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Comparative Study of Microwave Assisted and Conventional Synthesis of Furfuraldehyde Based Hydrazone Derivatives and their Metal Complexes with Biological Evaluation

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A series of acyl hydrazone derivatives were synthesized by the condensation of different hydrazides (benzohydrazide, isoniazid, nicotinic acid hydrazide and salicylhydrazide) and 5-(4'-nitrophenyl) furan-2-carbaldehyde. These hydrazones were subjected for metal complexation to yield copper(II) and nickel(II) complexes using conventional and microwave irradiation method. The microwave method was found to be successful with nearly the same or higher yields and shorter reaction time. The synthesized compounds were characterized by EIMS, CHN analysis, FTIR and NMR spectroscopy. All the synthesized compounds were screened for their antibacterial and antioxidant activities.

Keywords: Furfuraldehyde, Benzohydrazide, Isoniazid, Nicotinic acid hydrazide, Salicylhydrazide, Antibacterial, Antioxidant.

INTRODUCTION

Hydrazones and their derivatives are attractive targets for researchers due to their versatility [1], distinctive structural features and a wide range of pharmacological and biological applications such as antimicrobial, analgesic, anticonvulsant [2], anti-inflammatory, antituberculosis [3], antitumor, anti-HIV [4,5], antimalarial [6], antiviral, antifungal [7], antioxidant and vasodilator activities [8-11]. These are important precursors for drug design to treat the genetic disorders like thalassemia [12,13]. Hydrazone derivatives also act as herbicides, insecticides, nematocides, rodenticides and plant growth regulators [14]. These play an important role as ligands in coordination chemistry by forming stable complexes with most transition metal ions [15]. Some hydrazone metal complexes have not only shown significant antibacterial, antioxidant and antitumor activities [16] but also act as enzyme inhibitors [17] and corrosion inhibitors [18]. Also, the metal complexes of hydrazones have potential applications such as catalysts, luminescent probes and membrane sensors [19].

Microwave-assisted synthesis has a broad range of applications in both organic and coordination chemistry [20]. It is being used for carrying out chemical transformation which are eco-friendly, low cost and offer high yields together with simplicity in processing and handling [21-24]. Reports on the synthesis of hydrazones and their metal complexes by microwave methods have been comparatively less [25]. So the new and efficient methodology for synthesis of furfuraldehyde based hydrazone derivatives and their metal complexes by both conventional and microwave irradiation technique is of great interest. We hereby report the synthesis, spectral investigations, antibacterial and antioxident activities of N'-[{5-(4-nitrophenyl)furan-2-yl}methylene]benzohydrazide (**L1**), N'-[{5-(4-nitrophenyl)furan-2-yl}methylene]isonicotinohydrazide (**L2**), N'-[{5-(4-nitrophenyl)furan-2-yl}methylene]-nicotinohydrazide (**L3**) and 2-hydroxy-N'-[{5-(4-nitrophenyl)-furan-2-yl}-methylene]benzohydrazide (**L4**) and their complexes with copper(II) and nickel(II).

EXPERIMENTAL

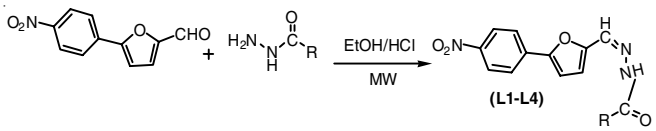
All the chemicals and solvents were purchased from Merck/Aldrich and used as such. Melting points were recorded on a GallenKamp apparatus and are uncorrected. The progress of the reaction and the purity of the target compounds were monitored by TLC using aluminium sheets coated with silica gel 60 F254. FTIR spectra were recorded on Vector 22 FTIR spectrophotometer. ^{1}H NMR and ^{13}C NMR spectra were recorded on Bruker AV 400 and AV 300 spectrophotometer respectively. Elemental analysis for C, H, N, Cl and metal were

carried out by Thermo Scientific FLASH 2000 elemental analyzer. Mass spectra were recorded on MAT 312 mass spectrometer. For microwave mediated reactions microwave oven with Model No. DW-631 was used.

Synthesis of ligands

Conventional method: 5-(4'-Nitrophenyl)furan-2-carbaldehyde was synthesized according to the reported method [26]. Similarly hydrazides (benzohydrazide, isoniazid, nicotinic acid hydrazide and salicylhydrazide) was synthesized by both conventional method and microwave irradiation method as reported in literature [27,28]. Equimolar amounts of 5-(4'-nitrophenyl)furan-2-carbaldehyde (10 mmol) and hydrazide (10 mmol) were dissolved in ethanol with few drops of concentrated hydrochloric acid as a catalyst and heated under reflux for 3-5 h. The completion of reaction was checked by TLC in a mixture of *n*-hexane:ethyl acetate (2:1). The mixture was cooled, filtered and recrystallized from a mixture of ethanol and ethyl acetate (5:1) to yield target hydrazone ligands (**L1-L4**) as coloured compounds **(Scheme-I).** Physical and spectral data of ligands is summarized in Tables 1 and 2.

Microwave irradiation method: A mixture of 5-(4-nitrophenyl)furan-2-carbaldehyde (10 mmol) and hydrazide (benzohydrazide, isoniazid, nicotinic acid hydrazide and salicylhydrazide) (10 mmol) in ethanol (2 mL) and two drops of concentrated hydrochloric acid was subjected to microwave irradiation 600 W for 2-3 min. The solid product obtained was checked for completion of the reaction by TLC with a solvent system *n*-hexane: ethyl acetate (2:1). The resulting compounds **L1-L4** were recrystallized from ethanol and ethyl acetate (5:1).



Scheme-I

Synthesis of metal complexes

Conventional method: A solution of metal(II) chlorides (10 mmol) in ethanol (10 mL) was added to a warm solution of ligand (**L1-L4**) (10 mmol or 20 mmol) in ethanol and DMF (3:2) (50 mL). The mixture was heated under reflux for 0.5-5 h. The reaction was monitored by TLC with solvent system *n*-hexane:ethyl acetate (1:1). The precipitates thus formed after cooling to room temperature were filtered and washed successively with DMF and ethanol mixture (1:2) to get the

TABLE-1
PHYSICAL DATA FOR LIGANDS

Ligands	Time		Yield (%)		Colour	m.p. (°C)	m.w.	Elemental analysis (%): Calcd. (Found)		
	CM (h)	MW (min)	CM	MW				C	H	N
L1	1.5	2.10	62.10	85.37	Golden yellow	243	335	64.47 (64.4)	3.91 (3.88)	12.53 (12.50)
L2	3.0	3.00	66.90	80.95	Dark yellow	225-226	336	60.71 (60.63)	3.60 (3.38)	16.66 (16.37)
L3	3.0	3.00	60.71	77.68	Yellow	245	336	60.7 (60.6)	3.60 (3.38)	16.66 (16.58)
L4	4.0	3.40	66.10	88.30	Bright yellow	236-238	351	61.54 (61.7)	3.73 (3.57)	11.96 (11.74)

CM = (a) Conventional method; MW = Microwave irradiation method

TABLE-2
FTIR, ^{1}H NMR AND ^{13}C NMR DATA FOR LIGANDS

Ligands	FTIR (cm^{-1})	^{1}H NMR δ (ppm) (DMSO)	^{13}C NMR δ (ppm) (DMSO)
L1	$3268.3_{(m)}$ (N-H), $1650.3_{(sh)}$ (C=O), $1514.3_{(sh)}$ & $1333.5_{(sh)}$ (Asym and sym -NO_2), $1603.5_{(m)}$ (C=N), $1281.7_{(sh)}$ (C-O-C), $1146.1_{(m)}$ (C-N), $1030.6_{(m)}$ (N-N)	11.98 (1H, *s*, N-H), 8.43 (1H, *s*, C-H=N), 8.34-8.32 (2H, *d*, *J* = *8 Hz*, H-3,5), 8.07-8.05 (2H, *d*, *J* = *8 Hz*, H-2',6'), 7.93-7.91 (2H, *d*, *J* = *8 Hz*, H-2,4), 7.61-7.60 (1H, *d*, *J* = *4Hz*, H-2 furan), 7.567-7.527 (3H, *m*, Ar), 7.17-7.16 (1H, *d*, *J* = *4 Hz*, H-1 furan)	112.42 (C-2 furan), 116.16 (C-3 furan), 124.52, 124.60, 127.69, 128.49, 131.83, 133.26, 135.17, 136.97 (CH=N), 146.33, 151.01 (C-1 furan), 151.74 (C-NO_2), 152.41 (C-4 furan), 163.14 (C=O)
L2	$3219.0_{(m)}$ (N-H), $1664.9_{(sh)}$ (C=O), $1512.9_{(sh)}$ & $1330.7_{(sh)}$ (Asym and sym -NO_2), $1602.7_{(m)}$ (C=N), $1416.9_{(s)}$ (C=N of pyridine), $1286.5_{(sh)}$ (C-O-C), $1147.9_{(m)}$ (C-N), $1027.3_{(s)}$ (N-N)	12.2 (1H, *s*, N-H), 8.82-8.81 (2H, *d*, *J* = *4 Hz*, H-3', 5'), 8.44 (1H, *s*, C-H=N), 8.36-8.34 (2H, *d*, *J* = *8 Hz*, H-3,5), 8.07-8.06 (2H, *d*, *J* = *4 Hz*, H-2',6'), 7.85-7.83 (2H, *d*, *J* = *8 Hz*, H-2,4), 7.53-7.52 (1H, *d*, *J* = *4 Hz*, H-2 furan), 7.23-7.22 (1H, *d*, *J* = *4 Hz*, H-1 furan)	112.43 (C-2 furan), 116.92 (C-3 furan), 121.46, 124.52, 124.71, 135.08, 138.08 (CH=N) 140.27, 146.42 (C-1 furan), 150.36, 150.64 (C-NO_2), 152.71 (C-4 furan), 161.62 (C=O)
L3	$3182.4_{(s)}$ (N-H), $1651.5_{(sh)}$ (C=O), $1512.4_{(sh)}$ & $1333.6_{(sh)}$ (Asym and sym -NO_2), $1598.3_{(m)}$ (C=N), $1424.2_{(s)}$ (C=N of pyridine ring), $1295.5_{(sh)}$ (C-O-C), $1157.5_{(m)}$ (C-N), $1030.8_{(m)}$ (N-N)	12.12 (1H, *s*, N-H), 9.08 (1H, *s*, CH=N pyridine ring, H-1'), 8.79-8.77 (1H, *d*, *J* = *8 Hz*, H-5' pyridine ring), 8.41 (1H, *s*, C-H=N), 8.35-8.33 (3H, d, *J* = 8 Hz, H-3, 5, 3'), 8.08-8.06 (2H, *d*, *J* = *8 Hz*, H-2,6), 7.62-7.59 (1H, *d* of *d*, H-4' pyridine ring), 7.515-7.505 (1H, *d*, *J* = *4 Hz*, H-2 furan), 7.22-7.21 (1H, *d*, *J* = *4 Hz*, H-1 furan)	112.40 (C-2 furan), 116.61 (C-3 furan), 123.60, 124.49, 124.65, 135.10 (CH=N), 135.40, 137.52, 146.36 (C-1 furan), 148.51, 150.73 (C-NO_2), 152.34 (CH=N pyridine), 152.58 (C-4 furan), 161.67 (C=O)
L4	$3428.3_{(b)}$ (O-H), $3241.7_{(sh)}$ (N-H), $1627.6_{(sh)}$ (C=O), $1505.5_{(sh)}$ & $1339.2_{(sh)}$ (Asym and sym -NO_2), $1600.9_{(s)}$ (C=N), $1226.6_{(sh)}$ (C-O-C), $1144.1_{(m)}$ (C-N), $1029.8_{(s)}$ (N-N)	11.95 (1H, *s*, N-H), 11.77 (1H, s, O-H), 8.44 (1H, s, C-H), 8.356-8.338 (2H, *d*, *J* = *7.2 Hz*, H-3, 5), 8.081-8.063 (2H, *d*, *J* = *7.2 Hz*, H-2,6), 7.887-7.875 (1H, d, *J* = *4.8 Hz*, H-2 furan), 7.51-7.48 (2H, *m*, Ar), 7.2-7.188 (1H, d, *J* = *4.8 Hz*, H-1 furan), 7.01-6.98 (2H, *m*, Ar)	112.45 (C-2 furan), 116.13(C-3 furan), 116.69, 117.24, 118.95, 124.54, 124.66, 128.62, 133.82, 135.13(CH=N), 137.66, 146.38 (C-1 furan), 150.79(C-NO_2), 152.59 (C-4 furan), 158.81 (C-OH), 164.66 (C=O)

TABLE-3
PHYSICO-CHEMICAL DATA OF COMPLEXES

Comp.	Time		Yield (%)		Colour	m.p. (°C)	m.w.	Elemental analysis (%): Calcd. (Found)			
	CM (h)	MW (min)	CM	MW				C	H	N	M
L1-Cu	0.5	1	76	83	Dark green	241	732.16	59.06 (59.01)	3.30 (3.36)	11.48 (11.43)	8.68 (8.60)
L1-Ni	4.5	2	62	74	Crimson red	Above 330	727.3	59.45 (59.49)	3.33 (3.35)	11.56 (11.52)	8.07 (8.01)
L2-Cu	0.5	1	67	81	Black	268	434.29	47.01 (48.00)	2.55 (2.62)	12.90 (13.09)	14.63 (14.65)
L2-Ni	2	1.50	62	77	Brick red	266-269	429.44	47.55 (47.64)	2.58 (2.41)	13.05 (13.03)	13.67 (13.65)
L3-Cu	0.5	1.30	78	83	Rust	168-170	434.29	47.01 (47.06)	2.55 (2.54)	12.90 (12.99)	14.63 (14.53)
L3-Ni	3	2.50	54	68	Cherry	265-267	429.44	47.01 (47.60)	2.58 (2.69)	13.05 (13.03)	13.67 (13.60)
L4-Cu	1	1	77	82	Yellowish brown	245	764.16	56.58 (56.67)	3.17 (3.06)	11.00 (10.99)	8.32 (8.31)
L4-Ni	3.5	2.10	65	73	Orange red	233-234	759.3	56.94 (57.18)	3.19 (3.29)	11.07 (10.94)	7.73 (7.67)

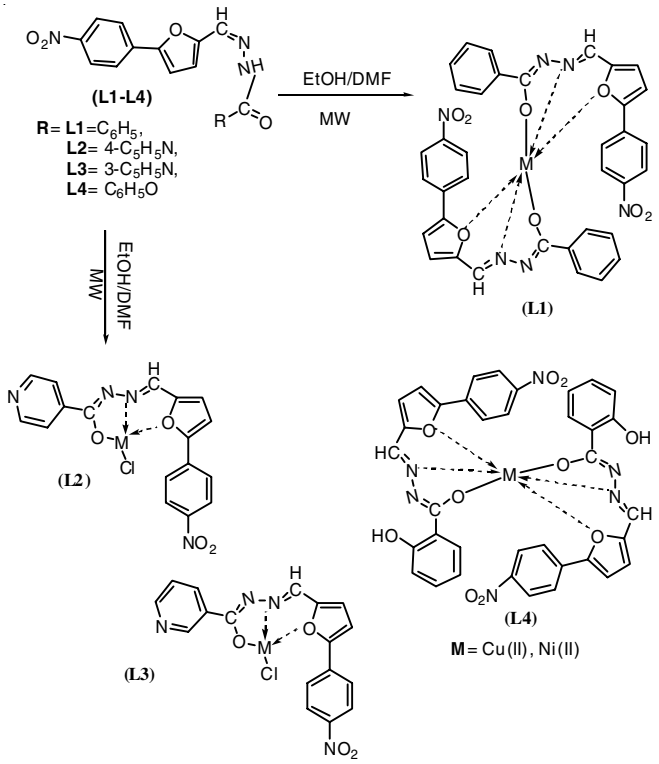
CM = (a) Conventional method; MW = Microwave irradiation method; *Decompose

target complexes (**Scheme-II**). The physical and spectral data of complexes is tabulated in Tables 3 and 4.

TABLE-4
FTIR (cm^{-1}) DATA OF THE METAL COMPLEXES

Compd.	FTIR (cm^{-1})
L1-Cu	$1514.9_{(sh)}$ & $1336.5_{(sh)}$ (Asym and sym -NO_2), $1611.2_{(s)}$ (C=N-N=C), $1281.1_{(s)}$ (C-O-C), $1107.9_{(s)}$ (C-O), $1022.8_{(m)}$ (N-N), $580.6_{(s)}$ (M-N), $459.1_{(s)}$ (M-O)
L1-Ni	$1500.7_{(sh)}$ & $1326.8_{(sh)}$ (Asym and sym -NO_2), $1597.0_{(m)}$ (C=N-N=C), $1271.0_{(m)}$ (C-O-C), $1102.9_{(m)}$ (C-O), $1022.4_{(m)}$ (N-N), $564.7_{(s)}$ (M-N), $496.8_{(s)}$ (M-O)
L2-Cu	$1512.7_{(sh)}$ & $1333.0_{(sh)}$ (Asym and sym -NO_2), $1600.3_{(m)}$ (C=N-N=C), $1423.8_{(s)}$ (C=N of pyridine), $1281.8_{(s)}$ (C-O-C), $1105.2_{(m)}$ (C-O), $1021.8_{(m)}$ (N-N), $546.9_{(s)}$ (M-N), $494.9_{(s)}$ (M-O)
L2-Ni	$1510.8_{(sh)}$ & $1333.1_{(sh)}$ (Asym and sym -NO_2), $1598.7_{(m)}$ (C=N-N=C), $1421.0_{(s)}$ (C=N of pyridine), $1275.4_{(s)}$ (C-O-C), $1106.1_{(m)}$ (C-O), $1021.0_{(m)}$ (N-N), $562.2_{(s)}$ (M-N), $454.9_{(s)}$ (M-O)
L3-Cu	$1599.8_{(sh)}$ (C=N-N=C), $1514.4_{(sh)}$ & $1338.5_{(sh)}$ (Asym and sym -NO_2), $1420.2_{(s)}$ (C=N of pyridine), $1283.1_{(s)}$ (C-O-C), $1107.7_{(m)}$ (C-O), $1017.4_{(s)}$ (N-N), $548.3_{(s)}$ (M-N), $485.7_{(s)}$ (M-O)
L3-Ni	$1598.8_{(s)}$ (C=N-N=C), $1513.7_{(sh)}$ & $1333.3_{(sh)}$ (Asym and sym -NO_2), $1421.3_{(s)}$ (C=N of pyridine ring), $1278.5_{(s)}$ (C-O-C), $1106.2_{(s)}$ (C-O), $1023.0_{(m)}$ (N-N), $457.4_{(s)}$ (M-O)
L4-Cu	$3251.0_{(b)}$ (O-H), $1514.7_{(sh)}$ & $1331.1_{(sh)}$ (Asym and sym -NO_2), $1597.7_{(m)}$ (C=N-N=C), $1253.0_{(s)}$ (C-O-C), $1103.4_{(s)}$ (C-O), $1035.9_{(m)}$ (N-N), $533.2_{(s)}$ (M-N), $485.1_{(S)}$ (M-O)
L4-Ni	$3443.2_{(b)}$ (O-H), $1514.4_{(sh)}$ & $1333.5_{(sh)}$ (Asym and sym -NO_2), $1596.7_{(m)}$ (C=N-N=C), $1258.7_{(s)}$ (C-O-C), $1100.5_{(s)}$ (C-O), $1048.8_{(s)}$ (N-N), $492.0_{(s)}$ (M-O)

Microwave irradiation method: A mixture of corresponding metal(II) chlorides (10 mmol) and (10 mmol or 20 mmol) of ligands (**L1-L4**) in ethanol (1 mL) and DMF (1 mL) was subjected to microwave irradiation at 600 W for 1-4 min. The solid product obtained was checked for completion of the reaction by TLC in a mixture of *n*-hexane:ethyl acetate (1:1). The resulting metal complexes were washed several times with DMF and ethanol mixture with 1:2. The physical and spectral data of complexes is tabulated in Tables 3 and 4.



Scheme-II

Antibacterial activity: The antibacterial activity of all the synthesized compounds was studied systematically against nine different bacterial strains including both the gram positive and gram negative bacteria by using disc diffusion method. The organisms were sub-cultured on nutrient broth Agar medium, incubated at 37 °C for 24 h and stored at 4 °C in the refrigerator to maintain stock culture. Petri plates were prepared with 20 mL of sterile Nutrient broth Agar medium and allowed to solidify. 100 µL of the cultures were spread on the top of the solidified media by spread-plate method and allowed to dry for 10 min. The tests were conducted at concentrations 500 µg/disc respectively of the synthetic derivatives.

TABLE-5
ANTIBACTERIAL ACTIVITY FOR LIGANDS (**L1**-**L4**) AND ITS METAL COMPLEXES

Compd.	Zone of inhibition in diameter (mm)								
	Gram-positive			Gram-negative					
	S. aureus	*Bas.*	*Asch.*	*Pseudomonas*	*B.b*	*S. typhi*	*Shigella*	*E. coli*	*Salmonella*
L1		8	–	–	–	–	–	–	8
L1-Cu	–	–	–	–	–	–	–	–	9
L1-Ni	–	–	–	–	–	–	10	–	–
L2	–	–	–	–	–	–	–	9	–
L2-Cu	–	–	–	–	–	–	–	13	–
L2-Ni	–	–	–	–	–	–	–	10	–
L3	–	–	–	9	–	–	–	–	–
L3-Cu	–	–	–	12	–	–	8	–	–
L3-Ni	–	–	–	–	–	9	13	–	–
L4	–	–	–	–	–	–	–	–	–
L4-Cu	9	–	–	10	–	–	–	–	–
L4-Ni	8	–	–	–	–	–	–	–	–
Standard	11	11	12	16	24	10	25	27	17

The loaded discs were placed on the surface of the medium and left for 0.5 h at room temperature for compound diffusion. Negative control was prepared by using respective solvent (DMSO). Ampicillin (50 µg/mL) was used as positive control. The plates were incubated for 24 h at 37 °C. The zone of inhibition was recorded in millimetres [29,30] (Table-5).

Free radical scavenging activity: From the stock solution 50 µL of synthesized compounds as well as standard compound (ascorbic acid) were taken and the volume was made uniformly to 150 µL using methanol. Each of the samples was then further diluted with methanol up to 3 mL and to each 150 µL DPPH (4.3 mg DPPH/3.3 mL) was added. Absorbance was taken after 15 min at 517 nm using methanol as blank and 3 mL methanol with 150 µL DPPH as control [31,32].

Total antioxidant capacity: From the stock solution 50 µL of synthesized compound solution in DMSO as well as standard was combined with 3 mL of reagent solution (0.6 M sulphuric acid, 28 mM sodium phosphate and 4 mM ammonium molybdate). The solutions were incubated at 95 °C for 90 min. and cooled to room temperature. The absorbance of the solutions measured at 695 nm against blank and standard (ascorbic acid). A typical blank solution contained 3mL of the reagent solution and the appropriate volume of DMSO and it was incubated under the same condition as the rest of samples [33-35].

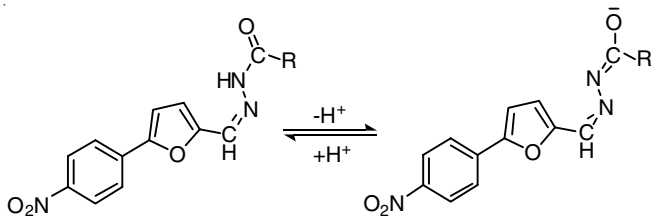
Nitric oxide scavenging assay: From the stock solution 50 µL of each of the compound as well as ascorbic acid (standard compound) were mixed with 150 µL with methanol. 2 mL of sodium nitroprusside 10 mM in phosphate buffer solution was added in each of the compound solution. The solutions were incubated at room temperature for 2.5 h and 5 mL of griess reagent (1 % sulphanilamide, 0.1 % naphthylethylenediamine dichloride and 3 % phosphoric acid) was added including control. The absorbance of chromophore formed was measured at 546 nm on UV-visible spectrometer. Ascorbic acid was used as positive control [36,37].

RESULTS AND DISCUSSION

All the synthesized compounds are coloured, solid and stable. Ligands are soluble more or less in organic solvents while complexes are only soluble in DMSO. The ligands confirmed by the spectroscopic data (^{1}H NMR, ^{13}C NMR, FTIR, EIMS and CHN). The elemental analysis and FTIR of complexes possess 1:2 stoichiometry in case of **L1** and **L4** while 1:1 stoichiometry in case of **L2** and **L3** with coordinated water molecules.

All the synthesized hydrazone ligands exhibit keto-enol tautomerism [13]. In solid state these ligands exist in keto form while when reacted with metal(II) ions, the ligands get deprotonated from amide moiety. Suggested tridentate, monobasic (mono-negative) hydrazone ligands and the metal(II) complexes are formed.

EIMS, ^{1}H NMR and ^{13}C NMR of the hydrazone ligands: Hydrazone ligands usually exist in keto-enol tautomeric form (**Scheme-III**). The presence of keto form of ligands were indicated by ^{1}H NMR spectroscopy since the enolic OH signal of enolic forms of ligands were not observed but amide NH signal of keto forms appeared around 11.98-12.2 ppm. Furthermore one singlet of C-**H**=N appeared around 8.44-8.41 ppm which indicated ketonic form of ligands. The other obtained values for ^{1}H NMR chemical shifts of these compounds (Table-2) also support the structures of the ligands. Similarly in ^{13}C NMR spectra of ligands signals of (-C=O) appears at δ 161-164 ppm and signals of HC=N appears at δ135-138 ppm which confirms the ketonic forms of ligands. The signals for (C-NO_2) appear around δ 150-151 ppm while others signals observed (Table-2).



Scheme-III: Tautomeric forms of hydrazone ligands

Mass spectra of ligands confirms the structures of target compounds by showing not only the molecular ion peaks at 335 (**L1**), 336 (**L2**), 336 (**L3**) and 351 (**L4**) but also fragmentation peaks like **L1** (335 [M^+], 214 [M^+- $C_6H_4NO_2$], 105 [PhCO], 77 [C_6H_5]), **L2** (336 [M^+], 306 [M^+-NO], 214 [M^+-$C_6H_4NO_2$], 106 [M^+-$C_{11}H_8N_3O_3$], 78 [M^+-$C_{12}H_8N_3O_4$]), **L3** (336 [M^+], 306 [M^+-NO], 214 [M^+- $C_6H_4NO_2$], 106 [M^+-$C_{11}H_8N_3O_3$],

78 [M^+-$C_{12}H_8N_3O_4$] and **L4** (351 [M^+], 306 [M^+- NO_2], 121[M^+-$C_{11}H_8N_3O_3$], 93 [C_6H_5O], 77 [C_6H_5]).

In FTIR spectra of the carbonyl (C=O) group is justified by an absorption bands around 1664-1627 cm^{-1}, (C-N) by an absorption bands around 1157-1144 cm^{-1}. Amide (N-H) stretching bands of these ligands observed at 3200-3100 cm^{-1} suggest that the ligands are in keto form.

The IR spectra of complexes show significant differences from free ligands like absence of N-H, C=O and C-N absorption bands and appearance of absorption bands of (C=N-N=C) around 1611-1596 cm^{-1}. The structures of complexes are further confirmed by the bands approximately 850-848 cm^{-1} of 1,4-disubstituted benzene in all ligands as well as metal complexes. The lower frequency region of the spectra of complexes furnishes some vital information regarding the mode of coordination of the ligand with the metal ion. The bands are in the region 580-533 cm^{-1} assignable for M-N and at 496-454 cm^{-1} for M-O.

Biological evaluation

Antibacterial activity: The synthesized compounds were evaluated for antibacterial activity at the concentration of 500 µg/mL by using disc diffusion assay where ampicillin was used as standard (Table-5). It is clear that some compounds showed significant antibacterial activity. In case of L1 and its complexes, the free ligand show moderate activities against *Bacillus subtilis* and *Salmonella* while *c*opper complexation caused the activity to increase in case of *Salmonella* but show no activity against *Bacillus subtilis,* similarly nickel complexation caused the activity to increase in case of *Shigella* but inactive against all other strains. In case of **L2** and its complexes, **L2** showed moderate activity against *E. coli* while its metal complexes show some good activity against the same strain while inactive against other strains. **L3** ligand is active against *Pseudomonas* and *E. coli*, copper complex showed increase in activity against *Pseudomonas* while nickel complex show increase in activity against *S. typhi* and *Shigella*. Hydrazone ligand **L4** is inactive against all strains and its complexes are only active against *Pseudomonas* and *S. aureus*.

Antioxidant activity: Table-6 shows the percentage of DPPH radical scavenged by standard that is ascorbic acid and metal complexes of hydrazones. It is evident from the data that **L1**-Cu, **L2**-Cu and **L3**-Cu possess hydrazone donating capabilities and free radical scavenging ability and can act as moderate antioxidants.

From all the tested compounds, **L4** and **L2**-Cu exhibited moderate NO radical scavenging activity (45.95 and 46.34 %, respectively). Hence these may act as moderate NO radical scavengers.

All the metal complexes showed significant total antioxidant activities as compared to the ligands. L4-Cu complex exhibited maximum activity 77.35 %. These complexes can act as moderate to strong antioxidants with comparable results.

TABLE-6
ANTIOXIDENT ACTIVITIES FOR LIGANDS AND THE METAL COMPLEXES

Compd.	Antioxidant (percentage scavenging)		
	Free radical scavenging	Total antioxidant capacity	Nitric oxide scavenging
L1	15.06	32.40	27.94
L1-Cu	30.80	44.25	26.76
L1-Ni	10	75.14	3.52
L2	22.29	25.09	16.58
L2-Cu	31.38	65.27	46.34
L2-Ni	1.03	66.90	11.49
L3	27.13	6.04	21.15
L3-Cu	31.61	64.11	24.15
L3-Ni	4.14	42.28	24.80
L4	13.56	12.54	45.95
L4-Cu	1.03	77.35	17.75
L4-Ni	20.57	66.31	1.04
Control	–	–	–
Ascrobic acid	78.16	96.05	84.33

Conclusion

Hydrazones derived from 5-(4'-nitrophenyl) furan-2-carbaldehyde and their metal complexes were synthesized by microwave assisted reactions in higher yields and in shorter time, compared to traditional techniques. From all the synthesized compounds copper complexes show maximum yields up to 83 % in less than 1 h (CM) and in 1 min to 1.30 min (MW). These hydrazone ligands bind with metal ions in tridentate, mono basic manner, with ONO donor sites. The compounds were evaluated for antibacterial activities using disk diffusion method against nine bacterial strains and antioxidant activities. As a result of these studies, among the target compounds some compounds show moderate antibacterial activities while most are inactive. In case of antioxidant activities, **L2**-Cu showed maximum DPPH activity and NO scavenging, while **L4**-Cu exhibited maximum total antioxidant activity.

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