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RESEARCH

ORIGINAL RESEARCH

Antimicrobial and antioxidant activities of new metal complexes derived from (E)-3-((5-phenyl-1,3,4-oxadiazol-2-ylimino)methyl)naphthalen-2-ol

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Abstract (E)-3-((5-phenyl-1,3,4-oxadiazol-2-ylimino)methyl) naphthalen-2-ol (**LH**) has been synthesized and used as a ligand for the formation of V(IV), Cr(III), Mn(II), Co(II), Ni(II), and Cu(II) complexes. The chemical structures were characterized using different spectroscopic methods. The elemental analyses revealed that the complexes have the general formula $[ML_2(H_2O)_2]$ [where M = Mn(II), Co(II), and Cu(II)], while the Cr(III) complex has the formula $[CrL_2(H_2O)_2]Cl$, V(IV) complex has the formula $[VO_2L_2]$, and Ni(II) complex has the formula $[NiL_2]$. The molar conductance data revealed that all the metal chelates except the Cr(III) are non-electrolytes. From the magnetic susceptibility measurement and UV–Visible spectra, it is found that the structures of Cr(III), Mn(II), Co(II), and Cu(II) complexes are octahedral, V(IV), complex is square pyramid and Ni(II) complex is square planar. The stability of the prepared complexes was studied theoretically using density function theory. The total energy for the complexes was calculated and it was shown that the copper complex is the most stable. Complexes were tested against selected types of microbial organisms and showed significant activities. The free radical scavenging activity of metal complexes have been determined by their interaction with the stable DPPH-free radicals. All the compounds have shown encouraging antioxidant activities.

Keywords Antimicrobial · Complexes · DPPH · Oxadiazol · Scavenging · Vanadium

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Introduction

Drug resistance has become a growing problem in the treatment of infectious diseases caused by bacteria and fungi (Raman *et al.*, 2007). The serious medical problem of bacterial and fungal resistance and the rapid rate at which it develops has led to increasing levels of resistance to classical antibiotics (Rice *et al.*, 1999; Ironmonger *et al.*, 2007). The discovery and development of effective antibacterial and antifungal drugs with novel mechanism of action has become an urgent task for infectious disease research programs (Kumar *et al.*, 2011). Schiff bases and their complexes are largely studied because of their interesting and important properties such as their ability to reversibly bind oxygen (Muhammad *et al.*, 2011) to redox system, biological systems (Park *et al.*, 1998) and oxidation of DNA (Landy, 1989). Antioxidants have become one of the major areas of scientific research (Gursoy and Yukse, 2010). Antioxidants are extensively studied for their ability to protect organism and cell from damage that are induced by oxidative stress. Scientists in many different disciplines become more interested in new compounds, either synthesized or obtained from natural sources that could provide active components to prevent or reduce the impact of oxidative stress on cell (Hussain *et al.*, 2003). The synthesis of compounds incorporating oxadiazole ring have been attracting widespread attention due to their diverse pharmacological properties such as antimicrobial, anti-inflammatory, analgesic, and antitumor activities (Amir and Shikha, 2004; Holla and Shivananda, 2002; Neslihan, 2005; Hakan *et al.*, 2010; Scovill and Franchino, 1982). The preparation of a (E)-3-((5-phenyl-1,3,4-oxadiazol-2-ylimino)methyl)naphthalen-2-ol, used as a ligand for the formation of V(IV), Cr(III), Mn(II), Co(II), Ni(II), and Cu(II) complexes, is presented in this study. The chemical structures of the newly synthesized complexes were confirmed by spectroscopic techniques and CHN analysis. The microbial activities of all synthesized compounds and their in vitro antioxidant activities were also investigated.

Experimental

General

All chemicals used in this study were of reagent grade (AR) supplied by either Sigma-Aldrich or Fluka, and used without purification. The FT-IR spectra were recorded in the (4,000–200) cm^{-1} range on Cesium iodide disks using a Shimadzu FTIR 8300 Spectrophotometer. Proton NMR spectra were recorded on Bruker-DPX 300 MHz spectrometer with TMS as internal standard. The UV–Visible spectra were measured in ethanol using a Shimadzu UV–Vis. 160A spectrophotometer in the range (200–1,000) nm. Magnetic susceptibility measurement for complexes was obtained at room temperature using a Magnetic Susceptibility Balance Model MSB-MKI. The flame atomic absorption of a Shimadzu AA-670 elemental analyzer was used for metal determination. Elemental microanalysis was carried out using a CHN elemental analyzer model 5500-Carlo Erba instrument. A Gallenkamp M.F.B.600.010 F melting point apparatus was used to measure the melting points of all the prepared compounds.

Chemistry

Synthesis of the ligand

A mixture of equimolar quantity of 3-hydroxy-2-naphthaldehyde and 2-amino-5-phenyl-1,3,4-oxadizole in minimum amount of ethanol was refluxed for 2 h. After cooling to room temperature the product was separated out and washed with distilled water, ether and finally several times with cold ethanol, dried, and then recrystallized from acetone which gave yellow needle shaped crystals of (E)-3-((5-phenyl-1,3,4-oxadiazol-2-ylimino)methyl)naphthalen-2-ol (**LH**) (Al-Amiery *et al.*, 2011a, b), yield 87%, m.p. 216°C; ^1H-NMR ($CDCl_3$): δ 5.4 (s, 1H) for –O–H, δ 6.3 (s, 1H) for –N=C–H), δ 7.30 (m, 1H) for aromatic ring) and δ 7.90 (m, 1H) for aromatic ring); IR: 2400 m cm^{-1} (OH, hydroxy), 1630 cm^{-1} (C=N), 1570 cm^{-1} (C=C, Alkene), 1050 and 1230 cm^{-1} (sym. and asym. C–O); Anal. Calcd. for $C_{19}H_{13}N_3O_2$: C 72.37%, H 4.16%, N 13.33%. Found: C 72.10%, H 4.02%, N 13.30%.

Synthesis of the metal complexes

Bis((E)-3-((5-phenyl-1,3,4-oxadiazol-2-ylimino)methyl) naphthalen-2-ol)nickel (II) The ethanolic solution of brown colored nickel (II) complex was obtained by mixing the solutions of nickel chloride (0.28 g in 100 ml),and ligand (0.63 g in 100 ml) in 1:2 molar ratio followed by dropwise addition of 10% sodium acetate (pH 7.5) was refluxed for 2 h over a water bath. On keeping the reaction mixture overnight, dark brown solids separated out. The adduct was filtered, washed with ethanol, and petroleum ether and finally dried under vacuum.

Bis((E)-3-((5-phenyl-1,3,4-oxadiazol-2-ylimino)methyl) naphthalen-2-ol)vanadium(II) **LH** (0.63 g, 0.002 mol) in 100 ml of ethanol was added with stirring to the $VOSO_4\cdot 5H_2O$ solution (0.001 mol, 0.253 g) in 2:1 molar ratio. The pH of the solution was raised up to 7.0 by adding 5 ml of 10% sodium acetate solution. The reaction mixture was refluxed for half an hour. Pink color complex was separated out then washed and filtered under suction. Further washing with water, ethanol, and petroleum ether to remove unreacted ligand and dried over anhydrous $CaCl_2$.

Bis((E)-3-((5-phenyl-1,3,4-oxadiazol-2-ylimino)methyl) naphthalen-2-ol)diaqua, cobalt(II), manganese(II), copper(II) or chromium(III) chloride, complexes Acidic solutions of metal ($CrCl_3\cdot 6H_2O$, $MnCl_2\cdot 4H_2O$, $CoCl_2\cdot 6H_2O$, and $CuCl_2\cdot 2H_2O$) (1 mmol) in hot ethanol (20 ml) were mixed with hot ethanolic solution 50 ml of the ligand (2 mmol) and dropwise addition of 10% (w/v) sodium acetate till the complexes precipitated out (pH 8.5). The closed complexes were filtered, washed with water, ethanol, and dried under vacuum. Purity of the complexes was checked by thin layer chromatography (TLC). The TLC plate prepared with precoated silica gel aluminum plate 60_F-254 and the stationary face having a thickness of about 0.5 mm. 5 µl each of test solution was applied on silica gel plate (20 × 10 cm). The TLC plate was kept in a developing chamber saturated ethyl acetate:methanol: acetone (25:25:50) solvent systems (Kadhum *et al.*, 2011).

Study of complex formation in solution

The complexes of the ligand with metal ions were studied in dimethylformamide (DMF), to determined M:L ratio in the complex following the molar ratio method. Several series of solutions were prepared having constant concentration (10^{-3} M) of the metal ion and (L). The M:L ratio was determined from the relationship between the absorption of light (Al-Amiery *et al.*, 2011a, b) and the M:L molar ratio. The results of complexes formation in solution are listed in Table 2.

Pharmacology

Evaluation of antibacterial activities The in vitro biological screening of all the compounds was carried out to evaluate their antibacterial activity against *Escherichia coli*, *Klebsiella pneumoniae*, *Pseudomonas vulgaris*, *Pseudomonas aeruginosa*, *Staphylococcus aureus*, and *Bacillus cereus* by the disk diffusion method, using agar nutrient as the medium and ciprofloxacin as the standard. The antifungal activity of the compounds was evaluated by the disk diffusion method against the fungi *Aspergillus niger* and *Candida albicans* cultured on potato dextrose agar as medium and ketoconazole as the standard. The stock solution (10^{-2} M) was prepared by dissolving the compounds in DMSO and the solutions were serially diluted to find the minimum inhibitory concentration (MIC) values. In a typical procedure (Al-Amiery *et al.*, 2009), the disk was filled with the test solution using a micropipette and the plate was incubated 24 h for bacteria and 72 h for fungi. During this period, the test solution diffused and the growth of the inoculated microorganisms was affected.

Evaluation of antioxidant activity Stock solution (1 mg/ml) was diluted to final concentrations of 20–100 µg/ml. Ethanolic DPPH solution (1 ml, 0.3 mmol) was added to sample solutions in DMSO (3 ml) at different concentrations (50–300 µg/ml) (Chen *et al.*, 1999). The mixture was shaken vigorously and allowed to stand at room temperature for 30 min. The absorbance was then measured at 517 nm in a UV–Vis spectrophotometer. The lower absorbance of the reaction mixture indicates higher free radical scavenging activity. Ethanol was used as the solvent and ascorbic acid as the standard. The DPPH radical scavenger was calculated using the following equation:

$$\text{Scavenging effect }(\%) = \frac{A_0 - A_1}{A_0} \times 100,$$

where A_0 is the absorbance of the control reaction and A_1 is the absorbance in the presence of the samples or standards. $A_0 - A_1$.

Results and discussion

Chemistry

(E)-3-((5-Phenyl-1,3,4-oxadiazol-2-ylimino)methyl)naphthalen-2-ol (Fig. 1) is the key intermediate for the metal complexes synthesized in this study.

These data shows that the atomic charges have been affected by the presence of substituent of rings as shown in Table 1. As a reference compound the (E)-3-((5-phenyl-1,3,4-oxadiazol-2-ylimino)methyl)naphthalen-2-ol (Fig. 1), data for minimized geometry and the 3D-geometrical structure is shown in Fig. 2.

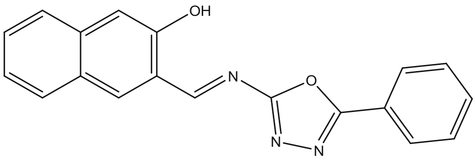


Fig. 1 The structure of (E)-3-((5-phenyl-1,3,4-oxadiazol-2-ylimino)methyl)naphthalen-2-ol (**LH**)

Table 1 The atomic charges of **LH**

Atom	Charge
[C(1)]	C −0.175
[C(2)]	C 0.257
[C(3)]	C −0.004
[C(4)]	C −0.063
[C(5)]	C 0.018
[C(6)]	C −0.044
[C(7)]	C −0.059
[C(8)]	C −0.038
[C(9)]	C −0.066
[C(10)]	C 0.050
[O(11)]	O −0.206
[C(12)]	C 0.148
[N(13)]	N −0.213
[O(14)]	O −0.107
[C(15)]	C 0.469
[N(16)]	N −0.324
[N(17)]	N −0.266
[C(18)]	C 0.350
[C(19)]	C 0.043
[C(20)]	C −0.052
[C(21)]	C −0.027
[C(22)]	C −0.055
[C(23)]	C −0.028
[C(24)]	C −0.051
[H(25)]	H 0.026
[H(26)]	H 0.021
[H(27)]	H 0.022
[H(28)]	H 0.025
[H(29)]	H 0.025
[H(30)]	H 0.023
[H(31)]	H 0.194
[H(32)]	H −0.013
[H(33)]	H 0.021
[H(34)]	H 0.025
[H(35)]	H 0.025
[H(36)]	H 0.025
[H(37)]	H 0.023

The data obtained shows that the highest atomic charge in **LH** molecule is at [N(16) −0.324] the next charge value is at [N(13) −0.213] and [O(11) −0.206]. These data

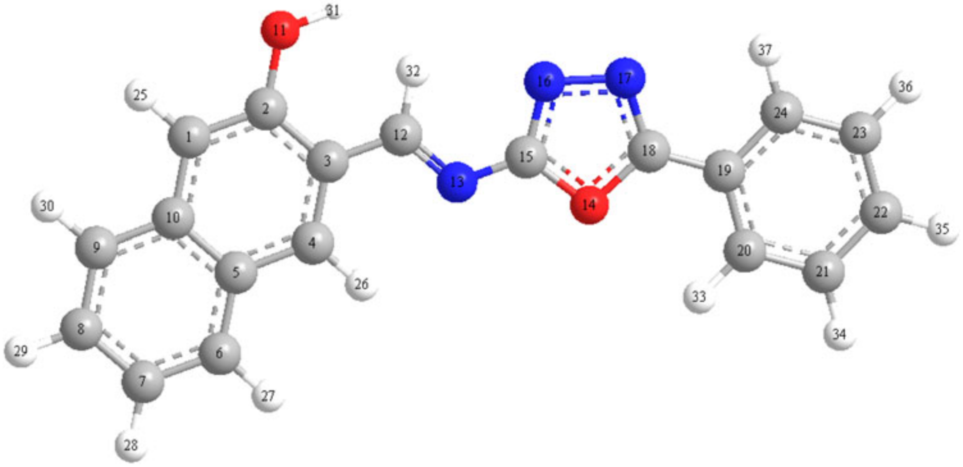
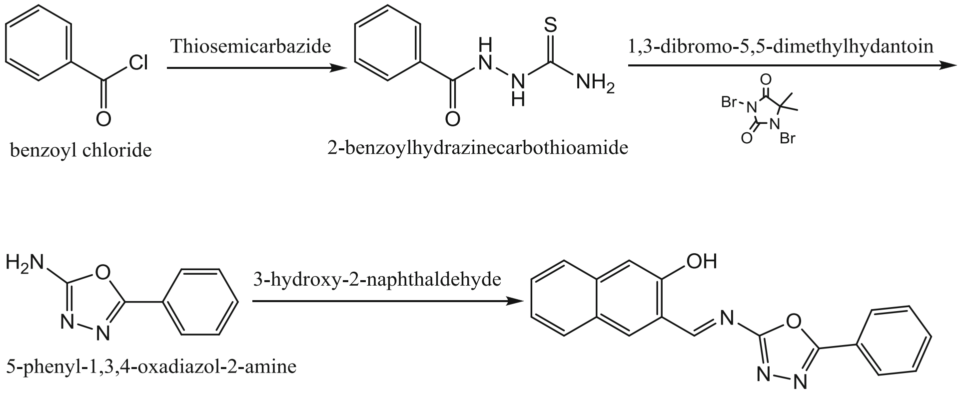


Fig. 2 The 3D structure of **LH**



Scheme 1 Formation of the ligand

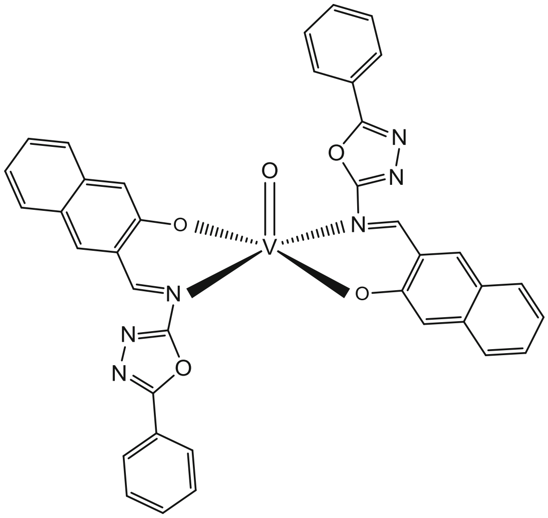
Table 2 Analytical data for the metal complexes

No.	Compounds	M:L	M.P. °C/color	Elemental analysis found/calculated			
				C%	H%	N%	M%
C_1	$[VO(L)_2]$	1:2	266d/light green	65.42/65.62	3.44/3.48	12.05/12.08	7.60/7.32
C_2	$[CrL_2(H_2O)_2]Cl$	1:2	272d/green	60.51/60.68	3.71/3.75	11.15/11.17	7.16/6.91
C_3	$[MnL_2(H_2O)_2]$	1:2	245/dark brown	63.42/63.42	3.89/3.92	11.68/11.68	7.60/7.63
C_4	$[CoL_2(H_2O)_2]$	1:2	280d/light pink	63.24/63.07	3.86/3.90	11.65/11.61	7.90/8.14
C_5	$[NiL_2]$	1:2	268d/orange	66.47/66.40	3.49/3.52	12.24/12.23	8.40/8.54
C_6	$[Cu(H_2O)_2L_2]$	1:2	292d/green	62.72/62.68	3.84/3.88	11.54/11.54	8.71/8.73

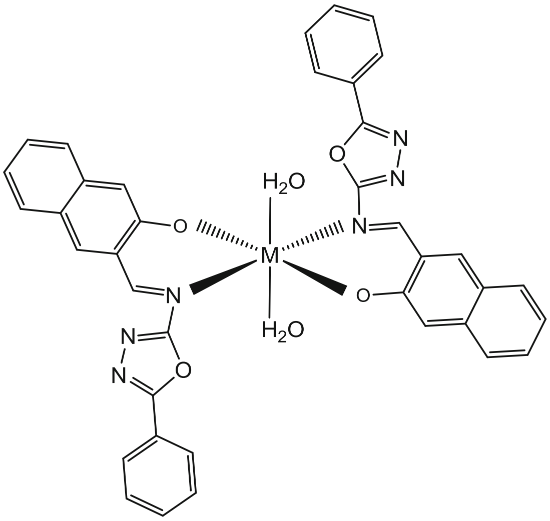
(Table 1) show clearly that oxygen atom [N(16)] is the most reactive toward the bonding with the metal. The determined bond angle, twist angle, 3D geometrical structure (Fig. 2), and stereochemistry [C(12)–N(13): (E)] indicate that this molecule is planar.

The synthesis of (E)-3-((5-phenyl-1,3,4-oxadiazol-2-ylimino)methyl)naphthalen-2-ol was performed by vigorously refluxing 3-hydroxy-2-naphthaldehyde and 2-amino-5-phenyl-1,3,4-oxadizole. 87% yield (Scheme 1).

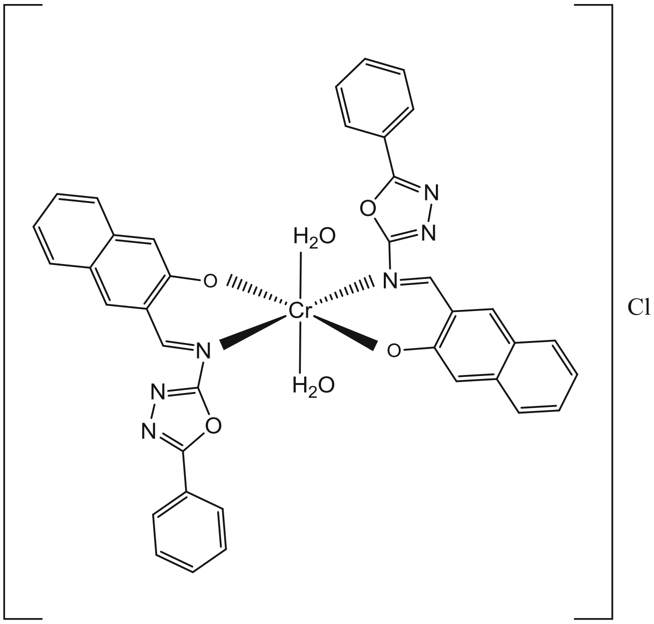
The complexes were synthesized by the reactions of **LH** with the metal ions, in which the ligand behaves as a bidentate ligand through its oxygen and nitrogen atoms. The analytical data of these complexes are presented in Table 2. All the complexes are fairly stable and can be stored for long periods at room temperature. The solid colored complexes are stable toward heat, air, and moisture, and they dissolved in dimethyl formamide and dimethyl sulfoxide. The analytical data of the complexes are consistent with the proposed molecular structures (Fig. 3), with molar metal to ligand ratio of (1:2). The stability for the prepared complexes was studied theoretically using density function theory (DFT). The total energy



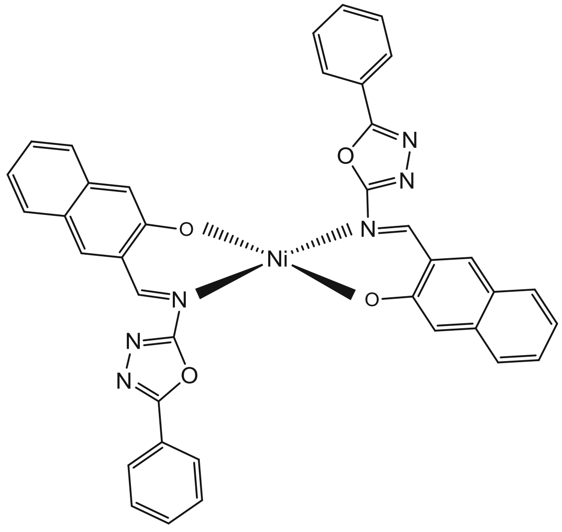
Square pyramidal geometry V(IV) complex



Octahedral geometry Mn(II), Co(II) and Cu(II) complex



Octahedral geometry Cr(III) complex



Square planer geometry Ni(II) complex

Fig. 3 The proposed structures for the complexes

for the complexes was calculated and it was shown that the copper complex is the most stable and the chromium complex is the least stable as follows: Cu(II) > Ni(II) > Co(II) > Mn(II) > Cr(III) > V(IV). In all our study on metal complexes (in which we have used different ligands with the ion metals Cu, Ni, Co, and Cr), we found out that the copper complex is consistently the more stable.

Elemental analysis

The compositions of the complexes are summarized in Table 2. The C, H, N, and M contents (both theoretically calculated values and actual values) are in accordance with the formula $ML_2(H_2O)_2$, [M = Mn(II), Co(II), and Cu(II)] while Cr(III) complex with formula $[ML_2(H_2O)_2]Cl$, Ni(III) complex with formula $[NiL_2]$, and V(IV) complex with formula $[VOL_2]$ (Table 2). The complexes are generally soluble in common organic solvents.

Infrared spectra

A study and comparison of the infrared spectra of **LH** and its complexes imply that **LH** is bidentate, with the oxygen and nitrogen as the two coordination sites. The ligand (**LH**) shows two moderately strong bands at 3,400 and 1,630 cm^{-1} assigned as ν O–H and ν C=N groups. On complex formation the latter band shifts to lower energy while the phenolic O–H group disappears in the prepared complexes, this supports the deprotonation and linkage of Oxygen atom to the central metal ion (Scovill and Franchino, 1982). However, the exceptionally higher value of 1,030 cm $^{-1}$ is in conformity with the C–O group in oxadiazole ring. The absorption band in the range (460–515) and (380–430) cm^{-1} were assigned to (M–N) and (M–O) bands. Moreover, the strong absorption at 970 cm^{-1} for C_1 complex investigate the V=O group, as well as the stretching of O–H groups for coordinated water molecular are showed in the region 3,615–3,490 cm^{-1} (Hakan *et al.*, 2010; Sreekanth and Kurup, 2003) as broad band which indicates the participation of water molecular in coordination with metal ion except for Ni(II) complex (Table 3).

Table 3 FT-IR (cm^{-1}) bands of metal complexes

No.	C=N	C=C	*v*C–O	M–O	*v*M–N	V=O	H_2O
C_1	1,570	1,572	1,025	395 (m)	460 (m)	970	3,660
C_2	1,580	1,573	1,020	415 (m)	510	–	3,490
C_3	1,605	1,577	1,015	380	515	–	3,515
C_4	1,610	1,572	1,015	420	490	–	–
C_5	1,663	1,577	1,010	418	465	–	3,470
C_6	1,660	1,020	1,580	430	477	–	3,615

^{1}H-NMR spectra

The ^{1}H NMR spectrum of the ligand (**LH**) show characteristic signals due to the (O–H) protons at 5.4 ppm. Moreover, the peaks observed at 7.3 ppm (m) and 7.9 ppm (m) were assigned to the (C–$H_{aromatic}$) protons of the ligand. The band located at 6.3 ppm may be assigned to (=C–H_{vinyl}) proton for ligand.

Molar conductance

The molar conductance values of all the complexes determined in nitrobenzene at room temperature are given in Table 4. The value for the Cr(III) complex indicates that one chloride ion is present outside the coordination sphere. The molar conductance values V(IV), Mn(II), C(II), Ni(II), and Cu(II) complexes are quite low to correspond to an ionic complex; hence, these complexes are considered to be neutral and the chloride ions are assumed to be situated within the coordination sphere.

Magnetic moment and UV–Vis spectra

The ultraviolet spectrum of the synthesized ligand showed two absorption bands, the position of the first band at 240 nm (41,666 cm^{-1}), which represents the ($\pi \rightarrow \pi^*$) transition, while the second band (which has higher intensity than the first band due to conjugated system) appeared at 315 nm (31,746 cm^{-1}) and represents the ($n \rightarrow \pi^*$) transition. Generally, the bands of the newly synthesized complexes are either shifted to shorter or longer wavelengths than that of the ligand, but the high intensity of the band is an indication for complex formation.

In these complexes the bands observed over 300 nm could be assigned to nitrogen-metal charge transfer absorption. The electronic absorption bands for the ligand and complexes are classified into two distinct groups, first those that belong to ligand transitions appeared in the UV region while *d–d* transitions which appeared in the visible region. These transitions are assigned in relevance to the structures of the complexes (Table 4). The Cr(III) complex showed a 3.2 B.M magnetic moment, which supports the high spin octahedral geometry. The Cr(III) complex showed four bands with absorbance maxima at 43478.2, 27777.7, 23809.5, and 16260.16 cm^{-1} which were assigned to the $^4A_2g(F) \rightarrow {}^4T_{2g(F)}$, $^4A_{2g(F)} \rightarrow {}^4T_{1g(F)}$, $^4A_{2g(F)} \rightarrow {}^4T_{1g(P)}$ absorption bands, respectively. These transitions suggest an octahedral geometry for the Cr(III) complex.

The electronic spectrum of vanadyl complex shows an absorption at 390 cm^{-1} of high intensity which refers to LMCT transition of (O=V), this suggest the overlapping of *d–d* transition at 413 nm with this change transform with indicates the square pyramid geometry around V-ion, Table 4. However, the spin forbidden transition at 2,000 cm^{-1} for Mn(II) complex investigates the octahedral geometry (John and David, 1965).

The nickel complex at a room temperature magnetic moment of 0.0 B.M., which is consistent with an square

Table 4 Physical data of the synthesized compounds

No.	λ_{max} nm (E_{max})	Magnetic moment μ (B.M.)	Λ ohm^{-1} cm^2 mol^{-1}	Structure
C_1	240, 390, 413	0.00	18	Square pyramid
C_2	230, 360, 420, 615 (106)	3.20	90	Octahedral
C_3	240, 375 (25000), 505 (80)	4.50	30	Octahedral
C_4	230, 325, 500, 625 (120)	2.90	24	Octahedral
C_5	225, 380 (19500), 505 (118)	0.00	28	Square planar
C_6	230, 350 (3500), 525 (80)	1.35	22	Octahedral

planar field. The electronic absorption spectrum showed absorption band at 19,220 cm^{-1} which is considered as $A_2g_1 \rightarrow A_2g_2$. The absence of any band below 10,000 cm^{-1} eliminates the possibility of a tetrahedral environment in this complex. The room temperature magnetic moment of 1.35 B.M. indicates an octahedral structure for the Cu(II) ion complex. The electronic absorption spectrum of Cu(II) complex shows only one band at 20,500 cm^{-1} assigned to $Eg_2 \rightarrow T_2g_2$, which is in conformity with octahedral geometry (Hakan *et al*., 2010; Sreekanth and Kurup, 2003).

Suggested stereostructures of the complexes

The proposed structures of complexes based on the above mentioned data (UV–Vis, IR, and NMR spectra, conductivity, molar ratio, and magnetic properties) are depicted in Fig. 3. The water molecules in the metal complexes of except Ni(II) and V(IV) are in the octahedral coordination sphere, but for the Cr(III) complex, the water molecules are in spherical coordination and the chloride is in the outer of the spherical coordination, as implied by the molar conductance.

Pharmacology

Antibacterial activity

The antibacterial screening data shows that the complexes exhibit antimicrobial properties, and we note that the metal chelates exhibit more inhibitory effects than the parent ligand. The increased activity of the metal chelates can be explained on the basis of chelation theory (Sengupta *et al*., 1998). It is known that chelation tends to make the ligand act as powerful and potent bactericidal agents, thus killing more of the bacteria than the ligand alone. It is observed that, in a complex, the positive charge of the metal is partially shared with the donor atoms present in the ligands, and there may be π-electron delocalization over the whole chelating space (Rohaya *et al*., 2005). This increases the lipophilic character of the metal chelate and favors its permeation through the lipoid layer of the bacterial membranes. The increased lipophilic character of these complexes seems to be responsible for their enhanced potent antibacterial activity. It may be suggested that these complexes deactivate various cellular enzymes, which play a vital role in various metabolic pathways of these microorganisms. It has also been proposed that the ultimate action of the toxicant is the denaturation of one or more proteins of the cell, which as a result, impairs normal cellular processes. There are other factors which also increase the activity, which are solubility, conductivity, and bond length between the metal and the ligand. As a result from the study of antibacterial of the prepared metal complexes (Table 5), the following points were concluded.

The activity of the ligand and metal complexes was tested against some human pathogenic bacteria including Gram-positive (*S. aureus* and *B. cereus*) Gram negative (*E. coli*, *P. aeruginosa*, *K. pneumoniae*, and *P. vulgaris*) (Table 5). From the results obtained from the method, it was found that the ligand and metal complexes were highly active even at low concentrations as shown in Table 5.

Antifungal activities

Metal ions are adsorbed on the surface of the cell wall of microorganisms and disturb the respiration process of the cell and thus block the synthesis of the proteins that restricts further growth of the organisms. So, metal ions are essential for the growth-inhibitor effect (Dharmaraj *et al*., 2001). According to Overtone's concept of cell permeability, the lipid membrane that surrounds the cell favors the passage of only the lipid soluble materials due to which liposolubility is an important factor, which controls the antifungal activity. On chelation, the polarity of metal ion will be reduced to a greater extent due to the overlap of the ligand orbital and partial sharing of the positive charge of

Table 5 The effect of tested compounds (**LH** and C_1–C_6) toward tested bacteria compare with ciprofloxacin as standard

Compounds	Zone of inhibition (mm)/concentration of compounds (10 μg/ml)					
	E. coli	*K. pneumoniae*	*P. vulgaris*	*P. aeruginosa*	*S. aureus*	*B. cereus*
LH	15	12	8	7	16	6
C_1	16	18	16	16	22	12
C_2	19	19	21	24	28	18
C_3	45	25	19	23	19	21
C_4	30	28	25	25	29	21
C_5	26	26	18	16	26	22
C_6	31	29	23	26	30	16
Ciprofloxacin	29	27	25	28	29	23
DMSO	0	0	0	0	0	0

the metal ion with donor groups. Further, it increases the delocalization π-electrons over the whole chelate ring and enhances the lipophilicity of the complexes. This increased lipophilicity enhances the penetration of the complexes into lipid membrane and restricts further multiplicity of the microorganisms. The variation in the effectiveness of different compounds against different organisms depends either on the impermeability of the cells of the microbes or on differences in ribosome of microbial cells (Joseyphus and Nair, 2008). Although, the exact mechanism is not understood biochemically, mode of action of antimicrobials may involve various targets in microorganisms. (i) Interference with the cell wall synthesis, damage as a result of which cell permeability may be altered (or) they may disorganize the lipoprotein leading to the cell death. (ii) Deactivate various cellular enzymes, which play a vital role in different metabolic pathways of these microorganisms. (iii) Denaturation of one or more proteins of the cell, as a result of which the normal cellular processes are impaired. (iv) Formation of a hydrogen bond through the azomethine group with the active center of cell constituents, resulting in interference with the normal cell process (Malhota *et al*., 1993). In vitro *antifungal* screening effects of the investigated compounds were tested against some fungal species (*A. niger* and *C. albicans*). The results of antifungal activity show that the ligand it selves dose not exhibit antifungal activities, but all complexes exhibit good antifungal activities. The Cu(II) complex shows more activity than Ni(II) and shows more activity than the Co(II) complex, due to the higher stability of Cu(II) complex than the Ni(II) and Co(II) complexes (Table 6).

Effect of hetero atoms From the observation (Table 6), the higher inhibition of microbial growth is due to uncoordinated hetero atom. In the complexes, the ligand has uncoordinated donor atom (nitrogen atom) which enhance the activity of the complexes by bonding with trace elements present in microorganisms. This may combine with the uncoordinated site and inhibit the growth of microorganisms (Malhota *et al*., 1993).

Table 6 The effect of tested compounds (**LH** and C_1–C_6) toward tested fungi compare with ketoconazole as standard

Compounds	Zone of inhibition (mm)/concentration of compounds (10 μg/ml)	
	A. niger	*C. albicans*
LH	2	4
C_1	11	9
C_2	22	19
C_3	2	6
C_4	24	24
C_5	14	16
C_6	25	29
Ciprofloxacin	27	26

Effect of azomethine (>C=N) group The mode of action of the compounds may involve formation of a hydrogen bond through the azomethine group (>C=N–) with the active centers of cell constituents (Soares *et al*., 1997; Mishra and Singh, 1993) resulting in interferences with the normal cell process.

In vitro antifungal screening effects of the ligand and metal complexes were tested against some fungal spices (*A. niger* and *C. albicans*). Complex (C4) was found to exhibit antifungal activity against all the fungi in this study. Thus, complex (C6) displayed potential antifungal activity against *A. niger* and *C. albicans* as shown in Table 6.

Radical scavenging activity

The 2,2″-diphenyl-1-picrylhydrazyl (DPPH) radical assay provides an easy and rapid way to evaluate the antiradical activities of antioxidants. Determination of the reaction kinetic types DPPHH is a product of the reaction between $DPPH^{\bullet}$ and an antioxidant:

$$DPPH^{\bullet} + AH \rightarrow DPPHH + A^{\bullet}$$

The reversibility of the reaction is evaluated by adding DPPHH at the end of the reaction. If there is an increase in the percentage of remaining $DPPH^{\bullet}$ at the plateau, the reaction is reversible, otherwise it is a complete reaction.

DPPH was used as stable free radical electron accepts or hydrogen radical to become a stable diamagnetic molecule (Dharmaraj *et al*., 2001). DPPH is a stable-free radical containing an odd electron in its structure and usually used for detection of the radical scavenging activity in chemical analysis (Nithiya *et al*., 2011). The reduction capability of DPPH radicals was determined by decrease in its absorbance at 517 nm induced by antioxidants (Matthaus, 2002). The graph was plotted with percentage scavenging effects on the *y*-axis and concentration (μg/ml) on the *x*-axis. The scavenging ability of the metal complexes was compared with ascorbic acid as a standard. The metal complexes showed good activities as a radical scavenger compared with ascorbic acid, Fig. 4. These results were in agreement with previous metallic complexes studies where the ligand has the antioxidant activity and it is expected that the metal moiety will increase its activity (Bukhari *et al*., 2009, 2008; Gabrielska *et al*., 2006).

Conclusions

In this study, V(IV), Cr(III), Mn(II), Co(II), Ni(II), and Cu(II) complexes of (E)-3-((5-phenyl-1,3,4-oxadiazol-2-

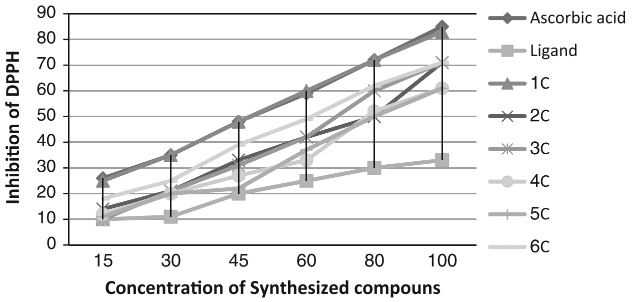


Fig. 4 Scavenging effect of metal complexes, and ascorbic acid at different concentrations (15, 30, 45, 60, 80, and 100 μg/ml)

ylimino)methyl)naphthalen-2-ol have been successfully synthesized and characterized by using various spectroscopic methods, elemental analysis, magnetic moment, and molar conductance studies. The synthesized complexes were tested for antioxidant and antimicrobial activities. Out of these complexes, Cu(II) indicated significant antimicrobial activities as compared to other metals ion. In addition, the Cu(II) complex is also found to be a superior antioxidant complex as compared to ascorbic acid.

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