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Metal Complexes of Semicarbazone and Thiosemicarbazone with Vanillin and 2-acetyl furan: Synthesis and Characterization with Preliminary Anti-bacterial and Anti-fungal activities

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ABSTRACT

This study reports the synthesis of ligands, D1 i.e. *((E)-2 (1-(furan-2-yl)ethylidene) hydrazine-1-carbothioamide)* and D6 i.e. *((E)-2-(4-hydroxy-3-methoxybenzylidene)* hydrazinecarbothioamide), utilizing a green, aqueous-based method. The structural properties and coordination behavior with metal(II) ions were analyzed systematically. Both ligands demonstrated effective bidentate coordination, offering two donor sites for each metal ion and all metal complexes are four coordinated. The biological evaluation indicated that complex M4C means (D6-Copper complex) exhibited significant antibacterial and antifungal activity against *E. coli, P. chrysogenum*, and *F. oxysporum*, whereas M4A complex means (D6-Nickel complex) demonstrated notable efficacy against *S. aureus*. Additionally, the complex M5C i.e. (D1-Copper complex) shown significant anti-bacterial activity with *S. aureus* and *E. coli* and, antifungal efficacy against *F. oxysporum*. The M5D i.e. (D1-Zinc complex) demonstrated significant antifungal efficacy against *P. chrysogenum*. The findings highlight the potential of these ligands and their complexes in the development of effective metal-based antibacterial and anti-fungal agents.

Keywords: 4 hydroxy-3-methoxy benzaldehyde, Acetylfuran, Semicarbazone, Thiosemicarbazone, Anti-microbial, Antifungal activities.

INTRODUCTION

Semicarbazones and thiosemicarbazones are well-known organic ligands that use oxygen, nitrogen, and sulfur atoms as donors for coordination with transition metal ions. Furthermore, numerous semicarbazones are of high pharmacological interest as anticancer, antibacterial, antifungal, and anti-inflammatory drugs. Furthermore, Thiosemicarbazones have been of tremendous interest in the realm of medicinal chemistry due to their varied coordination chemistry and probable pharmacological effects[1,2]. Typically, thiosemicarbazide is condensed with aldehydes or ketones to create compounds that may efficiently chelate metal ions, including transition metal species like copper, iron, nickel, and zinc. Coordination chemistry is the study of complex molecules generated by the interaction of metal atoms or ions with ligands. Ligands are molecules that give electron pairs to create coordinated covalent connections with central metal ions.

The present study explores the green synthesis and biological evaluation of metal-ligand complex formed with the combination of four selected ligands: vanillin, acetyl furan, semicarbazones, and thiosemicarbazones. Each of these ligands was chosen based on their known chemical reactivity, coordination potential, and previously reported pharmacological profiles. The white monoclinic crystalline phenolic aldehyde vanillin (4-hydroxy 3-methoxy benzaldehyde) has an aldehyde, hydroxyl, and ether group surrounding an arene. Changing phenol and aldehyde reactive groups can organically modify vanillin[3,4].

Building on our earlier study[5-7,16,17,18-22], and taking into account the previously described uses, we provide the synthesis, characterization, and preliminary antifungal and antibacterial evaluations of several Copper, Zinc, Cobalt, and Nickel complexes with ligand. The ligand was created by combining semicarbazide hydrochloride with vanillin. Adding an aromatic substituent to the semicarbazone (keto and enol) improves electron charge density delocalization (Fig. 1). These compounds frequently react with metallic cations to generate complexes having semicarbazone characteristics. Coordination of chelating ligands with metal centers enhances delocalization via metal chelate rings. If the substituent contains more donor atoms, the coordination options expand even further. Semicarbazone is often generated as a tridentate ligand, but it may also function as a quadridentate when the nitrogen (pyridyl) coordinates[8-9]. Furans are common heterocyclic chemicals that are vital to many pharmaceuticals. The planar ring furan has five members and dissolves in the majority of organic solvents. It's the most reactive five-membered heterocyclic. A non-polar chemical. Furan's electrophilic substitution reactions occur mostly in the second position[10]. Acetyl furan derivatives have shown potential as antibacterial and cancer therapies[11-15,23-24]. The study examines the synthesis, structural characterization, and biological assessment of these metal-ligand complexes, emphasizing their potential as new therapeutic agents.

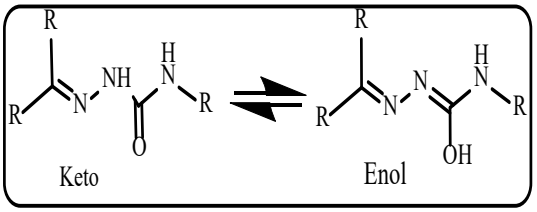


Fig. 1. Keto enol tautomerism of semicarbazones

MATERIAL AND METHOD

Reagents and chemicals were procured from Sigma-Merck and Fisher Chemical. The list of chemicals & reagents used for research work were represented in supplementary file (supplementary Table 1).

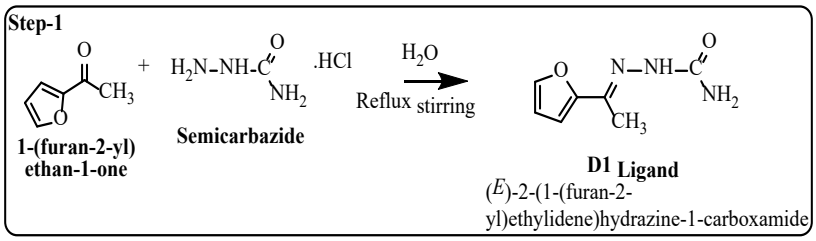
Preparation of Ligands

Preparation of ((E)-2-(1-(furanyl)ethylidene) hydrazinecarboxamide)–D1

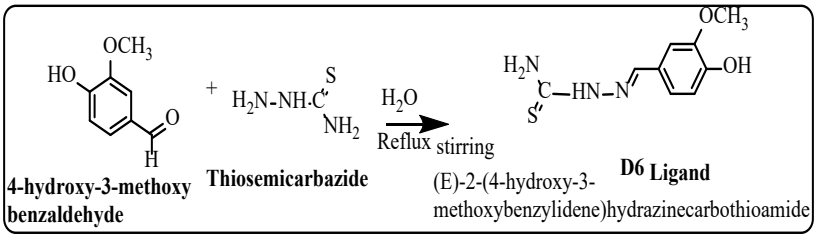
Semicarbazide (2.223 g, 19.931mmol) in hot aqueous solution (20 mL) and 2-acetyl furan (2.196 g, 19.943mmol) also in hot aqueous solution (20 mL) were mixed in 1:1 ratio (refluxed for four hours). The resultant solid was subjected to filtration, followed by recrystallization from ethanol and subsequent drying (Scheme 1).

Preparation of ((E)-2-(4-hydroxy-3methoxy -benzylidene) hydrazinecarbothioamide)–D6

Thiosemicarbazide (1.270 g, 13.936mmol) in hot aqueous solution (20 mL) and vanillin (2.122 g, 13.946mmol) in hot aqueous solution (20 mL) was mixed in 1:1 ratio. Four hours were spent refluxing the reaction mixture. After filtering and recrystallizing from ethanol, the solid product was dried (Scheme 2).



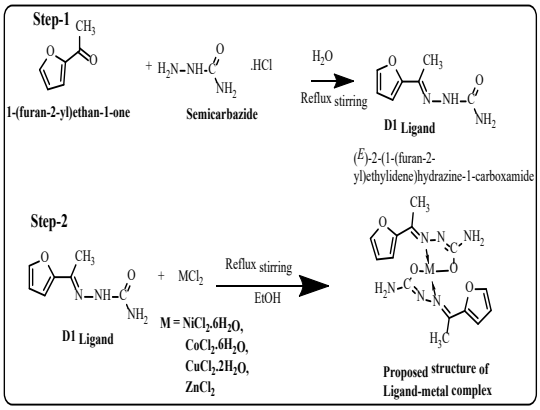
Scheme 1. Preparation of D1 ligand



Scheme 2. Preparation of D6 ligand

Synthesis of Metal Complexes with D1 Ligand

The metal-ligand complex was synthesized through the incorporation of a heated aqueous solution of metal chloride (Ni: 0.710 g, 5.98mmol; Co: 0.711 g, 2.99mmol; Cu: 0.509 g, 2.99mmol; Zn: 0.395 g, 2.99mmol) to a ethanolic solution (refluxing; dropwise) of the ligand (1.000 g, 2.990mmol) until the metal to ligand ratio reached 1:2. The combination remained at this temperature for four hours. The solid separated was filtered, washed (ethanol) and dried.



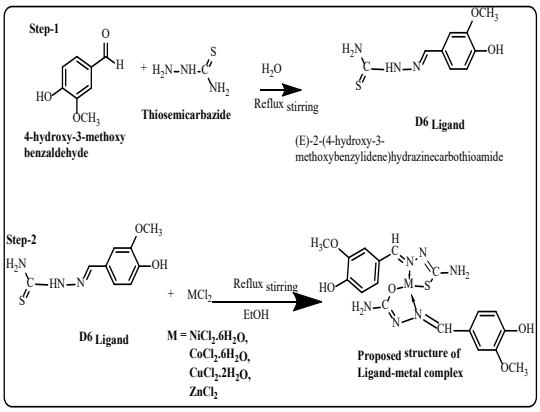
Scheme 3. Green synthesis of Ligand D1 and Metal Complexes (M5A-M5D)

Following abbreviations have been used for newly synthesized ligand metal complexes:

Sr. No.	Ligand-Metal complex	Abbreviated as
1.	D1-Nickel complex	M5A
2.	D1-Cobalt complex	M5B
3.	D1-Copper complex	M5C
4.	D1-Zinc complex	M5D

Synthesis of Metal Complexes with D6 Ligand

The preparation of the metal-ligand complex involved the meticulous addition of a hot aqueous solution of metal chloride (Ni: 0.527 g, 2.219mmol; Co: 0.528 g, 2.219mmol; Cu: 0.378 g, 2.219mmol; Zn: 0.302 g, 2.219mmol) in a dropwise manner to ethanolic solution of ligand (1.000 g, 4.439mmol) until the desired metal to ligand ratio (1:2) was achieved. The mixture was sustained at the reflux temperature for a duration of four hours. The solid that was separated underwent filtration, followed by washing with ethanol and subsequent drying.



Scheme 4. The green synthesis of ligand D6 and metal complexes (M4A-M4D)

Following abbreviations have been used for newly synthesized ligand metal complexes:

Sr. No.	Ligand-Metal complex	Abbreviated as
1.	D6-Nickel complex	M4A
2.	D6-Cobalt complex	M4B
3.	D6-Copper complex	M4C
4.	D6-Zinc complex	M4D

Characterization

NMR spectra of respective metal complexes had been recorded on a Bruker (Ascend 300 MHz) system. NMR (NMR) of all ligands and respective complexes, was noted in D6-DMSO making use of Tetramethylsilane (TMS)–an internal reference. All ligands' and their corresponding complexes' infra-red spectra were obtained using a Perkin Elmer spectrophotometer (Spectrum-Version10.4.00; 4000-400 cm^{-1}) employing the KBr method. The IR studies were performed out at Accuphychem analytics, Jaipur. UV-Vis. spectroscopy measures the extent to which molecules absorb ultraviolet and visible light. It facilitates the analysis of electronic

transitions, namely n→π* and π→π* transitions in conjugated systems. Electronic absorption spectra were recorded using a SHIMADZU 1800 spectrophotometer at Material Research Centre, MNIT, Jaipur. Mass spectrometry (MS) is an analytical method that detects substances according to their mass-to-charge ratio (m/z). It ionizes molecules, categorizes ions by mass, and detects them. The TOF MS ES+ technique is used to detect mass spectroscopy. The mass spectrometry studies were carried out at Accuphychem Analytics, Jaipur.

Antibacterial assay

The anti-bacterial activity of the produced complexes was determined by well-diffusion technique. Nutrient Agar was used to subculture bacterial cultures of *E. coli* and *S. aureus*, which were incubated for twenty-four hours at 36-38°C. Then, the cultures were swabbed onto petri plates that contained nutrient agar using a sterilized cotton swab. Wells measuring 6 mm in diameter were created in the agar plates, into which sample solutions ranging from 25 to 100 µg/mL were introduced. The plates underwent incubation, and the measurement of the zone of inhibition for each well was conducted. Streptomycin (30 µg/mL) served as a control to evaluate the efficacy of samples in relation to the tested bacteria. The activity index was determined by dividing the IZ of the test sample by antibiotic drug (IZ). The experiments were carried out in 3 sets.

Antifungal assay

The antifungal potential was evaluated using a modified agar well diffusion method. Petri plates containing PDA medium were utilized for the inoculation of individual fungal strains, which were seven days old and suspended in saline solution. The ligand metal complex was assessed for antifungal activity against two strains, *P. chrysogenum* and *F. oxysporum*, at concentrations ranging from 25 to 100 µg/mL. The plates were allowed to dry at RT (15 minutes). Cork-borers were utilized to perforate wells measuring 6 mm in diameter on the agar. The well was also prepared with effective distance control. The samples were diluted with 10% dimethyl -sulphoxide (DMSO), and various concentrations (200-1000 µg/mL) of all extracts were prepared. Various samples and standard drugs at different concentrations were seeded into petri plates. Plates Seeded were incubated (28°C) for 48 hours. Subsequently, anti-fungal activities were assessed by measuring the diameter of the IZ (in mm). Experiments were conducted three times, and the mean value was recorded. Ketoconazole (30 µg/mL) served as the standard control. In addition to inhibition zone, the activity index (AI) was calculated.

RESULTS

The chemical reaction of metal chlorides with ligands in a 1:2 molar ratio resulted in metal- ligand complexes, where M is Co/Zn/Cu/Ni and L is the corresponding ligand. These newly synthesized compounds are soluble in ethanol. The coordinating ability of the synthesized ligands was confirmed through their interaction with metal(II) ions.

D1

Yield% 74, m.p. 148°C. IR: υmax/cm^{-1} 3524 s(N-H), 1591 s(C=N), 1389 s(C-O); ^{1}H-NMR (DMSO-d6) δ: 11.22 (s, 1H), 9.42 (s, 1H), 8.08 (s, 1H), 7.90 (dd, J = 11.1, 1.7 Hz, 2H), 7.43 (d, J = 1.9 Hz, 1H), 6.98 (dd, J = 8.1, 1.9 Hz, 1H), 6.73 (d, J = 8.1 Hz, 1H), 3.78 (s, 3H). ^{13}C NMR (DMSO-d6) δ: 177.88, 149.31, 148.62, 143.39, 126.12, 122.90, 115.70, 109.74, 56.26, 40.65, 40.44, 40.23, 40.02, 39.81, 39.60, 39.39. Mass spectrum: m/z: 168.0771.

(M5A)

Yield% 75, m.p. 180-185°C. IR: υmax/cm^{-1} 3412 s(N-H), 1530 s(C=N), 1385 s(C-O), 683 v(M-N), 573 v(M-O); ^{1}H-NMR δ: 7.09 (s, 1H), 6.13 (s, 2H), 1.59 (s, 4H). ^{13}CNMR (DMSO-d6) δ: 149.17, 148.35, 143.41, 125.80, 122.71, 115.56, 109.58, 56.24.

(M5B)

Yield% 70, m.p. 148-152°C. IR: υmax/cm^{-1} 3611 s(N-H), 1593 s(C=N), 1388 s(C-O), 582 v(M-N), 518 v(M-O); ^{1}HNMR δ: 9.32 (s, 1H), 7.64 (s, 1H), 6.84 (s, 1H), 6.49 (s, 1H), 6.33 (s, 2H), 2.05 (s, 3H). ^{13}CNMR δ: 157.49, 152.82, 143.99, 137.30,

112.37, 109.45, 40.64, 40.43, 40.22, 40.01, 39.81, 39.60, 39.39, 13.39.

(M5C)

Yield% 68, m. p. 170-180°C. IR: υmax/ cm^{-1} 1587 s(C=N), 1373 s(C-O), 743 v(M-N), 584 v(M-O); ^{1}HNMR δ: 11.75 (s, 1H), 8.65 (s, 1H), 8.57 (s, 1H), 7.96 (s, 1H), 7.48 (s,1H), 7.38–7.24 (m, 1H), 7.08–6.99 (m, 1H), 6.92–6.86 (m, 1H), 6.74 (d, J = 7.9 Hz, 1H), 3.77 (s, 5H). ^{13}CNMR δ: 152.82, 143.99, 137.31, 112.36, 109.47, 40.64, 40.43, 40.23, 40.02, 39.81, 39.60, 39.39, 13.43.

(M5D)

Yield% 78, m. p. 168-172°C. IR: υmax/ cm^{-1} 3494 s(N-H), 1530 s(C=N), 1393 s(C-O), 721 v(M-N), 572 v(M-O); ^{1}HNMR δ: 9.34 (s, 4H), 7.66 (dd, J = 1.8, 0.9 Hz, 4H), 6.86 (dd, J = 3.4,0.8 Hz, 4H), 6.54–6.45 (m, 5H), 6.35 (s, 6H), 5.53 (s, 1H), 2.18 (s, 2H), 2.06 (s, 12H). ^{13}CNMR δ: 157.52, 152.82, 144.00, 137.31, 112.38, 109.46, 40.65, 40.44, 40.23, 40.02, 39.82, 39.61, 39.40, 13.40.

(E)-2-(4-hydroxy-3-methoxybenzylidene) hydrazinecarbothioamide (D6)

Yield% 68, m. p. 195-198°C. IR: υmax/cm^{-1} 3373 s(N-H), 1686 s(C=N), 3149 v(C-H; benzene ring), 725 v(C-H); ^{1}HNMR δ: 9.13 (s, 1H), 7.45 (dd, J = 1.8, 0.8 Hz, 1H), 6.66 (dd, J = 3.4, 0.8 Hz, 1H), 6.30 (dd, J = 3.4, 1.8 Hz, 1H), 6.15 (s, 1H), 1.86 (s, 3H). ^{13}CNMR δ: 157.33, 152.63, 143.77, 137.07, 112.16, 109.21, 40.44, 40.23, 40.02, 39.81, 39.60, 39.39, 39.18, 13.15. Mass spectrum: m/z: 226.067.

(M4A)

Yield% 64.88, m. p. 240°C. IR: max/cm^{-1} 3430 s(N-H), 1636 s(C=N), 3150 v(C-H; benzene ring), 815 v(C-H), 608 v(M-N); ^{1}HNMR δ: 10.93 (s, 1H), 9.32 (s, 1H), 7.81 (s, 1H), 7.75 (s, 1H), 7.64 (s, 1H), 7.18–7.03 (m, 2H), 6.71 (d, J = 7.3 Hz, 2H), 6.51 (d, J = 7.2 Hz, 1H), 3.50 (d, J = 4.5 Hz, 5H). ^{13}CNMR δ: 149.17, 148.35, 143.41, 125.80, 122.71, 115.56, 109.58, 56.24.

(M4B)

Yield% 54, m. p. 252°C. IR: υmax/cm^{-1} 3325 s(N-H), 1579 s(C=N), 786 v(C-H), 599 v(M-N); ^{1}HNMR δ: 9.20 (s, 1H), 6.92 (s, 1H), 3.76 (d, J = 11.7 Hz, 4H), 1.19 (s,5H), 1.01 (s, 1H), 0.81 (s, 1H). ^{13}CNMR δ: 205.82, 200.22, 192.19,189.05, 179.92, 167.20, 162.63, 155.87, 153.68, 140.66, 134.35,123.80, 118.52, 106.56.

(M4C)

Yield% 70, m. p. 215°C. IR: υmax/cm^{-1} 3095 s(N-H), 1585 s(C=N), 740 v(C-H), 567 v(M-N); ^{1}H-NMR δ: 11.75 (s, 1H), 8.65 (s, 1H), 8.57 (s, 1H), 7.96 (s, 1H), 7.48 (s,1H), 7.38 – 7.24 (m, 1H), 7.08–6.99 (m, 1H), 6.92–6.86 (m, 1H), 6.74 (d, J = 7.9 Hz, 1H), 3.77 (s, 5H). ^{13}C NMR δ: 191.55, 173.62, 153.51, 149.98, 148.63, 146.87, 129.19, 126.61, 125.30, 123.68, 115.89, 115.71, 111.14, 110.01, 56.28, 56.10, 41.26, 41.05, 40.83, 40.62, 40.41.

(M4D)

Yield% 68, m. p. 270°C. IR: υmax/cm^{-1} 3287 s(N-H), 1590 s(C=N), 3178 v(C-H; benzene ring), 829 v(C-H), 632 v(M-N); ^{1}HNMR δ: 11.21 (s, 1H), 11.01 (s, 1H), 8.29 (s, 1H), 8.20 (s, 1H), 8.06 (s, 1H), 7.87 (s, 3H), 7.68 (s, 1H), 7.42 (s, 1H), 7.20 (s, 1H), 7.08 (s, 1H), 6.97 (s, 2H), 6.73 (s, 2H), 6.54 (s, 1H), 6.20 (s, 1H), 5.90 (s,1H), 3.86 (s, 2H), 3.77 (s, 6H), 3.73–3.64 (m, 6H), 3.60 (s, 2H), 1.01 (t, J = 6.9 Hz, 1H). ^{13}CNMR δ: 176.68, 148.32, 143.35, 143.26, 115.49, 97.89, 78.47, 56.32, 55.99.

Anti-fungal and Anti-bacterial Activities

The ligand and metal combination demonstrated significant action against the strains (Table 2 & 3, Fig. 1-4). The (E)-2-(4-hydroxy-3-methoxybenzylidene) hydrazinecarbothioamide ligand and ligand metal complexes (M4A-M4D) was analyzed for anti-bacterial activity for two strains i.e. *E. coli* and *S. aureus* at concentrations and for antifungal activity against two strains, *P. chrysogenum* and *F. oxysporum*, at concentrations of 25-100 µg/mL (supplementary figures S33-S36). Similarly, the (E)-2-(1-furanyl)ethylidene) hydrazinecarboxamide) ligand and ligand metal complexes (M5A-M5D) was analyzed for same. The ligand and metal complexes have shown appreciable activity against strains.

Table 2: Anti-bacterial activity of ligand D1 and D6 and their complexes against *E. coli*

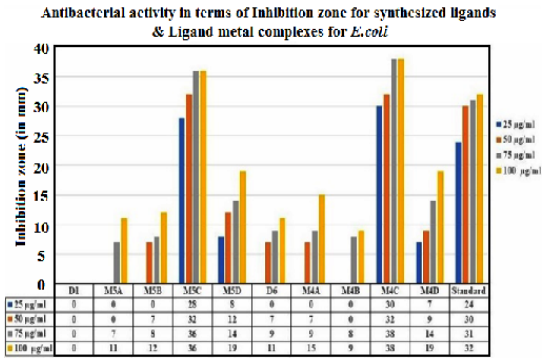
				E. coli				
		25 µg/mL		50 µg/mL		75 µg/mL		100 µg/mL
Compound name	IZ	AI	IZ	AI	IZ	AI	IZ	AI
D1	-	-	-	-	-	-	-	-
M5A	-	-	-	-	7	0.22	11	0.34
M5B	-	-	7	0.23	8	0.25	12	0.37
M5C	28	1.16	32	1.06	36	1.16	36	1.12
M5D	8	0.33	12	0.4	14	0.45	19	0.59
D6	-	-	7	0.23	9	0.29	11	0.34
M4A	-	-	7	0.23	9	0.29	15	0.46
M4B	-	-	-	-	8	0.25	9	0.28
M4C	30	1.25	32	1.06	38	1.22	38	1.18
M4D	7	0.29	9	0.3	14	0.45	19	0.59
Streptomycin	24	0	30	0	31	0	32	0
				S. aureus				
Compound name	IZ	AI	IZ	AI	IZ	AI	IZ	AI
D1	-	-	-	-	7	0.19	8	0.21
M5A	7	0.22	8	0.22	9	0.25	11	0.28
M5B	-	-	-	-	-	-	-	-
M5C	17	0.54	19	0.54	20	0.55	22	0.57
M5D	7	0.22	11	0.31	12	0.33	14	0.36
D6	7	0.22	9	0.25	10	0.27	11	0.28
M4A	10	0.32	14	0.4	19	0.52	21	0.55
M4B	10	0.32	11	0.31	12	0.33	14	0.36
M4C	15	0.48	17	0.48	19	0.52	21	0.55
M4D	10	0.32	12	0.34	15	0.41	17	0.44
Streptomycin	31	0	35	0	36	0	38	0

Note: IZ: Zone of Inhibition; AI: Activity Index; "-" :NA

Table 3: Anti-fungal activity of ligand D1 and D6 and their complexes against *F. oxysporum*

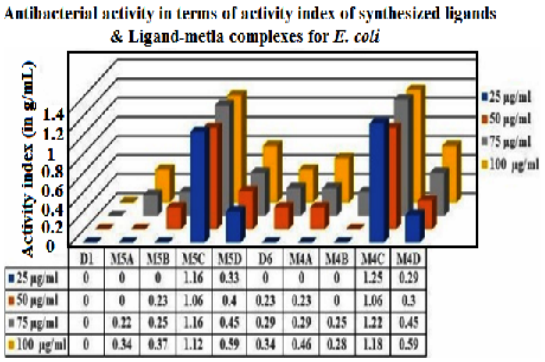
				P. chrysogenum				
		25 µg/mL		50 µg/mL		75 µg/mL		100 µg/mL
Compound name	IZ	AI	IZ	AI	IZ	AI	IZ	AI
D1	-	-	-	-	7	0.3	9	0.37
M5A	8	0.4	10	0.47	12	0.52	13	0.54
M5B	7	0.35	7	0.33	10	0.43	11	0.45
M5C	7	0.35	8	0.38	9	0.39	15	0.62
M5D	-	-	14	0.66	17	0.73	19	0.79
D6	-	-	7	0.33	9	0.39	11	0.45
M4A	8	0.4	12	0.57	14	0.6	15	0.62
M4B	-	-	7	0.33	8	0.34	9	0.37
M4C	7	0.35	13	0.61	17	0.73	19	0.79
M4D	7	0.35	10	0.47	11	0.47	14	0.58
Ketokenazole	20	0	21	0	23	0	24	0
				F. oxysporum				
Compound name	IZ	AI	IZ	AI	IZ	AI	IZ	AI
D1	-	-	-	-	-	-	7	0.28
M5A	7	0.46	8	0.42	8	0.38	9	0.36
M5B	7	0.46	8	0.42	10	0.47	12	0.48
M5C	7	0.46	9	0.47	9	0.42	13	0.52
M5D	-	-	8	0.42	10	0.95	11	0.44
D6	-	-	7	0.36	8	0.38	10	0.4
M4A	7	0.46	7	0.36	9	0.42	10	0.4
M4B	7	0.46	7	0.36	10	0.47	10	0.4
M4C	15	1	18	0.94	20	0.95	23	0.92
M4D	8	0.53	10	0.52	11	0.52	14	0.56
Ketokenazole	15	0	19	0	21	0	25	0

Note: Abbreviations same as Table 1



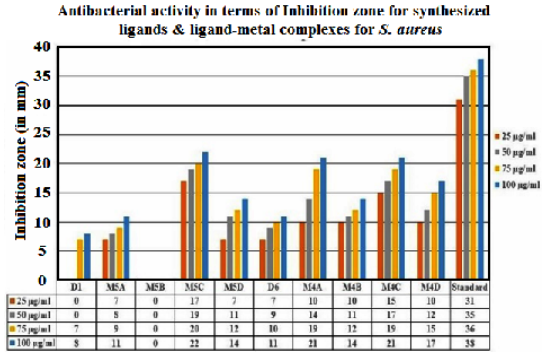
	D1	M5A	M5B	M5C	M5D	D6	M4A	M4B	M4C	M4D	Standard
25 µg/ml	0	0	0	25	8	0	0	0	30	7	24
50 µg/ml	0	0	7	32	12	7	7	0	32	9	30
75 µg/ml	0	7	8	36	14	9	9	8	38	14	31
100 µg/ml	0	11	12	36	19	11	15	9	38	19	32

Fig. 1. Anti-bacterial activity *(E. coli)* in Inhibition zone of ligand (D1and D6) and their complexes



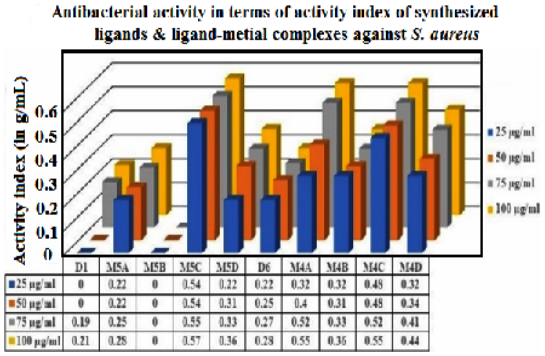
	D1	M5A	M5B	M5C	M5D	D6	M4A	M4B	M4C	M4D
25 µg/ml	0	0	0	1.16	0.33	0	0	0	1.25	0.29
50 µg/ml	0	0	0.23	1.06	0.4	0.23	0.23	0	1.06	0.3
75 µg/ml	0	0.22	0.25	1.16	0.45	0.29	0.29	0.25	1.22	0.45
100 µg/ml	0	0.34	0.37	1.12	0.59	0.34	0.46	0.28	1.18	0.59

Fig. 2. Anti-bacterial *(E. coli)* activity in Activity index of ligand D1 and their complexes



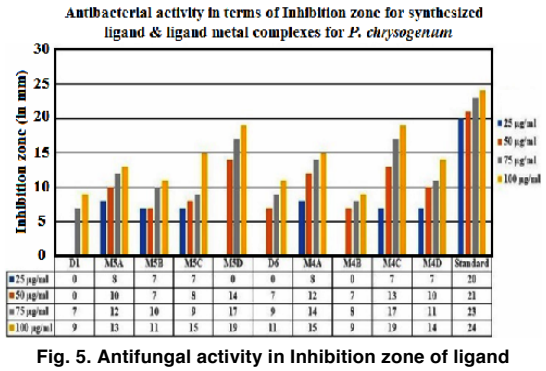
	D1	M5A	M5B	M5C	M5D	D6	M4A	M4B	M4C	M4D	Standard
25 µg/ml	0	7	0	17	7	7	10	10	15	10	31
50 µg/ml	0	8	0	19	11	9	14	11	17	12	35
75 µg/ml	7	9	0	20	12	10	19	12	19	15	36
100 µg/ml	8	11	0	22	14	11	23	14	21	17	38

Fig. 3. Antibacterial activity in Inhibition zone of ligand (D1and D6) and their complexes against *S. aureus*



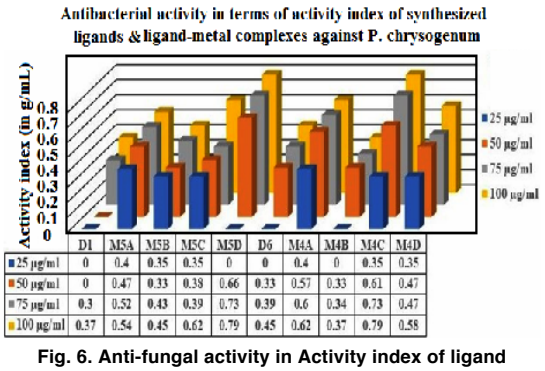
	D1	M5A	M5B	M5C	M5D	D6	M4A	M4B	M4C	M4D
25 µg/ml	0	0.22	0	0.54	0.22	0.22	0.32	0.32	0.48	0.32
50 µg/ml	0	0.22	0	0.54	0.31	0.25	0.4	0.31	0.48	0.34
75 µg/ml	0.19	0.25	0	0.55	0.33	0.27	0.52	0.33	0.52	0.41
100 µg/ml	0.21	0.28	0	0.57	0.36	0.28	0.55	0.36	0.55	0.44

Fig. 4. Antibacterial activity in Activity index of ligand (D1and D6) and their complexes against *S. aureus*



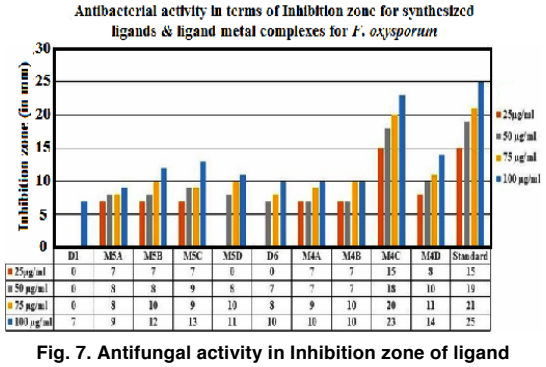
	D1	M5A	M5B	M5C	M5D	D6	M4A	M4B	M4C	M4D	Standard
25 µg/ml	0	8	7	7	0	0	8	0	7	7	20
50 µg/ml	0	10	7	8	14	7	12	7	13	10	23
75 µg/ml	7	12	10	9	17	9	14	8	17	11	23
100 µg/ml	9	13	11	15	19	11	15	9	19	14	24

Fig. 5. Antifungal activity in Inhibition zone of ligand (D1and D6) and their complexes against *P. chrysogenum*



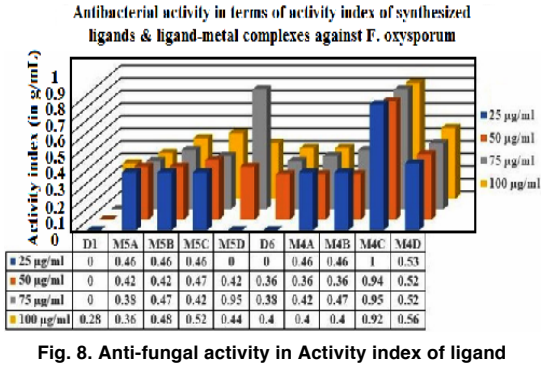
	D1	M5A	M5B	M5C	M5D	D6	M4A	M4B	M4C	M4D
25 µg/ml	0	0.4	0.35	0.35	0	0	0.4	0	0.35	0.35
50 µg/ml	0	0.47	0.33	0.38	0.66	0.33	0.57	0.33	0.61	0.47
75 µg/ml	0.3	0.52	0.43	0.39	0.73	0.39	0.6	0.34	0.73	0.47
100 µg/ml	0.37	0.54	0.45	0.62	0.79	0.45	0.62	0.37	0.79	0.58

Fig. 6. Anti-fungal activity in Activity index of ligand (D1and D6) and their complexes against *P. chrysogenum*



	D1	M5A	M5B	M5C	M5D	D6	M4A	M4B	M4C	M4D	Standard
25µg/ml	0	7	7	7	0	0	7	7	15	8	15
50 µg/ml	0	8	8	9	8	7	7	7	18	10	19
75 µg/ml	0	8	10	9	10	8	9	10	20	11	21
100 µg/ml	7	9	12	13	11	10	10	10	23	14	25

Fig. 7. Antifungal activity in Inhibition zone of ligand (D1and D6) and their complexes against *F. oxysporum*



	D1	M5A	M5B	M5C	M5D	D6	M4A	M4B	M4C	M4D
25 µg/ml	0	0.46	0.46	0.46	0	0	0.46	0.46	1	0.53
50 µg/ml	0	0.42	0.42	0.47	0.42	0.36	0.36	0.36	0.94	0.52
75 µg/ml	0	0.38	0.47	0.42	0.95	0.38	0.42	0.47	0.95	0.52
100 µg/ml	0.28	0.36	0.48	0.52	0.44	0.4	0.4	0.4	0.92	0.56

Fig. 8. Anti-fungal activity in Activity index of ligand (D1and D6) and their complexes against *F. oxysporum*

DISSCUSSION

The ligand D1 was characterized by various spectroscopic techniques. In its IR spectrum, key stretching bands for N-H, C=N, and C-O appeared at 3373, 1686, 1591, and 1428 cm^{-1}. Proton NMR data showed signals for primary amine at 7.90 ppm, a methyl singlet at 3.78 ppm, and an NH peak at 9.42 ppm, while ^{13}C NMR peaks for C-O and C=N were observed at 143.39 ppm and 149.31 ppm respectively. The MS showed a peak at m/z 168.0771 (molecular ion), matching its molecular weight. UV-Vis. spectroscopy revealed major absorption bands at 314 and 332 nm (supplementary figures S1 to S32).

Similarly, the ligand D6, showed IR bands at 3373, 1686, and 3271 cm^{-1} for N-H, C=N, and OH, respectively. In the proton NMR spectrum, primary amine, methyl, and NH protons appeared at 7.46, 1.86, and 9.13 ppm. In the ^{13}C NMR spectrum, C=N and C-O resonated at 157.33 and 152.63 ppm. The molecular ion peak at m/z 226.0667 was consistent with its molecular weight, and its UV-Vis. spectrum showed bands in the 250–363 nm range.

The metal complexes M4A–M4D showed characteristic IR bands for N-H between 3095–3430 cm^{-1}, and for C=N between 1579–1636 cm^{-1}. M-N coordination bonds were observed in the range of 567–632 cm^{-1}. In the proton NMR spectra of these complexes, signals for primary amine appeared between 6.92–7.96 ppm, methyl singlets between 3.50–3.86 ppm, and NH protons between 8.29–9.32 ppm. The ^{13}C NMR spectra revealed C=N peaks ranging from 148.32–153.68 ppm and C-O peaks from 143.35–153.68 ppm. For the D1-based metal complexes M5A–M5D, the IR spectra showed shifts in C=N bands to lower values at 1530–1593 cm^{-1} and in C-O bands to 1373–1393 cm^{-1}, confirming coordination. M-N bonds appeared at 582–743 cm^{-1} and M-O bonds at 518–584 cm^{-1}. In the ^{1}H NMR spectra, primary amine peaks were recorded between 7.09–7.96 ppm, methyl singlets between 1.59–3.77 ppm, and NH peaks between 8.65–9.32 ppm. The ^{13}C NMR spectra showed C=N signals from 149.17–157.52 ppm and C-O peaks between 143.41–144.00 ppm. UV-Vis spectra for these complexes displayed absorption bands at 359 and 325 nm (M5A), 500 and 501 nm (M5B), 394 and 509 nm (M5C), and 332 and 407 nm (M5D). These spectroscopic findings collectively confirm the formation and structural integrity of all ligand-metal complexes.

CONCLUSION

Based on the findings from the present study, two ligands D1 and D6 were synthesized using an environmentally friendly method in aqueous media. Their structural characteristics and interactions with metal (II) ions were thoroughly investigated. Both ligands demonstrated effective coordination abilities, each providing two donor sites for metal ion binding and four coordinated. These structural insights highlight the potential of these ligands in forming stable metal-ligand complexes with distinct geometrical configurations. The M4C (D6-Cu complex) has shown appreciable antifungal and anti-bacterial activity *(E. coli, P. chyysogenum,* and *F. oxysporum)*. The complex M4A (D6-Ni Complex) demonstrated promising activity against *S. aureus*. The M5D (D1-Zn Complex) compound demonstrated significant antifungal efficacy against *P. chrysogenum*. The findings highlight the potential of these ligands in the development of effective metal-based antimicrobial and anti-fungal agents.

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Conflict of interest

The author declare that we have no conflict of interest.

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