

## Investigating the Antimicrobial Efficacy of Copper(II) Complexes with 7-Hydroxy-Naphtho[2,1-c]chromen-6-one and Quinazolinone Schiff Bases

Milansinh.J.Gohil<sup>a</sup>, G.J.Kharadi<sup>a\*</sup>, Samat.R.Ram<sup>b</sup>

<sup>a</sup> Navjivan science college, Department of chemistry, Dahod, Gujarat, India

<sup>b</sup> Parekh brothers science college, Department of chemistry, Kapadwanj, Gujarat, India

\* Corresponding author

---

### Abstract

Six copper(II) complexes with mixed ligands were synthesized, utilizing 7-hydroxy-9,10,11,12-tetrahydro-6H-naphtho[2,1-c]chromen-6-one (ligand A) and six different quinazolinone-derived Schiff bases (ligands B1 through B6). To understand their structure and composition, these complexes underwent a series of analyses, including elemental analysis, infrared (IR) spectroscopy, proton nuclear magnetic resonance (1H-NMR) spectroscopy, fast atom bombardment mass spectrometry (FAB-MS), magnetic susceptibility measurements, and thermal analysis. We then assessed the antimicrobial activity of the complexes, as well as the individual ligands and copper salt, against various microorganisms, with comparisons to standard antimicrobial drugs. The data revealed that the newly synthesized copper complexes exhibited significantly higher antimicrobial activity compared to the free ligands and the copper salt alone. These results suggest that these mixed-ligand copper(II) complexes could be valuable in the ongoing search for effective antimicrobial agents.

### Keywords

Organometallic Compounds, Quinazolinone Schiff bases, Infrared Spectroscopy (IR), Antimicrobial Activity.

---

Date of Submission: 01-05-2024

Date of acceptance: 12-05-2024

---

### I. Introduction

Nitrogen-containing heterocyclic compounds form a crucial class of molecules, found in many natural products and synthesized substances with various biological activities [1]. Quinazolinone, a type of nitrogen-containing heterocycle, is composed of a benzene ring fused with a pyrimidine ring [2]. Extensive research has focused on quinazolinone structures containing an imine (-C=N) group [3], and these compounds have gained attention due to their diverse biological properties. These activities include antibacterial [4], anticancer [5], anticytotoxic, analgesic, diuretic, antipyretic, antihistamine, antidepressant, and vasodilatory effects [6] [7]. Given these properties, quinazolinone Schiff base and its derivatives have become significant targets for synthesis.

The synthesis of quinazolinone Schiff base derivatives typically involves the condensation reaction between 2-amino benzoyl hydrazide and aromatic aldehydes. Additionally, research has focused on creating complexes by reacting copper salts with synthesized ligands. In this context, copper(II) complexes with mixed ligands have drawn considerable interest due to their versatile coordination geometries and promising applications in various fields, including catalysis, medicine, and materials science [8]. Copper(II) ions, among the most studied transition metal ions, play essential roles in biological systems and pharmacology [9]. Notably, copper(II) complexes with nitrogen- and oxygen-donor heterocycles are particularly active, often serving as pharmacological agents or biological sensors.

Research into coumarin, another heterocyclic compound, has also expanded. Coumarin (2H-chromene 2-one) consists of a fused phenyl ring, yielding benzocoumarin and its derivatives when fused at the third and fourth positions [10]. These compounds have natural and synthetic origins and display a variety of bioactivities, including antidyslipidemic [11], anti-inflammatory [12], vasodilatory [13], antimicrobial [14], anti-thrombotic, anti-mutagenic, antioxidant [15], anti-allergic [16], antiviral [17], and anti-carcinogenic properties [18].

In this study, we aimed to synthesize and characterize a series of quinazolinone Schiff base derivatives, coumarin derivative-7-hydroxy-9,10,11,12-tetrahydro-6H-naphtho[2,1-c]chromen-6-one, and their copper(II) complexes, using various analytical and spectroscopic methods. Techniques like 1H-NMR spectroscopy, infrared spectroscopy, thermogravimetric analysis, and elemental analysis helped to elucidate the structure and stability of these compounds. The magnetic properties of the copper(II) complexes suggested an octahedral geometry, and FAB mass spectrometry confirmed the molecular weight and stability of the fragments.

Additionally, we assessed the antimicrobial activity of these complexes using the zone of inhibition method, targeting against four microorganism-E. coli, S. aureus, S. marcescens, and B. subtilis. The results from these biological assays were compared to those obtained with the ligands and standard drug.

This study's objective was to gain a comprehensive understanding of the structural features, properties, and biological activity of mixed ligand copper(II) complexes. The insights gained from this work could inform the development of new metal-based drugs and materials, highlighting the potential of these complexes as promising antimicrobial agents.

## II. Experimental

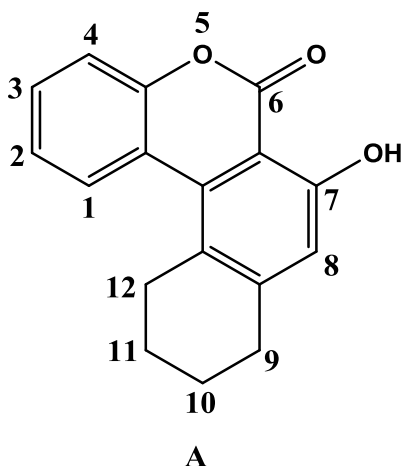
### Materials and Methods

This research utilized solely analytical grade chemicals and reagents. Salicylaldehyde, Ethylacetoacetate, piperidine, ether, chloroform, bromine, toluene, pyridine, cyclohexanone, benzaldehyde, 4-nitrobenzaldehyde, 4-methoxy-benzaldehyde, 4-dimethylamino benzaldehyde, furfural, and Copper nitrate were acquired from Sigma-Aldrich.

### Preparation of Ligands

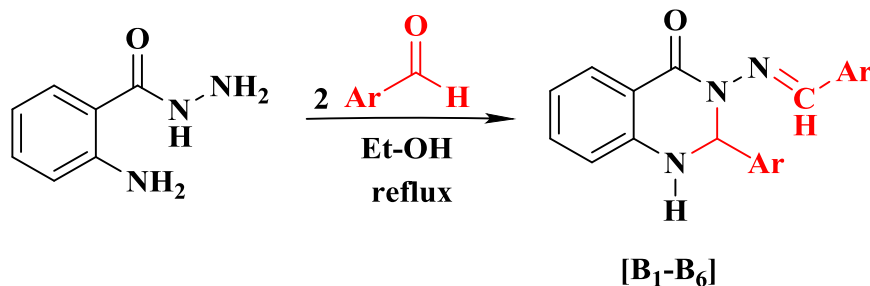
- **7-hydroxy-9,10,11,12-tetrahydro-6H-naphtho[2,1-c]chromen-6-one (A)**

The target compound, 7-hydroxy-9,10,11,12-tetrahydro-6H-naphtho[2,1-c]chromen-6-one (A), was synthesized following a tailored literature protocol. The synthesis entailed the reaction of a modified coumarinoyl methyl pyridinium derivative with cyclohexanone and sodium acetate, ultimately producing the ligand[19]. Yield, 71%, m.p., 210-212 °C. Found (%): C, 76.55; H, 5.12.  $C_{17}H_{14}O_3$  (266.30 g/mol) requires (%):C, 76.68; H, 5.30.  $^1H$  NMR ( $CDCl_3$ , 400 MHz)  $\delta/ppm$ : 11.61, (s, 1H, OH); 8.12, (d, 1H, H<sub>1</sub>); 7.20–7.45, (m, 3H, H<sub>2,3,4</sub>); 6.81, (s, 1H, H<sub>8</sub>); 3.18, (t, 2H, H<sub>12</sub>); 2.95, (t, 2H, H<sub>9</sub>); 1.80-1.82 (4H, m, H<sub>10,11</sub>). IR (KBr, 4000–400  $cm^{-1}$ ): 3420,  $\nu$ (O-H); 3040,  $\nu$ (C-H); 1610, 1410,  $\nu$ (C=C); 2950  $\nu$ (C-H, cyclohexane ring); 1672  $\nu$ (C=O).



- **Synthesis of Quinazolinone Schiff base ligands(B<sub>1</sub>-B<sub>6</sub>)**

The Quinazolinone Schiff bases B<sub>1</sub>-B<sub>6</sub>, as listed in Table-1, were synthesized by adapting the method outlined in the literature[20] [21]. In Scheme 1, the synthesis process involved stirring a mixture containing 2-amino benzoyl hydrazide and aromatic aldehyde in ethanol for 10 minutes, followed by refluxing for 2 hours. The resulting solid was then filtered and washed with water to isolate the product.



Scheme 1 Synthesis of Quinazolinone schiff base

**Table-1** Aromatic aldehyde and identification of Quinazolinone Schiff bases B<sub>1</sub>-B<sub>6</sub>

| Entry | Ar   | Quinazolinone Schiff base | Yield(%) |
|-------|--|---------------------------|----------|
| 1     | C <sub>6</sub> H <sub>5</sub>                                    | B <sub>1</sub>            | 84       |
| 2     | 4-NO <sub>2</sub> C <sub>6</sub> H <sub>4</sub>                  | B <sub>2</sub>            | 82       |
| 3     | 4-CH <sub>3</sub> OC <sub>6</sub> H <sub>4</sub>                 | B <sub>3</sub>            | 79       |
| 4     | 4-(CH <sub>3</sub> ) <sub>2</sub> NC <sub>6</sub> H <sub>4</sub> | B <sub>4</sub>            | 83       |
| 5     | 2-furyl  | B <sub>5</sub>            | 85       |
| 6     | 4-ClC <sub>6</sub> H <sub>4</sub>                                | B <sub>6</sub>            | 83       |

**1. (E)-3-(benzylideneamino)-2-phenyl-2,3-dihydroquinazolin-4(1H)-one(B<sub>1</sub>):**

Yield, 84%, m.p., 166-167 °C.

Found(%): C, 77.1, H, 5.17, N, 12.77. C<sub>21</sub>H<sub>17</sub>N<sub>3</sub>O(327.39) requires(%)C, 77.04, H, 5.23, N, 12.84. <sup>1</sup>H NMR (ppm): 7.95 (s, -HC=N), 6.69-7.97 (m, Ar-H), 5.92 (s, C-H), 6.12 (s, -NH).

IR(KBr,cm<sup>-1</sup>): 3283(-N-H str. vib.), 1660(-C=O str. vib.), 1618(-CH=N str. vib.), 3040(aromatic C-H).

**2. (E)-3-((4-nitrobenzylidene)amino)-2-(4-nitrophenyl)-2,3-dihydroquinazolin-4(1H)-one(B<sub>2</sub>):**

Yield, 82%, m.p., 215-217 °C.

Found(%): C, 60.28, H, 3.55, N, 16.71. C<sub>21</sub>H<sub>15</sub>N<sub>5</sub>O<sub>5</sub>(417.38) requires(%)C, 60.43, H, 3.62, N, 16.78. <sup>1</sup>H NMR (ppm): 8.12 (s, -HC=N), 6.52-8.12 (m, Ar-H), 5.96 (s, C-H), 6.18 (s, -NH).

IR(KBr,cm<sup>-1</sup>): 3284(-N-H str. vib.), 1641(-C=O str. vib.), 1612(-CH=N str.vib.), 1561(-C-N str. vib.), 3100(aromatic C-H).

**3. (E)-3-((4-methoxybenzylidene)amino)-2-(4-methoxyphenyl)-2,3-dihydroquinazolin-4(1H)-one(B<sub>3</sub>):**

Yield, 79%, m.p., 223-234 °C.

Found(%):C, 71.17, H, 5.41, N, 10.79. C<sub>23</sub>H<sub>21</sub>N<sub>3</sub>O<sub>3</sub>(387.44) requires (%)C, 71.30, H, 5.46, N, 10.85. <sup>1</sup>H NMR (ppm): 8.29(s, -HC=N), 6.62-7.78 (m, Ar-H), 5.94 (s, C-H), 6.19 (s, -NH), 3.78(s,-OCH<sub>3</sub>).

IR(KBr,cm<sup>-1</sup>): 3335(-N-H str. vib.), 1609(-C=O str. vib.), 1572(-CH=N str. vib.), 1251(-C-O str. vib.), 2966(aromatic C-H).

**4. (E)-3-((4-(dimethylamino)benzylidene)amino)-2-(4-(dimethylamino)phenyl)-2,3-dihydroquinazolin-4(1H)-one(B<sub>4</sub>):**

Yield,83%,m.p.,252-254 °C

Found(%):C, 72.48, H, 6.47, N, 16.82. C<sub>25</sub>H<sub>27</sub>N<sub>5</sub>O(413.53)requires(%)C, 72.61, H, 6.58, N, 16.94.

<sup>1</sup>H NMR (ppm): 8.29 (s, -HC=N), 6.45-7.32 (m, Ar-H), 5.96 (s, C-H), 6.18 (s, -NH), 2.96(s,-NCH<sub>3</sub>)

IR(KBr,cm<sup>-1</sup>): 3462 (-N-H str. vib.), 1714(-C=Ostr.vib.), 1604(-CH=Nstr.vib.), 1228(-C-Nstr.vib.)2915(aromatic C-H).

**5. (E)-2-(furan-2-yl)-3-((furan-2-ylmethylene)amino)-2,3-dihydroquinazolin-4(1H)-one(B<sub>5</sub>):**

Yield, 85%, m.p., 170 - 172 °C.

Found(%): C, 66.32, H, 4.15, N, 13.61. C<sub>17</sub>H<sub>13</sub>N<sub>3</sub>O<sub>3</sub>(301.31)requires(%)C, 66.44, H, 4.26, N, 13.67.

<sup>1</sup>H NMR (ppm): 8.26 (s, -HC=N), 6.41-7.74 (m, Ar-H), 5.92 (s, C-H), 6.18 (s, -NH). IR(KBr,cm<sup>-1</sup>): 3252(-N-H str. vib.), 1655(-C=O str. vib.), 1611(-CH=N str. vib.), 3145(aromatic C-H).

**6. (E)-3-((4-chlorobenzylidene)amino)-2-(4-chlorophenyl)-2,3-dihydroquinazolin-4(1H)-one(B<sub>6</sub>):**

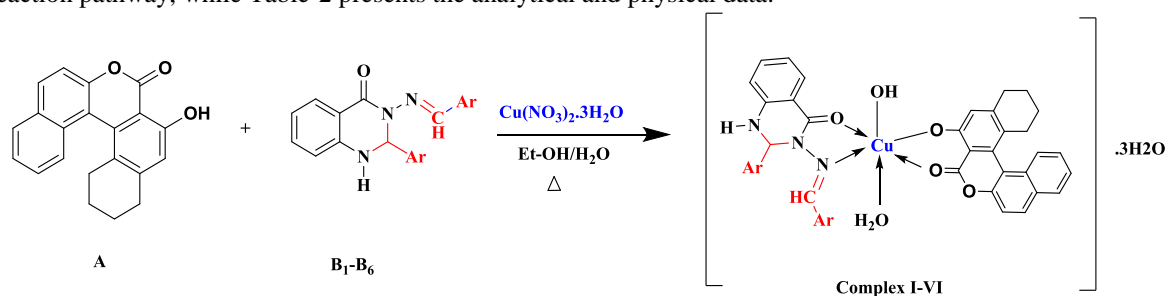
Yield, 83%, m.p, 230 – 232 °C.

Found(%): C, 63.44, H, 3.74, N 10.53. C<sub>21</sub>H<sub>15</sub>Cl<sub>2</sub>N<sub>3</sub>O (396.27) requires: %C, 63.53, H, 3.82, N, 10.60. <sup>1</sup>H NMR (ppm): 8.32 (s, -HC=N), 6.52-7.92 (m, Ar-H), 5.21(s, C-H), 6.17 (s, -NH).

IR(KBr,cm<sup>-1</sup>): 3435(-N-H str. vib.), 1625(-C=O str. vib.), 1591(-CH=N str. vib.), 810(-C-Cl str. vib.), 3050(aromatic C-H).

• **Synthesis of Cu(II) complexes(I - VI)**

The complexes were synthesized using a standardized approach. Initially, a solution containing Cu(NO<sub>3</sub>)<sub>2</sub>·3H<sub>2</sub>O (10 mmol) in water was combined with a solution of ligand A (10 mmol) in dimethylformamide. Subsequently, Quinazolinone Schiff base ligand B<sub>1</sub>–B<sub>6</sub> (10 mmol) in ethanol was added. The resulting mixture underwent refluxing on a water bath for 7 hours. The resultant dark green precipitate was filtered, washed with ethanol and hot water, and then dried under vacuum at room temperature[22]. Scheme 2 illustrates the general reaction pathway, while Table-2 presents the analytical and physical data.

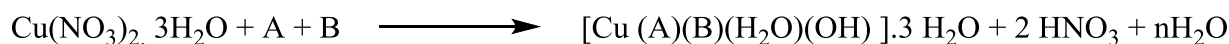


**Table-2** Analytical and physical data of Cu(II) complexes.

| Complex | Chemical Formula  | Color      | Yield( %) | Molecular weight | Melting Point (°C) | % found (required) |             |             |             |
|---------|---|------------|-----------|------------------|--------------------|--------------------|-------------|-------------|-------------|
|         |   |            |           |                  |                    | C                  | H           | N           | Cu          |
| I       | C <sub>38</sub> H <sub>39</sub> CuN <sub>3</sub> O <sub>9</sub>                 | Dark green | 64        | 745.24           | >350               | 65.92 (66.03)      | 4.78 (4.81) | 6.01 (6.08) | 9.12 (9.19) |
| II      | C <sub>38</sub> H <sub>37</sub> CuN <sub>3</sub> O <sub>13</sub>                | Dark green | 65        | 835.24           | >350               | 58.38 (58.42)      | 3.91 (4.00) | 8.81 (8.96) | 8.07 (8.13) |
| III     | C <sub>40</sub> H <sub>43</sub> CuN <sub>3</sub> O <sub>11</sub>                | Dark green | 62        | 805.30           | >350               | 63.91 (63.95)      | 4.88 (4.96) | 5.51 (5.59) | 8.41 (8.46) |
| IV      | C <sub>42</sub> H <sub>49</sub> CuN <sub>3</sub> O <sub>9</sub>                 | Dark green | 62        | 831.38           | >350               | 64.80 (64.89)      | 5.51 (5.58) | 8.89 (9.01) | 8.11 (8.17) |
| V       | C <sub>34</sub> H <sub>35</sub> CuN <sub>3</sub> O <sub>11</sub>                | Dark green | 61        | 725.17           | >350               | 60.81 (60.85)      | 4.28 (4.36) | 6.12 (6.26) | 9.41 (9.47) |
| VI      | C <sub>38</sub> H <sub>37</sub> Cl <sub>2</sub> CuN <sub>3</sub> O <sub>9</sub> | Dark green | 65        | 814.13           | >350               | 60.01 (60.04)      | 4.08 (4.11) | 5.49 (5.53) | 8.31 (8.36) |

**III. Result & Discussion**

Table 2 presents the physical data and elemental analysis findings of the copper(II) complexes synthesized using mixed ligands. The reaction depicted below elucidates the process employed for the formation of these complexes.



Where A = Ligand A & B = Ligand B<sub>1</sub>-B<sub>6</sub>

The copper(II) complexes synthesized demonstrated insolubility in the majority of organic solvents. Nevertheless, they exhibited a slightly elevated solubility when subjected to dimethyl sulfoxide.

**Analysis of Magnetic Characteristics in Copper(II) Complexes**

The electronic spectral data and magnetic moment measurements summarized in Table 3 reveal key details about the structure of mixed ligand complexes containing Cu(II). These complexes exhibit two distinct absorption bands at around 10,400 and 14,600 cm<sup>-1</sup>, corresponding to transitions involving dz<sup>2</sup> → dx<sup>2</sup>-y<sup>2</sup>, as well as dxz, dyz, → dx<sup>2</sup>-y<sup>2</sup> orbitals. The magnetic moment values for these copper(II) complexes, ranging from 1.79 to 1.91 Bohr Magnetons (B.M.), are consistent with the expected spin-allowed value of 1.73 B.M. Based on this combination of spectral and magnetic data, it's reasonable to conclude that the copper(II) ion in these complexes likely has an octahedral configuration [23].

**Table-3** electronic spectroscopy and magnetic measurement data of metal complexes

| Complexes | d-d transition in $\text{cm}^{-1}$ | Assignment  | $\mu_{\text{eff}}$ |
|-----------|------------------------------------|---|--------------------|
| I         | 14,000-10,400                      | $d_{z^2} \longrightarrow d_{x^2-y^2}, d_{xz}, d_{yz} \longrightarrow d_{x^2-y^2}$ | 1.81               |
| II        | 14,200-10,500                      | $d_{z^2} \longrightarrow d_{x^2-y^2}, d_{xz}, d_{yz} \longrightarrow d_{x^2-y^2}$ | 1.87               |
| III       | 14,100-10,400                      | $d_{z^2} \longrightarrow d_{x^2-y^2}, d_{xz}, d_{yz} \longrightarrow d_{x^2-y^2}$ | 1.79               |
| IV        | 14,500-10,600                      | $d_{z^2} \longrightarrow d_{x^2-y^2}, d_{xz}, d_{yz} \longrightarrow d_{x^2-y^2}$ | 1.82               |
| V         | 14,300-10,900                      | $d_{z^2} \longrightarrow d_{x^2-y^2}, d_{xz}, d_{yz} \longrightarrow d_{x^2-y^2}$ | 1.86               |
| VI        | 14,600-10,800                      | $d_{z^2} \longrightarrow d_{x^2-y^2}, d_{xz}, d_{yz} \longrightarrow d_{x^2-y^2}$ | 1.91               |

### IR spectra

Table 4 presents key infrared spectral bands obtained from KBr disks for the synthesized complexes, with corresponding assignments. The initial  $\text{V}(\text{C}=\text{O})$  band for ligand A, indicating a lactone carbonyl ketone, was observed at  $1672 \text{ cm}^{-1}$ . After complexation, this band shifted downward to  $1620 \text{ cm}^{-1}$ , suggesting that the carbonyl oxygen atom was involved in coordination with the metal.

For the quinazolinone Schiff bases, the  $\text{V}(\text{C}=\text{N})$  band originally ranged from  $1565$  to  $1625 \text{ cm}^{-1}$ , and it consistently shifted to lower frequencies in all the mixed ligand complexes, indicating coordination between the imine nitrogen and the copper ion.

Additionally, new bands in the far-infrared region appeared at  $500$ - $510 \text{ cm}^{-1}$  and  $536$ - $544 \text{ cm}^{-1}$ , which are attributed to  $\text{V}(\text{Cu}-\text{O})$  and  $\text{V}(\text{Cu}-\text{N})$  vibrations, respectively, confirming the coordination of copper with oxygen and nitrogen atoms.

In the IR spectra, a broad, faint band at  $3065 \text{ cm}^{-1}$ , along with a distinct band at  $2925 \text{ cm}^{-1}$ , are characteristic of aromatic C-H stretching and methyl group C-H stretching, respectively. The broad bands in the  $3200$ - $3400 \text{ cm}^{-1}$  range in the mixed ligand complexes are attributed to the presence of coordinated water molecules. Additionally, bands at  $860 \text{ cm}^{-1}$  and  $715 \text{ cm}^{-1}$  were identified as the rocking and wagging modes of the  $-\text{OH}$  group, respectively [24].

**Table- 4** Selected IR data ( $\text{cm}^{-1}$ ) for the Cu(II) complexes.

| Complexes | $\text{V}(\text{CH}=\text{N}) \text{ cm}^{-1}$ | $\text{V}(\text{CH}=\text{O}) \text{ cm}^{-1}$ [Qn] | $\text{V}(\text{N}-\text{H}) \text{ cm}^{-1}$ | $\text{V}(\text{Cu}-\text{O}) \text{ cm}^{-1}$ [A] | $\text{V}(\text{Cu}-\text{N}) \text{ cm}^{-1}$ [Qn] |
|-----------|--|---|---|--|---|
| I         | 1603(w)  | 1652(s)   | 3278  | 507  | 540   |
| II        | 1595(w)  | 1639(s)   | 3279  | 508  | 545   |
| III       | 1554(w)  | 1596(s)   | 3324  | 505  | 541   |
| IV        | 1583(w)  | 1691(s)   | 3479  | 508  | 539   |
| V         | 1592(w)  | 1639(s)   | 3248  | 506  | 535   |
| VI        | 1574(w)  | 1622(s)   | 3424  | 506  | 544   |

### Thermogravimetric Analysis of Mixed-Ligand Complexes

Thermogravimetric analysis stands out as a powerful tool for probing the thermal properties of various materials. In our investigation, we employed this technique to delve into the thermal stability and decomposition pathways of mixed-ligand complexes. Carried out under a  $\text{N}_2$  atmosphere, with a heating rate of  $10^\circ\text{C}$  per minute, the analysis spanned a temperature range from  $10$  to  $900^\circ\text{C}$  [25].

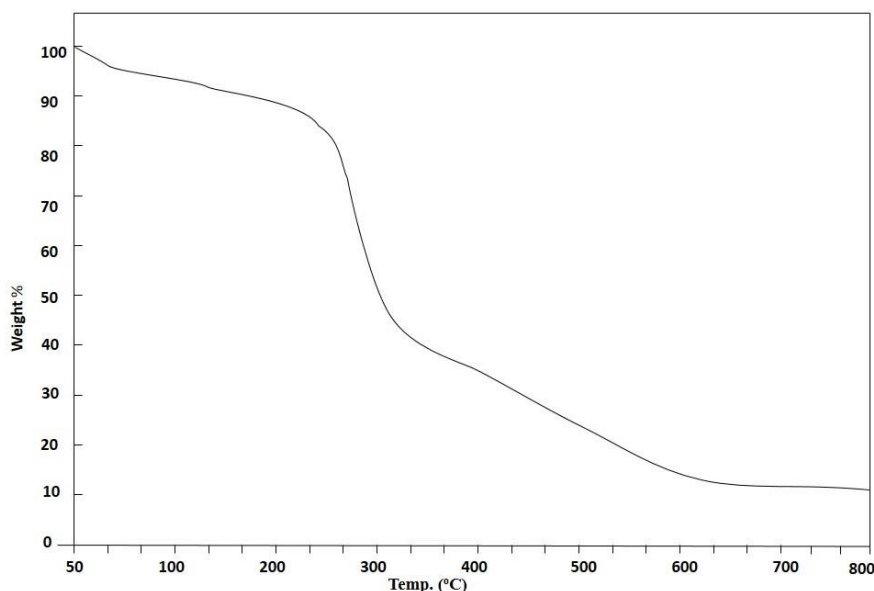
Our primary objective was to uncover the differences in composition among the mixed-ligand complexes and to characterize any associated water molecules. Our findings unveiled intriguing insights. For instance, the  $[\text{Cu}(\text{A})(\text{B}_1)\text{H}_2\text{O}.\text{OH}].3\text{H}_2\text{O}$  complex exhibited a complex thermal behavior, manifesting in four distinct decomposition stages upon heating.

Initially, between  $65$  and  $120^\circ\text{C}$ , three water molecules were lost, indicating the presence of water of crystallization. Following this, the second stage, spanning  $120$  to  $240^\circ\text{C}$ , involved the decomposition of one coordinated hydroxyl and water molecules. Subsequent stages saw the elimination of ligand A between  $240$  and  $320^\circ\text{C}$ , and ligand  $\text{B}_2$  between  $320$  and  $750^\circ\text{C}$ , leaving behind copper oxide as the residual product.

The TG curves for Cu(II) complex-I are illustrated in Figures 1, while Table 5 presents the thermal data extracted from the curves, corroborating findings from other studies. Utilizing thermogravimetric analysis to evaluate mixed-ligand complexes can provide invaluable insights into their thermal stability and decomposition mechanisms. Such knowledge plays a pivotal role in understanding decomposition mechanisms and optimizing synthesis and storage conditions for these complexes.

**Table 5** Thermal decomposition analytical data of complexes

| Complex | TG range (°C) | Mass loss (%)<br>Obs.(cal.) | Assignment                                       |
|---------|---------------|-----------------------------|--|
| I       | 65-120 °C     | 7.19 (7.24)                 | Loss of three lattice water molecules            |
|         | 120-240 °C    | 4.42(4.47)                  | Loss of coordinated water and hydroxyl molecules |
|         | 240-320 °C    | 35.61(35.73)                | Removal of ligand A                              |
|         | 320-750 °C    | 43.61(43.93)                | Removal of ligand B <sub>1</sub>                 |
| II      | 75-150 °C     | 6.41(6.46)                  | Loss of three lattice water molecules            |
|         | 150-260 °C    | 4.12(4.19)                  | Loss of coordinated water and hydroxyl molecules |
|         | 260-330 °C    | 31.78(31.88)                | Removal of ligand A                              |
|         | 330-750 °C    | 49.91(49.97)                | Removal of ligand B <sub>2</sub>                 |
| III     | 70-130 °C     | 6.63(6.70)                  | Loss of three lattice water molecules            |
|         | 130-220 °C    | 4.21(4.34)                  | Loss of coordinated water and hydroxyl molecules |
|         | 220-340 °C    | 33.01(33.06)                | Removal of ligand A                              |
|         | 340-750 °C    | 48.08(48.11)                | Removal of ligand B <sub>3</sub>                 |
| IV      | 70-140 °C     | 6.38(6.49)                  | Loss of three lattice water molecules            |
|         | 140-220 °C    | 4.11(4.20)                  | Loss of coordinated water and hydroxyl molecules |
|         | 220-300 °C    | 31.88(32.03)                | Removal of ligand A                              |
|         | 300-750 °C    | 49.11(49.74)                | Removal of ligand B <sub>4</sub>                 |
| V       | 85-120 °C     | 7.41(7.44)                  | Loss of three lattice water molecules            |
|         | 120-260 °C    | 4.71(4.82)                  | Loss of coordinated water and hydroxyl molecules |
|         | 260-320 °C    | 36.61(36.72)                | Removal of ligand A                              |
|         | 320-750 °C    | 42.31(42.37)                | Removal of ligand B <sub>5</sub>                 |
| VI      | 70-130 °C     | 6.61(6.63)                  | Loss of three lattice water molecules            |
|         | 130-250 °C    | 4.18(4.29)                  | Loss of coordinated water and hydroxyl molecules |
|         | 250-330 °C    | 32.66(32.70)                | Removal of ligand A                              |
|         | 330-750 °C    | 48.58(48.67)                | Removal of ligand B <sub>6</sub>                 |



**Fig.1** TGA curve for complex II

**Mass spectra**

Distinctive molecular ion peaks characterize the mass spectra of complexes I through VI, manifesting at  $m/z = 745, 835, 805, 831, 725,$  and  $814$  respectively. In the FAB-Mass spectrum for complex I, a conspicuous molecular ion peak emerges at  $745 m/z$ . Furthermore, several other peaks are discerned at varying  $m/z$  values including  $691, 656, 600, 548, 353, 309,$  and  $177$ . Notable doublets are also apparent at  $745:747, 691:623,$  and  $548:550 m/z$  values, indicating fragments containing a Cu atom. These findings are meticulously illustrated in Figure 2's mass spectra.

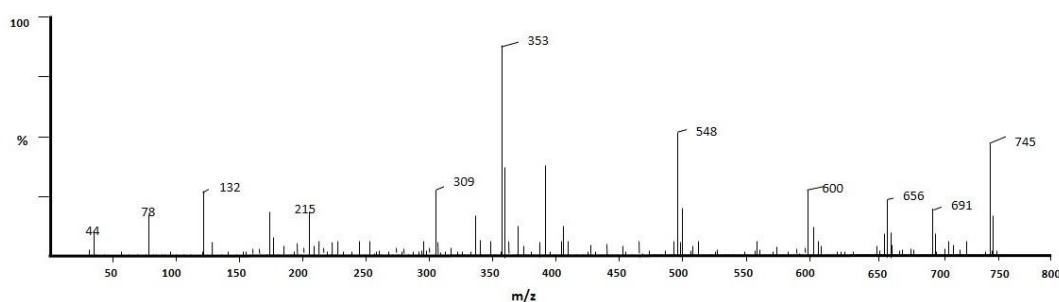


Fig.2 Mass spectra of synthesized complex I

### Antibacterial Activity of complexes

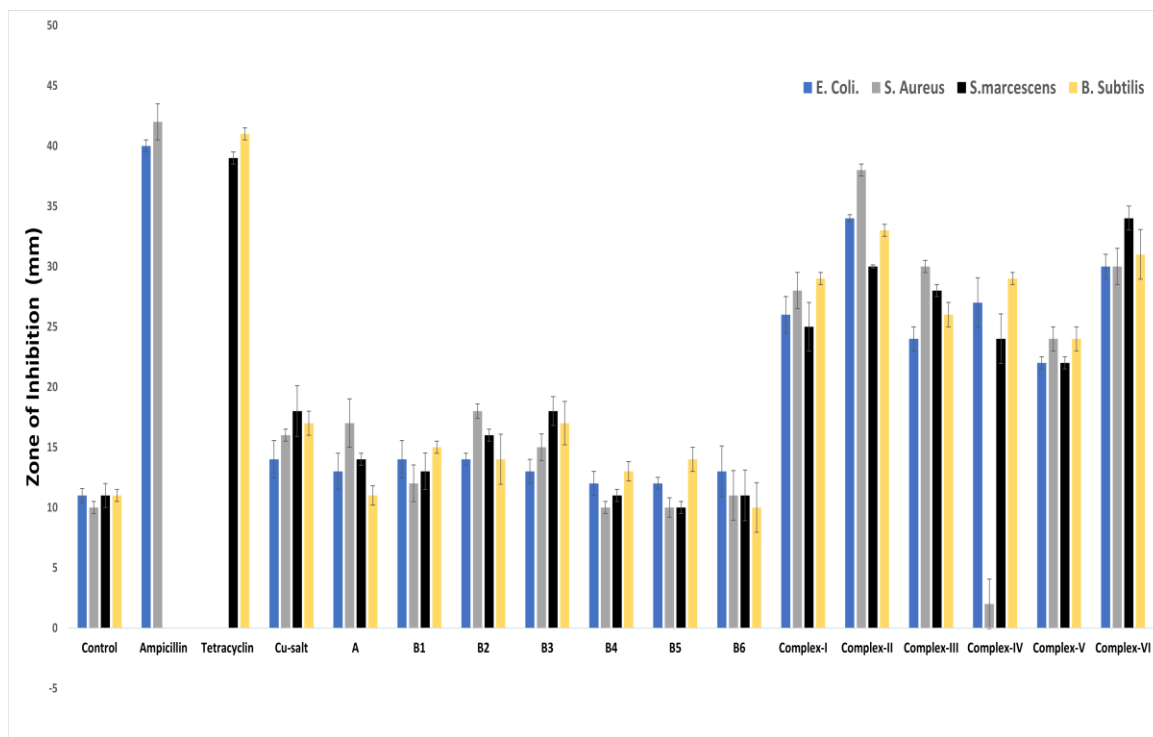
A 10 mg/mL stock solution was prepared by dissolving the compound in DMSO and diluting it to the required volume with double-distilled water. Agar plates were created by dissolving bacteriological agar and Luria broth in distilled water, followed by autoclaving to sterilize. Target microorganisms were activated in liquid Luria broth and then incubated with two 10 mm wells. After inoculating the agar plate with the active cultures, sterilized stock solutions were added to the wells. The plates were then incubated, and the zone of inhibition was measured. Control experiments were performed with solvents that did not contain test compounds. The measured zones of inhibition were compared to those obtained with a standard reference drug.

To assess the biological activity of the ligands and their corresponding metal complexes, they were tested against the bacteria *Escherichia coli*, *Staphylococcus aureus*, *Serratia marcescens*, and *Bacillus subtilis*. The metal complexes demonstrated greater antibacterial potency compared to the ligands, as indicated by the zone of inhibition. Among the tested complexes, Complex II exhibited the highest activity against all four bacteria, particularly against *Staphylococcus aureus* and *Serratia marcescens*. These results suggest the potential use of coordination compounds in biological applications. Detailed results are provided in Table 6 and illustrated in Figure 3.

TABLE 6 Antibacterial activity data of synthesized ligands and complexes  
Zone of inhibition (mm)

|                | E. Coli.  | S. aureus | S.marcescens | B. subtilis |
|----------------|-----------|-----------|--------------|-------------|
| Control        | 11 ± 0.58 | 10 ± 0.5  | 11 ± 1       | 11 ± 0.5    |
| Ampicillin     | 40 ± 0.5  | 42 ± 1.5  | -            | -           |
| Tetracyclin    | -         | -         | 39 ± 0.5     | 41 ± 0.5    |
| Cu-salt        | 14 ± 1.55 | 16 ± 0.5  | 18 ± 2.1     | 17 ± 1      |
| A              | 13 ± 1.5  | 17 ± 2.01 | 14 ± 0.5     | 11 ± 0.8    |
| B <sub>1</sub> | 14 ± 1.55 | 12 ± 1.53 | 13 ± 1.53    | 15 ± 0.5    |
| B <sub>2</sub> | 14 ± 0.5  | 18 ± 0.6  | 16 ± 0.5     | 14 ± 2.08   |
| B <sub>3</sub> | 13 ± 1    | 15 ± 1.1  | 18 ± 1.2     | 17 ± 1.8    |
| B <sub>4</sub> | 12 ± 1    | 10 ± 0.5  | 11 ± 0.5     | 13 ± 0.8    |
| B <sub>5</sub> | 12 ± 0.5  | 10 ± 0.8  | 10 ± 0.5     | 14 ± 1      |
| B <sub>6</sub> | 13 ± 2.1  | 11 ± 2.06 | 11 ± 2.1     | 10 ± 2.06   |
| Complex-I      | 26 ± 1.5  | 28 ± 1.5  | 25 ± 2       | 29 ± 0.5    |
| Complex-II     | 34 ± 0.28 | 38 ± 0.5  | 30 ± 0.13    | 33 ± 0.5    |
| Complex-III    | 24 ± 1    | 30 ± 0.5  | 28 ± 0.5     | 26 ± 1      |
| Complex-IV     | 27 ± 2.06 | 28 ± 2.06 | 24 ± 2.06    | 29 ± 0.5    |
| Complex-V      | 22 ± 0.5  | 24 ± 1    | 22 ± 0.5     | 24 ± 1      |
| Complex-VI     | 30 ± 1    | 30 ± 1.5  | 34 ± 1       | 31 ± 2.06   |

E. coli = *Escherichia coli*, S. aureus = *Staphylococcus aureus*, S.marcescens = *Serratia marcescens*  
B. subtilis = *Bacillus subtilis* (n = 3) ± standard deviation of three replicates.



**Fig.3 Comparative analysis for biological activity**

#### IV. Conclusion

- The ligands employed in this study have shown remarkable ability to act as strong electron donors, functioning as Lewis bases to form complexes with octahedral geometry. This conclusion is supported by the magnetic properties of the complexes, which are consistent with an octahedral structure.
- The distinctive mass fragmentation patterns, along with the molecular ion peak, provide unique identifiers for each compound. We utilized these characteristic patterns to determine the molecular mass and gain structural insights into different complexes.
- Thermal analyses revealed the degradation patterns of the various complexes, offering a glimpse into the degradation rate of the organic components and the residual inorganic composition.
- The synthesized ligands and complexes were evaluated for their potential antibacterial activity through a screening process. The results revealed significant antibacterial effects against all four bacterial strains: *Escherichia coli*, *Staphylococcus aureus*, *Serratia marcescens*, and *Bacillus subtilis*. Notably, the complexes demonstrated superior antibacterial activity compared to both the ligands and the corresponding metal salts. These findings point to the promising potential for further development of these complexes as antibacterial agents.

#### Acknowledgements

The authors extend their gratitude to Navjivan Science College, Dahod, Shri Govind Guru University, Godhra-389001 Gujarat, India, and Parekh Brothers Science College, Kapadwanj, Gujarat, India, for their generous provision of laboratory facilities. They also express their appreciation for the analytical support provided by the Sophisticated Instrumentation Centre for Applied Research & Testing (SICART), Vallabh Vidyanagar, Gujarat, India.

#### REFERENCES

- [1]. Kerru, N., Gummidi, L., Maddila, S., Gangu, K.K., & Jonnalagadda, S.B. (2020) "A review on recent advances in nitrogen-containing molecules and their biological applications." *Molecules*, Vol. 25, No. 8, pp. 1909.
- [2]. Khan, I., Ibrar, A., Abbas, N., Saeed, A., & Asiri, A.M. (2015) "Synthetic approaches, functionalization and therapeutic potential of quinazoline and quinazolinone skeletons: The advances continue." *European Journal of Medicinal Chemistry*, Vol. 90, pp. 124-169.
- [3]. Zhou, X., Ding, Y., & Huang, H. (2020) "Palladium- Catalyzed Carbonylative Difunctionalization of C= N Bond of Azaarenes or Imines to Quinazolinones." *Chemistry—An Asian Journal*, Vol. 15, No. 11, pp. 1678-1682.
- [4]. Gatadi, S., Lakshmi, T.V., & Nanduri, S. (2019) "4 (3H)-Quinazolinone derivatives: Promising antibacterial drug leads." *European Journal of Medicinal Chemistry*, Vol. 170, pp. 157-172.
- [5]. Ravez, S., Mouawad, F., & Urani, C. (2015) "Quinazoline derivatives as anticancer drugs: a patent review (2011–present)." *Expert Opinion on Therapeutic Patents*, Vol. 25, No. 7, pp. 789-804.
- [6]. Labade, V.B., Shinde, P.V., & Shingare, M.S. (2013) "A facile and rapid access towards the synthesis of 2, 3-dihydroquinazolin-4 (1H)-ones." *Tetrahedron Letters*, Vol. 54, No. 43, pp. 5778-5780.



- [7]. Ghorbani-Choghamarani, A., & Norouzi, M. (2014) "Synthesis of copper (II)-supported magnetic nanoparticle and study of its catalytic activity for the synthesis of 2, 3-dihydroquinazolin-4 (1H)-ones." *Journal of Molecular Catalysis A: Chemical*, Vol. 395, pp. 172-179.
- [8]. Gawande, M.B., Goswami, A., Asefa, T., & Guo, H. (2016) "Cu and Cu-based nanoparticles: synthesis and applications in catalysis." *Chemical Reviews*, Vol. 116, No. 6, pp. 3722-3811.
- [9]. Iakovidis, I., Delimaris, I., & Piperakis, S.M. (2011) "Copper and its complexes in medicine: a biochemical approach." *Molecular Biology International*, Vol. 2011, Article ID 593667.
- [10]. Pratap, R., & Ram, V.J. (2014) "Natural and synthetic chromenes, fused chromenes, and versatility of dihydrobenzo [h] chromenes in organic synthesis." *Chemical Reviews*, Vol. 114, No. 20, pp. 10476-10526.
- [11]. Kostova, I., Petrova, T., & Manolov, I. (2011) "Coumarins as antioxidants." *Current Medicinal Chemistry*, Vol. 18, No. 25, pp. 3929-3951.
- [12]. Indulatha, V., Gopal, N., & Jayakar, B. (2011) "Anti-inflammatory activity of newly synthesised N-[4'-Oxo-2'-(substituted aryl/heteryl)-thiazolidin-3'-yl]-3-carboxamido-2H-chromen-2-one derivatives." *International Journal of ChemTech Research*, Vol. 3, No. 4, pp. 1930-1937.
- [13]. Najmanova, I., Moravcikova, L., & Kunes, J. (2015) "Cardiovascular effects of coumarins besides their antioxidant activity." *Current Topics in Medicinal Chemistry*, Vol. 15, No. 9, pp. 830-849.
- [14]. Ajani, O.O., & Nwinyi, O.C. (2010) "Microwave- assisted synthesis and evaluation of antimicrobial activity of 3- {3- (s- aryl and s- heteroaromatic acryloyl)- 2H- chromen- 2- one derivatives." *Journal of Heterocyclic Chemistry*, Vol. 47, No. 1, pp. 179-187.
- [15]. Al-Ayed, A.S. (2011) "Synthesis, spectroscopy and electrochemistry of new 3-(5-aryl-4, 5-dihydro-1H-pyrazol-3-yl)-4-hydroxy-2H-chromene-2-one 4, 5 as a novel class of potential antibacterial and antioxidant derivatives." *International Journal of Organic Chemistry*, Vol. 1, No. 3, pp. 87.
- [16]. Sánchez-Recillas, A., & Ramírez, R. (2014) "Semisynthesis, ex vivo evaluation, and SAR studies of coumarin derivatives as potential antiasthmatic drugs." *European Journal of Medicinal Chemistry*, Vol. 77, pp. 400-408.
- [17]. Benazzouz, A., Zouhair, R., & Benakhla, K. (2015) "A facile synthesis of new coumarin-3, 4-dihydropyrimidin-2 (1H)-ones/thiones dyads." *Tetrahedron*, Vol. 71, No. 23, pp. 3890-3894.
- [18]. Emami, S., & Dadashpour, S. (2015) "Current developments of coumarin-based anti-cancer agents in medicinal chemistry." *European Journal of Medicinal Chemistry*, Vol. 102, pp. 611-630.
- [19]. Kharadi, G. (2011) "Antitubercular and fluorescence studies of copper (II) complexes with quinolone family member, ciprofloxacin." *Spectrochimica Acta Part A: Molecular and Biomolecular Spectroscopy*, Vol. 79, No. 5, pp. 898-903.
- [20]. Sawant, V., Patil, S., & Apte, S. (2009) "Synthesis, structural characterization, thermal and electrochemical studies of mixed ligand Cu (II) complexes containing 2-phenyl-3-(benzylamino)-1, 2-dihydroquinazoline-4-(3H)-one and bidentate N-donor ligands." *Spectrochimica Acta Part A: Molecular and Biomolecular Spectroscopy*, Vol. 74, No. 5, pp. 1100-1106.
- [21]. Hricovíni, M., Asher, J.R., & Hricovíni, M. (2022) "A study of the photochemical behaviour and relaxation mechanisms of anti-syn isomerisation around quinazolinone-N-N [double bond, length as m-dash] bonds." *RSC Advances*, Vol. 12, No. 42, pp. 27442-27452.
- [22]. Kharadi, G., & Patel, K. (2009) "Antibacterial, spectral and thermal aspects of drug-based Cu (II) mixed ligand complexes." *Applied Organometallic Chemistry*, Vol. 23, No. 10, pp. 391-397.
- [23]. Hathaway, B., Thorpe, J., & Hall, A. (1981) "The stereochemistry and electronic properties of fluxional six-coordinate copper (II) complexes." *Coordination Chemistry Reviews*, Vol. 36, No. 3, pp. 267-324.
- [24]. Yusuf, M.O. (2023) "Bond characterization in cementitious material binders using Fourier-transform infrared spectroscopy." *Applied Sciences*, Vol. 13, No. 5, pp. 3353.
- [25]. Bannov, A.G., Popov, M.V., & Kurmashov, P.B. (2020) "Thermal analysis of carbon nanomaterials: advantages and problems of interpretation." *Journal of Thermal Analysis and Calorimetry*, Vol. 142, No. 1, pp. 349-370.