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Synthesis, Characterization and Antimicrobial Evaluation of Cobalt(III) Complexes of 4-(2-Substituted Phenylimino)-2-(4-Substituted Phenyl)-4*H*-chromen-3-ol

ASHOK K. SINGH[1,*], SURESH K. PATEL[1] and ASIF JAFRI[2]

[1]Department of Chemistry, University of Lucknow, Lucknow-226007, India
[2]Department of Zoology, University of Lucknow, Lucknow-226007, India

*Corresponding author: E-mail: singhaks3@rediffmail.com

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A series of eight Co(III) complexes $[CoL^{1-8}(H_2O)_2Cl]$ (**I-1** to **I-8**) incorporating 4-(2-substituted phenylimino)-2-(4-substituted phenyl)-4*H*-chromen-3-ol, as a tridentate imino flavone ligands (L_1 to L_8, 2-sub. = NH_2, SH, 4-sub. = OMe, OH, Cl, NMe_2) have been synthesized, characterized and the geometry of the complexes were optimized by DFT. The chemical structure of synthesized imino flavone ligands and their complexes were characterized by elemental analysis, ^{1}H NMR, ^{13}C NMR, UV-visible, IR, ESI-mass spectral data, conductometric and magnetic measurements. The synthesized compounds have been screened for their *in vitro* antibacterial activities against bacteria *Vibrio cholerae*, *Salmonella typhi*, *Staphylococcus aureus*, *Escherichia coli* and antifungal activities against fungi *Candida albicans* and *Aspergillus flavus* by paper disc diffusion method. The complexes **I-3**, **I-4**, **I-7** and **I-8** showed good antimicrobial activities against pathogens.

Keywords: Iminoflavone, Co(III) complexes, Optimized geometry, Antimicrobial activities.

INTRODUCTION

Antibiotics have become revolutionary medicine in the treatment of various pathogenic diseases [1]. But recently intensive use of it, resulted in the emergence of microbial resistance against present antimicrobial agents, which concern with the global health problem of 21st century [2]. Therefore, to design the improved versions of antimicrobial drug with novel mode of action is urgently needed in present and near future. Now a days, in order to synthesizing new antimicrobial drugs, cobalt complexes have highly attracted the researchers as they possess diverse biological activities such as antiviral [3,4], antitumor [5], tumor imaging agent [6], antimycobacterial [7], anti-inflamatory activities [8], *etc*. Cobalt is a trace mineral which is needed by human body in small amount [9]. Vitamin B_{12} (cobalamine) contains a cobalt ion, is necessary for the prevention of pernicious anaemia [10], formation of red blood corpuscles and involved many other functions too [8,11]. Flavones, a naturally occurring heterocyclic compound have possessed versatile biological activity against several diseases [12-14]. The presence of imine group in ligands with potent donor atom *i.e.* O, N, S enhanced the biological activity of parent compound [15,16]. Further, the binding of ligands with metal enhance the lipophilicity, selectivity and activity of parent compound [17-19]. Thus, binding of iminoflavones to a metal ions will enhance its biological and medicinal activities. In order to explore the biological activities of 3-hydroxyflavone, we have synthesized iminoflavone ligands containing imine group and their Co(III) complexes. These ligands and Co(III) complexes (**I-1** to **I-8**) were screened for the antibacterial and antifungal activities by the disc diffusion, micro-dilution broth techniques using streptomycin and fluconazole as positive control. These synthesized complexes showed significant antimicrobial activity against *Vibrio cholerae*, *Salmonella typhi*, *Staphylococcus aureus*, *Escherichia coli* and antifungal against *Candida albicans* and *Aspergillus flavus*.

EXPERIMENTAL

All chemicals used were purchased from Sigma-Aldrich. The solvents used were purified by reported method [20]. Double distilled water has been used whereever necessary. The purity of the compound was monitored by TLC ($CHCl_3$/CH_3OH, 9:1),

using silica gel plate (Merck). Melting points were determined with SSU melting point apparatus. Euro Vector E 3000 Elemental Analyzer was used for elemental analysis. UV-visible spectra were recorded on a double beam UV-Vis near IR Labtronics LT-2900 instrument. IR spectra (KBr discs) were recorded on Agilent Cary 360 FTIR spectrometer. ^{1}H NMR, ^{13}CNMR spectra were recorded on Brucker Advance 400 MHz FT-NMR spectrometer. ESI mass spectrum was recorded on Waters UPLC-TQD mass spectrometer.

***in vitro* Antibacterial and antifungal assay:** The cobalt(III) complexes (**I-1** to **I-8**) have been tested for *in vitro* antimicrobial activity against *Escherichia coli*, *Vibrio cholerae*, *Salmonella typhi*, *Staphylococcus aureus*, *Candida albicans* and *Aspergillus flavus* by paper disc diffusion method [21]. All the selected microorganisms were cultured on sterile petri-discs containing agar medium. The synthesized compounds were dissolved in DMSO and then 5 mm diameter and 1 mm thickness Whatman filter paper disc were soaked in 0.25, 0.5, 1.0 and 2.0 % of tested compounds. The Whatman discs were then subjected to the petri-discs of selected microorganism and incubated at 37 ºC for 36 h. Streptomycin and fluconazole containing discs was used as a positive control for antibacterial and antifungal activities, respectively for the antimicrobial analysis.

Synthesis of imino flavones and their Co(III) complexes: The iminoflavones ligands and their cobalt(III) complexes were synthesized by reported procedure [22,23] with some minor modifications. To a solution of 3-hydroxy-4-substituted flavone derivative (10 mmol) (sub.= 0.268 g (-OCH_3), 0.254 g (-OH), 0.364 g (-Cl), 0.281 g (-$N(CH_3)_2$) in methanol, *o*-phenylenediamine (0.108 g, 10 mmol))/*o*-aminothiophenol (0.125 g, 10 mmol) dissolved in methanol (20 mL) and few drops of glacial acetic acid were added. Then, the mixture was refluxed for 7 h at 70-80 ºC. The resulting solution was cooled to room temperature, and then poured into ice with constant stirring. The product thus obtained was filtered and washed with 10 % ethanol and diethyl ether. The ligand was recrystallized with hot ethanol and dried *in vacuo* over anhydrous $CaCl_2$. Further, the synthesized imino flavones were interacted with $CoCl_2{\cdot}6H_2O$. To the solution of $CoCl_2{\cdot}6H_2O$ (0.714 g, 3 mmol) in 10 mL of methanol, an imino flavone (3 mmol, **L-1** = 1.075 g, **L-2** = 1.033 g, **L-3** = 1.087 g, **L-4** = 1.113g, **L-5** = 1.126 g, **L-6** = 1.084 g, **L-7** = 1.139 g and **L-8** = 1.165 g in methanol) was added. The mixture was stirred magnetically, refluxed for 3 h by adding 3 mmol of sodium acetate and the reaction was monitored by TLC. The volume of reaction mixture was reduced up to 5 mL. On cooling the reaction mixture at room temperature, the precipitate was formed, which was filtered, washed with 10 % ethanol and ether and dried in vacuum over anhydrous $CaCl_2$. The complexes were recrystallized in hot ethanol (**Scheme-I**). The product formed was purified by column chromatography using silica gel. The change in colour of mixture from violet red to brown during the synthesis under aerobic conditions shows the occurrence of oxidation process induced by oxygen in air ($Co^{II} \rightarrow Co^{III}$).

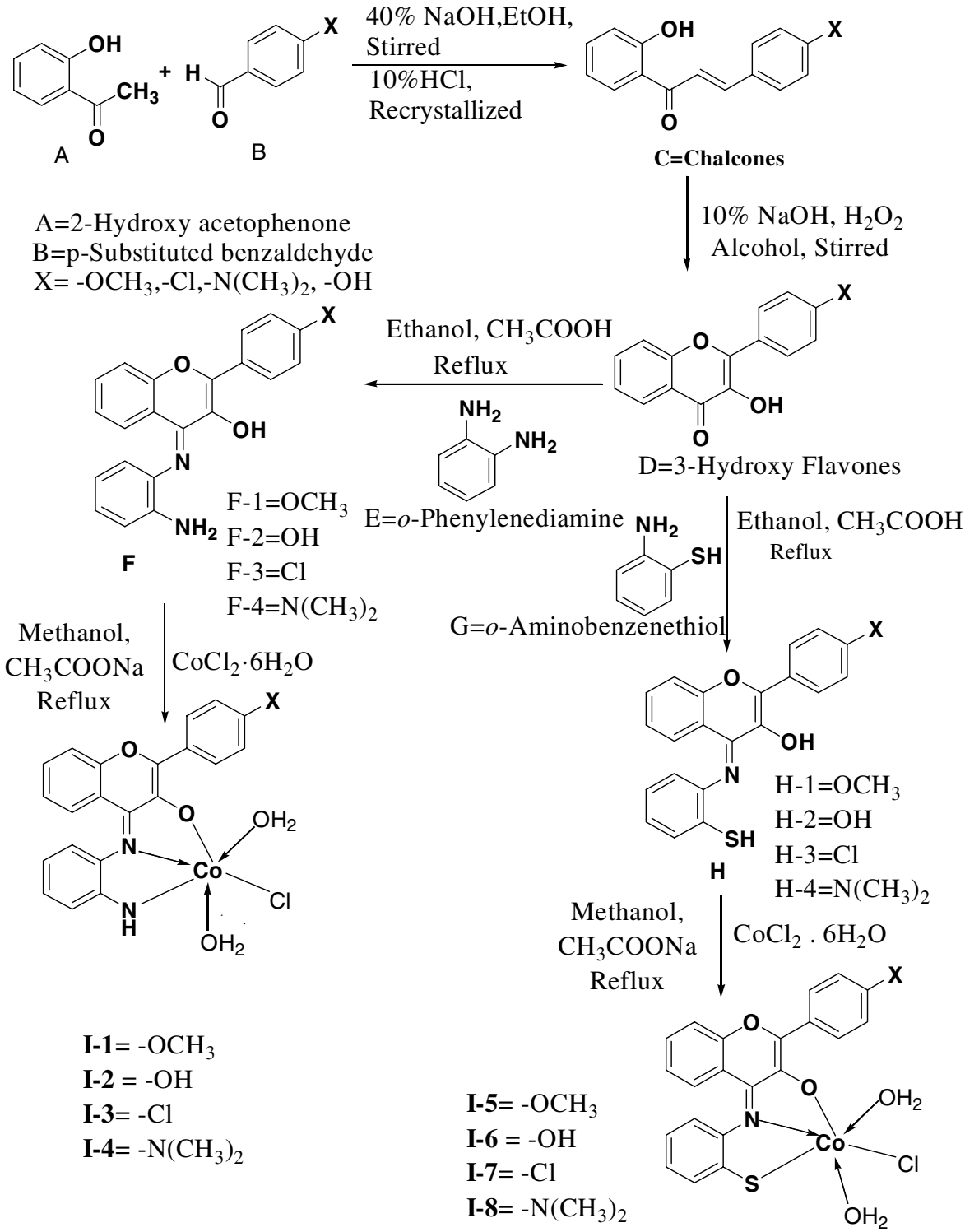
(*E*)-4-((2-Aminophenyl)imino)-2-(4-methoxyphenyl)-4*H*-chromen-3-ol (L^1): Yield: 78 % (0.281 g), colour: brown, m.p.: 113 ºC. IR (KBr, ν_{max}, cm^{-1}): 3513 (OH), 3312 (NH), 2812 (CH), 1609 (C=N), 1582 (C=C), 1236 (C-O); ^{1}H NMR (400 MHz, DMSO-d_6), δ (ppm): 3.47 (3H, s), 4.26 (2H, s), 6.79 (2H, d, *J* = 8.28Hz), 6.69-6.84 (4H, m), 7.02-7.19 (4H, m), 7.75 (2H, d, *J* = 8.68 Hz), 9.56 (1H, s); ^{13}C NMR (100 MHz, DMSO-d_6), δ (ppm): 69.11, 69.11, 114.24, 114.24, 115.32, 116.22, 119.48, 120.58, 120.58, 127.56, 132.99, 132.99, 137.21, 137.21, 137.87, 146.11, 146.11, 150.97, 150.97, 150.97, 152.92; Elemental analysis (%) of $C_{22}H_{18}N_2O_3$ calcd. (found): C, 73.73 (73.75); H, 5.06 (5.12); N, 7.82 (7.85); ESI-MS: $[M+1]^+$ 359.39 (obs.), 358.39 (calcd.). UV-vis.: λ_{max} in nm (in DMSO, 2×10^{-4} M), 256 (π -π* transition), 360 (n-π* transition).

(*E*)-4-((2-Aminophenyl)imino)-2-(4-hydroxyphenyl)-4*H*-chromen-3-ol (L^2): Yield: 62 % (0.22 g), colour: reddish brown, m.p.: 210 ºC. IR (KBr, ν_{max}, cm^{-1}): 3523 (OH), 3308 (NH), 2906 (CH), 1606 (C=N), 1573 (C=C), 1196 (C-O); ^{1}H NMR (400 MHz, DMSO-d_6), δ (ppm): 4.16 (2H, brs), 6.98 (2H, d, *J* = 8.3, Hz), 7.06 (2H, d, *J* = 8.3, Hz), 7.28 (4H, m), 7.19-7.29 (4H, m), 9.11 (2H, s); ^{13}C NMR (100 MHz, DMSO-d_6), δ (ppm): 113.74, 115.10, 115.72, 115.72, 118.65, 120.53, 123.79, 124.24, 124.77, 128.10, 129.27, 131.34, 131.42, 131.43, 136.23, 137.87, 154.36, 155.69, 155.82, 157.84, 159.61. Elemental analysis (%) of $C_{21}H_{16}N_2O_3$ calcd. (found): C, 73.24 (73.76); H, 4.68 (5.02); N, 8.13 (8.85); ESI-MS: $[M+1]^+$ 345.36 (obs.), 344.36 (calcd.). UV-vis.: λ_{max} in nm (in DMSO, 2×10^{-4} M), 271, (π-π* transitions), 343 (n-π* transition).

(*E*)-4-((2-Aminophenyl)imino)-2-(4-chlorophenyl)-4*H*-chromen-3-ol (L^3): Yield: 68 % (0.25 g), colour: brownish black, m.p.: 121 ºC. IR (KBr, ν_{max}, cm^{-1}): 3569 (OH), 3348 (NH), 2869 (CH), 1553 (C=N), 1564 (C=C), 723 (C-Cl); ^{1}H NMR (400 MHz, DMSO-d_6), δ (ppm): 4.03 (2H, s), 7.19 (2H, d, *J* = 8.4 Hz), 7.14 (4H, m), 7.00-7.10 (4H, m), 7.29 (2H, s), 9.62 (1H, brs); ^{13}C NMR (100 MHz, DMSO-d_6), δ (ppm): 113.74, 115.13, 118.66, 120.53, 123.79, 124.24, 124.75, 126.68, 126.70, 128.10, 128.96, 128.97, 129.25, 131.35, 135.65, 136.20, 137.87, 154.36, 155.64, 155.80, 159.59. Elemental analysis (%) of $C_{21}H_{15}N_2O_2Cl$ calcd. (found): C, 69.52 (70.12); H, 4.17 (4.42); N, 7.72 (7.85). ESI-MS: $[M+1]^+$ 363.81 (obs.), 362.81 (calcd.). UV-vis.: λ_{max} in nm (in DMSO, 2×10^{-4} M), 262 (π-π* transitions), 385 (n-π* transition).

(*E*)-4-((2-aminophenyl)imino)-2-(4-(dimethylamino)-phenyl)-4*H*-chromen-3-ol (L^4): Yield: 73 % (0.27 g), colour: brown, m.p.: 135 ºC. IR (KBr, ν_{max}, cm^{-1}): 3469 (OH & NH), 2879 (CH), 1607 (C=N), 1576 (C=C), 1278 (C-O), 1214 (C-N); ^{1}H NMR (400 MHz, DMSO-d_6), δ (ppm): 2.88 (6H, s), 4.69 (2H, s), 6.93 (2H, d, *J* = 7.5 Hz), 6.99-7.17 (4H, m), 7.24 (4H, m), 7.19-7.26 (2H, s), 9.50 (1H, brs); ^{13}C NMR (100 MHz, DMSO-d_6), δ (ppm): 40.31, 40.32, 113.71, 113.83, 113.86, 115.10, 118.63, 120.53, 123.79, 124.24, 124.75, 126.40, 126.41, 129.26, 131.32, 136.24, 137.87, 151.44, 154.36, 155.64, 159.60. Elemental analysis (%) of $C_{23}H_{21}N_3O_2$ calcd. (found): C, 74.37 (75.10); H, 5.70 (5.83); N, 11.31 (11.86); ESI-MS: $[M+1]^+$ 372.43 (obs.), 371.43 (calcd.). UV-vis.: λ_{max} in nm (in DMSO, 2×10^{-4} M), 265 (π-π* transitions), 440 (n-π* transition).

(*E*)-4-((2-Mercaptophenyl)imino)-2-(4-methoxyphenyl)-4*H*-chromen-3-ol (L^5): Yield: 73 % (0.27 g), colour: yellowish brown, m.p.: 121 ºC, IR (KBr, ν_{max}, cm^{-1}): 3530 (OH), 2850 (CH), 1550 (C=N), 1524 (C=C), 2562 (SH), 1247 (C-S), 1220 (C-O); ^{1}H NMR (400 MHz, DMSO-d_6), δ (ppm): 2.92(1H, s, SH), 3.95 (3H, s), 6.89 (2H, d, *J* = 8.0 Hz), 7.07(2H, d *J* = 8.0 Hz), 7.10



Scheme-I: Synthesis of ligands and their cobalt(III) complexes

(4H, m), 7.17 (4H, m), 9.8 (1H, s); ^{13}C NMR (100 MHz, DMSO-d_6), δ (ppm): 55.46, 111.82, 113.72, 118.68, 120.51, 124.79, 127.12, 127.49, 127.70, 128.09, 128.10, 131.72, 131.33, 131.75, 114.44, 114.42, 144.99, 154.35, 155.66, 155.80, 159.60, 160.41. Elemental analysis (%) of $C_{22}H_{17}NO_3S$ calcd. (found): C, 70.38 (70.95); H, 4.56 (4.83); N, 3.73 (3.96); S, 8.54 (8.72). ESI-MS: $[M+1]^+$ 376.44 (obs.), 375.44 (calcd.). UV-vis.: λ_{max} in nm (in DMSO, 2×10^{-4} M), 270 (π-π* transitions), 430 (n-π* transition).

(*E*)-2-(4-Hydroxyphenyl)-4-((2-mercaptophenyl)imino)-4*H*-chromen-3-ol (L^6): Yield: 76 % (0.28 g), colour: brown m.p.: 186 ºC. IR (KBr, ν_{max}, cm^{-1}): 3486 (OH), 2950 (CH), 1565 (C=N), 1530 (C=C), 2580 (SH), 1241 (C-S), 1243 (C-O); ^{1}H NMR (400 MHz, DMSO-d_6), δ (ppm): 2.78 (1H, s, SH), 6.97 (2H, d, J = 8.3 Hz), 7.03 (2H, d, J = 8.3 Hz), 7.11 (4H, m), 7.25 (4H, m), 9.32 (2H, s, OH); ^{13}C NMR (100 MHz, DMSO-d_6), δ (ppm): 111.82, 113.74, 115.74, 115.75, 118.68, 120.55, 124.80, 127.13, 127.48, 127.70, 128.10, 128.10, 131.33, 131.38,

131.39, 144.96, 154.35, 155.67, 155.80, 157.82, 159.60. Elemental analysis (%) of $C_{21}H_{15}NO_3S$ calcd. (found): C, 69.79 (70.95); H, 4.18 (4.63); N, 3.88 (3.96); S, 8.87 (8.98); ESI-MS: $[M+1]^+$ 362.41 (obs.) 361.41 (calcd.). UV-vis.: λ_{max} in nm (in DMSO, 2×10^{-4} M), 268 (π-π* transitions), 365 (n-π* transition).

(*E*)-2-(4-Chlorophenyl)-4-((2-mercaptophenyl)imino)-4*H*-chromen-3-ol (L^7): Yield: 68 % (0.26 g), colour: yellowish brown, m.p.: 132 ºC. IR (KBr, ν_{max}, cm^{-1}): 3433 (OH), 2950 (CH), 1565 (C=N), 1530 (C=C), 2580 (SH), 1239 (C-S), 1243 (C-O); ^{1}H NMR (400 MHz, DMSO-d_6), δ (ppm): 3.00(1H, s, SH), 6.90 (2H, d, *J* = 7.9, Hz), 7.00 (2H, d, *J* = 8.3, Hz), 7.14 (4H, m), 7.26 (4H, m), 9.57 (1H, s, OH); ^{13}C NMR (100 MHz, DMSO-d_6), δ (ppm): 111.82, 113.72, 118.62, 120.51 124.78, 126.71, 126.72, 127.01, 127.49, 127.71, 128.10, 128.10, 128.96, 128.97, 131.34, 135.68, 144.98, 154.36, 155.66, 155.81, 159.60. Elemental analysis (%) of $C_{21}H_{14}NO_2SCl$ calcd. (found): C, 66.40 (66.95); H, 3.71 (3.83); N, 3.69 (3.96); Cl, 9.33 (9.47); S, 8.44 (8.52); ESI-MS: $[M+1]^+$ 380.86 (obs.) 379.86 (calcd.). UV-vis.: λ_{max} in nm (in DMSO, 2×10^{-4} M), 275 (π-π* transitions), 355 (n-π* transition).

(*E*)-2-(4-(Dimethylamino)phenyl)-4-((2-mercaptophenyl)imino)-4*H*-chromen-3-ol (L^8): Yield: 66 % (0.26 g), colour: reddish brown, m.p.: 145 ºC. IR (KBr, ν_{max}, cm^{-1}): 3464 (OH), 2897 (CH), 1593 (C=N), 1578 (C=C), 2571 (SH), 1235 (C-S), 1206 (C-O), 1277 (C-N); ^{1}H NMR (400 MHz, DMSO-d_6), δ (ppm): 2.89 (6H, s), 2.86 (1H, s, SH), 6.61 (2H, d, *J* = 8.8 Hz), 7.04 (2H, d, *J* = 7.5Hz), 7.40-7.56 (4H, m), 7.31 (4H, m), 9.93 (1H, s, OH); ^{13}C NMR (100 MHz, DMSO-d_6), δ (ppm): 40.31, 40.31, 111.78, 118.66, 113.77, 113.84, 113.84, 120.53, 124.75, 126.42, 126.44, 127.11, 127.49, 127.69, 128.09, 128.10, 131.34, 144.99, 151.40, 154.34, 155.68, 155.81, 159.59. Elemental analysis (%) of $C_{23}H_{20}N_2O_2S$ calcd. (found): C, 71.11 (71.75); H, 5.19 (5.63); N, 7.21 (7.77); S, 8.25 (8.68). ESI-MS: $[M+1]^+$ 389.48 (obs.), 388.48 (calcd.). UV-vis.: λ_{max} in nm (in DMSO, 2×10^{-4} M), 273 (π-π* transitions), 347 (n-π* transition).

(*E*)-((4-((2-Aminophenyl)imino)-2-(4-methoxyphenyl)-4*H*-chromen-3-yl)oxy)cobalt dihydrate chloride (I-1): Colour: brown; Yield 73 %, m. p.: > 350 ºC. IR (KBr, ν_{max}, cm^{-1}): 3530 (OH), 3356 (NH), 2859 (CH), 1557 (C=N), 1548 (C=C), 1298 (C-O), 527 (O-Co), 492 (N-Co), 352 (Co-Cl); ^{1}H NMR (DMSO-d_6, 400 MHz, 25 ºC, TMS), δ (ppm): 3.47 (3H, s), 3.78 (2H, s), 7.00-9.80 (m, Ar-H). Elemental analysis (%) of $C_{22}H_{20}N_2O_5ClCo$ calcd. (found): C, 54.28 (54.76); H, 4.14 (4.28); N, 5.75 (5.74); Cl, 7.28 (7.31); Co, 12.11 (12.12). ESI-MS: $[M+1]^+$ 504.82 (obs.), 504.2 (calcd.). UV-vis.: λ_{max} in nm (in DMSO, 2×10^{-4} M), 257 (π-π* transitions), 402 (n-π* transition), 542 (*d-d* transition).

(*E*)-((4-((2-Aminophenyl)imino)-2-(4-hydroxyphenyl)-4*H*-chromen-3-yl)oxy)cobalt dehydrate chloride (I-2): Colour: blackish brown; Yield 65 %, m.p.: > 360 ºC. IR (KBr, ν_{max}, cm^{-1}): 3523 (OH), 3327 (NH), 2837 (CH), 1563 (C=N), 1629 (C=C), 1302 (C-O), 545 (O-Co), 497 (N-Co), 3364 (Co-Cl); ^{1}H NMR (DMSO-d_6, 400 MHz, 25 ºC, TMS), δ (ppm): 3.88 (2H, s), 6.59 (s, 2H), 6.86-8.96 (m, Ar-H). Elemental analysis (%) of $C_{21}H_{18}N_2O_5ClCo$ calcd. (found): C, 53.35 (53.37); H, 3.84 (3.86); N, 5.93 (5.92), Cl, 7.50 (7.49); Co, 12.47 (12.46). ESI-MS: $[M+1]^+$ 473.56 (obs.), 472.76 (calcd.). UV-vis.: λ_{max} in nm (in DMSO, 2×10^{-4} M), 274 (π-π* transitions), 402 (n-π* transition), 575 (*d-d* transition).

(*E*)-((4-((2-Aminophenyl)imino)-2-(4-chlorophenyl)-4*H*-chromen-3-yl)oxy)cobalt dihydrate chloride (I-3): Colour: brown; Yield 68 %, m. p. > 300 ºC. IR (KBr, ν_{max}, cm^{-1}): 3486 (OH), 3308 (NH), 3033 (CH), 1585 (C=N), 1624 (C=C), 1314 (C-O), 538 (O-Co), 499 (N-Co), 367 (Co-Cl); ^{1}H NMR (DMSO-d_6, 400 MHz, 25 ºC, TMS), δ (ppm): 4.08 (2H, s), 7.3 (s, 2H), 7.46-9.23 (m, Ar-H). Elemental analysis (%) of $C_{21}H_{17}N_2O_4Cl_2Co$ calcd. (found): C, 51.35 (51.37); H, 3.49(3.50); N, 5.70 (5.69); Cl, 14.43 (14.43); Co, 12.00 (11.98). ESI-MS: $[M+1]^+$ 491.20 (obs.), 491.21 (calcd.). UV-vis.: λ_{max} in nm (in DMSO, 2×10^{-4} M) 264 (π-π* transitions), 407 (n-π* transition), 527 (*d-d* transition).

(*E*)-((4-((2-Aminophenyl)imino)-2-(4-(dimethylamino)-phenyl)-4*H*-chromen-3-yl)oxy)cobalt dihydrate chloride (I-4): Colour: brown; Yield 58 %, m. p.: > 300 ºC. IR (KBr, ν_{max}, cm^{-1}): 3526 (OH), 3326 (NH), 3021 (CH), 1585 (C=N), 1654 (C=C), 1296 (C-O), 528 (O-Co), 495 (N-Co), 344 (Co-Cl); ^{1}H NMR (DMSO-d_6, 400 MHz, 25 ºC, TMS), δ (ppm): 2.88 (6H, s), 3.96 (2H, s), 7.02 (s, 2H), 7.16-9.86 (m, Ar-H). Elemental analysis (%) of $C_{23}H_{23}N_3O_4ClCo$ calcd. (found): C, 55.27 (55.34); H, 4.64 (4.67); N, 8.41 (8.40), Cl, 7.09 (7.11); Co, 11.79 (11.75). ESI-MS: $[M+1]^+$ 500.64 (obs.), 499.83 (calcd.). UV-vis.: λ_{max} in nm (in DMSO, 2×10^{-4} M), 266 (π-π* transitions), 382 (n-π* transition), 562 (*d-d* transition).

(*E*)-((4-((2-Aminophenyl)imino)-2-(4-(dimethylamino)-phenyl)-4*H*-chromen-3-yl)oxy)cobalt dihydrate chloride (I-5): Colour: yellow brown; Yield 72 %, m.p.: > 360 ºC. IR (KBr, ν_{max}, cm^{-1}): 3545 (OH), 2890 (CH), 1590 (C=N), 1564 (C=C), 1293 (C-S), 1297 (C-O), 527 (O-Co), 498 (N-Co), 356 (Co-Cl), 471(Co-S); ^{1}H NMR (DMSO-d_6, 400 MHz, 25 ºC, TMS), δ (ppm): 3.95 (3H, s), 6.96-8.76 (m, Ar-H). Elemental analysis (%) of $C_{22}H_{19}NO_5SClCo$ calcd. (found): C, 52.44 (52.47); H, 3.80 (3.83); Cl, 7.04 (7.03); N, 2.78 (2.77); S, 6.36 (6.35); Co, 11.70 (11.71). ESI-MS: $[M+1]^+$ 504.32 (obs.), 503.84 (calcd.). UV-vis.: λ_{max} in nm (in DMSO, 2×10^{-4} M), 270 (π-π* transitions), 390 (n-π* transition), 550 (*d-d* transition).

(*E*)-((4-((2-Mercaptophenyl)imino)-2-(4-methoxyphenyl)-4*H*-chromen-3-yl)oxy)cobalt dihydrate chloride (I-6): Colour: reddish brown; Yield 69 %, m.p.: > 320 ºC. IR (KBr, ν_{max}, cm^{-1}): 3547 (OH), 2990 (CH), 1576 (C=N), 1614 (C=C), 1281 (C-S), 1307 (C-O), 537 (O-Co), 502 (N-Co), 362 (Co-Cl), 478 (C-S); ^{1}H NMR (DMSO-d_6, 400 MHz, 25 ºC, TMS), δ (ppm): 9.78 (s, OH), 6.96-8.93 (m, Ar-H). Elemental analysis (%) of $C_{21}H_{17}NO_5SClCo$ calcd. (found): C, 51.49 (51.51); H, 3.50 (3.52); Cl, 7.24 (7.23); N, 2.86 (2.84); S, 6.55 (6.53); Co, 12.03 (12.06); ESI-MS: $[M+1]^+$ 490.58 (obs.), 489.81 (calcd.). UV-vis.: λ_{max} in nm (in DMSO, 2×10^{-4} M), 269 (π-π* transitions), 372 (n-π* transition), 532 (*d-d* transition).

(*E*)-((2-(4-Hydroxyphenyl)-4-((2-mercaptophenyl)-imino)-4*H*-chromen-3-yl)oxy)cobalt dihydrate chloride (I-7): Colour: blackish brown; Yield 66 %, m.p.: > 300 ºC. IR (KBr, ν_{max}, cm^{-1}): 3507 (OH), 2870(CH), 1570 (C=N), 1627 (C=C), 1274 (C-S), 1316 (C-O), 525 (O-Co), 499 (N-Co), 372 (Co-Cl), 486(C-S); ^{1}H NMR (DMSO-d_6, 400 MHz, 25 ºC, TMS), δ (ppm): 6.72-8.82 (m, Ar-H). Elemental analysis (%) of $C_{21}H_{16}NO_4SCl_2Co$

calcd. (found): C, 49.63 (49.65); H, 3.17 (3.19); Cl, 13.95 (13.94); N, 2.76 (2.75); S, 6.31 (6.30); Co, 11.60 (11.62). ESI-MS: $[M+1]^+$ 509.22 (obs.) 508.26 (calcd.). UV-vis.: λ_{max} in nm (in DMSO, 2×10^{-4} M), 277 (π-π* transitions), 390 (n-π* transition), 520 (*d-d* transition)..

(*E*)-((2-(4-Chlorophenyl)-4-((2-mercaptophenyl)-imino)-4*H*-chromen-3-yl)oxy)cobalt dihydrate chloride (I-8): Colour: reddish brown; Yield 71 %, m.p.: > 310 ºC. IR (KBr, ν_{max}, cm^{-1}): 3542 (OH), 2965 (CH), 1562 (C=N), 1579 (C=C), 1263 (C-S), 1309 (C-O), 525 (O-Co), 492 (N-Co), 347 (Co-Cl), 474 (C-S); ^{1}H NMR (DMSO-d_6, 400 MHz, 25 ºC, TMS), δ (ppm): 3.31 (6H, s), 7.52-9.87 (m, Ar-H). Elemental analysis (%) of $C_{23}H_{22}N_2O_4SClCo$ calcd. (found): C, 53.44 (53.47); H, 4.29 (4.30); N, 5.42 (5.41); Cl, 6.86 (6.89); S, 6.20 (6.22), Co, 11.40 (11.38). ESI-MS: $[M+1]^+$ 517.45 (obs.), 516.88 (calcd.). UV-vis.: λ_{max} in nm (in DMSO, 2×10^{-4} M), 274 (π-π* transitions), 397 (n-π* transition), 517 (*d-d* transition).

RESULTS AND DISCUSSION

FT-IR spectra: The band of substituted 3-hydroxyimino -flavone was compared with those of Co(III) complexes in order to infer the coordination mode. The stretching frequency of ligands were observed at 3600-3500 cm^{-1} ν(O-H) phenolic, at 3450-3370 cm^{-1} ν(N-H) (**I-5** to **I-8**), at 1625-1600 cm^{-1} ν(C=N), at 1300-1250 cm^{-1} ν(C-O) phenolic, at 1250-1230 cm^{-1} ν(C-S), at 1225-1175 cm^{-1} ν(C-N) and at 2550-2500 cm^{-1} ν(S-H). In all complexes, ν(C=N) band is shifted to lower frequency, 1605-1580 cm^{-1} indicated the coordination of amino flavones through azomethine N-atom. A strong band observed at 1300-1250 cm^{-1} in the free imino flavones is due to phenolic C-O stretching. In complexes, the C-O stretching vibration appears at higher frequency 1322-1295 cm^{-1} inferred coordination occurred through phenolic O-atom. Moreover, the absorption due to ν(C-S) of the ligands (L^5 to L^8) at 1250-1230 cm^{-1} shifted to 1306-1266 cm^{-1} (**I-5** to **I-8**) and the absorption due to ν(C-N) of the ligands (L^1 to L^4) at 1225-1175 cm^{-1} shifted to 1260-1210 cm^{-1} in the complexes indicates the coordination through phenolic S and N atom. The disappearance of absoption bands due to ν(O-H) and ν(S-H) in the complexes occurred during coordination shows deprotonation of phenolic and thiophenolic protons. The broad band in the region 3450-3220 cm^{-1} and two weaker bands in the region 825-755 cm^{-1} in complexes due to ν(O-H) rocking and wagging mode of vibration respectively, indicated the presence of coordinated water molecule [24]. The new bands appeared in the metal complexes in the region 550-515, 504-488, 372-344 and 486-448 cm^{-1} are attributed to ν(Co-O), ν(Co-N), ν(Co-N) and ν(Co-S), respectively [25]. On the basis of vibrational bands, it is inferred that the ligands are behaving as a dibasic tridentate ligands.

^{1}H NMR spectra: ^{1}H NMR spectra of imino flavone ligands and its Co(III) complexes were recorded in DMSO-d_6 and the chemical shift δ (ppm) are referenced to internal TMS. The protons of imino flavones appeared in the region δ (ppm) 6.90-9.98, δ 3.20-3.80, δ 2.2-2.9, δ 8.90-9.83, δ 3.0-5.0 and δ 2.5-3.5 of aromatic (Ar-H), methoxy (-OCH_3, L^1, H-1 & **I-1**, **I-5**), N-methyl (NCH_3, L^4, H-4 and **I-4**, **I-8**), phenolic (OH), amino (NH, L^1 to L^4, **I-1** to **I-4**) and SH (H-1 to H-4) protons, respectively. The downfield shift of aromatic protons in the complexes from δ 6.90-9.98 to δ 6.25-8.63, shows metal ion coordinated to the ligand. Furthermore, the disappearance of the phenolic and thiophenolic proton in the complexes shows that the deprotonation occurred during complexation. The downfield shift of C-N-H protons from δ 3.0-5.0 to δ 2.6-4.5, indicate coordination of N of amino group with Co(III) metal ions with loss of one proton (**I-1** to **I-4**).

Electronic spectral and magnetic studies: The electronic spectral data of imino flavone and complexes were recorded in 1×10^{-3} M solution of DMSO. Electronic spectra of Co(III) complexes (**I-1** to **I-8**) exhibited three absorption bands in the region 250-280, 380-405 and 505-572 nm due to π -π*, n-π* and *d-d* transitions. The absorption bands of ligands due to π-π* and n-π* transitions shifted at higher wavelength in complexes and a new band observed in region 505-560 nm due to metal to ligand charge transfer (MLCT). This *d-d* bands originate from the $^1A_{1g} \rightarrow {}^1T_{1g}$ transition for the distorted octahedral Co(III) ion in complexes [26]. Thus spectral data confirm the octahedral geometry with low spin d^6 configuration.

Conductometric and magnetic moment measurements: The molar conductivity of Co(III) complexes was measured in DMF by digital TDS-conductivity meter. The molar conductance (in Ω^{-1} mol^{-1} cm^{-2}) of the complexes **I-1** to **I-8** was found 19, 23, 16, 21, 18, 25, 17 and 22, respectively which indicated that all the complexes are non-ionic.

The magnetic measurement of Co(III) complexes (**I-1** to **I-8**) exhibited very low value of magnetic moment, which showed the low spin d_6 octahedral complexes [27]. Thus, Co(III) ions in complexes are in a low spin magnetic state with S = 0 [28].

Optimized geometry of complexes (I-1 to I-8): Quantum chemical calculations were carried out with the Gauss View 5 and Gaussian 09 programs using B3LYP functional with 6-31G (d, p) basis set for carbon, hydrogen, nitrogen, oxygen and chlorine and LanL2DZ basis set for Co. The ground state energy of complexes **I-1** to **I-8** [(4-(2-substituted phenylimino)-2-(4-substituted phenyl)-4*H*-chromen-3-yl)oxy)cobalt dihydrate chloride] are found to be -1653.9461, 1653.9351, 1653.9241, 1653.9456, 1653.9125, 1653.9615, 1653.9561 and 1764.2356 Hartree. All complexes possess C1 symmetry and the optimized structure with numbering of atoms and symbols are presented in Fig. 1.

Antimicrobial analysis: The cobalt complexes [**I-1 to I-8**] have been tested for *in vitro* growth inhibition against *Escherichia coli*, *Vibrio cholerae*, *Salmonella typhi*, *Staphylococcus aureus*, *Candida albicans* and *Aspergillus flavus* by paper disc diffusion method. The complexes **I-3**, **I-4**, **I-7** and **I-8** showed good antibacterial activity against the pathogens (Table-1). Remaining complexes exhibited lesser activity against pathogens in comparison to that of standard drug. The variation in antimicrobial effectiveness of various compounds in different microorganisms mainly depends on the permeability of selected test compounds against microbial cells. Interestingly, the antibacterial activity of metal chelates increasing with concentration increment, because of the metal ion effect on a normal cell. Overtone′s concept and chelation theory explain the activity of metal chelates. In Overtone′s concept of cell permeability, the lipid membrane allows rapid soluble materials, these liposolubility

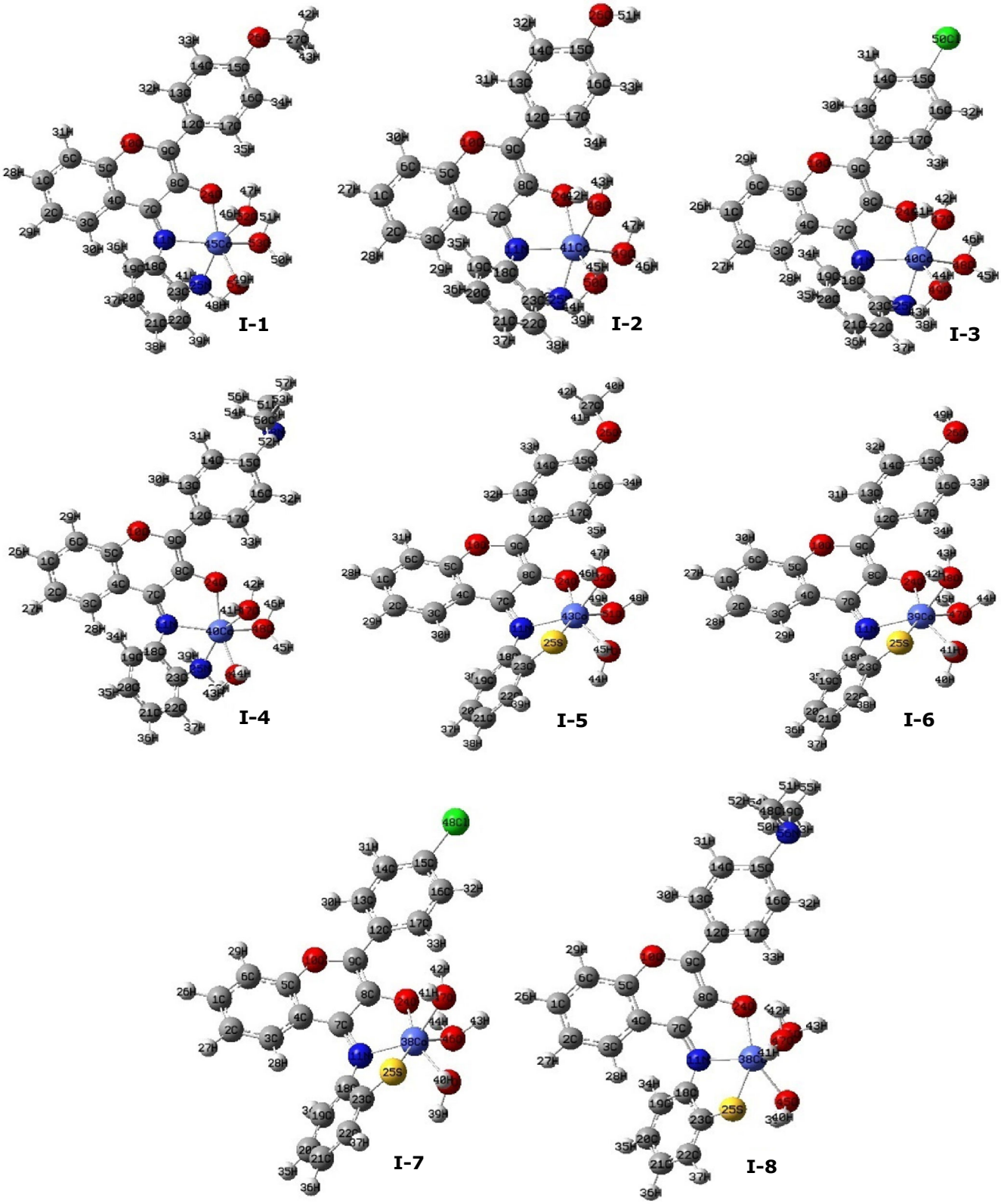


Fig. 1. Optimized geometry of the cobalt(III) complexes

properties mainly control the antimicrobial activity of various test compounds. In chelation theory, the metal ion polarity reduces due to the sharing of ligand orbital and partial delocalization of positive charge of the metal ion with their coordinating groups. In addition to this, metal ion delocalizes the π-electrons over the chelate ring and enhances the lipophilicity by enhancing the penetration power of complexes on the lipid membrane of microorganism.

Conclusion

Tridentate 3-hydroxy-4-substituted iminoflavone ligands (**L1-L4**), H(H1-H4) and their Co(III) complexes (**I1-I8**) were

TABLE-1
ANTIBACTERIAL AND ANTIFUNGAL EVALUATION OF Co COMPLEXES OF (4-((2-SUBSITUTED PHENYL)IMINO)-2-(4-SUBSITUTEDYPHENYL)-4*H*-CHROMEN-3-YL)OXY)COBALT TRIHYDRATE

Cobalt complexes	Diameter of inhibition zone (mm)					
	V. cholerae 0.25 %	*S. typhi* 0.5 %	*S. aureus* 1.0 %	*E. coli* 2.0 %	*C. albicans* 2.0 %	*A. flavus* 1.0 %
I-1	7	9	10	10	7	9
I-2	8	10	11	11	8	10
I-3	12	14	19	17	14	18
I-4	16	19	18	21	16	17
I-5	8	8	9	11	05	03
I-6	9	10	11	12	04	06
I-7	12	13	16	15	13	15
I-8	15	16	13	16	17	18
Streptomycin	18	20	22	24	–	–
Fluconazole	–	–	–	–	20	23

synthesized and characterized by spectroscopic methods and physical measurements. The spectral data and physical measurements showed all the Co(III) complexes are neutral having octahedral geometry of low spin d^6 configuration. The optimized structures of complexes (**I-1–I-8**) have been studied by Gaussian 09 program. The Co(III) complexes (**I-1–I-8**) were screened for the antibacterial and antifungal activities by the disc diffusion, microdilution broth techniques. The antimicrobial activities of Co(III) complexes exhibited better antimicrobial properties and showed enhanced inhibitory activities as compared to the standard drugs.

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CONFLICT OF INTEREST

The authors declare that there is no conflict of interests regarding the publication of this article.

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