Indian Journal of Chemistry
Vol. 65, March 2026, pp. 189-196
DOI: 10.56042/ijc.v65i3.11520

# Thermal and biological appraisal on Cu(II) based complexes using Ciprofloxacin with bromo-dicumarol derivative

Nikita Prajapati[a], Poonam Gautam*[a], Shalini Chaturvedi[b], Deepika Gautam[b] & Nitya Chawda[a]

[a] Department of Chemistry, Silver Oak Institute of Science, Silver Oak University, Ahmedabad 382 481, Gujarat, India

[b] Department of Chemistry, Shri R K Parikh Arts and Science College Petlad, Anand 388 450, Gujarat, India

E-mail: pmgautam83@gmail.com

*Received 30 May 2024; accepted (revised) 28 April 2025*

A series of novel Cu (II) complexes have been produced using the conventional thermal method. The biologically active ligands (L) are created by refluxing a dicumarol derivative with aldehydes in ethanol. The Cu (II) compounds have been synthesized by mixing an aqueous solution of the metal in a 1:1 molar ratio with ethanolic ligands and modified ciprofloxacin. The structures of the ligands and their copper complexes have been analyzed and confirmed through elemental analysis, FT-IR, $^{1}H$ and $^{13}C$ NMR, and mass spectrometry. The thermal properties of the newly synthesized mixed-phase Cu (II) complexes have been investigated using thermo-gravimetric analysis. Both the ligands and their complexes have been screened for their *in vitro* inhibition, anti-tubercular, and antimicrobial activities, which show significantly higher potency compared to the parent ligands used for complexation.

**Keywords**: Biological aspect, Thermal study, Ciprofloxacin, Metal complexes

Coumarins exhibit a wide range of forms due to the various substitutions possible in their basic structure, which significantly impact their biological activity[1-4]. Interest in coumarin chemistry has surged over the years, largely due to the widespread use of coumarin derivatives. Many structurally novel coumarin derivatives have been reported to exhibit significant cytotoxic and anti-HIV activity both *in vitro* and *in vivo*[2]. Coumarin derivatives are known to have diverse applications such as anti-HIV[5-8], anti-inflammatory[9-12], anthelminthic[13,14], antioxidant[15-17], anticoagulant, antitumor agents, or even as plant growth regulators[18-20]. Their ability to form complexes with various metal ions has been extensively studied and discussed in numerous investigations[21-24].

It has been discovered that the addition of a metal to the coumarin moiety can enhance or even augment its biological activity[25-27]. In recent years, metal ions such as copper (II), iron (II), iron (III), or platinum (II) have exhibited broad biological activity, including activity against tumor cells. Similarly, chromones, flavonoids, and coumarins are renowned for their similar properties. Based on these findings, complexes formed by these metals and ligands are expected to be more potent than the parent compounds alone. Some of these complexes have shown biological activity comparable to widely used carboplatin[28-32]. In addition to their medicinal, biological, and therapeutic applications, coumarins are utilized as sweeteners, perfume fixatives, additives in food and cosmetics, odor stabilizers in tobacco, and odor-masking agents in paints and rubber[33]. Ciprofloxacin is an antibiotic effective in treating various bacterial infections. When administered orally or intravenously, it can address conditions such as pneumonia, cellulitis, urinary tract infections, anthrax, plague, and certain types of infectious diarrhea. Its applications also extend to treating multidrug-resistant tuberculosis, often in combination with other medications. Additionally, ciprofloxacin can be used as eye drops for superficial bacterial eye infections and as ear drops for otitis when there's a perforation in the eardrum.

Quinolones, also known as quinolone-carboxylic acids or 4-quinolones, are a group of synthetic antimicrobial agents that function by effectively inhibiting DNA replication. They are commonly utilized in the treatment of various infections[34]. Ciprofloxacin stands out as one of the most frequently prescribed fluorinated quinolone antibiotics globally[35]. It exhibits broad-spectrum activity against a wide range of bacteria, including gram-positive and gram-negative aerobic bacteria, facultative anaerobic bacteria, chlamydia, as well as

some related organisms like mycoplasmas or mycobacteria[36]. Additionally, Schiff bases play a significant role in bioinorganic chemistry due to their remarkable biological activity. The acid hydrazides R–CO–NH–$NH_2$, a class of Schiff base, along with their corresponding aroyl hydrazones, R–CO–NH–N=CH–R and the manner in which they chelate with metal ions present in living systems are subjects of considerable interest[37].

The objective of this study was to synthesize mixed-substance complexes of Cu (II) using ofloxacin with anticoagulant derivatives and to investigate their properties. In this work, we detail the synthesis, characterization, thermal behavior, biological activity, and spectroscopic features of the newly synthesized mixed-substance Cu (II) and Cu (II) complexes.

## Experimental Section

### Materials

All chemical agents were of analytical reagent (AR) grade and were commercially sourced from Spectrochem Ltd., Mumbai, India, and used without further purification. Solvents employed were distilled, purified, and dried using standard procedures prior to usage[38]. The antimycotic agent was purchased from the Agro Chemical Division of Atul Limited, Valsad, Gujarat. The metal nitrates utilized were in an anhydrous form.

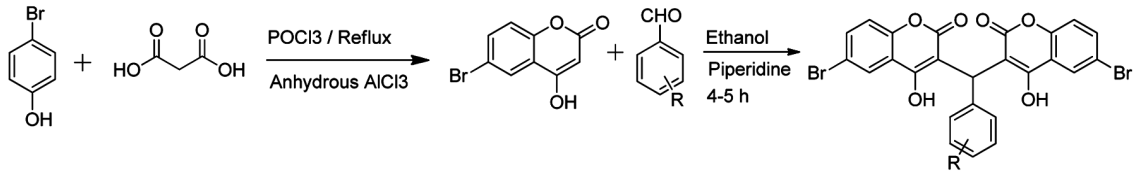
## Physical measurements

All reactions were monitored by thin-layer chromatography (TLC) using aluminum plates coated with silica gel 60 F254 (0.25 mm thickness, E. Merck, Mumbai, India), and the components were visualized under ultraviolet (UV) light or iodine vapor. Carbon, hydrogen, and nitrogen content was determined using an elemental analyzer (PerkinElmer, USA 2400-II C, H, N analyzer). Metal ion analyses were conducted by dissolving the solid complexes in concentrated hot acid, diluting with water, and filtering to remove precipitated organic ligands (Scheme 1). The remaining solution was neutralized with ammonia solution, and the metal ions were titrated against EDTA. $^1$H and $^{13}$C NMR measurements were performed on an Advance-II 400 Bruker NMR spectroscope at SAIF, Chandigarh. Chemical shifts were referenced to tetra methyl silane (TMS) used as an internal standard, and DMSO was used as the solvent. Infrared spectra of solids were recorded in the 4000-400 $cm^{-1}$ region using a Nicolet Impact 400D Fourier-Transform Infrared spectrometer with KBr pellets. The freezing points of the ligands and metal complexes were measured using the open tube method.

**3,3'-((3-Hydroxyphenyl)methylene)bis(6-bromo-4-hydroxy-2*H*-chromen-2-one), $L^1$**: Yield 70%. m.p.217°C. FT-IR (KBr): (-OH/$H_2O$) 3137, 3055, (C=O) 1664,1657 (C=C) 1625, 1576, (C-O) 1153, 1126, 1092, 815, 797, 774 $cm^{-1}$; $^1$H NMR (DMSO-$d_6$ 400 MHz): δ 6.35 (1H, Aliphatic), 6.97-7.74 (12H, m, Aromatic proton), 9.37, 10.34 (-OH phenolic); $^{13}$C NMR (DMSO-$d_6$ 100 MHz): δ 36.5 (C-9), 101.4 (C-3, 18), 113.7, 114.5, 116.3, 116.8, 120.3, 123.4 125.6, 128.8, 130.4, 142.2 (10C, Ar-C), 152.3(C-8a, 23a), 157.3(C-12, carbon attach to phenolic OH) 161.4(C-2, 17), 164.5(C-4, 19); ESI-MS: *m/z* 471.01(M +H)$^+$. Anal. Found (%): C, 60.09; H, 2.76. Calcd for $C_{25}H_{16}Br_2O_7$ (470.28): C, 60.38; H, 2.84%.

**3,3'-((3-Chlorophenyl)methylene)bis(6-bromo-4-hydroxy-2*H*-chromen-2-one), $L^2$**: Yield 70%. m.p.260°C. FT-IR (KBr): (-OH/$H^2O$) 3192, 3055, (C=O) 1664,1656, (C=C) 1648, 1557, (C-O) 1205, 1125, 1083, 817, 784, 744 $cm^{-1}$; 1H NMR (DMSO-$d_6$ 400 MHz): δ 6.44 ($^1$H, Aliphatic), 7.19-8.78 (12H, m, Aromatic proton), 10.43 (-OH phenolic); $^{13}$C NMR (DMSO-$d_6$ 100 MHz): δ 36.3 (C-9), 102.2 (C-3, 18), 116.4, 116.8, 123.5, 125.6, 125.7, 125.8, 128.4, 128.7, 131.3, 134.6, 144.7 (11C, Ar-C), 151.7(C-8a, 23a), 163.5(C-2, 17), 165.4(C-4, 19); ESI-MS: *m/z* 489.98(M +H)$^+$. Anal. Found (%): C, 67.20; H, 3.38. Calcd for $C_{25}H_{15}Br_2O_6$ (488.73): C, 58.22; H, 2.54%.

**3,3'-((3-Phenylmethylene)bis(6-bromo-4-hydroxy-2*H*-chromen-2-one), $L^3$**: Yield 67%. m.p. 225°C. FT-IR (KBr): (-OH/$H_2O$) 3183, 3053, (C=O) 1660,1653, (C=C) 1646, 1564, (C-O) 1177, 1122,




**Where R** = *p*-OH ($L^1$); *m*-Cl ($L^2$); *H* ($L^3$); *m*-$NO_2$ ($L^4$); *p*-$CH_3$ ($L^5$);

Scheme 1 — General procedure for the preparation of Coumarine chalcone (L)

1086, 822, 794, 749 $cm^{-1}$; $^1H$ NMR (DMSO-$d_6$ 400 MHz): δ 6.53 ($^1H$, Aliphatic), 7.11-7.94 (13H, m, Aromatic proton), 10.36 (-OH phenolic); $^{13}C$ NMR (DMSO-$d_6$ 100 MHz): δ 36.6 (C-9), 103.5 (C-3, 18), 116.3, 117.4, 123.5 125.4, 125.3, 127.73, 128.2, 128.3, 143.5(9C, Ar-C), 152.5(C-8a, 23a), 164.6(C-2, 17), 167.4(C-4, 19); ESI-MS: *m/z* 455.02$(M+H)^+$. Anal. Found (%): C, 62.28; H, 2.81. Calcd for $C_{25}H_{14}Br_2O_6$ (454.28): C, 62.39; H, 2.93%.

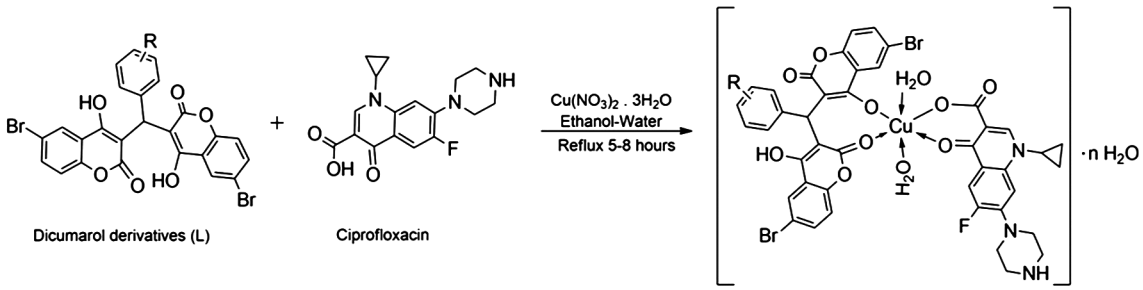
**3,3'-((3-Nitrophenyl)methylene)bis(6-bromo-4-hydroxy-2*H*-chromen-2-one), L[4]**: Yield 69%. m.p.287°C. FT-IR (KBr): (m,-OH/$H_2O$) 3159, 3034, (C=O) 1666,1653 (C=C) 1625, 1574, (C-O) 1161, 1125, 1078, 813, 781, 748 $cm^{-1}$; $^1H$ NMR (DMSO-$d_6$ 400 MHz): δ 6.41 (1H, Aliphatic), 7.19-8.25 (12H, m, Aromatic proton), 10.84 (-OH phenolic); $^{13}C$ NMR (DMSO-$d_6$ 100 MHz): δ 35.2 (C-9), 100.7 (C-3, 18), 115.9, 116.6, 119.6, 120.24, 121.6 122.5 124.52, 127.4, 133.3, 144.7, 148.2 (11C, Ar-C), 151.4(C-8a, 23a), 162.6(C-2, 17), 165.6(C-4, 19); ESI-MS: *m/z* 500.00. Anal. Found (%): C, 57.65; H, 23.31; N, 2.06. Calcd for $C_{25}H_{13}Br_2NO_8$ (499.28): C, 57.05; H, 2.49; N, 2.66%.

**3,3'-(3-Tolylmethylene)bis(6-bromo-4-hydroxy-2*H*-chromen-2-one), L[5]**: Yield 62%, m.p.270°C. FT-IR (KBr): (-OH/$H_2O$) 3151, 3035, (C-OH) 1344, 1332, (C=O) 1665, 1651, (C=C) 1625, 1573, (C-O) 1162, 1124, 1074, 812, 785, 744 $cm^{-1}$; $^1H$ NMR (DMSO-$d_6$ 400 MHz): δ 2.33 (3H, s, -$CH_3$), 6.52 (1H, Aliphatic), 7.11-7.90 (10H, m, Aromatic proton), 10.84 (-OH phenolic); $^{13}C$ NMR (DMSO-$d_6$ 100 MHz): δ 22.3 (-$CH_3$), 37.4 (C-9), 102.2 (C-3, 18), 116.3, 117.2, 124.3 126.25, 128.10, 128.8, 128.7, 136.4, 142.6 (9C, Ar-C), 152.3(C-8a, 23a), 162.8(C-2, 17), 165.8(C-4, 19); ESI-MS: *m/z* 463.03(M+H. Anal. Found (%): C, 67.43; H, 3.45. Calcd for $C_{26}H_{16}Br_2O_6$ (462.40): C, 67.53; H, 3.49%.

Data of all ligands are shown in Supplementary Information Figure S1 to S4.

**Synthesis of metal complexes**: **[M(L)(CF)$(H_2O)_2$](C)**

A solution of $Cu(NO_3)_2$•$3H_2O$ salt (10 mmol) was added to an ethanolic solution of ligand (L) (10 mmol), followed by the addition of an ethanolic solution of Ciprofloxacin (10 mmol) with continuous stirring. The *p*H was adjusted to 4.5-6.0 by adding diluted $NH_4OH$ solution. The resulting solution was refluxed for 5 hours and then heated on a steam bath to evaporate up to half of the volume. The reaction mixture was left overnight at RT. A fine colored crystalline product was obtained, which was washed with ether and dried in vacuum desiccators (Scheme 2). Complexes $C^2$- $C^5$were prepared using the same method, and their chemical parameters are summarized in Table 1. The artificial protocol of complexes is shown in theme a pair, while the FT-IR spectrum of $C^4$ is presented in Fig. 1.




Scheme 2 — General scheme for metal complexes

Table 1 — Analytical and physical parameters of complexes

| Compd | Elemental analysis Found % (Reqd.) | | | | m.p. (°C) | Yield (%) | Mol. Wt. | μeff/ B.M. |
|---|---|---|---|---|---|---|---|---|
| | C | H | N | Cu(II) | | | | |
| $C^1$ | 56.55(56.65) | 4.31(4.42) | 4.50(4.58) | 6.28(6.41) | >350 | 71 | 934.39 | 1.82 |
| $C^2$ | 56.46(56.66) | 4.13(4.29) | 4.41(4.56) | 6.16(6.28) | >350 | 71 | 952.93 | 1.84 |
| $C^3$ | 57.54(57.63) | 4.39(4.50) | 4.65(4.81) | 4.57(4.69) | >300 | 69 | 918.49 | 1.83 |
| $C^4$ | 54.85(54.96) | 4.08(4.28) | 5.82(5.92) | 6.09(6.18) | >350 | 72 | 963.49 | 1.88 |
| C5 | 57.96(58.04) | 4.54(4.69) | 4.51(4.62) | 6.29(6.37) | >350 | 66 | 932.52 | 1.85 |

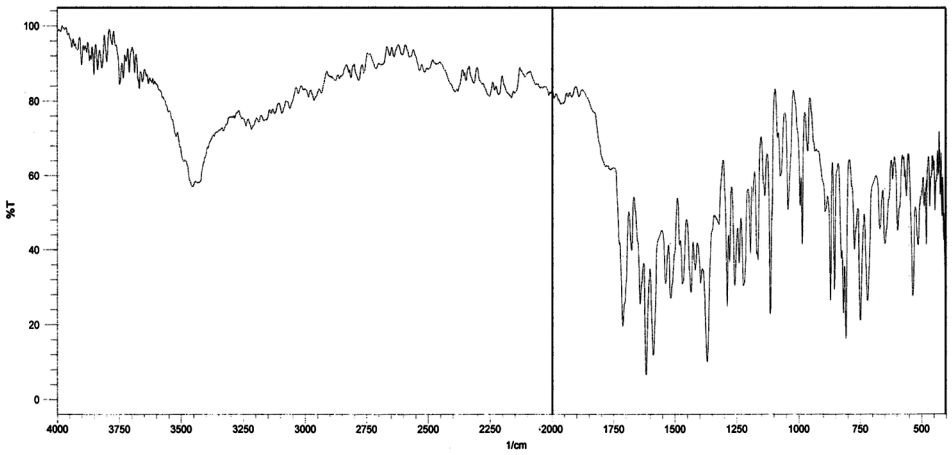



Fig. 1 — FT-IR Spectrum of $C^4$

**Antimicrobial activity**

All the ATCC culture was collected from Institute of microorganism technology, Bangalore. 2 Luria broth resolution was ready in water whereas, hydrogen ion concentration was adjusted to 7°C at temperature and sterilized by autoclaving at 15pound pressure for two min. The tested microorganism associate in nursing plant life strains were ready within the Luria broth and incubated at 37°C and 200 revolutions per minute in an orbital setup for long. Sample solutions were ready in DMSO for concentration of 200, 150, 100, 50, 25, 12 and 6µg/mL. Serial broth small dilution was adopted as a reference methodology. 10 resolution of check compound was inoculated in 5 mL Luria broth for every concentration severally and in addition one check tubes was unbroken as management. Each of the check tubes was inoculated with a suspension of normal being to be tested and incubated at 35°C for 24 h. At the period of time, the tubes were examined for the muddiness. Muddiness within the check tubes indicated that being growth has not reserved by the antibiotic contained within the medium at the check concentration. The antimicrobial action tests were run 3 times.

**Antioxidant studies**

Ferric reducing inhibitor power (FRAP) confirm victimization associate custom-made methodology[39]. The inhibitor potentials of the compounds were examined by their reducing power of the TPTZ-Fe(III) advanced to TPTZ-Fe(II) advanced for the full inhibitor capability of tested samples. This methodology was utilized because it is straightforward, quick, and yields reproducible results. Initially, the following solutions were prepared, A) acetate buffer, 300 mL *p*H 3.6 (3.1g atomic number 11 acetate trihydrate and 16 mL conc. ethanoic acid per L of buffer solution), B) 10 mM 2,4,6-tripyridyl-s-triazine in 40 mL HCl, C) 20 mL $FeCl_3 \bullet 6H_2O$ in water 1mM of antioxidant dissolved in 100 mL water. The FRAP working solution was prepared by mixing solutions (A), (B), and (C) in a ratio of 10:1:1, respectively. A mixture of 40.0 µL of 0.5 mM sample solution and 1.2 mL of FRAP reagent was incubated at 37°C for 15 minutes. It was essential to use the working solution immediately after preparation. Ascorbic acid was used as the standard antioxidant compound, and the results were expressed in comparison to it.

**Results and Discussion**

The synthesized Cu(II) complexes were characterized by elemental analysis and FTIR spectroscopy. The copper ion content in the complexes was determined after mineralization. The metal content for biochemical studies was estimated complexometrically[40]. The geometry of the complexes was elucidated using thermogravimetric analysis, electronic spectroscopy, and magnetic susceptibility measurements.

**Elemental analysis**

The analytical and physicochemical data of the complexes are presented in Table 1. The experimental results showed very good agreement with the calculated values. The complexes were colored, insoluble in water and most common organic solvents, but soluble in DMSO, and stable in air. The proposed structures of the complexes are based on the biochemical analysis summarized in Table 1.

**FT-IR spectra**

The coordination sites of ligand are elucidated using IR. The IR band assignments of dicoumarol derivatives and its complexes are included in Table 2. The IR data of free ligands and its metal complexes were carried out within the IR range 4000-400 $cm^{-1}$. The IR spectra of the dicoumarol derivatives show weak bands at ~3125-3055 $cm^{-1}$ and ~1323-335 $cm^{-1}$, corresponding to (O–H) and (C–OH) respectively. On complexation, O–H peak has nowhere to be found, indicating the deprotonation of O–H proton. The (C=O) of lactone rings observed at ~1645 and 1657 $cm^{-1}$ in free ligand is shifted to lower frequencies (~12-14 $cm^{-1}$ and 40-50 $cm^{-1}$) due to complex formation, and further supported by shifting of (C–C), (C–O), and (C–O–C) stretch frequencies to higher values. Two bands at ~1615 and ~1563 $cm^{-1}$ were assigned to stretching vibration of conjugate double bonding in the free ligand. The H–O–H bending mode occurring about ~1605 $cm^{-1}$ has not been observed because of the presence of strong absorbing group like methine group (–CH=). It is difficult to resolve both these bands. A broad band at ~3425-3454 $cm^{-1}$ observed in the complex was due to the (O–H) characteristic peak of a coordinated water molecule. The bands at ~1745 $cm^{-1}$ and ~1256 $cm^{-1}$ attributed to the stretching vibrations $(C=O)_{carboxylic}$ and $(C-O)_{carboxylic}$ respectively, of the carboxylic moiety (–COOH) of Ciprofloxacin, have been shifted in the range ~1583-1605 $cm^{-1}$ and ~1365-1395 $cm^{-1}$ assigned as antisymmetric, $(C=O)_{asym}$, and symmetric, $(C=O)_{sym}$, stretching vibrations of the carboxylato group, respectively. The difference $\Delta=[(C=O)_{asym} - (C=O)_{sym}]$, a useful characteristic tool for determining the coordination mode of the carboxylato ligands, reaches a value of ~203–232 $cm^{-1}$ indicative of a monodentate coordination mode. Whereas (C=O)p is shifted from ~1622–1653 $cm^{-1}$ upon bonding. The overall changes of the IR spectrum suggest that Ciprofloxacin and ligands are coordinated to the Cu(II) *via* the ketone oxygen and carboxylato oxygen. These changes in the IR spectra suggest that Ciprofloxacin is coordinated to metal *via* pyridone and one carboxylate oxygen atoms. These data are further supported by (Cu–O) which appear at ~522 $cm^{-1}$ (Fig. 1).

**Thermal studies of synthesized complexes**

Thermal data and kinetic parameters of the complexes are given in Table 3 and Table 4, respectively. The typical TG curves of the complexes $[Cu(L^2)(CF)(H_2O)_2]\bullet H_2O$ are characterized in Fig. 2. The anhydrous complexes show enormous thermal stability up to 250°C. Next two steps were occurring exothermic and endothermic related with removal of coordinated ligand (coumarins) as well as Ciprofloxacin, respectively. In the third subsequent stage, the decomposition and combustion of ligand (loss 48.75%) occurs at 260-430°C. Where in fourth subsequent stage for complex show the decomposition and combustion of Ciprofloxacin (loss 44.34%) occurring at 500-780°C. The removal of Ciprofloxacin undergoes decomposition forming CuO as the final residue. The thermodynamic activation parameters of the decomposition process of dehydrated complexes, such as activation entropy ($\Delta S$), pre-exponential factor ($A$), activation enthalpy ($\Delta H$) and free energy of activation ($\Delta G$), were calculated using the reported equations[41] and are tabulated in Table 4. All the complexes have negative entropy, which indicates that the studied complexes have more ordered systems than reactants[42]. The kinetic parameters, mainly energy of activation ($E_a$) was useful in conveying the strength of the bonding of ligand moieties with the metal ion. The calculated $E_a$ values of the investigated complexes for the

Table 2 — FT-IR data of synthesized compounds

| Sample No. | υ(O-H) $cm^{-1}$ (br) | υ(C=O) $cm^{-1}$ | υ(C=C) $cm^{-1}$ | υ(C-C), υ(C-O), υ(C-O-C) $cm^{-1}$ | υ(C=O) of pyridine $cm^{-1}$ | $\upsilon(COO)_s$ $cm^{-1}$ | $\upsilon(COO)_a$ $cm^{-1}$ | Δ | υ(Cu-O) $cm^{-1}$ (w) |
|---|---|---|---|---|---|---|---|---|---|
| $C^1$ | 3433 | 1636, 1603 | 1583 | 1182.1143,1124, 854,725 | 1632 | 1364 | 1575 | 212 | 562 |
| $C^2$ | 3435 | 1654, 1604 | 1592 | 1191,1154,1126, 836,754 | 1622 | 1364 | 1575 | 215 | 566 |
| $C^3$ | 3433 | 1654, 1613 | 1584 | 1193.1147,1123, 856,752 | 1634 | 1362 | 1586 | 214 | 565 |
| $C^4$ | 3422 | 1656, 1613 | 1584 | 1196,1136,1132, 833,756 | 1624 | 1362 | 1572 | 204 | 567 |
| $C^5$ | 3444 | 1655, 1613 | 1585 | 1189,1135,1127, 837,750 | 1621 | 1374 | 1574 | 215 | 565 |

Table 3 — Thermoanalytical results (TG and DTG) of metal complexes

| Complexes | TG range/°C | $DTG_{max}$/°C | Mass loss Obsd. % (Calcd) | Assignment |
|---|---|---|---|---|
| $C^1$ | 70-380 | 235 | 53.34(53.76) | Loss of Two $H_2O$ molecules |
| | | 343 | | Removal of $L^1$ ligand |
| | 380-800 | 552 | 37.25 | Removal of Ciprofloxacin ligand |
| | | >650 | 8.19 | Leaving CuO residue |
| $C^2$ | 70-370 | 83 | | Loss of one lattice water molecules |
| | | 219 | 48.75(48.92) | Loss of two $H_2O$ molecules |
| | | 305 | | Removal of $L^2$ ligand |
| | 380-800 | 540 | 44.34 | Removal of Ciprofloxacin ligand |
| | | >650 | 5.45 | Leaving CuO residue |
| $C^3$ | 80-380 | 95 | | Loss of one lattice water molecules |
| | | 245 | 54.35(54.62) | Loss of two $H_2O$ molecules |
| | | 354 | | Removal of $L^3$ ligand |
| | 380-800 | 562 | 38.16 | Removal of Ciprofloxacin ligand |
| | | >650 | 7.33 | Leaving CuO residue |
| $C^4$ | 80-375 | 98 | | Loss of one lattice water molecules |
| | | 232 | 54.28(54.46) | Loss of two $H_2O$ molecules |
| | | 354 | | Removal of $L^4$ ligand |
| | 375-800 | 568 | 38.30 | Removal of Ciprofloxacin ligand |
| | | >650 | 7.30 | Leaving CuO residue |
| $C^5$ | 70-370 | 93 | | Loss of one lattice water molecules |
| | | 247 | 53.15(53.49) | Loss of two $H_2O$ molecules |
| | | 355 | | Removal of $L^5$ ligand |
| | 370-800 | 545 | 39.11 | Removal of Ciprofloxacin ligand |
| | | >650 | 7.49 | Leaving CuO residue |

Table 4 — Thermodynamic data of the thermal decomposition of metal complexes

| Compd | TG range/°C | $E_a$/kJ mol$^{-1}$ | N | $A$/s$^{-1}$ | S*/J K$^{-1}$ mol$^{-1}$ | H*/kJ mol$^{-1}$ | G*/kJ mol$^{-1}$ |
|---|---|---|---|---|---|---|---|
| $C^1$ | 60-380 | 3.37 | 0.99 | 0.142 | -104.45 | 0.588 | 32.12 |
| | 380-800 | 8.0 | 1.31 | 0.059 | -101.14 | 0.020 | 44.37 |
| $C^2$ | 70-380 | 3.20 | 1.15 | 0.102 | -103.23 | 0.226 | 37.03 |
| | 380-800 | 8.7 | 1.25 | 0.082 | -101.21 | 0.030 | 45.68 |
| $C^3$ | 80-380 | 3.82 | 1.09 | 0.181 | -101.09 | 0.756 | 38.70 |
| | 380-800 | 10.02 | 1.21 | 0.025 | -98.12 | 0.89 | 43.10 |
| $C^4$ | 80-380 | 3.76 | 1.35 | 0.168 | -109.86 | 0.843 | 35.05 |
| | 380-800 | 3.47 | 1.31 | 0.073 | -95.56 | 0.076 | 53.11 |
| $C^5$ | 70-380 | 3.33 | 0.97 | 0.152 | -104.76 | 0.587 | 32.97 |
| | 380-800 | 10.05 | 1.18 | 0.061 | -103.43 | 0.061 | 48.58 |

dehydration stage of ligand ($A^n$) were in the range 3.20-3.82 kJ mol$^{-1}$. The relatively high $E_a$ value indicates that the ligand ($A^n$) strongly bonds with the metal ion. The final solid product of decomposition was CuO (7.45%) accompanied by broad exothermic effect on above 800°C TGA data of shown in Fig. 2.

## Antimicrobial bioassay

The ligand and its metal complexes were screened for their antibacterial and antifungal activities according to the respective literature protocol and the results obtained are presented in Table 5. The results were compared with those of the standard drug. All the metal complexes were more potent bactericides and fungicides than the ligand. $C^3$ and $C^4$ complexes were much less bacterial activity than the $C^2$ and $C^5$ complex while $C^1$ complex shows superior antifungal activity compare to other complexes.

## Antioxidant studies

A capacity to transfer a single electron *i.e.* the antioxidant power of all compounds was determined by a FRAP assay. The FRAP value was expressed as an equivalent of standard antioxidant ascorbic acid (mmol/100 g of dried compound). FRAP values indicate that all the compounds have a ferric reducing antioxidant power. The compounds $C^3$ and

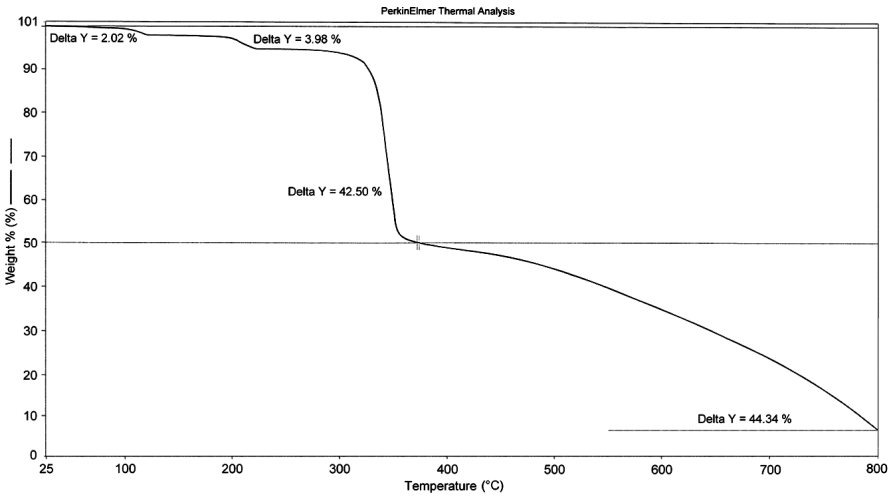



Fig. 2 — TGA Curve of $C^2$

Table 5 — Antimicrobial and antioxidant results of compound ($Cu^1$-$Cu^5$)

| Compd $C^1$-$C^5$ | Minimal Inhibition Concentration of microorganisms (µg/mL) | | | | | | | Antioxidant activity |
|---|---|---|---|---|---|---|---|---|
| | Bacteria | | | | Fungi | | | |
| | SA | BS | EC | PA | CA | AN | AC | |
| Cu(II)1 | 100 | 345.81 | >25 | >50 | 50 | 100 | 50 | >25 |
| Cu(II)2 | 12 | 425.24 | 25 | 12 | 25 | 25 | 12 | >12 |
| Cu(II)3 | 100 | 330.22 | >50 | 100 | >25 | 50 | >50 | 50 |
| Cu(II)4 | 25 | 345.40 | >25 | 50 | 100 | 50 | 25 | 25 |
| Cu(II)5 | 50 | 370.37 | 50 | >25 | 100 | >25 | 50 | >25 |
| Getifloxacin | 12 | NT | >6 | 12 | >12 | 12 | 12 | NT |
| Isoniazide | NT | NT | NT | NT | NT | NT | NT | 0.025 |
| Ethambutol | NT | NT | NT | NT | NT | NT | NT | 20 |
| Streptomycin | 12 | NT | 6 | 12 | NT | NT | NT | 6.25 |

$C^4$ showed relatively high antioxidant activity while compound $C^1$, $C^5$ and $C^2$ shows poor antioxidant power (Table 5).

## Conclusions

This study elucidates the synthesis of biologically active coumarin derivatives and their Cu(II) complexes ($C^1$–$C^5$). An octahedral geometry was assigned to the Cu(II) complexes based on thermogravimetric analysis and magnetic moment measurements. The complexes exhibited significantly enhanced antioxidant activity compared to their corresponding ligands. *In vitro* antimicrobial assays of all synthesized compounds demonstrated good activity, with a notable increase upon complexation with metal ions. This enhancement is likely due to the increased lipophilicity of the metal complexes. The structures of the ligands were confirmed through elemental analysis, FT-IR, $^1$H NMR, $^{13}$C NMR, and mass spectrometry.

## Supplementary Information

Supplementary information is available in the website http://nopr.niscpr.res.in/handle/123456789/58776.

## Acknowledgements

The authors are grateful to the Department of Chemistry and the Principal of SOIS, Silver Oak University for providing laboratory facilities.

## References

1 Gikas E, Parissi-Poulou M, Kazanis M & Vavagiannis A, *J Mol Struc*, 724 (2005) 135.
2 Zhao H N, Neamati, Hong H & Mazumder A, *J Med Chem*, 40 (1997) 242.
3 Raev L D, Voinova E, Ivanov I C & Popov D, *Pharmazie*, 45 (1990) 696.
4 Kostova I, *Curr Med Chem*, 5 (2005) 29.
5 Bedoya L M, Beltran M, Sancho R, Olmedo D A, Sanchez-Palomino S, Del lmo E, Lopez-Perez J L, Munoz E, Feliciano A & Alcam J, *Bioorg Med Chem Lett*, 15 (2005) 4447.

6 Lee K H, *J Nat Prod*, 67 (2004) 273.
7 Suvit T, Paul K T, Keith D W, Kong-Teck C, Howe W J, Chih-Ping Y, Strohbach W J, Turner R S & McGrath P J, *J Med Chem*, 37 (1994) 3200.
8 Kirkiacharian S, Thuy D.T, Sicsic S, Bakhchinian R, Kurkjian R & Tonnaire T, *II Farmaco*, 57 (2002) 703.
9 Appendino G, Mercalli E, Fuzzati N, Arnoldi L, Stavri M, Gibbons S, Ballero M & Maxia A, *J Nat Prod*, 67 (2004) 2108.
10 Khan K M, Saify Z S, Khan M Z, Zia-Ullah M I, Choudhary, Atta-Ur- Rahman S, Perveen Z H, Chohan C T & Supuran, *J Enzyme Inhib Med Chem*, 19 (2004) 373.
11 Lee B H, Clothier M F, Dutton F E, Conder G A & Johnson S S, *Bioorg Med Chem Lett*, 8 (1998) 3317.
12 Kontogiorgis C A & Hadjipavlou-Litina D, *J Med Chem*, 48 (2005) 6400.
13 Ghate M, Manohar D, Kulkarni V, Shobha R & Kattimani S Y, *Eur J Med Chem*, 38 (2003) 297.
14 Silvan A M, Abad M.J, Bermejo P, Sollhuber M & Villar A, *J Nat Prod*, 59 (1996) 1183.
15 Nicolaides D N, Fylaktakidou K C, Litinas K E & Hadjipavlou-Litina D, *Eur J Med Chem*, 33 (1998) 715.
16 Raj H G, Parmar V S, Jain S C, Goel S, Pooman, Himanshu S, Malhotra A, Singh C E & Wengel J O, *Bioorg Med Chem*, 6 (1998) 833.
17 Kontogiorgis C A & Hadjipavlou-Litina D, *Bioorg Med Chem Lett*, 14 (2004) 611.
18 Masche U P, Rentsch K.M, Felten A, Meier P J & Fittinger K E, *Eur J Clin Pharm*, 54 (1999) 865.
19 Luzzatto G, Fabris F, Zanon R D B & Giralami A, *Arzneim Forsch*, 36 (1986) 972.
20 Kostova I P, Manolov I, Nicolova I & Danchev N, *II Farmaco*, 56 (2001) 707.
21 Singh H B, *Acta Cienc Acta Cienc Indica Ser Chem*, 6 (1980) 88.
22 Teotia M P, Rastogi D K & Malik W U, *Inorg Chim Acta*, 7 (1973) 339.
23 Mandakmare A U & Navwade M L, *Orient J Chem*, 13 (1997) 155.
24 El-Ansary A L & Omar M M, *Egypt J Chem*, 31 (1988) 511.
25 Kostova I P, Manolov I, Nicolova I, Konstantinov S & Karaivanova M, *Eur J Med Chem*, 36 (2001) 339.
26 Kostova I P, Manolov I, Konstantinov S & Karaivanova M, *Eur J Med Chem*, 34 (1999) 63.
27 Manolov I I, Kostova I P, Konstantinov S & Karaivanova M, *Eur J Med Chem*, 34 (1999) 853.
28 Budzisz E, Krajewska U & Alski M R, *Pol J Pharmacol*, 56 (2004) 473.
29 Budzisz E, Małecka M, Lorenz I P, Mayer P, Kwiecien R A, Paneth P, Krajewska U & Alski M R, *Inorg Chem*, 45 (2006) 9688.
30 Miernicka M, Szulawska A, Czyz M, Lorenz I P, Mayer P, Karwowski B & Budzisz E, *J Inorg Biochem*, 102 (2008) 157.
31 Budzisz E, Keppler B.K, Giester G, Woznicka M, Kufelnicki A & Nawrot B, *Eur J Inorg Chem*, 22 (2004) 4412.
32 Budzisz E, Keppler B K, Małecka M, Keppler B, Arion V B & Andrijewski G, Rajewska U & Alski M R, *Eur J Inorg Chem*, 23 (2007) 3728.
33 Tyagi Y K, *Eur J Med Chem*, 40 (2005) 413.
34 Turel I, *Coord Chem Rev*, 232 (2002) 27.
35 Abd-Allah A R A, Gannam B B & Hamada F M A, *Pharm Res*, 42 (2000) 145.
36 Sanders J W E, *Clin Infect Dis*, 14 (1992) 539.
37 Savanini, Chiasserini L, Gaeta A & Pellerano C, *Bioorg Med Chem*, 10 (2002) 2193.
38 Vogel A I, *Practical Organic Chemistry*, *5th Ed.*, (Longman, London), 1989.
39 Angelusiu M V, Barbuceanu S F, Draghici C & Almajan G L, *Eur J Med Chem*, 45 (2010) 2055.
40 Singh V P & Katiyar A, *Pestic Biochem Physiol*, 92 (2008) 8.
41 Modi C K, Patel S H & Patel M N, *J Therm Anal Cal*, 87 (2007) 441.
42 El-Zaria M E, *Spectrochim Acta A*, 69 (2008) 216.