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Metal Based Sulfanilamides: A Note on Their Synthesis, Spectral Characterization, and Antimicrobial Activity[1]

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Abstract—Objectives of the current study were synthesis, spectral characterization and biological screening of sulfanilamide derived Schiff bases and their metal based compounds. Sulfanilamide Schiff bases ($\mathbf{L^1}$–$\mathbf{L^3}$) were synthesized by condensation of 4-aminobenzenesulfanilamide with 1-(furan-2-yl)ethanone, 1-(thiophene-2-yl)-ethanone, and 1-acetylindoline-2,3-dione. The ligands were used for preparation of their Co(II), Ni(II), Cu(II), and Zn(II) complexes by using metals chlorides in metal : ligand (1 : 2) molar ratio. All metal chelates had octahedral geometry with bidentate ligands. The ligands and their metal complexes were characterized by physical, spectral and analytical data, and screened for *in-vitro* antibacterial activity against six bacterial pathogens (*Escherichia coli*, *Shigella flexneri*, *Pseudomonas aeruginosa*, *Salmonella typhi*, *Staphylococcus aureus,* and *Bacillus subtilis*) and for *in vitro* antifungal activity against six fungal pathogens (*Trichophyton longifusus, Candida albicans, Aspergillus flavus, Microsporum canis, Fusarium solani,* and *Candida glabrata*). The results of antimicrobial studies revealed that the ligands activity was significantly increased upon chelation.

Keywords: sulfanilamides, metal(II) chelates, antimicrobial activity

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INTRODUCTION

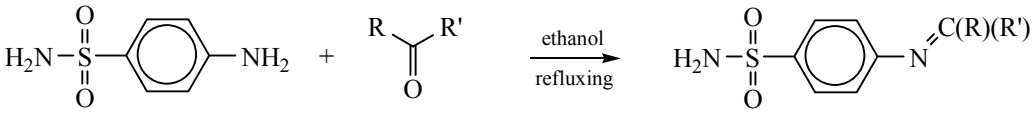
Sulfanilamide drugs have been used as potential chemotherapeutic agents [1, 2]. The mode of their action is hindering the synthesis of folic acid in bacteria [3] causing death of cells. From the time of discovery, sulfa drugs [4–6] attracted a remarkable attention as antiviral [7], antibacterial [8], anti-inflammatory [9], antifungal [10] and anticancer [11] agents. Usually biologically active compounds, including sulfa drugs, demonstrate enhanced activity upon chelation with metals [12, 13]. Isatin derived compounds are also known to display a wide range of biological [14, 15] and pharmacological activities [16–18]. Versatile medicinal importance of sulfanilamides and potential bioactivity of isatins, furanyl and thioenyl compounds, gave us a good reason for combining both types of molecules by synthesizing 3 novel Schiff base derivatives of sulfanilamide, 4-[1-(furan-2-yl)ethylideneamino]benzenesulfanilamide ($\mathbf{L^1}$), 4-[1-(thiophene-2-yl)ethylideneamino]benzenesulfanilamide ($\mathbf{L^2}$), and (*Z*)-4-[1-acetyl-2-oxoindolin-3-ylideneamino]benzenesulfanilamide ($\mathbf{L^3}$) (Scheme 1). In order to determine the effect of chelation, Co(II), Cu(II), Ni(II), and Zn(II) metal complexes **1–12** (Scheme 2) of these compounds that could be considered as a novel class of metal based potential antibacterial drugs. All the prepared compounds were screened for their bactericidal/fungicidal activity against some bacterial/fungal strains as reported herein.

RESULTS AND DISCUSSION

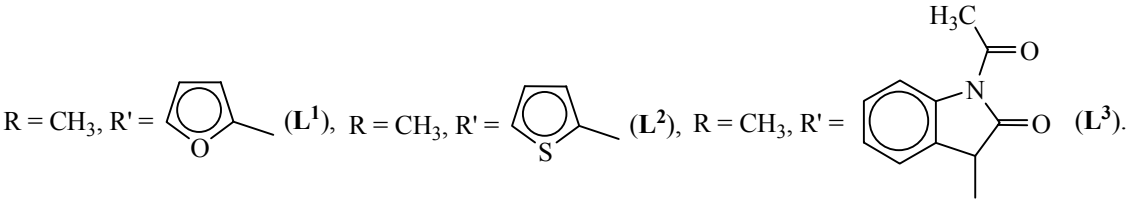
Schiff base ligands $\mathbf{L^1}$–$\mathbf{L^3}$ were synthesized in the reaction of 4-aminobenzenesulfanilamide with 1-(furan-2-yl)ethanone/1-(thiophene-2-yl)ethanone/1-acetylindoline-2,3-dione in an equimolar ratio (Scheme 1). The ligands were colored air and moisture stable compounds soluble in DMSO and DMF at room temperature and in methanol and ethanol upon heating. The ligands acted as bidentate and reacted readily with Co(II), Cu(II), Ni(II), and Zn(II) chlorides in ethanol to form the corresponding metal(II) complexes (Scheme 2).

[1] The text was submitted by the authors in English.

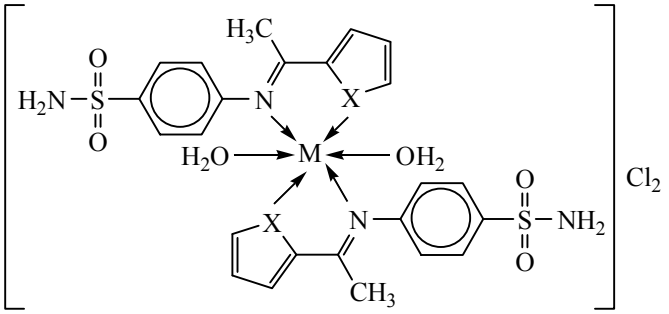
Scheme 1. Synthesis of Schiff base ligands $\mathbf{L^1}$–$\mathbf{L^3}$.



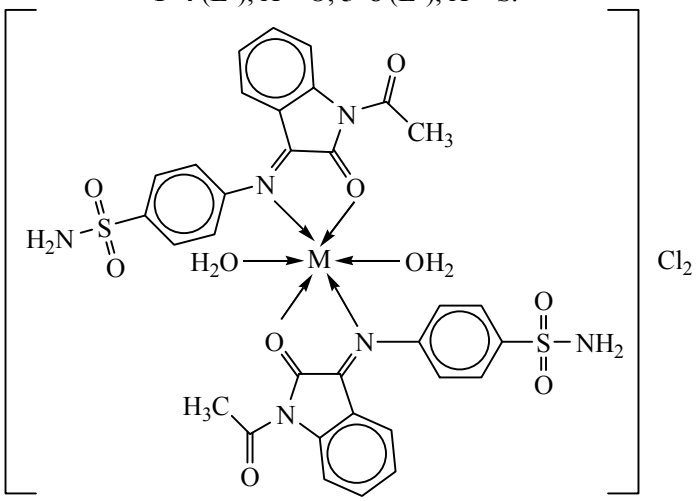
4-Aminobenzenesulfanilamide Substituted carbonyls $\mathbf{L^1}$–$\mathbf{L^3}$



Scheme 2. Proposed structure of metal(II) complexes **1–12**.



1–4 ($\mathbf{L^1}$); X = O, **5–8** ($\mathbf{L^2}$); X = S.



9–12 of ($\mathbf{L^3}$).

Attempts to produce large crystals of ligands and their metal complexes were unsuccessful.

All complexes were microcrystalline compounds soluble in DMSO and DMF.

IR spectra. In IR spectra (Table 2) of all synthesized Schiff base ligands one NH_2 band of sulfanilamide and C=O band of ketone moiety disappeared and a new band appeared at 1640–1658 cm^{-1} due to azomethine (C=N) linkage [19]. Other characteristic bands [20] also supported formation of the corresponding product. Comparison of the IR spectra of the ligands and their metal(II) complexes **1–12** justified coordination of the ligands to the metals bidentately. Azomethine ν(C=N) vibrations of all metal complexes were shifted to lower frequency by

Table 1. Physical measurements and analytical data of metal(II) complexes **1–12**

Comp. no.	Metal(II) complex	Yield, %	M_w	Formula	mp, °C	Calculated (found), %			
						C	H	N	M
1	$[Co(L^1)_2(H_2O)_2]Cl_2$	66	694.47	$C_{24}H_{28}N_4O_8S_2Cl_2Co$	312–314	41.51 (41.45)	4.06 (4.02)	8.07 (8.03)	8.49 (8.46)
2	$[Ni(L^1)_2(H_2O)_2]Cl_2$	68	694.23	$C_{24}H_{28}N_4O_8S_2Cl_2Ni$	317–318	41.52 (41.47)	4.07 (4.04)	8.07 (8.04)	8.45 (8.41)
3	$[Cu(L^1)_2(H_2O)_2]Cl_2$	74	699.08	$C_{24}H_{28}N_4O_8S_2Cl_2Cu$	325–326	41.23 (41.37)	4.04 (4.00)	8.01 (7.96)	9.09 (9.05)
4	$[Zn(L^1)_2(H_2O)_2]Cl_2$	71	700.95	$C_{24}H_{28}N_4O_8S_2Cl_2Zn$	234–235	41.12 (41.08)	4.03 (3.98)	7.99 (7.96)	9.33 (9.30)
5	$[Co(L^2)_2(H_2O)_2]Cl_2$	69	726.60	$C_{24}H_{28}N_4O_6S_4Cl_2Co$	309–311	39.67 (39.62)	3.88 (3.85)	7.71 (7.67)	8.11 (8.08)
6	$[Ni(L^2)_2(H_2O)_2]Cl_2$	68	726.36	$C_{24}H_{28}N_4O_6S_4Cl_2Ni$	333–334	39.69 (39.65)	3.89 (3.85)	7.71 (7.68)	8.08 (8.04)
7	$[Cu(L^2)_2(H_2O)_2]Cl_2$	70	731.21	$C_{24}H_{28}N_4O_6S_4Cl_2Cu$	307–309	39.42 (39.36)	3.86 (3.83)	7.66 (7.62)	8.69 (8.66)
8	$[Zn(L^2)_2(H_2O)_2]Cl_2$	69	733.08	$C_{24}H_{28}N_4O_6S_4Cl_2Zn$	239–240	39.32 (39.28)	3.95 (3.91)	7.64 (7.61)	8.92 (8.89)
9	$[Co(L^3)_2(H_2O)_2]Cl_2$	71	852.58	$C_{32}H_{30}N_6O_{10}S_6Cl_2Co$	231–232	45.08 (45.02)	3.55 (3.51)	9.86 (9.82)	6.91 (6.88)
10	$[Ni(L^3)_2(H_2O)_2]Cl_2$	74	852.34	$C_{32}H_{30}N_6O_{10}S_6Cl_2Ni$	217–218	45.09 (45.04)	3.55 (3.52)	9.86 (9.81)	6.89 (6.85)
11	$[Cu(L^3)_2(H_2O)_2]Cl_2$	76	857.20	$_{32}H_{30}N_6O_{10}S_6Cl_2Cu$	237–238	44.84 (44.78)	3.53 (3.50)	9.80 (9.76)	7.41 (7.37)
12	$[Zn(L^3)_2(H_2O)_2]Cl_2$	74	859.06	$C_{32}H_{30}N_6O_{10}S_6Cl_2Zn$	242–243	44.74 (44.69)	3.52 (3.47)	9.78 (9.75)	7.61 (7.58)

8 to15 cm^{-1} in the region of 1625–1650 cm^{-1} indicating coordination [21] of the C=N group with the Metal(II) ions. The new low-frequency weaker bands that appeared in the spectra of the metal complexes at 3477–3488, 546–555, 460–468, and 434–445 cm^{-1} were assigned to ν(H_2O), ν(M–N), ν(M–S), and ν(M–O), thus confirming the coordination [22] of metal atoms with ligands via furanyl-O, thienyl-S, isatin-O, and azomethine-N linkages. Position and intensities of ν(C–O) stretching of furanyl moiety, ν(C–S) of thienyl ring and ν(C=O) of isatin were shifted in IR spectra of the complexes supporting the above groups involvement in coordination/chelation [23].

^{1}H NMR spectra. ^{1}H NMR spectra of sulfonilamide derivatives **L^1–L^3** and their diamagnetic Zn(II) complexes demonstrated [24] distinctive amino (NH_2) protons signals at 9.14–9.25 ppm as a singlet which provided evidence for condensation of only one amino group of sulfanilamide. Coordination of the amino protons was evident by downfield shifting of all proton signals of Zn(II) complexes which was attributed to attraction of electronic density by Zn(II) metal. All other protons underwent downfield shift by 0.5–1.2 ppm due to increased conjugation upon coordination with Zn(II). Thus, the number of protons calculated from the integration curves [25] and CHN analysis data were in good agreement with the proposed structures.

^{13}C NMR spectra. Downfield shifting of the methyl and azomethine groups carbons in the spectra of Zn(II) complexes indicated electrons density interaction with Zn(II) ion. All carbon atoms of aromatic/heteroaromatic rings experienced the influence of chelation.

Table 2. Conductivity, magnetic and spectral data of metal(II) complexes **1–12**

Comp. no.	Ω_M, Ω^{-1} cm^2 mol^{-1}	μ_{eff}, BM[a]	λ_m, nm	IR spectrum, cm^{-1}
1	141.2	4.7	7296, 17498, 20508, 29373	3485 (H_2O), 1635 (C=N), 1111 (C–O), 554 (M–N), 432 (M–O)
2	139.2	3.3	10409, 15695, 26538, 29996	3480 (H_2O), 1632 (C=N), 1113 (C–O), 550 (M–N), 432 (M–O)
3	140.7	2.1	14984, 19184,30357	3483 (H_2O), 1636 (C=N), 1110 (C–O), 548 (M–N), 432 (M–O)
4	138.4	Dia	28985	3481 (H_2O), 1632 (C=N), 1114 (C–O), 551 (M–N), 432 (M–O)
5	139.3	4.6	7410, 17454, 20586, 29325	3488 (H_2O), 1625 (C=N), 870 (C–S), 546 (M–N), 468 (M–S)
6	135.4	3.1	10394, 15710, 26456, 29875	3480 (H_2O), 1628 (C=N), 868 (C–S), 551 (M–N), 465 (M–S)
7	140.5	2.1	14995, 19162, 30375	3486 (H_2O), 1630 (C=N), 871 (C–S), 549 (M–N), 460 (M–S)
8	139.7	Dia	28935	3483 (H_2O), 1631 (C=N), 874 (C–S), 554 (M–N), 467 (M–S)
9	142.0	4.8	7409, 17451, 20589, 29321	3477 (NH_2), 1712 (C=O), 1645 (C=N), 555 (M–N), 436 (M–O)
10	137.5	3.3	10398, 15709, 26457, 29878	3485 (H_2O), 1715 (C=O), 1646 (C=N), 550 (M–N), 433 (M–O)
11	139.1	2.4	15013, 19166, 30379	3483 (H_2O), 1710 (C=O), 1650 (C=N), 545 (M–N), 430 (M–O)
12	140.2	Dia	28939	3480 (H_2O), 1711 (C=O), 1648 (C=N), 551 (M–N), 435 (M–O)

[a] Dia is diamagnetic.

Molar conductance and magnetic measurements. Molar conductance measurements of the metal(II) complexes (DMF) were in the range of 135.4–142 Ω^{-1} cm^2 mol^{-1} thus indicating [26] the electrolytic (2 : 1) nature of the complexes. Magnetic moments of the Co(II) complexes (Table 2) were observed in the range of 4.6–4.8 BM indicating those as high-spin three unpaired electrons in an octahedral environment. Ni(II) complexes were likely to have an octahedral [27] geometry as well. The magnetic moments of 2.1–2.4 BM for Cu(II) complexes indicated one unpaired electron per Cu(II) ion for the d^9-system typical for octahedral [28] geometry. All Zn(II) complexes were measured to be diamagnetic [29].

Electronic spectra. Electronic spectra of Co(II) complexes generally displayed [30] three low to high transition intensity bands at 7296–7410, 17451–17498, and 20508–20589 cm^{-1} due to $^4T_{1g}$ (F) → $^4T_{2g}$ (F), $^4T_{1g}$ (F) → $^4A_{2g}$ (F) and $^4T_{1g}$ (F) → $^4T_{2g}$ (P) transitions in an octahedral environment. A high intensity band at 29321–29373 cm^{-1} was attributed to the metal → ligand charge transfer. Electronic spectral data of the Ni(II) complexes demonstrated [31] bands in the regions of 10394–10409, 15695–15710, and 26456–26538 cm^{-1} that were assigned to transitions, $^3A_{2g}$ (F) → $^3T_{2g}$ (F), $^3A_{2g}$ (F) → $^3T_{1g}$ (F) and $^3A_{2g}$ (F) → $^3T_{2g}$ (P) respectively, suggesting their octahedral geometry. Also a strong band due to metal to ligand charge transfer appeared at 29875–29996 cm^{-1}. The spectra of the Cu(II) complexes demonstrated two week bands at 14984–15013, 19162–19182 cm^{-1} that could be assigned to the transitions $^2B_{1g}$ → $^2A_{1g}$ and $^2B_{1g}$ → ^2E_g respectively, and their octahedral geometry [32]. A high intensity band at 30357-30379 cm^{-1} was assigned to the metal → ligand charge transfer. The Zn(II) complexes being diamagnetic demonstrated only *d–d* transitions and a strong band of high intensity at 28935–28985 cm^{-1} due to metal → ligand charge transfer [33].

Biological studies. *Antibacterial screening.* Sulfonilamide derived Schiff bases **L^1–L^3** and their Metal(II) complexes **1–12** have been screened for *in vitro* antibacterial activity against *Escherichia coli*, *Shigella*

Table 3. Antibacterial activity of ligands $\mathbf{L^1}$–$\mathbf{L^3}$ and metal(II) complexes **1–12**[a]

Comp. no.	Zone of inhibition, mm							
	g^-				g^+			
	Escherichia coli	*Pseudomonas aeruginosa*	*Salmonella typhi*	*Shigella flexneri*	*Staphylococcus aureus*	*Bacillus subtilis*	Statistical analysis	Average
$\mathbf{L^1}$	16	14	12	16	13	17	1.97	14.67
$\mathbf{L^2}$	12	15	13	14	16	12	1.63	13.67
$\mathbf{L^3}$	18	16	20	21	18	22	2.23	19.17
1	20	18	15	19	17	21	2.16	18.33
2	17	19	14	22	15	22	3.43	18.17
3	19	17	16	20	18	20	1.63	18.33
4	18	16	17	21	17	21	2.16	18.33
5	16	18	16	19	19	16	1.51	17.33
6	15	21	19	18	22	15	2.94	18.33
7	14	20	17	16	19	14	2.50	16.67
8	17	19	16	16	20	19	1.72	17.83
9	24	22	23	25	21	25	1.63	23.33
10	26	23	26	22	25	25	1.64	24.50
11	23	20	21	25	23	24	1.86	22.67
12	25	24	24	24	22	27	1.63	24.33
Standard drug (Imipenem)[b]	28	27	29	28	27	30	1.17	28.17

[a] Average activity of ligand $\mathbf{L^1}$–$\mathbf{L^3}$ = 15.84 mm, average activity of of **1–12** = 18.71 mm; [b] weaker = 0–10 mm, moderate = 10–15 mm, significant is above 16 mm.

flexneri, *Pseudomonas aeruginosa*, *Salmonella typhi*, *Staphylococcus aureus,* and *Bacillus subtilis* bacterial strains according to the standard procedure (Table 3) and were compared with those of the standard drug imipenum. Ligand ($\mathbf{L^1}$) exhibited significant (16–17 mm) activity against *Escherichia coli*, *Salmonella typhi* ,and *Bacillus subtilis* bacterial strains. The remaining strains demonstrated moderate (12–14 mm) activity. Likewise, ligand ($\mathbf{L^2}$) possessed overall moderate (12–15 mm) activity against all strains except *Staphylococcus aureus* (16 mm). But the ligand $\mathbf{L^3}$ demonstrated significant (16–22 mm) activity against all bacterial strains. The metal complexes **3–5** and **8–12** displayed exceptional (16–26 mm) activity against all strains. Overall, it was concluded that metal complexes demonstrated higher activity against one or more bacterial strains that support our earlier results [34]. The Ni(II) complex **10** of $\mathbf{L^3}$ was found to have the highest antibacterial activity.

Antifungal studies. Antifungal screening of all synthesized compounds was carried out against *Trichophyton longifusus, Candida albicans, Aspergillus flavus, Microsporum canis, Fusarium solani,* and *Candida glabrata* fungal strains (Table 4) according to the common protocol. It is noteworthy that the metal complexes **1** and **2** demonstrated high (55–65%) activity against all strains, except *Trichophyton longifusus* and *Fusarium solani*. The metal complexes **9–12** exhibited overall significant 56–77% activity against all fungal strains. The accumulated data (Table 4) indicated that the ligand $\mathbf{L^3}$ demonstrated the overall highest antifungal activity among all ligands. The Zn(II) complex **9** of $\mathbf{L^3}$ was determined to be the most

Table 4. Antifungal activity of ligands $\mathbf{L^1}$–$\mathbf{L^3}$ and metal(II) complexes **1–12**

Comp. no.	Percent of inhibition, mm							
	Trichophyton longifusus	*Candida albicans*	*Aspergillus flavus*	*Microsporum canis*	*Fusarium solani*	*Candida glabrata*	Statistical analysis	Average
$\mathbf{L^1}$	0	35.0	56	40	28.00	39.0	18.61	33.00
$\mathbf{L^2}$	59	46.0	0	31.0	26.00	49.0	21.05	35.17
$\mathbf{L^3}$	46	57.0	50	49.0	43.00	52.0	4.85	49.50
1	34	55.0	65	59.0	41.00	56.0	11.72	51.67
2	36	60.0	71	57.0	50.00	59.0	11.71	55.50
3	40	46.0	69	58.0	45.00	62.0	11.34	53.33
4	39	43.0	65	60.0	37.00	58.0	12.06	50.33
5	74	58.0	21	43.0	39.00	57.0	18.38	48.67
6	66	61.0	37	40.0	44.00	66.0	13.46	52.33
7	69	56.0	35	52.0	41.00	59.0	12.36	52.00
8	71	62.0	18	46.0	40.00	60.0	19.10	49.50
9	60	74.0	62	60.0	58.00	77.0	8.16	65.17
10	56	70.0	65	62.0	58.00	67.0	5.37	63.00
11	64	69.0	60	66.0	63.00	71.0	4.04	65.50
12	61	62.0	58	59.0	56.00	70.0	4.90	61.00
Standard drugs[b], μg/mL	70	110.8	20	98.4	73.25	110.8	–	–

[a] Average activity of ligands $\mathbf{L^1}$–$\mathbf{L^3}$ = 37.33%; average activity of **1–12** = 58.01%. [b] Standard drugs (MIC μg/mL); miconazole (*Trichophyton longifusus, Candida albicans, Microsporum canis, Fusarium solani, Candida glabrata*) and amphotericin B (*Aspergillus flavus*); weaker = 0–33%, moderate = 34–54%, significant = 55–100%.

active among all complexes. So, the metal(II) complexes were characterized by higher activity [35] than the free ligands.

EXPERIMENTAL

All chemicals of analytical grade were purchased from Sigma Aldrich and used without further purification. Synthesis of ligands was carried out in purified and dried solvents. Melting points were measured on a Fischer Scientific apparatus. IR spectra (KBr discs) were recorded on a 8400 Shimadzu FTIR Transform Infrared Spectrophotometer. Elemental analysis was carried out on a Perkin Elmer analyzer (USA model). ^{1}H and ^{13}C NMR spectra were measured in DMSO-d_6 on a Bruker Spectrospin Avance DPX-400 spectrometer using TMS as the internal standard. Electron impact mass spectra (EIMS) were recorded on a JEOL MSRoute instrument. UV-Vis spectra were recorded on a UV-Vis double beam PC scanning spectrophotometer UVD-2950 LAMBOED in the range of 250–800 nm. Conductivity meter Jenway model 70 was used for measuring conductivity of metal complexes using 0.001 molar solutions in DMF at room temperature. A Stanton SM12/S Gouy balance was used to measure the magnetic susceptibility of the metal complexes at room temperature using mercury acetate ligand as a standard. *In vitro* antibacterial and antifungal properties were studied at HEJ Research Institute of Chemistry, International Centre for Chemical Sciences, University of Karachi, Pakistan.

4-[1-(Furan-2-yl)ethylideneamino]benzenesulfanilamide ($\mathbf{L^1}$). 4-Aminobenzenesulfanilamide (0.002 M, 0.34g) in ethanol (10 mL) was added to a stirred solution of 1-(furan-2-yl)ethanone (0.002 M, 0.22 g) in ethanol (10 mL) followed by 2–3 drops of acetic acid. The reaction mixture was stirred for 4 h

with continuous monitoring by TLC. The mixture was left overnight at room temperature. Precipitate formed was filtered off, washed with cold ethanol, then with ether, dried, and recrystallized from a mixture of ethanol:dichloromethane (1 : 1). Ligands $\mathbf{L^2}$ and $\mathbf{L^3}$ were synthesized according to the same method. Light brown solid, yield 62%, mp 220°C. IR spectrum, ν, cm^{-1}: 3364 (NH_2), 1648 (C=N), 1317, 1162 (S=O), 1125 (C–O), 935 (S–N), 845 (C–S). ^{1}H NMR spectrum, δ, ppm: 2.15 s (3H), 7.01 d.d (1H, *J* = 4.8, 3.7 Hz), 7.35 d (1H, *J* = 4.8 Hz), 7.63 d (1H, *J* = 3.8 Hz), 7.65–7.91 m (4H, Ph), 9.25 s (2H, SO_2NH_2). ^{13}C NMR spectrum, δ, ppm: 15.1, 115.2, 121.9, 123.5, 124.1, 126.8, 127.7, 137.3, 140.6, 145.8, 151.2, 155.6, 163.9. MS (ESI): $[M]^+$ = 264 (264.30). Found, %: C 54.49; H 5.54; N 10.57. $C_{12}H_{12}N_2O_3S$. Calculated, %: C 54.53; H 4.58; N 10.60.

4-[1-(Thiophene-2-yl)ethylideneamino]benzenesulfanilamide ($\mathbf{L^2}$). Off white solid, yield 68%, mp 215°C. IR spectrum, ν, cm^{-1}: 3369 (NH_2), 1640 (C=N), 1321, 1162 (S=O), 930 (S–N), 883 (C–S, thienyl), 840 (C–S). ^{1}H NMR spectrum, δ, ppm: 2.06 s (3H), 6.97 d.d (1H, *J* = *4.8, 3.7* Hz), 7.30 d (1H, *J* = 4.8 Hz), 7.59 d (1H, *J* = 3.8 Hz), 7.47–7.81 m (4H, Ph), 9.14 s (2H, SO_2NH_2). ^{13}C NMR spectrum, δ, ppm: 14.8, 114.7, 121.3, 123.1, 123.8, 126.5, 127.5, 137.0, 140.1, 145.3, 150.7, 155.3, 163.1; MS (ESI): $[M]^+$ = 280 (280.37). Found, %: C 51.36: H 4.27; N 9.95. $C_{12}H_{12}N_2O_2S_2$. Calculated, %: C 51.41; H 4.31; N 9.99.

4-[1-Acetyl-2-oxoindolin-3-ylideneamino]benzenesulfanilamide ($\mathbf{L^3}$). Reddish brown solid, yield 65%, mp 200°C. IR spectrum, ν, cm^{-1}: 3380 (NH_2), 1725 (C=O), 1658 (C=N), 1348, 1184 (S=O), 1145 (C-N), 931 (S–N), 854 (C–S). ^{1}H NMR spectrum, δ, ppm: 2.11 s (3H), 7.30–7.55 m (4H, isatin), 7.71–7.89 m (4H, Ph), 9.22 s (2H, SO_2NH_2). ^{13}C NMR spectrum, δ, ppm: 18.7, 115.1, 121.9, 123.0, 123.7, 125.6, 126.8, 127.6, 129.0, 133.2, 136.0, 138.8, 154.7, 158.8, 164.6, 168.3. MS (ESI): $[M]^+$ = 343 (343.35). Found, %: C 55.91; H 3.78; N 12.10. $C_{14}H_{13}N_3O_4S$. Calculated, %: C 55.97; H 3.82; N 12.24.

Synthesis metal(II) complexes. All metal(II) complexes were prepared according to the standard procedure. To a metal chloride (5 mmol) in ethanol (10 mL) upon magnetic refluxing was added ethanol solution (20 mL) of a ligand (10 mmol). The mixture was refluxed for 3 h then cooled down to room temperature. The precipitate was filtered off, washed with ethanol and diethyl ether, dried, and recrystallized from a mixture of hot ethanol: methanol (1 : 1) to get the corresponding TLC pure compound (Table 1).

$[Zn(L^1)_2]$ (4). ^{1}H NMR spectrum, δ, ppm: 2.26 s (3H), 7.08 d.d (1H, *J* = 4.8, 3.7 Hz), 7.44 d (1H, *J* = 4.8 Hz), 7.69 d (1H, *J* = 3.8 Hz), 7.70–7.99 m (4H, Ph), 9.30 s (2H, SO_2NH_2). ^{13}C NMR spectrum, δ, ppm: 16.6, 116.0, 122.5, 124.2, 124.9, 127.3, 128.4, 138.0, 141.2, 146.5, 151.8, 156.4, 165.3.

$[Zn(L^2)_2]$ (8). ^{1}H NMR spectrum, δ, ppm: 2.19 s (3H), 7.04 d.d (1H, *J* = 4.8, 3.7 Hz), 7.32 d (1H, *J* = 4.8 Hz), 7.68 d (1H, *J* = 3.8 Hz), 7.53–7.94 m (4H, Ph), 9.19 s (2H, SO_2NH_2). ^{13}C NMR spectrum, δ, ppm: 15.5, 115.6, 121.9, 124.0, 124.9, 127.0, 128.2, 137.6, 140.9, 145.8, 151.4, 156.1, 164.4.

$[Zn(L^3)_2]$ (12). ^{1}H NMR spectrum, δ, ppm: 2.16 s (3H), 7.35–7.65 m (4H, isatin), 7.77–7.99 m (4H, Ph), 9.28 s (2H, SO_2NH_2). ^{13}C NMR spectrum, δ, ppm: 19.3, 115.8, 12.8, 123.7, 124.7, 126.5, 127.5, 128.4, 129.5, 133.8, 136.9, 139.4, 155.5, 159.6, 165.7, 169.9.

Antibacterial activity. The agar-well diffusion method [36] was used for testing toxicity of all newly synthesized ligands $\mathbf{L^1}$–$\mathbf{L^3}$ and their metal(II) complexes **1–12** in-vitro against four gram-negative (*E. coli, S. flexneri, P. aeruginosa, S. typhi*) and two gram-positive (*S. aureus, B. subtilis*) bacterial strains. The wells (6 mm in diameter) were introduced in the media with the help of a sterile metallic borer with centers at least 24 mm apart. Bacterial inoculum after 6–8 h of growth approximately having 10^4–10^6 colony forming units (CFU)/mL was used. The recommended concentration of the test sample (1 mg/mL in DMSO) was introduced in the respective well. Other wells supplemented with DMSO and reference antibacterial drug (imipenem) served as a negative and positive control, respectively. The plates were incubated at 37°C for 24 h. Activity was determined by measuring the diameter of zones which showed complete inhibition (mm). DMSO demonstrated no activity against any of the bacterial strains used in this study.

Antifungal activity. Antifungal activity of all compounds was studied against six fungal strains (*T. longifusus, C. albican, A. flavus, M. canis, F. solani* and *C. glabrata*). Sabouraud dextrose agar (Oxoid, Hampshire, England) was seeded with 10^5 (CFU)/mL fungal spore suspensions and transferred to petri plates. Discs soaked in 20 mL (200 μg/mL in DMSO) of the compounds were placed at different positions on the agar surface. The plates were incubated at 32°C for 7 days. The results

were recorded as percentage of inhibition and compared with standard drugs miconazole and amphotericin B.

CONCLUSIONS

The synthesized sulfanilamide Schiff bases acted as bidentate ligands in coordination with Co(II), Ni(II), Cu(II), and Zn(II) via azomethine-N, thienyl-S, furanyl-O, and acetyisatin-N. Physical, spectral and analytical data confirmed that the Schiff bases had octahedral geometry in the complexes. Antibacterial and antifungal activities data of the metal complexes demonstrated higher biological activity against one or more bacterial and/or fungal strains than non-chelated ligands. Probably oxygen of furanyl, sulphur of thioenyl, nitrogen of azomethine, and isatin were the sites potentially responsible for the enhancement of antibacterial and antifungal activities.

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