Synthesis, characterization and antimicrobial activity of copper (II) with 2-chloroquinoline-3-carbaldehyde thiosemicarbazide {1-((2-chloroquinolin-3-yl)methylene) thiosemicarbazide (2-Chloro-QAT)}

Shobha Sakharam Borhade
Department of Chemistry, S.M.B.S.T College Arts, Science and Commerce Sangamner, University of Pune Sangamner, Ahmednagar, (MH) - India

Abstract
Synthesis of 2-Chloroquinoline-3-carbaldehyde Thiosemicarbazide {1-(2-Chloroquinolin-3-yl)methylene} Thiosemicarbazide (2-Chloro-QAT), Melting point Elemental analysis, XRD, Effect of diverse ion and Antimicrobial Activity are studied. A simple, sensitive and specific spectrophotometric method for the determination of Cu (II) is developed based on the colour reaction between Copper (II) and 2-Chloroquinoline-3-carbaldehyde thiosemicarbazide {1-(2-Chloroquinolin-3-yl)methylene} thiosemicarbazide (2-Chloro-QAT). The optimum condition for complete colour development has been established by studying parameters like effect of medium, reagent concentration, time period. Stability constant, Dissociation constant and Change in free energy of the complex are determined. Composition of metal and ligand has been determined by Job’s variation and mole ratio method. Application of this 2-Chloro-QAT for antimicrobial activity has been performed.

Key-Words: Copper (II), 2-Chloroquinoline-3-carbaldehyde, Thiosemicarbazone (2-Chloro-QAT), Spectrophotometry, Antimicrobial Activities

Introduction
The abundance of copper is 70 parts per million in the igneous (Volcanic) rocks of the earth’s crust. Copper is not abundant but it is widely distributed as metal in sulfides, arsenides, chloride and carbonates. The commonest mineral is chalcopyrite CuFeS₂. Metal complexes of some peptide derivative complex formation of copper (II) with N-benzensulfonamides of some dipeptides have been reported [1]. Detection of Copper (II) & Cadmium (II) without cyanide in qualitative analysis have been done by Chakraborty [2]. Equilibrium study on the mixed ligand complex formation of copper (II) with boric acid & (N, N) bidentate ligands have been studied by Mukherjee [3]. The complex of copper (II), nickel (II) & cobalt (II) with schiffs base derived from 2-thiophenecarboxaldehyde & 2-monopropanolamine have been prepared [4].

Synthesis, structural & electrical studies of cobalt, nickel, copper & zinc (II) polymeric complexes have been studied [8]. Synthesis & antibacterial activity of copper (II) complexes with 2-(Thiomethyl-2'-benzimidazolyl)-1,3-diazaeyclopentadec-Δ'-ene have been studied [9]. Cheating resin containing s-bonded dithizone for the separation of copper (II) was studied by Shah [10]. Potentiometric study of copper (II) complexation with two high molecular weight poly (acrylic acids) have been done [11]. Potentiometric studies of copper (II) with 5-aryl-1-phenyl-4-pentene-1,3-diones have been done by Venugopalan [12].

Copper (II) compound has a distorted octahedral geometry. Studies on complexes of copper, cobalt, nickel, zinc & cadmium with Schiff base derived from 3-aminobenzofuran and salicyaldehyde have been studied by Kriza [5]. Studies on the solution equilibria involved in some copper (II) & zinc (II) Schiff base complex systems have been carried out [6]. Complexation of nickel, cobalt & copper (II) with L-3,4-dihydroxy-phenylalanine kinetic studies have been reported [7].

* Corresponding Author
E-mail: borhadesobhaga@gmail.com
Mob.: +919960872151

* Corresponding Author
E-mail: borhadesobhaga@gmail.com
Mob.: +919960872151
of copper (II) with L-α-Amino-δ-guanidinovaleric acid have been studied by Malhotra [13]. Patnaik [14] have studied the complex formation of copper with D (+) - Saccharic acid. Synthesis and characterization of copper complexes of morin have been studied [15]. The simultaneous determination of copper in human plasma & urine by inductively coupled plasma mass spectrometry (ICP-MS) is discussed [16]. Copper (II) complexes of Schiff bases with N or S donor sites have been studied [17]. Thiosemicarbazones usually react as chelating ligands with transition metal ions by bonding through sulphur and nitrogen atoms [18]. Thiosemicarbazones have been frequently used for spectrophotometric determination of inorganic ions and their analytical potentials have been reviewed [19, 20]. Thiosemicarbazone are important organic analytical reagents for the determination of metal ions in microgram quantities. They form coloured complexex with many metal ions and act as good chelating agents. In addition to the analytical utility [21, 22] Metal complexes formed with these reagents are of great medicinal value in the treatment of diseases like influenza [23], protozoa [24], smallpox [25]. Tumors [26] and pesticides [27]. A large number of thiosemicarbazides have been found to posses good antibacterial [28], antifungal [29], herbicidal [30], antitubercular [31, 32] activities. The pharmacological importance of metal complex with heterocyclic thiosemicarbazones [33].

Methodology
An Elico UV-visible spectrophotometer model UV-SL-164 equipped with 1 cm quartz cell used for spectrophotometric measurements. An Elico pH meter LI-610 is used for the pH measurements. The chemicals used are of AR grade. X-RD was taken on PW 3710 diffractometer using CuKα radiation has been taken on the instrument BRUKER AC 300F. Elemental analysis and antimicrobial activity was done in Laboratory approved by Central Government for AGMARK.

Synthesis of 2-Chloro-QAT
2-Chloroquinoline-3-carbaldehyde thiosemicarbazide (1-((2-Chloroquinolin-3-yl)methylene) thiosemicarbazide (2-Chloro-QAT) is prepared by taking equimolar quantity of 2-Chloroquinoline-3-Carbaldehyde & thiosemicarbazide in methanol and reflux 74 hours or more. It was allowed hydroxide to stand at room temp until the yellowish crystals were found.

The crude product is crystallized in methanol. The recrystallized product has melting point is 227°C and molecular weight by formula is 252.5.

Characterization of 2-Chloro-QAT
Absorption Spectra of 2-Chloro-QAT was recorded against a blank solution containing buffer (pH=2) and is shown in fig 1. Absorption spectra were recorded in the wave length range 250-570 nm. The complex shows an absorption maximum at 285 nm. At 285 nm wavelength the molar absorptivity of 2-Chloro-QAT is 0.9750 x 10^3 L.mol⁻¹.cm⁻¹.

Elemental analysis of 2-Chloro-QAT
The elemental analysis of 2-Chloro-QAT was done in the Laboratory approved by Central Government through AGMARK. It shows the result of elemental analysis in Table 1.

X-RD of 2-Chloro-QAT
X-RD spectra of 2-Chloro-QAT was taken on PW 1710 diffractometer using CuKα radiation (Wavelength 1.54060 to 1.54438 Å). The X-RD diffraction of 2-Chloro-QAT was recorded at angle 2Ø from 20.000-80.000. The data of X-ray diffraction of 2-Chloro-QAT were presented in Table 2. And X-ray spectrum in fig.2. For the determination of structure Hesse-Lipson procedure is used [34].

Antimicrobial Activity of 2-Chloro-QAT
Antimicrobial Activity of 2-Chloro-QAT has been done in the Laboratory approved by Central Government through AGMARK. The results are noted in Table 3.

Effect of Reagent concentration
Effect of Reagent concentration was studied by taking varying amount of reagent and fixed amount of Cu (II). Optimum pH of solution was maintained 1.988. It was noted that 0.13 ml reagent is sufficient for complete colour development. However by adding excess of reagent there is no substantial change in the absorbance value. Effect of reagent shown in fig. No.3.
Validity of Beer’s Law
For the study of Beer’s law the solutions were prepared which contained different amounts of Cu (II), same amount of 2-chloro-QAT and 1 ml of pH 2. It indicates that the validity of Beer’s law obeys up to 10 ppm is shown in fig No. 4.

Composition of Complex
The composition of the Cu (II)-2-chloro-QAT complexes is found to be 1:1. It was determined by studying Job’s method. The ratio of metal ion to ligand molecule in the coloured complex was found to be 1:1. Composition of complex shown in fig No. 5.

Physico-chemical Characteristic of Cu (III)-2-chloro-QAT
Physico-chemical and Analytical Characteristic of Cu (II)-2-chloro-QAT was studied and given in Table 4, and Tolerance limit of diverse ions in the determination of 2-Chloro-QAT shown in Table No. 5.

Results and Discussion
The Cu (II)-2-ChloroQAT shows an absorption maximum at 285 nm. At 285 nm wavelength the molar absorptivity of 2-Chloro-QAT is 0.9750 x 10^4 L mol^-1 cm^-1. The 0.13 ml reagent is sufficient for complete colour development. And the Beer’s law obeys up to 10 ppm. The ratio of metal ion to ligand molecule in the coloured complex was found to be 1:1. The stability constant, Dissociation constant and change in free energy are 3.3400 x 10^-4 and -11623.48 Cal /mole respectively. The Sandell’s Sensitivity is 0.003321 µg/cm². The XRD- of complex shown the structure.

References

Table 1: Elemental analysis of 2-chloro-QAT

<table>
<thead>
<tr>
<th>S/No.</th>
<th>Chemical Analysis</th>
<th>Percentage Found</th>
<th>Percentage Expected</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Carbon</td>
<td>48.38</td>
<td>47.52</td>
</tr>
<tr>
<td>2</td>
<td>Hydrogen</td>
<td>04.02</td>
<td>03.56</td>
</tr>
<tr>
<td>3</td>
<td>Sulphur</td>
<td>13.24</td>
<td>12.67</td>
</tr>
<tr>
<td>4</td>
<td>Nitrogen</td>
<td>22.60</td>
<td>22.18</td>
</tr>
<tr>
<td>5</td>
<td>Chlorine</td>
<td>14.33</td>
<td>14.06</td>
</tr>
</tbody>
</table>

Table 2: XRD for 2-chloro-QAT (Powder method)

<table>
<thead>
<tr>
<th>S/No.</th>
<th>2θ</th>
<th>hkl</th>
<th>Sin² θ Observed</th>
<th>Sin² θ Calculated</th>
<th>d (Å) Observed</th>
<th>d (Å) Calculated</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>25.695</td>
<td>211</td>
<td>0.04960</td>
<td>0.05162</td>
<td>3.4556</td>
<td>3.9556</td>
</tr>
<tr>
<td>2</td>
<td>28.350</td>
<td>211</td>
<td>0.04653</td>
<td>0.05068</td>
<td>3.8159</td>
<td>4.0556</td>
</tr>
<tr>
<td>3</td>
<td>30.950</td>
<td>220</td>
<td>0.07102</td>
<td>0.07998</td>
<td>2.8901</td>
<td>2.9102</td>
</tr>
<tr>
<td>4</td>
<td>35.500</td>
<td>222</td>
<td>0.08065</td>
<td>0.07225</td>
<td>2.4279</td>
<td>2.3093</td>
</tr>
<tr>
<td>5</td>
<td>44.730</td>
<td>210</td>
<td>0.03950</td>
<td>0.03950</td>
<td>4.6603</td>
<td>3.8753</td>
</tr>
<tr>
<td>6</td>
<td>50.775</td>
<td>211</td>
<td>0.05980</td>
<td>0.04780</td>
<td>4.4828</td>
<td>4.5220</td>
</tr>
<tr>
<td>7</td>
<td>53.330</td>
<td>110</td>
<td>0.06321</td>
<td>0.06821</td>
<td>3.8984</td>
<td>3.8779</td>
</tr>
<tr>
<td>8</td>
<td>72.520</td>
<td>111</td>
<td>0.07881</td>
<td>0.07328</td>
<td>3.9806</td>
<td>3.9857</td>
</tr>
<tr>
<td>9</td>
<td>74.720</td>
<td>111</td>
<td>0.08341</td>
<td>0.08333</td>
<td>4.0525</td>
<td>4.9765</td>
</tr>
</tbody>
</table>

\[ \begin{aligned}
  a &= 9.3682 \\
  b &= 6.8990 \\
  c &= 8.2506
\end{aligned} \]
Table 3: Antimicrobial activity of 2-Chloro-QAT

<table>
<thead>
<tr>
<th>S/No.</th>
<th>Microorganism</th>
<th>Activity</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Klebsiella Pneumoniae</td>
<td>Nil</td>
</tr>
<tr>
<td>2</td>
<td>Vibriae Cholerase</td>
<td>Nil</td>
</tr>
<tr>
<td>3</td>
<td>Bacillus Megaterium</td>
<td>Nil</td>
</tr>
<tr>
<td>4</td>
<td>Salmonella typhi</td>
<td>Nil</td>
</tr>
<tr>
<td>5</td>
<td>Shigella Flexneri</td>
<td>Nil</td>
</tr>
</tbody>
</table>

Table No. 4. Physico-chemical and analytical characteristic of 2-chloro-QAT

<table>
<thead>
<tr>
<th>S/No.</th>
<th>Characteristics</th>
<th>Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Absorption Spectra</td>
<td>285 nm</td>
</tr>
<tr>
<td>2</td>
<td>Molar absorptivity</td>
<td>0.9750 x 10⁻³ Lit. mol⁻¹. cm⁻¹</td>
</tr>
<tr>
<td>3</td>
<td>pH range ( optimum )</td>
<td>2.0</td>
</tr>
<tr>
<td>4</td>
<td>Reagent required for maximum complexation</td>
<td>0.13ml</td>
</tr>
<tr>
<td>5</td>
<td>pKa</td>
<td>6.587 x 10⁻⁸</td>
</tr>
<tr>
<td>6</td>
<td>Beer’s law validity range ( ppm)</td>
<td>10 ppm</td>
</tr>
<tr>
<td>7</td>
<td>Composition of complex ( M : L )</td>
<td>1:1</td>
</tr>
<tr>
<td>8</td>
<td>Stability Constant</td>
<td>3.3400 x 10⁻⁸</td>
</tr>
<tr>
<td>9</td>
<td>Dissociation Constant</td>
<td>2.994 x 10⁻⁹</td>
</tr>
<tr>
<td>10</td>
<td>Change in free energy</td>
<td>-11623.48 Cal /mole</td>
</tr>
<tr>
<td>11</td>
<td>Sandell’s Sensitivity ( µg/cm²)</td>
<td>0.003321 µg /cm²</td>
</tr>
</tbody>
</table>

Table 5: Tolerance limit of diverse ions in the determination of 2-chloro-QAT

<table>
<thead>
<tr>
<th>S/No.</th>
<th>Metal ion</th>
<th>Salt</th>
<th>Interference</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Mg (II)</td>
<td>MgSO₄</td>
<td>76</td>
</tr>
<tr>
<td>2</td>
<td>Au (II)</td>
<td>CuSO₄</td>
<td>98</td>
</tr>
<tr>
<td>3</td>
<td>Cd (II)</td>
<td>CdCl₂</td>
<td>54</td>
</tr>
<tr>
<td>4</td>
<td>Mn (II)</td>
<td>MnCl₂</td>
<td>27</td>
</tr>
<tr>
<td>5</td>
<td>Co (II)</td>
<td>CoSO₄</td>
<td>Interferes</td>
</tr>
<tr>
<td>6</td>
<td>Ce (IV)</td>
<td>Ce(SO₄)₂</td>
<td>43</td>
</tr>
<tr>
<td>7</td>
<td>Ba (II)</td>
<td>BaCl₂</td>
<td>42</td>
</tr>
<tr>
<td>8</td>
<td>Cr (III)</td>
<td>K₂Cr₂O₇</td>
<td>06</td>
</tr>
<tr>
<td>9</td>
<td>Hg (II)</td>
<td>HgCl₂</td>
<td>09</td>
</tr>
<tr>
<td>10</td>
<td>Ti (V)</td>
<td>K-titanyl oxalate</td>
<td>18</td>
</tr>
<tr>
<td>11</td>
<td>Ni (II)</td>
<td>NiCl₂</td>
<td>14</td>
</tr>
<tr>
<td>12</td>
<td>Sn (II)</td>
<td>SnCl₂</td>
<td>23</td>
</tr>
<tr>
<td>13</td>
<td>Pb (II)</td>
<td>PbSO₄</td>
<td>54</td>
</tr>
<tr>
<td>14</td>
<td>V (v)</td>
<td>V₂O₅</td>
<td>Interferes</td>
</tr>
<tr>
<td>15</td>
<td>Zn (II)</td>
<td>ZnSO₄</td>
<td>36</td>
</tr>
<tr>
<td>16</td>
<td>Al (III)</td>
<td>AlCl₃</td>
<td>Interferes</td>
</tr>
<tr>
<td>17</td>
<td>Pd (II)</td>
<td>PdCl₂</td>
<td>Interferes</td>
</tr>
<tr>
<td>18</td>
<td>Ni (II)</td>
<td>NiCl₂</td>
<td>23</td>
</tr>
</tbody>
</table>
Fig. 1: Absorption spectra of 2-chloro-QAT

Fig. 2: X-RD of 2-chloro-QAT

Fig. 3: Effect of Reagent concentration

Fig. 4: Validity of Beer’s Law

Fig. 5: Composition of Complex