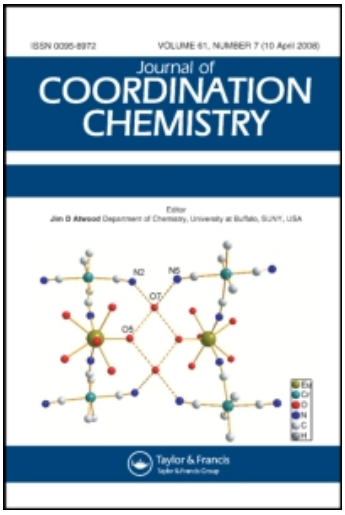

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Synthesis, spectroscopic, antibacterial and antifungal studies of nickel(II)5(2'-hydroxyphenyl)-3-(4-X-phenyl)pyrazolinates and their addition complexes with N and P donor ligands

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Synthesis, spectroscopic, antibacterial and antifungal studies of nickel(II)5(2′-hydroxyphenyl)-3-(4-X-phenyl)pyrazolinates and their addition complexes with N and P donor ligands

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A number of complexes of nickel(II) with 5(2′-hydroxyphenyl)-3-(4-X-phenyl)pyrazolines of the type $(C_{15}H_{12}N_2O \cdot X)_2Ni$ [where X = H, Cl, CH_3 and OCH_3] were synthesized by the reaction of anhydrous nickel(II) chloride with sodium salts of pyrazoline in 1 : 2 molar ratio. Their addition complexes with 2,2′-bipyridine, 1,10-phenanthroline and triphenylphosphine were prepared in 1 : 1 molar ratio. These complexes were characterized by elemental analyses, molecular weight, magnetic, conductivity, IR, electronic, ^1H, ^{13}C, ^{31}P NMR and FAB mass spectral data. All complexes are amorphous. Square planar geometry around nickel confirms the presence of two bidentate pyrazoline ligands in nickel(II)5(2′-hydroxyphenyl)-3-(4-X-phenyl)pyrazolinates. In the addition complexes pyrazoline is monodentate. Bidentate and monodentate pyrazoline was confirmed by IR, ^1H, ^{13}C and ^{31}P NMR spectral data. All the metal complexes exhibit very good antibacterial and antifungal activity. Coordination of metal ion has pronounced effect on the microbial activities of the ligand. The brine shrimp bioassay was also carried out to study their *in vitro* cytotoxic properties; all complexes and adducts display potent cytotoxic activity against *Artemia salina*.

Keywords: Antibacterial activity; Antifungal activity; Cytotoxicity; Nickel(II)pyrazolinates; Pyrazoline; Triphenylphosphine; 1,10-Phenanthroline; 2,2′-Bipyridine

1. Introduction

Pyrazolines possess wide-spread pharmacological properties such as analgesic, antipyretic, antidepressant and antirheumatic activities [1, 2], are also known for their pronounced anti-inflammatory activity [3] and are used as potent antidiabetic agents [4, 5]. Recently, pyrazolines were reported as DP-IV inhibitors and antitumor agents [6–8]. The coordination chemistry of pyrazole derived ligands has received attention, primarily due to their biological implications. Several studies have centered

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on the synthesis and structural studies of metal complexes of pyrazole containing bidentate ligands (N, O donors) due to the reported anticarcinogenic and antiviral activity of these donor ligands and complexes. It has been reported that substituted pyrazolones, pyrazolines and pyrazoles have potential biological activity [9, 10]. The metal complexes of 5(2′-hydroxyphenyl)-3-phenylpyrazoline with Ni(II), Co(II) and Cu(II) have been prepared in our laboratory by the method of extraction [11]. Similar types of ligands have been used to prepare complexes of cobalt, copper and nickel [12]. The synthesis, spectral and antimicrobial studies of diorganotin(IV), triorganotin(IV) and chlorodiorganotin(IV)3(2′-hydroxyphenyl)-5-(4-substituted-phenyl)pyrazolinates have been carried out in our laboratory [13–15]. In continuation of our work [16, 17], we synthesized the nickel(II)5(2′-hydroxyphenyl)-3-(4-X-phenyl)pyrazoline complexes [X = H, Cl, CH_3 and OCH_3] and their addition complexes with 2,2′-bipyridine, 1,10-phenanthroline and triphenylphosphine. We have investigated spectral, antibacterial and antifungal activities of these complexes. Nickel plays numerous roles in the biology of microorganisms and plants, the main constituent of various enzymes and coenzymes i.e. urease, NiFe-hydrogenases, F430, methanogenic archaea, carbon monoxide dehydrogenase [18], superoxide dismutase [19] and glyoxalase [20].

2. Experimental

All chemicals were analytical grade. Solvents were rigorously dried and purified before use by standard procedure [21]. The ligand 5(2′-hydroxyphenyl)-3-(4-X-phenyl)pyrazoline was prepared by reported procedure [22].

2.1. *Synthesis of 5(2′-hydroxyphenyl)-3-(4-X-phenyl)pyrazolinates of nickel*

The nickel(II)pyrazolinates were prepared by the following route:

$$NiCl_2 + 2(C_{15}H_{12}N_2O \cdot X)Na \xrightarrow[\text{Room Temp.}]{\text{Isopropanol}} (C_{15}H_{12}N_2O \cdot X)_2Ni + 2\,NaCl$$
$$[X = H, Cl, CH_3 \quad \text{and} \quad OCH_3]$$

Freshly cut sodium was taken in a flask containing isopropanol and refluxed (~1/2 h) till a clear solution of sodium isopropoxide was obtained. Solution of 5(2′-hydroxyphenyl)-3-(4-X-phenyl)pyrazoline [X = H, Cl, CH_3, OCH_3] in isopropanol was added and reaction was continued for 1 h when a constant yellow was obtained. The reaction mixture was cooled to room temperature and alcoholic solution of anhydrous nickel(II) chloride was added dropwise with constant stirring. The reaction mixture was further stirred for 20–24 h, till the color of the reaction mixture changed to dark brown. The reaction mixture was filtered under vacuum and the solid washed with hot water and alcohol. The solid so obtained was dried at 100°C. Data for synthesis of individual compounds are given in table 1.

Table 1. Synthetic, analytical and physical data for 5(2′-hydroxyphenyl)-3-(4-X-phenyl)pyrazolinates of nickel.

S.No. (Compd. No.)	Reactants: Anhydrous $NiCl_2$ g (mmole)	Reactants: Sodium g (mmole)	Reactants: Ligand g (mmole)	Molar ratio	Product (Color)	Yield %	M.P. (°C)	Mol. Wt. Found (Calcd)	Analysis, % Found (Calcd): C	H	N	Ni
			HPPP									
1	0.73 (5.63)	0.25 (11.26)	2.68 (11.26)	1 : 2 : 2	$Ni(L_a)_2$ (Light green)	94	>360	529.89 (532.69)	67.53 (67.64)	4.93 (4.92)	10.50 (10.52)	11.10 (11.02)
			HPCPP									
2	0.64 (4.98)	0.22 (9.97)	2.71 (9.97)	1 : 2 : 2	$Ni(L_b)_2$ (Green)	96	>360	602.52 (601.69)	59.88 (59.89)	4.00 (4.02)	9.33 (9.31)	9.74 (9.76)
			HPMPP									
3	0.69 (5.35)	0.24 (10.70)	2.69 (10.70)	1 : 2 : 2	$Ni(L_c)_2$ (Light green)	87	>360	556.13 (560.69)	68.53 (68.55)	5.37 (5.39)	9.91 (9.99)	10.48 (10.47)
			HPMeoPP									
4	0.65 (5.06)	0.23 (10.12)	2.71 (10.12)	1 : 2 : 2	$Ni(L_d)_2$ (Green)	90	>360	591.01 (592.69)	64.75 (64.85)	5.08 (5.10)	9.50 (9.45)	9.93 (9.91)

HPPP, L_a = 5(2′-hydroxyphenyl)-3-phenylpyrazoline.
HPCPP, L_b = 5(2′-hydroxyphenyl)-3-(4-chlorophenyl)pyrazoline.
HPMPP, L_c = 5(2′-hydroxyphenyl)-3-(4-methylphenyl)pyrazoline.
HPMeoPP, L_d = 5(2′-hydroxyphenyl)-3-(4-methoxyphenyl)pyrazoline.

2.2. *Synthesis of addition complexes of 5(2′-hydroxyphenyl)-3-(4-X-phenyl) pyrazolinates of nickel with N and P donor ligands*

A weighed amount of the nickel(II)pyrazolinate was dissolved in dry chloroform and a solution of 2,2′-bipyridine, 1,10-phenanthroline or triphenylphosphine in chloroform was added dropwise with constant stirring during 24 h at room temperature till the color changed. Reaction mixture was filtered under vacuum and the solid was washed with distilled water and finally with alcohol. The solid so obtained was dried at 100°C. The data for synthesis of individual compounds are given in tables 2–4.

2.3. *Physical measurements*

IR spectra were recorded as KBr pellets on a Perkin-Elmer RX1 spectrophotometer. Molecular weights were determined on a Knoauer Vapour pressure Osmometer in $CHCl_3$ at 45°C. Elemental analysis of nickel was done by standard procedure. Carbon, hydrogen and nitrogen were estimated on an Elementor Vario ELIII Carlo1108 elemental analyzer. Magnetic moment studies were conducted on a Gouy balance at room temperature. Conductivity measurements were made on a Systronics conductivity meter model-303 using DMSO as a solvent. Electronic spectra were recorded in chloroform solution on a Perkin-Elmer Lambda 15 spectrophotometer. ^{1}H and ^{13}C-NMR spectra were recorded on a Bruker DRX-300 spectrometer at room temperature. The FAB mass spectra were recorded on a JEOL SX 102/DA-6000 mass spectrometer. The ^{31}P NMR spectra were recorded in solid state on a Bruker Advance DRX-300 spectrometer at room temperature. The complexes were examined for crystalline/amorphous nature through XRD on a Philips compact X-ray diffraction analyzer model PW 1710.

2.4. *Biological activity*

2.4.1. Antibacterial bioassay. All the complexes were screened *in vitro* for their antibacterial activity against four Gram-negative (*Escherichia coli, Schigella flexenari, Pseudomonas aeruginosa, Salmonella typhi*) and two Gram-positive (*Bacillus subtilis, Staphylococcus aureus*) bacterial strains using the agar-well diffusion method [23]. Two to eight hour old bacterial inoculums containing approximately 10^4–10^6 colony-forming units (CFU)/ml were used in these assays. The wells were dug in the media with the help of a sterile metallic borer with centers at least 24 mm. Recommended concentration (100 μL) of the test sample (1 mg mL^{-1} in DMSO) were introduced in the respective wells. Other wells with DMSO and reference antibacterial drug (imipenum) served as negative and positive controls, respectively. The plates were incubated immediately at 37°C for 20 h. Activity was determined by measuring the diameter of zones showing complete inhibition (mm). Growth inhibition was compared [24] with the standard drug. DMSO showed no activity against any bacterial strains.

2.4.2. Antifungal activity. Antifungal activities were studied against six fungal cultures, *Trichophyton longifusus, Candida albicans, Aspergillus flavus, Microsporum canis, Aspergillus niger, Cumella glaberata*. Sabouraud dextrose agar was seeded with 10^5

Table 2. Synthetic, analytical and physical data for adducts of 5(2′-hydroxyphenyl)-3-(4-X-phenyl)pyrazolinates of nickel with 2,2′-bipyridine.

S.No. (Compd. No.)	Reactants		Molar ratio	Product (Color)	Yield %	M.P. (°C)	Mol. Wt. Found (Calcd)	Analysis, % Found (Calcd)			
	Complex g (mmole)	2,2′-Bipyridine $C_{10}H_8N_2$ g (mmole)						C	H	N	Ni
5	$Ni(L_a)_2$ 1.54 (2.90)	0.45 (2.90)	1 : 1	$Ni(L_a)_2$(bipy) (Light green)	88	>360	685.68 (688.88)	69.61 (69.68)	5.28 (5.27)	12.22 (12.20)	8.50 (8.52)
6	$Ni(L_b)_2$ 1.58 (2.63)	0.41 (2.63)	1 : 1	$Ni(L_b)_2$(bipy) (Light green)	89	>360	756.01 (757.88)	63.30 (63.34)	4.53 (4.52)	11.12 (11.10)	7.71 (7.75)
7	$Ni(L_c)_2$ 1.56 (2.78)	0.43 (2.78)	1 : 1	$Ni(L_c)_2$(bipy) (Greenish brown)	90	>360	718.24 (716.88)	70.29 (70.31)	5.61 (5.62)	11.69 (11.72)	8.15 (8.19)
8	$Ni(L_d)_2$ 1.58 (2.67)	0.41 (2.67)	1 : 1	$Ni(L_d)_2$(bipy) (Light green)	95	>360	743.86 (748.88)	67.30 (67.31)	5.39 (5.38)	11.23 (11.22)	7.81 (7.84)

Table 3. Synthetic, analytical and physical data for adducts of 5(2′-hydroxyphenyl)-3-(4-X-phenyl)pyrazolinates of nickel with 1,10-phenanthroline.

S.No. (Compd. No.)	Reactants: Complex g (mmole)	Reactants: 1,10-Phenanthroline $C_{12}H_8N_2$ g (mmole)	Molar ratio	Product (Color)	Yield %	M.P. (°C)	Mol. Wt. Found (Calcd)	Analysis, % Found (Calcd): C	H	N	Ni
	$Ni(L_a)_2$										
9	1.49 (2.80)	0.50 (2.80)	1 : 1	$Ni(L_a)_2$(phen) (Greenish brown)	86	>360	710.90 (712.90)	70.69 (70.70)	4.83 (4.81)	11.80 (11.79)	8.25 (8.24)
	$Ni(L_b)_2$										
10	1.53 (2.55)	0.46 (2.55)	1 : 1	$Ni(L_b)_2$(phen) (Greenish brown)	91	>360	783.89 (781.90)	64.49 (64.46)	4.15 (4.13)	10.70 (10.75)	7.50 (7.51)
	$Ni(L_c)_2$										
11	1.51 (2.69)	0.48 (2.69)	1 : 1	$Ni(L_c)_2$(phen) (Greenish brown)	89	>360	736.01 (741.90)	71.28 (71.27)	5.15 (5.17)	11.36 (11.34)	7.89 (7.92)
	$Ni(L_d)_2$										
12	1.53 (2.58)	0.46 (2.58)	1 : 1	$Ni(L_d)_2$(phen) (Greenish brown)	86	>360	774.56 (772.90)	68.35 (68.32)	4.86 (4.96)	10.89 (10.87)	7.56 (7.60)

Table 4. Synthetic, analytical and physical data for adducts of 5(2′-hydroxyphenyl)-3-(4-X-phenyl)pyrazolinates of nickel with triphenylphosphine.

S.No. (Compd. No.)	Reactants: Complex g (mmole)	Reactants: Triphenylphosphine $C_{18}H_{15}P$ g (mmole)	Molar ratio	Roduct (Color)	Yield %	M.P. (°C)	Mol. Wt. Found (Calcd)	Analysis, % Found (Calcd): C	H	N	Ni
	$Ni(L_a)_2$										
13	1.34 (2.51)	0.65 (2.51)	1 : 1	$Ni(L_a)_2(PPh_3)$ (Light green)	86	>360	789.96 (794.98)	72.55 (72.52)	5.21 (5.20)	7.00 (7.05)	7.37 (7.38)
	$Ni(L_b)_2$										
14	1.39 (2.31)	0.60 (2.31)	1 : 1	$Ni(L_b)_2(PPh_3)$ (Light green)	88	>360	864.58 (863.98)	66.72 (66.73)	4.50 (4.55)	6.52 (6.50)	6.83 (6.80)
	$Ni(L_c)_2$										
15	1.36 (2.43)	0.63 (2.43)	1 : 1	$Ni(L_c)_2(PPh_3)$ (Light green)	87	>360	819.62 (822.98)	72.99 (72.97)	5.53 (5.51)	6.79 (6.81)	7.16 (7.13)
	$Ni(L_d)_2$										
16	1.38 (2.33)	0.61 (2.33)	1 : 1	$Ni(L_d)_2(PPh_3)$ (Light green)	84	>360	852.98 (854.98)	70.21 (70.24)	5.35 (5.31)	6.45 (6.55)	6.79 (6.87)

(CFU) mL^{-1} fungal spore suspensions and transferred to petri plates. Discs soaked in 20 mL (10 μg mL^{-1} in DMSO) of all compounds were placed at different positions on the agar surface. The plates were incubated at 32°C for seven days. The results were recorded as zones of inhibition in mm and compared with the standard drug Miconazole.

2.4.3. Cytotoxicity. Brine shrimp (*Artemia salina* leach) eggs were hatched in a shallow rectangular plastic dish (22 × 32 cm) filled with artificial seawater, which was prepared [25] with commercial salt mixture and doubly-distilled water. An unequal partition was made in the plastic dish with the help of a perforated device. Approximately 50 mg of eggs were sprinkled into the large compartment, which was darkened while the matter compartment was opened to ordinary light. After two days, nauplii were collected by a pipette from the lighted side. A sample of the test compound was prepared by dissolving 20 mg of each compound in 2 mL of DMF. From this stock solution, 500, 50, 5 μg mL^{-1} were transferred to 9 vials (three for each dilution were used for each test sample and LD_{50} is the mean of three values) and one vial was kept as control having 2 mL of DMF only. The solvent was allowed to evaporate overnight. After two days, when shrimp larvae were ready, 1 mL of seawater and 10 shrimps were added to each vial (30 shrimps/dilution) and the volume was adjusted with seawater to 5 mL per vial. After 24 h, the numbers of survivors were counted. Data were analyzed by Finney computer program to determine the LD_{50} values [26].

3. Results and discussion

The 5(2′-hydroxyphenyl)-3-(4-X-phenyl)pyrazolinates of nickel and their adducts with 2,2′-bipyridine, 1,10-phenanthroline and triphenylphosphine are non-hygroscopic and stable at room temperature. These nickel(II) complexes are soluble in organic (chloroform, dichloromethane) and coordinating (pyridine, DMSO and tetrahydrofuran) solvents on slight heating. These complexes are monomeric in dilute chloroform at 45°C. The elemental analysis (C, H, N, Ni) data are in good accord with the stoichiometry proposed for respective complexes. The data are summarized in tables 1–4.

3.1. *Magnetic and conductivity measurements*

The magnetic moment measurements of pyrazolinates of nickel(II) were measured at room temperature. The nickel(II)pyrazolinates and their adduct complexes are diamagnetic ($\mu_{eff} = 0.00$ BM) indicating the square planar structure [27]. The conductance values of the synthesized complexes have been found to be in the range 12.6–17.3 $\Omega^{-1}\,cm^2\,mol^{-1}$ (table 5), which proposes to be non-electrolytic [28] in nature.

3.2. *Infrared spectra*

The assignments of infrared spectra for nickel(II)pyrazolinates and their addition complexes have been given in table 6. The band due to υ(OH) originally found at

Table 5. Electronic spectral data and conductivity data for 5(2′-hydroxyphenyl)-3-(4-X-phenyl)pyrazolinates of nickel.

Complex	Electronic spectral bands		Λ_m ($\Omega^{-1}\,cm^2\,mol^{-1}$)
	Assignment	Band (cm^{-1})	
1	$^1A_{1g} \rightarrow {}^1B_{1g}$ $^1A_{1g} \rightarrow {}^1B_{2g}$	20806 21800	15.7
2	$^1A_{1g} \rightarrow {}^1B_{1g}$ $^1A_{1g} \rightarrow {}^1B_{2g}$	20292 24537	16.4
3	$^1A_{1g} \rightarrow {}^1B_{1g}$ $^1A_{1g} \rightarrow {}^1B_{2g}$	20593 23982	17.3
4	$^1A_{1g} \rightarrow {}^1B_{1g}$ $^1A_{1g} \rightarrow {}^1B_{2g}$	20822 23333	17.1
5	$^1A_{1g} \rightarrow {}^1B_{1g}$ $^1A_{1g} \rightarrow {}^1B_{2g}$	20093 21790	14.5
6	$^1A_{1g} \rightarrow {}^1B_{1g}$ $^1A_{1g} \rightarrow {}^1B_{2g}$	20841 22981	13.8
7	$^1A_{1g} \rightarrow {}^1B_{1g}$ $^1A_{1g} \rightarrow {}^1B_{2g}$	20142 23333	12.6
8	$^1A_{1g} \rightarrow {}^1B_{1g}$ $^1A_{1g} \rightarrow {}^1B_{2g}$	20332 24933	15.3
9	$^1A_{1g} \rightarrow {}^1B_{1g}$ $^1A_{1g} \rightarrow {}^1B_{2g}$	20746 21490	14.6
10	$^1A_{1g} \rightarrow {}^1B_{1g}$ $^1A_{1g} \rightarrow {}^1B_{2g}$	20302 22637	12.8
11	$^1A_{1g} \rightarrow {}^1B_{1g}$ $^1A_{1g} \rightarrow {}^1B_{2g}$	20817 22387	12.9
12	$^1A_{1g} \rightarrow {}^1B_{1g}$ $^1A_{1g} \rightarrow {}^1B_{2g}$	20799 23714	13.7
13	$^1A_{1g} \rightarrow {}^1B_{1g}$ $^1A_{1g} \rightarrow {}^1B_{2g}$	20480 21893	13.2
14	$^1A_{1g} \rightarrow {}^1B_{1g}$ $^1A_{1g} \rightarrow {}^1B_{2g}$	20850 22110	14.7
15	$^1A_{1g} \rightarrow {}^1B_{1g}$ $^1A_{1g} \rightarrow {}^1B_{2g}$	20734 24700	15.5
16	$^1A_{1g} \rightarrow {}^1B_{1g}$ $^1A_{1g} \rightarrow {}^1B_{2g}$	20817 22145	15.9

3080–3050 cm^{-1} in the spectra of ligand is absent in the spectra of complexes, indicating involvement of phenolic OH in bond formation. The band in the region 3445–3412 cm^{-1} assigned to υ(N–H) is found at almost the same position with respect to the spectra of free pyrazoline ligand suggesting non-involvement of N–H in bond formation. The υ(C=N) in the region 1654–1600 cm^{-1} is shifted to higher wavenumber suggesting coordination through nitrogen of C=N [29–31]. This confirms the bidentate ligand in pure complexes. In addition complexes bands at 3442–3410 cm^{-1} and 1635–1584 cm^{-1} assigned to υ(N–H) and υ(C=N), respectively, are at the same position with respect to the ligand, suggesting non-involvement of N–H and C=N in bonding,

Table 6. IR spectral data for 5(2′-hydroxyphenyl)-3-(4-X-phenyl)pyrazolinates of nickel.

	Infrared (cm^{-1})			
Complex	υ(N–H)	υ(C=N)	υ(M–N)	υ(M–O)
1	3445	1654	418	536
2	3412	1600	430	558
3	3425	1600	410	470
4	3418	1601	424	486
5	3434	1592	398	545
6	3411	1596	420	529
7	3424	1584	427	508
8	3415	1593	413	543
9	3434	1585	425	548
10	3413	1597	390	560
11	3421	1590	406	518
12	3414	1589	412	555
13	3442	1635	–	480
14	3410	1600	–	478
15	3416	1602	–	483
16	3417	1604	–	510

indicating monodentate pyrazoline. New bands in the region 560–470 cm^{-1} and 430–390 cm^{-1} are assigned to υ(M–O) and υ(M–N) stretching vibrations.

3.3. *^{31}P NMR spectra*

The ^{31}P NMR spectra of addition complexes of nickel(II)pyrazolinates with triphenylphosphine in solid state observe a broad single peak in the range δ 36.3–31.2 ppm, indicating coordinaton between Ni(II) and triphenylphosphine [32–35].

3.4. *Electronic absorption spectra*

Electronic spectral data of pyrazolinates of nickel(II) and their addition complexes are given in table 6. The two absorption bands in the region 20850–20093 cm^{-1} and 24933–21490 cm^{-1} are assigned to $^1A_{1g} \rightarrow {}^1B_{1g}$ and $^1A_{1g} \rightarrow {}^1B_{2g}$ transitions, which are characteristic of square planar diamagnetic Ni(II) complexes [36–40].

3.5. *^{1}H NMR spectra*

The ^{1}H NMR spectra of nickel(II)pyrazolinates are summarized in table 7, recorded at 300 MHz in $CDCl_3$ and DMSO-d_6. The aromatic protons of nickel(II) complexes were observed as a multiplet from 6.69–8.07 ppm. The integration ratio indicates nine protons. The peak due to hydroxyl proton (originally present in the region 10.8–11.15 ppm in ligand) is absent from the spectra of the complexes suggesting the bonding through hydroxyl oxygen. The unaffected N–H in the region 4.01–5.08 ppm as a broad singlet suggests non-involvement of N–H in bond formation. The skeletal protons of five-membered rings are observed from 3.00–3.99 ppm and 2.03–2.50 ppm broad singlets assigned to CH and CH_2, respectively [36, 39, 41–43].

Table 7. ^{1}H NMR spectral data for 5(2′-hydroxyphenyl)-3-(4-X-phenyl)pyrazolinates of nickel.

	Chemical shift (in δ ppm)					
Complex	Ar–H	NH	CH_2	CH	CH_3	$–OCH_3$
1	7.61–7.85	5.08	2.50	3.47	–	–
2	7.40–7.60	4.57	2.08	3.50	–	–
3	7.27–7.39	4.99	2.39	3.43	1.86	–
4	7.32–7.45	5.01	2.15	3.62	–	3.80
5	7.37–7.80	4.65	2.49	3.70	–	–
6	6.86–7.45	4.43	2.22	3.57	–	–
7	7.98–8.07	5.02	2.19	3.10	1.82	–
8	7.00–7.89	4.32	2.43	3.38	–	3.61
9	7.34–7.90	4.79	2.41	3.69	–	–
10	6.98–7.79	4.87	2.39	3.86	–	–
11	7.28–8.00	4.35	2.16	3.99	1.84	–
12	7.88–8.02	4.01	2.11	3.00	–	3.52
13	7.63–7.99	5.07	2.03	3.67	–	–
14	6.69–7.89	4.39	2.45	3.72	–	–
15	7.22–7.65	4.66	2.35	3.54	1.72	–
16	7.14–7.96	5.03	2.31	3.18	–	3.73

Table 8. ^{13}C NMR spectral data for 5(2′-hydroxyphenyl)-3-(4-X-phenyl)pyrazolinates of nickel.

	Chemical shift (in δ ppm)				
Complex	Ar–C	C=N	CH_2	CH_3	$–OCH_3$
1	128–138	175	30.9	–	–
2	120–125	169	30.5	–	–
3	122–130	173	29.8	24.3	–
4	124–135	164	29.9	–	49.8
5	129–133	168	30.1	–	–
6	126–131	166	30.4	–	–
7	121–132	167	30.6	25.7	–
8	127–135	171	30.6	–	56.0
9	128–132	167	29.7	–	–
10	128–137	174	29.6	–	–
11	126–135	166	30.5	23.8	–
12	127–138	165	30.8	–	52.3
13	125–128	172	30.2	–	–
14	124–129	168	29.8	–	–
15	123–133	164	29.5	24.2	–
16	124–136	169	30.4	–	49.5

3.6. *^{13}C NMR spectra*

^{13}C NMR spectra of nickel(II)pyrazoline complexes are given in table 8 with assignments made on the basis of available literature and the spectrum of ligand. The spectra of nickel(II) complexes show all signals expected from the ligand: a broad singlet 120–138 ppm to aromatic carbons, C = N in the region 146–160 ppm in the ligands shifts to 164–175 ppm in the complexes showing coordination of imino nitrogen [36, 39, 41, 42]. All other signals were found at their respective positions as in the ligands.

Table 9. Antibacterial bioassay data of free pyrazolines and 5(2′-hydroxyphenyl)-3-(4-X-phenyl)pyrazolinates of nickel.

	Gram(−ve) bacteria				Gram(+ve) bacteria	
Compound	*E. coli*	*S. flexenari*	*P. aeruginosa*	*S. typhi*	*S. aureus*	*B. subtilis*
L_a	00	00	00	00	08	09
L_b	00	00	00	00	07	08
L_c	00	00	00	00	07	07
L_d	00	00	00	00	06	07
$Ni(L_a)_2$	10	06	14	15	18	17
$Ni(L_b)_2$	11	08	13	16	20	18
$Ni(L_c)_2$	11	10	14	14	21	15
$Ni(L_d)_2$	16	07	11	15	19	19
$Ni(L_a)_2$(bipy)	11	07	17	19	19	18
$Ni(L_b)_2$(bipy)	12	09	15	18	21	18
$Ni(L_c)_2$(bipy)	13	11	18	16	22	16
$Ni(L_d)_2$(bipy)	17	08	13	16	20	20
$Ni(L_a)_2$(phen)	12	08	16	18	20	19
$Ni(L_b)_2$(phen)	13	09	17	17	22	19
$Ni(L_c)_2$(phen)	13	12	16	15	20	17
$Ni(L_d)_2$(phen)	18	08	14	16	19	21
$Ni(L_a)_2(PPh_3)$	12	07	18	19	21	20
$Ni(L_b)_2(PPh_3)$	17	09	16	17	21	20
$Ni(L_c)_2(PPh_3)$	13	12	17	15	19	18
$Ni(L_d)_2(PPh_3)$	17	09	14	16	20	19
Standard drug (Imipenem)	30	27	27	26	30	28

(Diameter of inhibition zone measured in mm, article disc 5 mm, inhibition zone measured excluding article disc diameter, amount of complexes taken 1 mg mL^{-1} of DMSO).

3.7. *FAB mass spectra*

The FAB mass spectra of 5(2′-hydroxyphenyl)-3-(4-methylphenyl)pyrazoline and $[Ni(L_a)_2bipy]$ give a molecular ion peak (M^+) along with other characteristic peak showing fragmentation. The mass spectra of $Ni(L_c)_2$ exhibited the molecular ion peak at $m/z = 561$ and peaks at 468, 375, 284, 193, 154 and 115 m/z after successive removal of $-C_6H_5O^{\bullet}$, $-C_6H_5O^{\bullet}$, $-C_7H_7^{\bullet}$, $-C_7H_7^{\bullet}$, $-C_3H_3^{\bullet}$ and $-C_3H_3^{\bullet}$ groups. In the case of $[Ni(L_a)_2bipy]$, molecular peak at $m/z = 689$ suggests a monomer with other peaks 611, 533, 456, 379, 286, 193, 154 and 115 m/z after successive removal of $-C_5H_4N^{\bullet}$, $-C_5H_4N^{\bullet}$, $-C_6H_5^{\bullet}$, $-C_6H_5^{\bullet}$,$-C_6H_5O^{\bullet}$, $-C_6H_5O^{\bullet}$, $-C_3H_3^{\bullet}$ and $C_3H_3^{\bullet}$ groups, respectively.

3.8. *Biological activity*

The 5(2′-hydroxyphenyl)-3-(4-X-phenyl)pyrazolinates of nickel were screened for their antibacterial activity against *E. coli*, *S. flexenari*, *P. aeruginosa*, *S. typhi*, *B. subtilis* and *S. aureus* and for antifungal activity against *T. longifusus*, *C. albicans*, *A. flavus*, *M. canis*, *A. niger* and *C. glaberata*. The results are listed in tables 9 and 10.

The 5(2′-hydroxyphenyl)-3-(4-X-phenyl)pyrazolinates of nickel(II) have higher activities than free ligand, explained on the basis of Overtone's concept and chelation theory [44].

These complexes disturb the respiration process of the cell and thus block the synthesis of proteins which restricts further growth of organisms. In the present study it can be clearly seen that the substitution of the central metal atom of the

Table 10. Antifungal bioassay data of free pyrazolines and 5(2′-hydroxyphenyl)-3-(4-X-phenyl)pyrazolinates of nickel.

Compound	Organism					
	T. longifusus	*C. albicans*	*A. flavus*	*M. canis*	*A. niger*	*C. glaberata*
L_a	00	00	10	00	08	00
L_b	00	00	10	00	07	00
L_c	00	00	07	00	05	00
L_d	00	00	07	00	05	00
$Ni(L_a)_2$	11	07	20	02	09	04
$Ni(L_b)_2$	05	09	21	01	08	00
$Ni(L_c)_2$	12	10	18	02	06	00
$Ni(L_d)_2$	10	04	19	03	06	00
$Ni(L_a)_2$(bipy)	12	08	21	02	08	04
$Ni(L_b)_2$(bipy)	07	10	22	01	07	00
$Ni(L_c)_2$(bipy)	13	12	20	03	07	00
$Ni(L_d)_2$(bipy)	12	06	20	04	06	00
$Ni(L_a)_2$(phen)	14	08	22	03	09	05
$Ni(L_b)_2$(phen)	06	11	21	04	08	00
$Ni(L_c)_2$(phen)	14	12	19	02	06	00
$Ni(L_d)_2$(phen)	11	05	22	01	07	00
$Ni(L_a)_2(PPh_3)$	12	09	21	03	08	05
$Ni(L_b)_2(PPh_3)$	07	10	22	04	08	00
$Ni(L_c)_2(PPh_3)$	14	11	19	02	07	00
$Ni(L_d)_2(PPh_3)$	11	08	19	03	06	00
Standard drug (Miconazole)	30	27	30	26	27	27

(Diameter of inhibition zone measured in mm, article disc 5 mm, inhibition zone measured excluding article disc diameter, amount of complexes taken 200 $\mu g\,mL^{-1}$.)

complexes with different ligands provides a variation among the observed biological activities.

3.9. *Cytotoxic bioassay*

All complexes were screened for cytotoxicity (brine shrimp bioassay) using the protocol of Meyer *et al.* [45]. From data recorded in table 11, all complexes and adducts displayed potent cytotoxic activity as $LD_{50} = 7.012 \times 10^{-4}$ to 8.325×10^{-4} against *Artemia salina*, while all ligands were almost inactive for this assay.

4. Conclusions

On the basis of analytical and spectral data, square planar geometry [46–49] around nickel(II) is proposed. The four coordination of nickel(II) complexes indicates two bidentate pyrazoline ligands in $(C_{15}H_{12}N_2O \cdot X)_2Ni$ while in the addition complexes pyrazoline is monodentate. In PPh_3 complexes the fourth coordination site is satisfied by solvent. On the basis of XRD all complexes are amorphous. The antimicrobial studies show that the 5(2′-hydroxyphenyl)-3-(4-X-phenyl)pyrazolinates of nickel(II) have greater activity towards all tested bacteria than free pyrazolines and also exhibit greater antifungal activity. Generally, it is suggested that the nickel complexes deactivate various cellular enzymes, which play a vital role in metabolic pathways of

Table 11. Brine shrimp bioassay data of free pyrazolines and 5(2′-hydroxyphenyl)-3-(4-X-phenyl)pyrazolinates of nickel.

Compound	LD_{50} ($M\,mL^{-1}$)
L_a	1.112×10^{-3}
L_b	1.609×10^{-3}
L_c	1.750×10^{-3}
L_d	1.246×10^{-3}
$Ni(L_a)_2$	7.012×10^{-4}
$Ni(L_b)_2$	7.096×10^{-4}
$Ni(L_c)_2$	7.321×10^{-4}
$Ni(L_d)_2$	7.125×10^{-4}
$Ni(L_a)_2$(bipy)	8.025×10^{-4}
$Ni(L_b)_2$(bipy)	7.896×10^{-4}
$Ni(L_c)_2$(bipy)	8.325×10^{-4}
$Ni(L_d)_2$(bipy)	7.921×10^{-4}
$Ni(L_a)_2$(phen)	7.898×10^{-4}
$Ni(L_b)_2$(phen)	8.213×10^{-4}
$Ni(L_c)_2$(phen)	7.565×10^{-4}
$Ni(L_d)_2$(phen)	8.225×10^{-4}
$Ni(L_a)_2(PPh_3)$	7.939×10^{-4}
$Ni(L_b)_2(PPh_3)$	8.315×10^{-4}
$Ni(L_c)_2(PPh_3)$	8.127×10^{-4}
$Ni(L_d)_2(PPh_3)$	7.776×10^{-4}

the microorganisms. The role of 5(2′-hydroxyphenyl)-3(4-X-phenyl)pyrazolinates of nickel at the cellular/enzymatic level is an area of further research.

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