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Antibacterial and Antifugal Mono- and Di-substituted Symmetrical and Unsymmetrical Triazine-derived Schiff-bases and their Transition Metal Complexes

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A new series of antibacterial and antifungal triazine-derived mono- and di-substituted (symmetrical and unsymmetrical) Schiff-bases and their cobalt(II), copper(II), nickel(II) and zinc(II) metal complexes have been synthesized and characterized by their elemental analyses, molar conductances, magnetic moments and IR and electronic spectral measurements. IR spectra indicated the ligands to act as tridentate towards divalent metal ions via a trazine-N, the azomethine-N and, indole-NH and deprotonated-O of salicylaldehyde. The magnetic moments and electronic spectral data suggest octahedral geometry for the Co(II), Ni(II) and Zn(II)complexes and square-pyramid for Cu(II) complexes. NMR spectral data of the ligands and their diamagnetic zinc(II) complexes well-define their proposed structures/geometries. Elemental analyses data of the ligands and metal complexes agree with their proposed structures/geometries. The synthesized ligands, along with their metal complexes were screened for their antibacterial activity against *Escherichia coli*, *Bacillus subtillis*, *Shigella flexneri*, *Staphylococcus aureus*, *Pseudomonas aeruginosa* and *Salmonella typhi* and for antifungal activity against *Trichophyton longifusus*, *Candida albicans*, *Aspergillus flavus*, *Microsporum canis*, *Fusarium solani* and *Candida glaberata*. The results of these studies show the metal complexes to be more antibacterial/antifungal against two or more species as compared to the uncomplexed Schiff-base ligands.

Keywords: Triazines; Schiff's-bases; Transition metal complexes; Antibacterial; Antifungal

INTRODUCTION

Triazines are known to possess interesting biological activities: they act as antibacterial, antiviral, antimalarial and anti-inflammatory agents among others.[1–4] Their anticancer, antileukemia and anti-HIV activities have also been evaluated and found to show promising properties in some instances.[5–8] The therapeutic properties of certain salicylaldehyde and indoles are also reported and show bactericidal activity.[9,10] It is known that the existence of metal ions bonded to biologically active compounds may enhance their activities.[11–15] Our ongoing research has established[16–19] that non-biologically active compounds become biologically active and less biologically active compounds become more active upon coordination/chelation with metal ions. In order to expand this emerging area of metal-based drug chemistry we, now, wish to report a series of novel antibacterial and antifungal triazine-derived mono- and di-substituted (symmetrical and unsymmetrical) Schiff-bases ($\mathbf{L_1}$–$\mathbf{L_5}$) and their cobalt(II), copper(II), nickel(II) and zinc(II) metal complexes (**1**–**20**). The synthesized Schiff-bases and their metal complexes have been characterized by their molar conductances, magnetic moments, and elemental analyses. All the Schiff-base ligands, along with their metal complexes were screened for their antibacterial activity against *Escherichia coli*, *Bacillus subtillis*, *Shigella flexneri*, *Staphylococcus aureus*, *Pseudomonas aeruginosa* and *Salmonella typhi* and for antifungal activity against *Trichophyton longifusus*, *Candida albicans*, *Aspergillus flavus*, *Microsporum canis*, *Fusarium solani* and *Candida glaberata*. The Schiff-bases showed varied antibacterial and

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antifungal activity against one or more strains respectively and their activity was enhanced on coordination/chelation. These reported compounds are not only good candidates potentially for use as antibacterial and antifungal but also, a promising addition to metal-based drug chemistry.

MATERIAL AND METHODS

Solvents used were analytical grades; all metal (II) were used as their chloride salts. IR spectra were recorded on a Philips Analytical PU 9800 FTIR spectrophotometer. NMR spectra were recorded on a Perkin-Elmer 283B spectrometer. UV-Visible spectra were obtained in DMF on a Hitachi U-2000 double-beam spectrophotometer. Butterworth Laboratories Ltd (U.K.) carried out C, H and N analyses. Conductance of the metal complexes was determined in DMF on a Hitachi (Japan) YSI-32 model conduct meter. Magnetic measurements were carried out on solid complexes using Gouy's method. Melting points were recorded on a Gallenkamp (UK) apparatus and are uncorrected. The complexes were analyzed for their metal contents by EDTA titration.[17] Antibacterial and antifungal screening was done at HEJ Research Institute of Chemistry, International Center for Chemical Sciences, University of Karachi, Pakistan.

Preparation of Triazine-derived Schiff Bases (L^1–L^5) and Metal (II) Complexes (1–20)

To a stirred solution of 2,6-diamino-4-phenyl-1,3,5-triazine (3.0 g, 0.01 mmol) in warm ethanol (20 mL) was added salicylaldehyde (1.3 g, 0.01 mmol) in ethanol (10 mL). Then 2–3 drops of conc. H_2SO_4 were added and the mixture refluxed for 2 h. The completion of reaction was monitored by TLC. After completion of reaction the mixture was cooled to afford a solid product. The solid residue was filtered, washed with ethanol, then with ether and dried. Crystallization from hot ethanol gave $\mathbf{L^1}$. The same method was applied for the preparation of $\mathbf{L^2}$–$\mathbf{L^5}$ by using the corresponding aldehydes, working under the same conditions with their respective molar ratio. TLC of the unsymmetrical ligand, $\mathbf{L_5}$, showed a mixture of mainly two compounds, 20% of which was symmetrical di-substituted and the rest was the desired unsymmetrically di-substituted ligand $\mathbf{L_5}$ which were separated by column chromatography.

For the preparation of metal (II) complexes, a solution (30 mL) of the corresponding ligand (0.02 mmol) in hot ethanol was added to a stirred solution of metal (II) chloride (0.01 mmol) in ethanol (25 mL). The mixture was refluxed for 1 h and then cooled to room temperature when solidification on cooling. The solid thus obtained was filtered, washed with ethanol, then with ether and dried in air. Crystallization from aqueous/ethanol (30:70) gave the desired metal complex. The same method was used for the preparation of all other complexes by using their respective metal (II) salts.

Biological Activity

All the synthesized ligands and their corresponding metal(II) chelates were screened in vitro for their antibacterial activity against *Escherichia coli*, *Bacillus subtillis*, *Shigella flexneri*, *Staphylococcus aureus*, *Pseudomonas aeruginosa* and *Salmonella typhi* and for antifungal activity against *Trichophyton longifusus*, *Candida albicans*, *Aspergillus flavus*, *Microsporum canis*, *Fusarium solani* and *Candida glaberata* using the agar well diffusion method.[20,21] Two to eight hours 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. The concentration (100 μl) of the test sample (1 mg/ml in DMSO) was introduced into the corresponding wells. Other wells were supplemented with DMSO and reference antibacterial drugs 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). Imipenum was used as a standard drug for antibacterial activity and, miconazole and amphotericin B for antifungal activity.

RESULTS AND DISCUSSION

Chemistry

The Schiff-bases ($\mathbf{L^1}$–$\mathbf{L^5}$, Figure 1) were prepared by refluxing the appropriate amount of 2,6-diamino-4-phenyl-1,3,5-triazine with the corresponding salicylaldehyde and indole-3-carboxaldehyde in ethanol, in 1:1 molar ratio to obtain the Schiff-bases $\mathbf{L_1}$ and $\mathbf{L_3}$ while in a 1:2 molar ratio to achieve $\mathbf{L_2}$, $\mathbf{L_4}$ (symmetrical) and $\mathbf{L_5}$ (unsymmetrical) Schiff-base ligands. The structures of the synthesized ligands were established with the aid of their IR, NMR and microanalytical data. All metal complexes (**1**–**20**) of these ligands were air-and moisture stable and prepared by the stoichiometric reaction of the corresponding metal(II) chloride with the ligand, in a molar ratio (M:L) of 1:2. These complexes are intensely colored and amorphous solids, which decomposed without melting. They were insoluble in common organic solvents and only soluble in water, DMF and DMSO. Molar conductance values

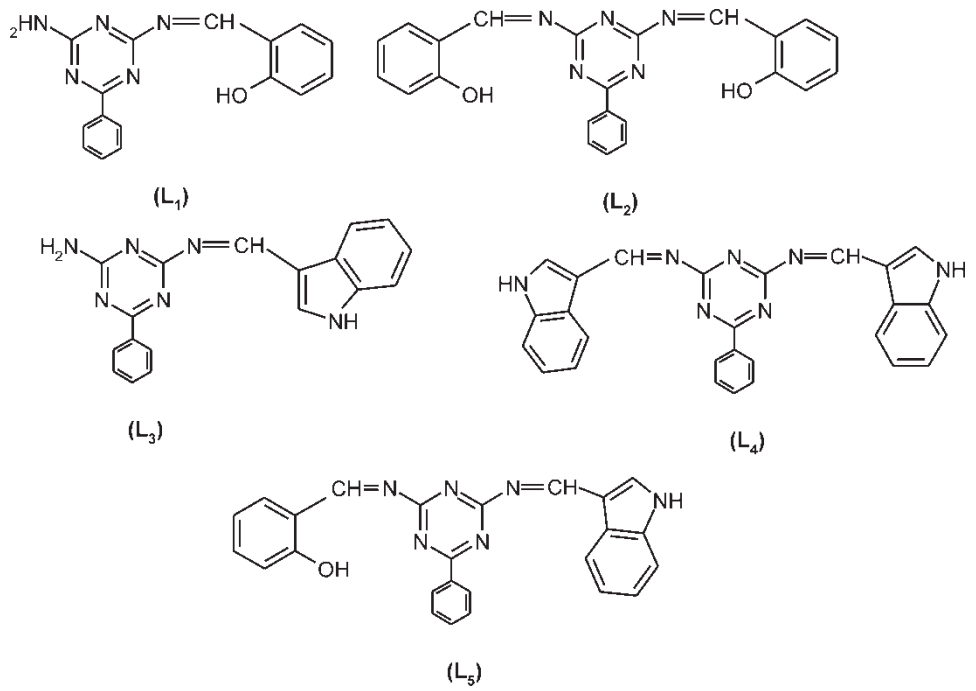

FIGURE 1 Proposed structure of the ligands ($\mathbf{L^1}$–$\mathbf{L^5}$).

of the soluble complexes in DMF (10^3 M solution at 25°C), indicated that complexes of copper (II) have initially lower values (54–58 $ohm^{-1}\,cm^{-2}\,mol^{-1}$) indicating that they are all less-electrolytic in nature[22] with the involvement of one chloride ion in bonding with the copper metal ion. It was interesting to note that after heating the Cu(II) complexes to 50°C they behaved as more electrolytic (77–82 $ohm^{-1}\,cm^{-2}\,mol^{-1}$) in nature. This is probably due to the replacement of the bonded chloride as shown in the following equations: this phenomenon has been previously reported[23] for copper(II) complexes.

$$CuCl_2 + 2(L)_2 \xrightarrow{25^{\circ}C} [Cu(L)_2X]X \quad (1)$$

$$CuCl_2 + 2(L)_2 \underset{X=Cl}{\overset{50^{\circ}C}{\longrightarrow}} [Cu(L)_2]X_2 \quad (2)$$

However, the complexes of cobalt(II), nickel(II) and zinc(II), showed higher molar conductance values (82–98 $ohm^{-1}\,cm^{-2}\,mol^{-1}$) indicating that they are all electrolytic[22] in nature, in turn, suggesting non-involvement of chlorides in bonding. The elemental analyses data agree well with the proposed formulae for the ligands and also confirmed the $[M(L)_2]Cl_2$ composition of the metal (II) chelates. Efforts to grow good crystals of the ligands and their metal chelates for X-ray diffraction studies were unsuccessful due to their poor solubility in common organic solvents.

IR Spectra

The selected IR spectra of the ligands and their metal complexes along with their tentative assignments are reported in Tables I and III, respectively. The IR spectra of the complexes (Table III) showed shifts to lower wave numbers in ν(HC═N) of both the azomethine and triazine ν(C═N) moieties by 15–20 cm^{-1}, respectively and shifts to higher wave numbers in the ν(C═N) of the triazine ring when compared[24] with the corresponding values of the ligands. This data suggests that both

TABLE I Physical, spectral and analytical data of the ligands $\mathbf{L^1}$–$\mathbf{L^5}$

Ligand/Mol. Form	M.P (°C)	IR (cm^{-1})	C, H, N; Calc. (Found) %	Yield (%)
$\mathbf{L^1}$ [291.0] ($C_{16}H_{13}N_5O$)	117	3315 (OH), 3175 (NH_2), 1620 (CH═N), 1565 (C═N)	66.0 (66.3), 4.5 (4.7), 24.1(24.4)	68
$\mathbf{L^2}$ [395.0] ($C_{23}H_{17}N_5O_2$)	147	3325 (OH), 1620 (CH═N), 1565 (C═N)	69.9 (70.2), 4.3 (4.1), 17.7 (17.4)	65
$\mathbf{L^3}$ [314.0] ($C_{18}H_{14}N_6$)	160	3210 (NH), 3175 (NH_2), 1620 (CH═N), 1565 (C═N)	68.8 (68.5), 4.5 (4.8), 26.8 (26.5)	70
$\mathbf{L^4}$ [441.0] ($C_{27}H_{19}N_7$)	185	3215 (NH) 1620 (CH═N), 1565 (C═N)	73.5 (73.8), 4.3 (4.1), 22.2 (22.5)	65
$\mathbf{L^5}$ [418.0] ($C_{25}H_{18}N_6O$)	192	3315 (OH), 3215 (NH), 1625 (CH═N), 1565 (C═N)	71.8 (71.4), 4.3 (4.5), 20.1 (20.5)	58

TABLE II ^{1}H NMR and ^{13}C NMR data of the ligands (L^{1}–L^{5}) and Zn (II) complexes (**16**–**20**)

No.	^{1}H NMR (DMSO-d_6) (ppm)	^{13}C NMR (DMSO-d_6) (ppm)
L^{1}	3.3 (s, 1H, CH═N), 4.7 (s, 2H, NH_2), 9.6 (s, 1H, OH), 6.5–8.2 (m, 5H, phenyl), 7.1–8.7 (m, 4H, phenol)	115.6, 130.3, 155.2, 121.5, 135.5, 124.7 (phenol),148.6, 126.5, 128.4, 126.7 (phenyl), 142.5 (C═N), 152.8, 156.5, 158.9 (triazine)
L^{2}	3.5 (s, 2H, CH═N), 9.7 (s, 2H, OH), 6.6–8.4 (m, 5H, phenyl), 7.2–8.8 (m, 8H, phenol)	115.7, 130.3, 155.3, 121.5, 135.6, 124.7 (phenol), 148.7, 126.5, 128.5, 126.7 (phenyl), 142.6 (C═N), 152.8, 156.5, 158.9 (triazine)
L^{3}	3.4 (s, 1H, CH═N), 4.7 (s, 2H, NH_2), 6.9 (dd, 1H, indol), 6.5–8.2 (m, 5H, phenyl), 7.3–7.6 (m, 4H, indol), 8.3 (s, IH, indol-NH)	122.6, 123.6, 124.4, 124.5, 126.7, 139.6, 152.2, 155.2, (indol), 148.6, 126.5, 128.4, 126.7 (phenyl), 142.5 (C═N), 152.8, 156.5, 158.9 (triazine)
L^{4}	3.6 (s, 2H, CH═N), 6.9 (dd, 2H, indol), 6.5–8.3 (m, 5H, phenyl), 7.4–7.7 (m, 8H, indol), 8.5 (s, 2H, indol-NH)	122.6, 123.6, 124.4, 124.5, 126.7, 139.6, 152.2, 155.2, (indol), 148.6, 126.5, 128.4, 126.7 (phenyl), 142.5 (C═N), 152.8, 156.5, 158.9 (triazine)
L^{5}	3.6 (s, 2H, CH═N), 6.8 (dd, 1H, indol), 6.5–8.3 (m, 5H, phenyl), 7.1–8.7 (m, 4H, phenol), 7.4–7.8 (m, 4H, indol), 8.4 (s, 1H, indol-NH), 9.6 (s, 1H, OH)	115.7, 130.3, 155.3, 121.5, 135.6, 124.7 (phenol), 122.6, 123.6, 124.4, 124.5, 126.7, 139.6, 152.2, 155.2, (indol), 148.6, 126.5, 128.4, 126.7 (phenyl), 142.5 (C═N), 152.8, 156.5, 158.9 (triazine)
16	3.7 (s, 1H, CH═N), 4.9 (s, 2H, NH_2), 9.8 (s, 1H, OH), 6.6–8.4 (m, 5H, phenyl), 7.3–8.9 (m, 4H, phenol)	115.9, 130.3, 155.4, 121.6, 135.6, 124.7 (phenol), 148.8, 126.5, 128.6, 126.7 (phenyl), 142.7 (C═N), 152.9, 156.8, 158.9 (triazine)
17	3.8 (s, 2H, CH═N), 9.7 (s, 2H, OH), 6.7–8.4 (m, 10H, phenyl), 7.3–8.8 (m, 8H, phenol)	115.8, 130.4, 155.3, 121.5, 135.7, 124.7 (phenol), 148.7, 126.6, 128.5, 126.7 (phenyl), 142.8 (C═N), 152.9, 156.6, 158.9 (triazine)
18	3.7 (s, 1H, CH═N), 4.7 (s, 2H, NH_2), 6.9 (dd, 1H, indol), 6.6–8.2 (m, 5H, phenyl), 7.4–7.6 (m, 4H, indol), 8.5 (s, IH, indol-NH)	122.6, 123.7, 124.5, 124.7, 126.7, 139.6, 152.4, 155.2, (indol), 148.7, 126.5, 128.4, 126.7 (phenyl), 142.7 (C═N), 152.9, 156.7, 158.9 (triazine)
19	3.8 (s, 2H, CH═N), 6.9 (dd, 2H, indol), 6.6–8.4 (m, 5H, phenyl), 7.5–7.8 (m, 8H, indol), 8.7 (s, 2H, indol-NH)	122.7, 123.6, 124.5, 124.7, 126.7, 139.7, 152.2, 155.3, (indol), 148.7, 126.6, 128.4, 126.8 (phenyl), 142.7 (C═N), 152.9, 156.6, 158.9 (triazine)
20	3.8 (s, 2H, CH═N), 6.9 (dd, 1H, indol), 6.6–8.3 (m, 5H, phenyl), 7.2–8.7 (m, 4H, phenol), 7.5–7.8 (m, 4H, indol), 8.6 (s, 1H, indol-NH), 9.6 (s, 1H, OH)	115.7, 130.3, 155.3, 121.5, 135.6, 124.7(phenol),122.6, 123.6, 124.4, 124.5, 126.7, 139.6, 152.2, 155.2, (indol), 148.6, 126.5, 128.4, 126.7 (phenyl), 142.5 (C═N), 152.8, 156.5, 158.9 (triazine)

the azomethine and triazine nitrogen atoms are involved in coordination with the metal ions. The band located at 3315 and 3210 cm^{-1} in the ligands are attributed[25] to ν(C–OH) and ν(HN) moieties of salicylaldehyde-OH and indole-NH. The band due to ν(C–OH) disappear in the spectra of the metal complexes and instead, a new band at 1580 cm^{-1} appeared suggesting deprotonation and coordination of this group with the metal ions. Similarly, the band due to ν(HN) disappeared and a new band at 355 cm^{-1} appeared indicating the involvement of NH in coordination. The far IR spectra of the metal complexes in Table III exhibited new bands which are not present in the spectra of the ligands. These bands are located at 425, 390 and 375 cm^{-1}, assigned[26] to ν(M–O), of salicyl-O, ν(M–N) of azomethine nitrogen and ν(M–N) of the triazine, supporting the bonding of the salicyl oxygen, azomethine and triazine nitrogen atoms to the metal ions. Only the IR spectra of the Cu(II) complexes showed a band at 315 cm^{-1}, suggesting[27] coordination of ν(M–Cl) in the $[Cu(L)_2Cl]Cl$ complexes which finally disappeared on heating the complex at 50°C and formation of the stable complex, $[Cu(L)_2]Cl_2$.

According to the above mentioned data the ligands behave as tridentate towards cobalt(II), nickel(II) and zinc(II) complexes via two nitrogen atoms, one derived from the triazine ring and the other from the azomethine linkage, and one deprotonated oxygen atom of the salicylaldehyde moiety and/or via indole-NH.

NMR Spectra

The ^{1}H NMR and ^{13}C NMR spectra of the free ligands and their diamagnetic Zn(II) chelates were run in DMSO-d_6. The ^{1}H NMR spectral data are reported along with the possible assignments in Table II. All the protons due to heteroaromatic and/or aromatic groups were found to be in the expected region.[28,29] The conclusions drawn from these studies lend further support to the mode of bonding discussed in their IR spectra. In the spectra of diamagnetic Zn (II) complexes (**16**–**20**) these signals shifted downfield due to the increased conjugation and coordination to the metal atoms. The number of protons calculated from the integration curves, and those obtained from the values of the expected CHN analyses are in

TABLE III Physical and analytical data for the metal (II) complexes **1–20**

No.	Metal chelate/Mol. formula	M.P (°C)	B.M (μ_{eff})	C, H, N; Calc. (Found) %	Yield (%)
1	$[Co(L^1)_2]Cl_2$ [709.9] ($C_{32}H_{24}N_{10}CoCl_2O_2$)	218–220	3.8	54.1 (54.5), 3.4 (3.7), 19.7 (19.6)	68
2	$[Co(L^2)_2]Cl_2$ [917.9] ($C_{46}H_{32}N_{10}CoCl_2O_4$)	230–232	3.7	60.1 (60.3), 3.5 (3.2), 15.3 (15.5)	70
3	$[Co(L^3)_2]Cl_2$ [757.9] ($C_{36}H_{28}N_{12}CoCl_2$)	220–222	4.2	57.0 (56.8), 3.7 (3.3), 22.2 (22.4)	72
4	$[Co(L^4)_2]Cl_2$ [1011.9] ($C_{54}H_{38}N_{14}CoCl_2$)	234–236	4.1	64.0 (64.4), 3.8 (3.5), 19.4 (19.2)	69
5	$[Co(L^5)_2]Cl_2$ [963.9] ($C_{50}H_{34}N_{12}CoCl_2O_2$)	231–233	3.8	62.2 (59.9), 3.5 (3.7), 17.4 (17.7)	71
6	$[Cu(L^1)_2Cl]Cl$ [714.5] ($C_{32}H_{24}N_{10}CuCl_2O_2$)	228–230	1.8	53.7 (53.9), 3.4 (3.7), 19.6(19.2)	68
7	$[Cu(L^2)_2Cl]Cl$ [922.5] ($C_{46}H_{32}N_{10}CuCl_2O_4$)	216–218	1.6	59.8 (59.9), 3.5 (3.7), 15.2 (19.7)	70
8	$[Cu(L^3)_2Cl]Cl$ [762.5] ($C_{36}H_{28}N_{12}CuCl_2$)	222–223	1.4	56.7 (56.2), 3.7 (3.5), 22.0 (22.4)	65
9	$[Cu(L^4)_2Cl]Cl$ [1016.5] ($C_{54}H_{38}N_{14}CuCl_2$)	230–232	1.7	63.7 (63.9), 3.7 (3.5), 19.3 (19.7)	71
10	$[Cu(L^5)_2Cl]Cl$ [968.5] ($C_{50}H_{34}N_{12}CuCl_2O_2$)	238–240	1.6	62.0 (62.4), 3.5 (3.7), 17.3 (17.7)	70
11	$[Ni(L^1)_2]Cl_2$ [709.7] ($C_{32}H_{24}N_{10}NiCl_2O_2$)	215–217	3.1	54.1 (54.3), 3.4 (3.7), 19.7 (19.3)	69
12	$[Ni(L^2)_2]Cl_2$ [917.7] ($C_{46}H_{32}N_{10}NiCl_2O_4$)	225–227	3.4	60.2 (59.8), 3.5 (3.2), 15.3 (15.1)	67
13	$[Ni(L^3)_2]Cl_2$ [757.7] ($C_{36}H_{28}N_{12}NiCl_2$)	233–235	3.3	57.0 (57.4), 3.7 (3.5), 22.2 (22.7)	70
14	$[Ni(L^4)_2]Cl_2$ [1011.9] ($C_{54}H_{38}N_{14}NiCl_2$)	217–219	3.2	64.1 (64.3), 3.8 (3.7), 19.4 (19.7)	68
15	$[Ni(L^5)_2]Cl_2$ [963.7] ($C_{50}H_{34}N_{12}NiCl_2O_2$)	225–228	3.3	62.3 (62.0), 3.5 (3.9), 17.4 (17.0)	71
16	$[Zn(L^1)_2]Cl_2$ [716.4] ($C_{32}H_{24}N_{10}ZnCl_2O_2$)	215–217	Dia	53.6 (53.9), 3.4 (3.0), 19.5 (19.3)	67
17	$[Zn(L^2)_2]Cl_2$ [924.4] ($C_{46}H_{32}N_{10}ZnCl_2O_4$)	222–224	Dia	59.7 (59.5), 3.5 (3.8), 15.1 (15.5)	69
18	$[Zn(L^3)_2]Cl_2$ [764.4] ($C_{36}H_{28}N_{12}ZnCl_2$)	230–232	Dia	56.5 (56.2), 3.7 (3.4), 22.0 (22.4)	71
19	$[Zn(L^4)_2]Cl_2$ [1018.4] ($C_{54}H_{38}N_{14}ZnCl_2$)	235–237	Dia	63.6 (63.3), 3.7 (3.6), 19.2 (19.7)	67
20	$[Zn(L^5)_2]Cl_2$ [970.4] ($C_{50}H_{34}N_{12}ZnCl_2O_2$)	238–240	Dia	61.8 (61.5), 3.5 (3.9), 17.3 (17.5)	68

agreement. In the ^{13}C NMR spectra, the ligands and their Zn(II) complexes display signals assigned respectively to heteroaromatic and aromatic carbons. These signals also appear downfield in comparison with the corresponding signals indicating[29] coordination and complexation with the central metal atom. It was observed that DMSO did not have any coordinating effect on either the spectra of the ligands or on their metal complexes.

Electronic Spectra

The Co(II) complexes exhibited well-resolved, low-energy bands at 7,685–7,775 cm^{-1} and 17,440–17,585 cm^{-1} and a strong high-energy band at 20,615–20,785 cm^{-1} (Table III) and are assigned[30] to the transitions $^4T_{1g}(F) \rightarrow {}^4T_{2g}(F)$, $^4T_{1g}(F) \rightarrow {}^4A_{2g}(F)$ and $^4T_{1g}(F) \rightarrow {}^4T_{2g}(P)$ for a high-spin octahedral geometry.[31,32] A high intensity band at 28,565–29,215 cm^{-1} was assigned to the metal to ligand charge transfer. The magnetic susceptibility measurements (3.8–4.2 B.M) for the solid Co (II) complexes are also indicative of three unpaired electrons per Co(II) ion suggesting[33] consistency with their octahedral environment.

The electronic spectra of the Cu(II) complexes (Table III) showed two low-energy weak bands at 15,210–15,325 cm^{-1} and 19,520–19,645 cm^{-1} and a strong high-energy band at 30,255–30,420 cm^{-1}. The low-energy bands in this position typically are expected for a square-planar configuration and may be assigned to $^2B_{1g} \rightarrow {}^2A_{1g}$ and $^2B_{1g} \rightarrow {}^2E_g$ transitions, respectively.[34] The strong high-energy band, in turn, is assigned to metal → ligand charge transfer. Also, the magnetic moment values (1.4–1.8 B.M) (Table IV) for the copper (II) are indicative of anti-ferromagnetic spin–spin interaction through molecular association. Hence, the copper(II) complexes appear to be in the square-planar geometry with $d_x^2 - d_y^2$ ground state.[33]

The electronic spectra of the Ni(II) complexes showed d–d bands in the region 26,465–26,550, 15,715–15,810 and 10,285–10,375 cm^{-1}. These are assigned[34] to the transitions $^3A_{2g}(F) \rightarrow {}^3T_{2g}(F)$, $^3A_{2g}(F) \rightarrow {}^3T_{1g}(F)$ and $^3A_{2g}(F) \rightarrow {}^3T_{2g}(P)$, respectively, consistent with their well-defined octahedral configuration. The band at 29,815–30,335 cm^{-1} was assigned to metal → ligand charge transfer. The magnetic measurements (3.1–3.4 B.M) showed two unpaired electrons per Ni(II) ion suggesting[33] also an octahedral geometry for the Ni (II) complexes. The electronic spectra of the Zn (II) complexes exhibited only a high-intensity band at 28,350–29,145 cm^{-1} and are assigned[32] to a ligand-metal charge transfer.

Biological Activity

The antibacterial and antifungal activity results presented in Tables V and VI, show clearly that all the newly synthesized compounds ($\mathbf{L^1}$–$\mathbf{L^5}$) and their metal complexes (**1–20**) containing Co(II), Cu(II), Ni(II) and Zn(II) possess good biological activity. The new derivatives ($\mathbf{L^1}$–$\mathbf{L^5}$) obtained by condensation of the amino group of triazine with aromatic and heteroaromatic aldehydes and screened for their antibacterial and antifungal effect against *E. coli*, *B. subtillis*, *S. flexenari*, *S. aureus*, *P. aeruginosa* and *S. typhi* and for antifungal activity against *T. longifusus*, *C. albicans*, *A. flavus*, *M. canis*, *F. solani* and *C. glaberata*

TABLE IV Spectral data for the metal chelates **1–20**

No.	IR (cm^{-1})	λ_{max} (cm^{-1})
1	3175 (NH_2), 1610 (CH═N), 1580 (C–O), 1550 (C═N), 425 (M–O), 390 (M–N, azomethine-N), 375 (M–N, triazine)	7,685, 17,440, 20,615, 28,565
2	3325 (OH), 1605 (CH═N), 1580 (C–O), 1555 (C═N), 425 (M–O), 390 (M–N, azomethine-N), 375 (M–N, triazine)	7,775, 17,585, 20,785, 29,215
3	3175 (NH_2), 1605 (CH═N), 1580 (C–O), 1555 (C═N), 390 (M–N, azomethine-N), 375 (M–N, triazine), 355 (M–NH)	7,770, 17,475, 20,645, 28,875
4	1605 (CH═N), 1555 (C═N), 390 (M–N, azomethine-N), 375 (M–N, triazine), 355 (M–NH)	7,690, 17,580, 20,675, 28,890
5	1605 (CH═N), 1580 (C–O), 1550 (C═N), 390 (M–N, azomethine-N), 375 (M–N, triazine), 355 (M–NH)	7,695,17,480, 20,655, 29,110
6	3175 (NH_2), 1610 (CH═N), 1580 (C–O), 1555 (C═N), 425 (M–O), 390 (M–N, azomethine-N), 375 (M–N, triazine), 315 (M–Cl)	15,210 19,645, 30,255
7	3325 (OH), 1605 (CH═N), 1580 (C–O), 1555 (C═N), 425 (M–O), 395 (M–N, azomethine-N), 375 (M–N, triazine), 315 (M–Cl)	15,325, 19,520, 30,420
8	3175 (NH_2), 1605 (CH═N), 1580 (C–O), 1555 (C═N), 390 (M–N, azomethine-N), 375 (M–N, triazine), 355 (M–NH), 315 (M–Cl)	15,270, 19,595, 30,335
9	1605 (CH═N), 1555 (C═N), 390 (M–N, azomethine-N), 370 (M–N, triazine), 355 (M–NH), 315 (M–Cl)	15,310, 19,540, 30,315
10	1605 (CH═N), 1580 (C–O), 1550 (C═N), 390 (M–N, azomethine-N), 375 (M–N, triazine), 355 (M–NH), 315 (M–Cl)	15,220, 19,615, 30,290
11	3175 (NH_2), 1610 (CH═N), 1580 (C–O), 1550 (C═N), 425 (M–O), 390 (M–N, azomethine-N), 375 (M–N, triazine)	10,285, 15,715, 26,465, 30,285
12	3325 (OH), 1605 (CH═N), 1580 (C–O), 1555 (C═N), 425 (M–O), 390 (M–N, azomethine-N), 375 (M–N, triazine)	10,375, 15,810, 26,550, 30,210
13	3175 (NH_2), 1605 (CH═N), 1580 (C–O), 1555 (C═N), 390 (M–N, azomethine-N), 375 (M–N, triazine), 355 (M–NH)	10,290, 15,785, 26,495, 30,915
14	1605 (CH═N), 1555 (C═N), 390 (M–N, azomethine-N), 375 (M–N, triazine), 355 (M–NH)	10,315, 15,755, 26,535, 29,815
15	1605 (CH═N), 1580 (C–O), 1550 (C═N), 390 (M–N, azomethine-N), 375 (M–N, triazine), 355 (M–NH)	10,355, 15,760, 26,515, 30,335
16	3175 (NH_2), 1610 (CH═N), 1580 (C–O), 1550 (C═N), 425 (M–O), 390 (M–N, azomethine-N), 375 (M–N, triazine)	29145
17	3325 (OH), 1605 (CH═N), 1580 (C–O), 1555 (C═N), 425 (M–O), 390 (M–N, azomethine-N), 375 (M–N, triazine)	28,350
18	3175 (NH_2), 1605 (CH═N), 1580 (C–O), 1555 (C═N), 390 (M–N, azomethine-N), 375 (M–N, triazine), 355 (M–NH)	28,775
19	1605 (CH═N), 1555 (C═N), 390 (M–N, azomethine-N), 375 (M–N, triazine), 355 (M–NH)	28,915
20	1605 (CH═N), 1580 (C–O), 1550 (C═N), 390 (M–N, azomethine-N), 375 (M–N, triazine), 355 (M–NH)	28,990

exhibited a marked enhancement of activity on coordination with the metal ions against all the test bacterial/fungal strains. The compounds generally showed moderate antibacterial activity against two or four species and good activity against one or two species. However, they showed greater antifungal activity. It was evident from the data that this activity of the compounds was significantly increased upon coordination. This enhancement in the activity of ($\mathbf{L^1}$–$\mathbf{L^5}$) may be rationalized on the basis that their structures, possess an additional (C═N) bond with an heterocyclic or an aromatic ring. It has been suggested that the ligands with nitrogen and oxygen donor systems might inhibit enzyme production, since the enzymes which require these groups for their activity appear to be especially more susceptible to deactivation by the metal ions upon chelation. Chelation reduces the polarity[35,36] of the metal ion mainly because of the partial sharing of its positive charge with the donor groups and possibly the π-electron delocalization[37–39] within the whole chelate ring system thus formed during coordination. This process of chelation thus increases the lipophilic nature of the central metal atom, which in turn, favors its permeation through the lipoid layer of the membrane.[38,39] It has also been observed that some moieties containing groups such as azomethine or heteroaromatic systems present in the ligands exhibit extensive biological activities. These in turn, are responsible for increasing the hydrophobic character and liposolubility of the molecule in crossing cell membrane of the microorganism and hence enhance the biological utilization ratio and activity of the drug.

TABLE V Antibacterial activity data of compounds $\mathbf{L^1}$–$\mathbf{L^5}$ and **1–20**

Compound	Diameter of zones showing complete inhibition of growth (mm)					
	E. coli	*P. aeruginosa*	*B. subtillis*	*S. flexenari*	*S. aureus*	*S. typhi*
$\mathbf{L^1}$	6	13	7	12	6	8
$\mathbf{L^2}$	8	12	8	11	7	9
$\mathbf{L^3}$	10	13	7	14	8	10
$\mathbf{L^4}$	8	12	8	13	10	8
$\mathbf{L^5}$	12	14	9	15	7	9
1	10	15	10	14	8	10
2	14	17	11	13	10	11
3	12	14	10	16	11	12
4	15	15	12	15	10	13
5	27	13	11	15	9	10
6	14	15	13	14	12	10
7	15	14	12	18	11	11
8	16	14	11	17	10	12
9	15	13	14	15	9	11
10	13	16	15	17	12	10
11	14	13	12	15	12	10
12	16	12	12	15	11	12
13	12	14	11	13	10	13
14	12	17	14	17	13	11
15	13	12	12	18	12	10
16	14	14	14	17	12	11
17	13	13	12	16	11	12
18	12	14	13	17	10	11
19	11	11	15	15	13	11
20	14	14	14	18	12	10
	10					

>14 mm = significant activity; 7–13 mm = moderate activity; <7 mm = weak activity.[21]

TABLE VI Antifungal activity data of the compounds $\mathbf{L^1}$–$\mathbf{L^5}$ and **1–20**

Compound	Diameter of zones showing complete inhibition of growth (mm)					
	T. longifusus	*C. albicans*	*A. flavus*	*M. canis*	*F. solani*	*C. glaberata*
$\mathbf{L^1}$	20	13	20	22	21	18
$\mathbf{L^2}$	21	12	21	20	20	15
$\mathbf{L^3}$	21	13	20	21	18	14
$\mathbf{L^4}$	22	12	21	22	19	13
$\mathbf{L^5}$	23	10	22	20	20	15
1	24	15	25	24	22	20
2	25	13	28	23	23	21
3	26	18	27	23	21	22
4	23	15	27	24	22	20
5	25	16	28	23	25	22
6	24	15	28	24	26	23
7	22	15	27	22	25	24
8	26	14	26	23	27	23
9	27	13	29	24	26	25
10	26	14	27	26	25	22
11	25	13	28	24	24	20
12	27	12	25	24	23	23
13	26	14	27	23	26	24
14	23	18	24	25	23	24
15	26	13	27	25	25	23
16	27	14	26	25	25	25
17	27	13	28	23	23	25
18	28	14	27	24	25	24
19	27	15	28	25	24	26
20	26	14	27	26	26	25

>24–14 mm = significant activity; 7–13 mm = moderate activity; <7 mm = weak activity.[21]

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