. aureus* and compared with standard drugs Ciprofloxacin and Ampicillin, the result indicated that the activity increased upon complexation of the ligand. Simultaneously, antifungal activity was estimated on selected fungal strains *C. albicans*, *A. flavus*, *A. niger*, *C. neoformans* using standard drugs Miconazole and Fluconazole. Some of the metal complexes showed good antibacterial activity, however, all the compounds exhibited very poor antifungal activity as compared to standard drugs. All the compounds also exhibited better antioxidant activity as compared to ascorbic acid as standard and the cobalt complex showed pBR

322 DNA cleavage in the presence of H₂O₂.

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Appendix A. Supplementary data

Supplementary data related to this article can be found at <https://doi.org/10.1016/j.molstruc.2017.09.112>.

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