CU (II) MEDIATED SYNTHESIS OF 2-IMINOBENZOPYRAN ANALOGUES VIA SOLVENT FREE GREEN CHEMISTRY TECHNIQUE AND THEIR LARVICIDAL, ANTIFEEDANT, AND MOLECULAR DOCKING STUDIES

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\textbf{ABSTRACT}

To synthesize novel benzopyran analogues via solvent free green chemistry technique by using CuCl\textsubscript{2}.2H\textsubscript{2}O as a catalyst and investigate for their larvicidal, antifeedant and molecular docking studies. The compounds (1a-c) were synthesized and characterized by FT-IR, \textsuperscript{1}H NMR, \textsuperscript{13}C NMR, mass spectral and elemental analyses. Larvicidal activity was assessed using 2\textsuperscript{nd} instar mosquito larvae of \textit{Culexquinquefasciatus}. Among the synthesized compounds (1a-c) the compound 1b was extremely active with the LD\textsubscript{50} value of 54.64 µg/mL. From the synthesized compounds (1a-c) the compounds 1a, and 1c was shows moderate activity against \textit{Culexquinquefasciatus} with the LD\textsubscript{50} value of 86.20, and 66.66µg /mL than the control Bergaptan with the LD\textsubscript{50} value of 62.23µg/mL respectively. Marine fishes of \textit{Oreochromimossambicus} was chosen as a target organism for antifeedant activity. Among the synthesized compounds (1a-c) the compound 1a was less toxic with 66% mortality at 100 µg/mL. The compound 1a was extremely active with the LD\textsubscript{50} value of 57.14 µg/mL than other compounds. The molecular docking studies also supports that compound 1b (Binding energy: -7.6 kcal/mol) was the potent compound than control Bergaptan(Binding energy: -7.3 kcal/mol) in mosquito larvicidal screening.

\textbf{KEYWORDS:} Antifeedant activity, Benzopyran, CuCl\textsubscript{2} catalysis, Grindstone method, Larvicidal activity, Molecular docking.

\textbf{Introduction}

Coumarins are significant group of benzopyran compounds extensively dispersed in nature and also fashioned synthetically for commercial purposes like pharmaceuticals, agrochemicals, fragrances, cosmetics, food additives, and optical brightening agents\textsuperscript{[1]}. Coumarin and its derivatives were synthesized by numerous approaches, which comprises Pechmann reaction\textsuperscript{[2]}, Knoevenagal reaction\textsuperscript{[3]}, Perkin reaction\textsuperscript{[4]}, Wittig reaction\textsuperscript{[5]}, Reformatsky reaction\textsuperscript{[6]}, Michael condensation\textsuperscript{[7]}, and Claisen rearrangement\textsuperscript{[8]}. From these reactions, Pechmann reaction is the most commonly used method for the synthesis of coumarins meanwhile it incomes from simple starting materials and also gives good yields. Coumarins can be synthesized by using several catalysts such as H\textsubscript{2}SO\textsubscript{4}\textsuperscript{[9]}, trifluoroacetic acid\textsuperscript{[10]}, AlCl\textsubscript{3}\textsuperscript{[11]}, W/ZrO\textsubscript{2}\textsuperscript{[12]}, POCl\textsubscript{3}\textsuperscript{[13]}, Nafion-H catalyst\textsuperscript{[14]}, montmorillonite clay\textsuperscript{[15]}, solid acid catalysts\textsuperscript{[16]}, and chloroaluminate ionic liquid\textsuperscript{[17]}. Coumarin derivatives having a broad scale of biological activities like anti-inflammatory\textsuperscript{[18]}, anti-HIV\textsuperscript{[19]}, antibacterial\textsuperscript{[20]}, anticoagulant\textsuperscript{[21]}, antifungal\textsuperscript{[22]}, and antitumor activity\textsuperscript{[24,25]}. Some important bio-active coumarin analogues were shown in Figure 1. Olfaction plays a key role in organisms and tangled in major activities such as food detection, host-seeking, reproduction, and also identification of predators\textsuperscript{[26]}. OBP (odorant-binding proteins) transport the odorants to olfactory receptors to induce signal transduction\textsuperscript{[27,28]}. Keep this in mind, we have choose OBP of \textit{Culexquinquefasciatus} as a target protein for molecular docking studies. Based on the above literature observation, we are focused on the synthesis of 2-iminobenzopyran derivatives via Schiff base reaction by employing novel green chemistry technique (grindstone method) using simple,
inexpensive, commercially available, CuCl$_2$:2H$_2$O as a catalyst and inspected their larvicidal, antifeedant and molecular docking studies.

![Bergaptan](image1) ![Psoralen](image2) ![5-Ethoxy-chromen-2-one](image3) ![Gernayloxypsoralen](image4) ![Imperatorin](image5) ![Heracelenin](image6)

**Fig. 1.** Biologically active Natural benzopyran compounds.

**Materials and Methods**

**Chemistry**
Both of the chemicals were bought from Sigma-Aldrich, Merck, and utilized without extra washing. Pre-use solvents is purified and dried. For analytical TLC, Merck's silica gel plates (pre-coated) with the use of fluorescent indicator. For TLC, Ethyl acetate-hexane was utilized as an eluting solvent. Melting points were registered and uncorrected in open capillary tubes. On a Shimadzu 8201pc spectrometer was used to take the FT-IR spectra at (4000-400 cm$^{-1}$). Bruker DRX spectrometer was utilized to acquire the $^1$H and $^{13}$C NMR spectra at 300, 75 MHz. Chemical changes of the $^1$H and $^{13}$C NMR spectra in the downfield of tetramethylsilane is represented in ppm.

**Preparation of 7-Hydroxy-4-methyl-chromen-2-one (I).**
A solution comprising 1.1 gm resorcinol and 1.3 mL ethyl acetoacetate (EAA) was applied drop wise with stirring to 10 mL conc. H$_2$SO$_4$. To preserve the temperature that should not increase above 10 °C, the reaction mixture was maintained in the ice bath. Then the complete addition mixture reaction was held for 24 hours at room temperature and then pumped into the ice and water mixture with intense stirring. The precipitated was drained off and cleaned with cold water, and dried to have the crude stable mass under decreased strain. For the neutralisation of the material, 5 percent of sodium hydroxide solution was applied to the crude and it was fully dissolved in it. After neutralisation, a proportion of hydrochloric acid solution is applied to regenerate the solid mass in its pure condition. To produce a pure oil, 95% ethanol is recrystallized.

**7-Hydroxy-4-methyl-chromen-2-one (I).**
White solid; mw: 176.17; mp 185°C; IR(cm$^{-1}$): 3787.3 (OH), 3074.57 (Ph-CHstr), 3090.2 (C=C), 2923.5 (CH), 1612.5 (C=O), 1270.5 (C-O-C); $^1$H NMR (300MHz, DMSO-d$_6$): δ 10.56 (1H, s, OH), 7.58 (1H, d, $J$=6.21Hz, Phenyl), 6.80 (1H, dd, $J$=7.33Hz, $J$=7.37Hz Ph), 6.70 (1H, d, $J$=7.35Hz Ph), 6.12 (1H, d, - CH), 2.36 (3H, s, -CH$_3$); $^{13}$C NMR(300MHz, DMSO-d$_6$): 161.8 (1C, C=O), 160.3 (1C, -C=CH$_3$), 102.19 (1C, -C=C-), 110.28, 112.04, 112.88, 126.65, 153.58, 154.86 (6C, Ar ring), 18.14 (1C, -CH$_3$); Elemental analysis: Calculated for C$_{10}$H$_8$O$_3$: C, 68.18; H, 4.58; %. Found: C, 68.17; H, 4.60; %

**Preparation of 2-((2-aminoethyl)imino)-4-methyl-2H-chromen-7-ol (1a).**
The compounds 7-hydroxy-4-methyl coumarin (0.001mol, 0.18g), ethylenediamine (0.002mol, 0.12mL), CuCl$_2$:2H$_2$O (0.002mol, 0.34g), are mixed together in a mortar. To this few drops of conc.HCl was added and mixed well. TLC technique was utilized to monitor the reaction progress. The precipitate was washed with excess of ice-cold water filtered and dried. The product was recrystallized in ethanol to get pure product.

**2-((2-aminoethyl)imino)-4-methyl-2H-chromen-7-ol (1a)**
Dust White solid; mw: 218.25; mp:110°C; IR(cm\(^{-1}\)): 3883.8 (OH), 3305 (-NH\(_2\)), 2928 (CH), 2857.8 (C=C), 1669.5 (C=O), 1270.5 (C-O-C); \(^1\)H NMR (300MHz, DMSO-\(d_6\)) \(\delta\): 10.56 (1H, s, OH), 7.60 (1H, d, \(J=6.21\)Hz, Phenyl), 6.81 (1H, d, \(J=7.37\)Hz Ph), 6.70 (2H, s, NH\(_2\)), 2.72 (2H, m, N-CH\(_2\)),2.50 (1H, s, Ph), 2.36 (3H, s, -CH\(_3\)), 1.75 (2H, m, -CH\(_2\)); \(^1\)C NMR(300MHz, DMSO-\(d_6\)): 161.28 (1C, C-CH\(_3\)), 163.00 (1C, C=CN), 154.78, 153.55, 126.60, 112.82, 111.98, 110.20 (6C, Ar ring), 102.12 (1C, C=), 48.12 (1C, CH\(_2\)-N), 43.71 (1C, CH\(_2\)-NH), 18.42 (1C, -CH\(_3\)).

**Preparation of 2-(2-((2-hydroxyethyl)amino)(ethyl)limino)-4-methyl-2H-chromen-7-ol (1b).**

The compounds 7-hydroxy-4-methyl coumarin (0.001mol, 0.18g), aminoethylethanolamine (0.002mol, 0.20mL), CuCl\(_2\).2H\(_2\)O (0.002mol, 0.34g), are mixed together in a mortar. To this few drops of con.HCl was added and mixed well. TLC technique was utilized to monitor the reaction progress. The precipitate was washed with excess of ice-cold water filtered and dried. The product was recrystallized in ethanol to get pure product.

2-(2-((2-hydroxyethyl)amino)(ethyl)limino)-4-methyl-2H-chromen-7-ol (1b)

Pale brown solid; mw: 262.30; mp:217°C; IR(cm\(^{-1}\)): 3831.2 (OH), 3498 (NH\(_2\)), 2919 (CH), 1603.7 (C=O), 1279.2 (C-O-C); \(^1\)H NMR (300MHz, DMSO-\(d_6\)) \(\delta\): 10.18 (1H, s, OH), 8.65 (1H, s, OH), 7.62 (1H, d, \(J=6.21\)Hz, Phenyl), 6.84 (1H, d, \(J=7.37\)Hz Ph), 6.74 (1H, s, NH), 3.47 (2H, m, -CH\(_2\)), 2.74 (2H, m, -CH\(_2\)),2.60 (2H, m, -CH\(_2\)), 2.52 (1H, s, Ph), 2.38 (3H, s, -CH\(_3\)), 1.61 (2H, m, -CH\(_2\)); \(^1\)C NMR(300MHz, DMSO-\(d_6\)): 163.01 (1C, C=CN), 160.30 (1C, C-CH\(_3\)), 154.80, 153.57, 126.62, 112.84, 111.99, 110.22 (6C, Ar ring), 102.14 (1C, -C=), 61.50 (1C, CH\(_2\)-OH), 51.92 (1C, CH\(_2\)-NH), 50.90 (1C, CH\(_2\)-NH), 45.92 (1C, CH\(_2\)-N), 18.42 (1C, -CH\(_3\)); Elemental analysis: Calculated. For C\(_{14}\)H\(_{16}\)N\(_2\)O\(_2\): C, 64.10; H, 6.92; N, 10.68%. Found: C, 64.12; H, 6.90; N, 10.70%.

**Preparation of 2-(2-((2-aminoethyl)amino)(ethyl)limino)-4-methyl-2H-chromen-7-ol (1c).**

The compounds 7-hydroxy-4-methyl coumarin (0.001mol, 0.18g), N-(2-aminoethyl)ethane-1,2-diamine (0.002mol, 0.20mL), CuCl\(_2\).2H\(_2\)O (0.002mol, 0.34g), are mixed together in a mortar. To this few drops of con.HCl was added and mixed well. TLC technique was utilized to monitor the reaction progress. The precipitate was washed with excess of ice-cold water filtered and dried. The product was recrystallized in ethanol to get pure product.

2-(2-((2-aminoethyl)amino)(ethyl)limino)-4-methyl-2H-chromen-7-ol (1c)

Yellow solid; mw: 261.32; mp:240°C; IR(cm\(^{-1}\)): IR(cm\(^{-1}\)): 3838.3 (OH), 3305 (-NH\(_2\)), 2928 (CH), 1599.3 (C=C), 1384.5 (C-O-C); \(^1\)H NMR (300MHz, DMSO-\(d_6\)) \(\delta\): 10.60 (1H, s, OH), 7.64 (2H, d, \(J=6.21\)Hz, Phenyl), 6.86 (2H, d, \(J=7.37\)Hz Ph), 6.78 (2H, s, NH\(_2\)), 3.49 (2H, m, -CH\(_2\)), 2.76 (2H, m, -CH\(_2\)),2.62 (2H, m, -CH\(_2\)), 2.54 (1H, s, Ph), 2.38 (3H, s, -CH\(_3\)), 1.62 (2H, m, -CH\(_2\)); \(^1\)C NMR(300MHz, DMSO-\(d_6\)): 163.04 (1C, C=CN), 160.32 (1C, C-CH\(_3\)), 154.82, 153.59, 126.64, 112.86, 111.97, 110.24 (6C, Ar ring), 102.16 (1C, C=), 51.94 (1C, CH\(_2\)-NH), 50.92 (1C, CH\(_2\)-NH), 45.94 (1C, CH\(_2\)-N), 43.74 (1C, CH\(_2\)-NH), 18.44 (1C, -CH\(_3\)); Elemental analysis: Calculated. For C\(_{14}\)H\(_{16}\)N\(_2\)O\(_2\): C, 64.35; H, 7.33; N, 16.08%. Found: C, 64.32; H, 7.35; N, 16.10%.

**Larvicidal activity**

On a dead/alive basis, judgments were made. Assessment is based on a 0-100 percentage scale, which is equivalent to 0 for no operation and 100 for absolute kill. The bioassay was replicated three times as well as an average of these replicates is the product of bioactivity. The results are comparable with the Switlenocoumarin B positive regulation. Using probit analysis, the LD50 values of certain active title compounds were measured and the findings were examined by using programme SPSS v16.

**Larvicidal Activity against Mosquito Culexquinquefasciatus**

The larvicidal behaviour of compounds (1a-1c) were tested by the water immersion system under conditions of (27 ±2) °C, 10:14 photoperiod (light: dark) and 50-70 percent relative humidity at the preliminary test concentration of 100 and 50 µg/mL toward the fourth-instar
Culexquinquefasciatus. After 24 hours of care, all test beakers holding 20 Culexquinquefasciatus were tested. The findings were reported in terms of overall mortality percentage.

**Antifeedant activity**

For the assessment of ichthyotoxic ability, fishes (1.5–2.0 cm) of marine acclimatised Oreochromis mossambicus were utilized. In control and investigational beakers, ten fishes were added, each comprising one litre of salt water and the chosen compound concentrations (1a-1c). Immediate reflex shifts and mortality were consistently detected for the first 6 hours, and then for the next 12 hours at 1-hour intervals. The amount of dead and live fish was counted after 24 hours of exposure.

**Molecular Docking**

Compounds (1a-1c) and mosquito odorant-binding protein associations and binding modes were tested by molecular docking utilising AutoDockVina 1.1.2\(^{[29]}\). The crystal structure was taken from the Protein Data Bank (http://www.rcsb.org) of the mosquito odorant-binding protein (PDB ID: 3OGN). Through ChemDraw Ultra 12.0 and Chem3D Pro 12.0 program packages, the 3D assemblies of compounds (1a-1c) were calculated. The AutoDockVina input files were generated via AutoDock Tools 1.5.6 programme. The 3OGN protein quest grid was placed at centre x, y, z: 18.681, 49.660, 11.409 with dimensions: size x, y, z: 22, 20, 22 at intervals of 1.0 Å. The meaning of exhaustiveness has been set at 8. For Vina docking, other constraints remained fixed to normal. The best-scoring compound was the compound with the least binding affinity, and the findings were visually evaluated using tools from Discovery Studio 2019.

![Scheme 1. Synthesis of 7-hydroxy-4-methyl coumarin.](image-url)
Results and discussion
The compound 1 was equipped conferring to the synthesis categorizations demonstrated in scheme 1. The compounds (1a-1c) were primed conferring to the synthesis categorizations demonstrated in scheme 2. Compound 1 was synthesised by Beckmann condensation reaction with using resorcinol reacted with Ethyl acetoacetate in con.H$_2$SO$_4$ medium (Scheme 1). The compound 1a was synthesised by compound 1 reacted with various amine compounds and CuCl$_2$.2H$_2$O by Schiff base method (Scheme 2). The compounds were confirmed through the IR, $^1$H NMR and $^{13}$C NMR spectra recording. The physiochemical characterization of compounds (1a-1c) were represented in Table 1.

The IR spectrum of compound 1 conformed by important characterization bands at 3787.3, 3090.2, 1612.5 and 1270.5 cm$^{-1}$ conforming the OH, C=C, C=O and C-O-C groups individually.

The $^1$H NMR spectra of compound 1 was confirmed the protons peaks appeared at $\delta$10.56, 6.12 and 2.36 corresponding to OH, CH and CH$_3$ protons respectively. The$^{13}$C NMR spectra of compound 1 was confirmed the carbon peaks appeared at $\delta$161.8, 160.3 and 18.4 agreeing to carbons C=O, C=N and CH$_3$ individually.

The IR spectrum of compound 1a conformed by important characterization bands at 3883.8, 3305, 1669.5 and 1270.5 cm$^{-1}$ resultant the OH, NH$_3$, C=N and C-O-C groups. The $^1$H NMR spectra of compound 1a was confirmed the protons peaks appeared at $\delta$10.56, 6.70 and 2.36 corresponding to OH, NH$_2$ and CH$_3$ protons respectively. The$^{13}$C NMR spectra of compound 1a
was confirmed the carbon peaks appeared at δ 163.00, 102.12 and 18.42 agreeing to carbons C=N, C=C, and CH₃.

The IR spectrum of compound 1b conformed by important characterization bands at 3831.2, 3498, 1603.7, and 1270.5 cm⁻¹ resultant the OH, NH₂, C=N, and C-O-C groups. The ¹H NMR spectra of compound 1 was confirmed the protons peaks appeared at δ 10.58, 6.74, and 2.38 corresponding to OH, NH₂, and CH₃ protons respectively. The ¹³C NMR spectra of compound 1b was confirmed the carbon peaks appeared at δ 163.01, 102.14, and 18.42 agreeing to carbons C=N, C=C, and CH₃.

The IR spectrum of compound 1c conformed by important characterization bands at 3883.8, 3305, 1599.3, and 1384.5 cm⁻¹ resultant to OH, NH₂, C=N, and C-O-C groups respectively. The ¹H NMR spectra of compound 1c was confirmed the protons peaks appeared at δ 10.60, 6.78, and 2.38 corresponding to OH, NH₂, and CH₃ protons respectively. The ¹³C NMR spectra of compound 1c was confirmed the carbon peaks appeared at δ 163.04, 102.16, and 18.44 agreeing to carbons C=N, C=C, and CH₃.

Table 1. Physiochemical characterization of compounds (1a-1c)

<table>
<thead>
<tr>
<th>Compound. No</th>
<th>-R</th>
<th>Catalyst</th>
<th>Time (min)</th>
<th>Yield (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1a</td>
<td>(CH₂)₂NH₂</td>
<td>CuCl₂.2H₂O</td>
<td>5</td>
<td>92</td>
</tr>
<tr>
<td>1b</td>
<td>(CH₂)₂NH(CH₂)₂OH</td>
<td>CuCl₂.2H₂O</td>
<td>5</td>
<td>90</td>
</tr>
<tr>
<td>1c</td>
<td>(CH₂)₂NH(CH₂)₂NH₂</td>
<td>CuCl₂.2H₂O</td>
<td>5</td>
<td>94</td>
</tr>
</tbody>
</table>
Fig. 4. $^{13}$C NMR spectra of 1

Fig. 5. IR spectra of 1a

Fig. 6. $^1$H NMR spectra of 1a

Fig. 7. $^{13}$C NMR spectra of 1a
Fig. 8. IR spectra of 1b

Fig. 9. H NMR spectra of 1b

Fig. 10. $^{13}$C NMR spectra of 1b

Fig. 11. IR spectra of 1c
Larvicidal activity
Compound 1b exhibited high activity against C. quinquefasciatus with the LD$_{50}$ value of 54.64 µg/mL than compound 1a and 1c with the LD$_{50}$ values of 86.20 and 66.66 µg/mL. Among the compounds (1a-1c) the compound 1a displayed less activity against C. quinquefasciatus with the LD$_{50}$ value of 86.20 µg/mL individually. The synthesized compounds 1c was moderately active and 1 was less active compared to Bergaptan with the LD$_{50}$ value of 62.23 µg/mL due to the presence of free OH atom. The results were abridged in Table 2.

Table 2. Larvicidal activity of compounds (1a-1c)

<table>
<thead>
<tr>
<th>Comp.No.</th>
<th>Mortality (%)</th>
<th>Room temp</th>
<th>Concentration(µg/mL)</th>
<th>LD$_{50}$</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>100</td>
<td></td>
</tr>
<tr>
<td>1a</td>
<td>100</td>
<td>40 ± 1.29</td>
<td></td>
<td>86.20</td>
</tr>
<tr>
<td>1b</td>
<td>60 ± 1.20</td>
<td>0± 0.0</td>
<td></td>
<td>54.64</td>
</tr>
<tr>
<td>1c</td>
<td>80± 1.44</td>
<td>20± 1.30</td>
<td></td>
<td>66.66</td>
</tr>
<tr>
<td>Bergaptan</td>
<td>-</td>
<td>-</td>
<td></td>
<td>62.23</td>
</tr>
</tbody>
</table>

*Value were the means of three replicates ± SD.

Antifeedant activity
Compound 1a exhibited high toxicity associated with other compounds 1b and 1c. Compound 1b produced 100% mortality in 24hr at both 100 and 50 µg/mL respectively. Toxicity was dignified as percentage death at 24hr. Compound 1a produced 66% mortality in 24hr at 100 µg/mL. Among the synthesized compounds (1a-1c) the compound 1a displayed high toxicity with the LD$_{50}$ value of 57.14 µg/mL compared to 7-Methanesulfonyloxycoumarin with the LD$_{50}$ values of 62.4 µg/mL. The results were abridged in Table 3.

Table 3. Antifeedant activity of compounds (1a-1c)
Docking
The docking behavior of compounds (1a-1c) were studied using 3OGN protein and AutoDockVina simulation software. Figure 14 show the 3D structures of mosquito odorant-binding protein (PDB ID: 3OGN). Compound 1b had more binding affinity (-9.6 vs. -6.1 kcal/mol) for 3OGN protein than hydantocidin (-7.6 kcal/mol) than compound 1a (-7.3 kcal/mol) and 1c (-7.5 kcal/mol). Compound 1b showes one hydrogen bond collaboration with the 3OGN receptor. The residue of amino acid His121 was tangled in hydrogen bond relations with the bond length of 2.25 Å. The residues of amino acids Leu76, His77, Leu80, Met84, Ala88, Met89, Met91 and Trp114 were tangled in hydrophobic connections. Figure 15 shows contacts between 1b and 3OGN protein. The Compound 1a shows one hydrogen bond collaboration with the 3OGN receptor. The residue of amino acid Tyr10 was tangled in hydrogen bond collaboration with the bond length of 2.07 Å. The residues of amino acids Leu76, Leu80, Ala88, Met91 and Trp114 were tangled in hydrophobic contacts. Figure 16 shows relations between 1a and 3OGN protein. The Compound 1c shows one hydrogen bond collaboration with the 3OGN receptor. The residue of amino acid His121 was tangled in hydrogen bond contact with the bond length of 2.84 Å. The residues of amino acids Leu76, His77, Leu80, Met84, Ala88, Met91 and Trp114 were tangled in hydrophobic contacts. Figure 17 shows connections between 1c and 3OGN protein. The control Bergaptan did not form any hydrogen bond interaction with the receptor 3OGN. The amino acid residues Leu76, Leu80, Ala88, Met91, Trp114, His121 and Phe123 were involved in hydrophobic interactions. The interactions of compound Bergaptan with 3OGN protein were shown in Figure 18. The results show that 1b inhibited the odorant-binding protein 3OGN of C. quinquefasciatus more effectively than 1a, 1c and control Bergaptan. Table 4 summarizes the results.

Table 4. Interaction of compounds (1a-1c) and Bergaptan

<table>
<thead>
<tr>
<th>Compounds</th>
<th>3OGN Binding affinity (kcal/mol)</th>
<th>No. of H-bonds</th>
<th>H-bonding residues</th>
</tr>
</thead>
<tbody>
<tr>
<td>1a</td>
<td>-7.3</td>
<td>1</td>
<td>Tyr10</td>
</tr>
<tr>
<td>1b</td>
<td>-7.6</td>
<td>1</td>
<td>His121</td>
</tr>
<tr>
<td>1c</td>
<td>-7.5</td>
<td>1</td>
<td>His121</td>
</tr>
<tr>
<td>Bergaptan</td>
<td>-7.3</td>
<td>0</td>
<td>-</td>
</tr>
</tbody>
</table>

Value were the means of three replicates ± SD.

**Journal of Natural Remedies**
Vol. 21, No.9(1), (2021)

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Fig. 14 Structure of 3OGN.

Fig. 15. Interaction modes of compound 1a with 3OGN.
Fig. 16. Interaction modes of compound 1b with 3OGN.
**Fig. 17.** Interaction modes of compound 1c with 3OGN.

**Fig. 18.** Interaction modes of control Bergaptan with 3OGN.

**Conclusion**

It can be inferred from the current research that the potency of the 7-hydroxy-4-methyl coumarin moiety in larvicidal and antifeedant bioassays demonstrated substantial activity. In contrast with positive regulation, compound 1b demonstrated substantial behavior against mosquito larvae and showed low toxicity in antifeedant screening. Compound 1b was also inferred from molecular docking experiments with an impressive inhibition potential (binding affinity: -7.6 Kcal/mol)
relative to other compounds. These compounds may also be a possible basis for environmentally valuable bioactive compounds, like biopharmaceuticals, and ecological insecticides to be created.

Acknowledgments
Authors are acknowledge the Management of Srinivasan College of arts and science, Perambalur and Bishop Heber College for providing the opportunity to carry out the Research work.

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