

# THEORETICAL STUDY OF SOME 7,8-DYHYDROXYFLAVONE ANALOGUES AS TROPOMYOSIN-RELATED KINASE B AGONISTS

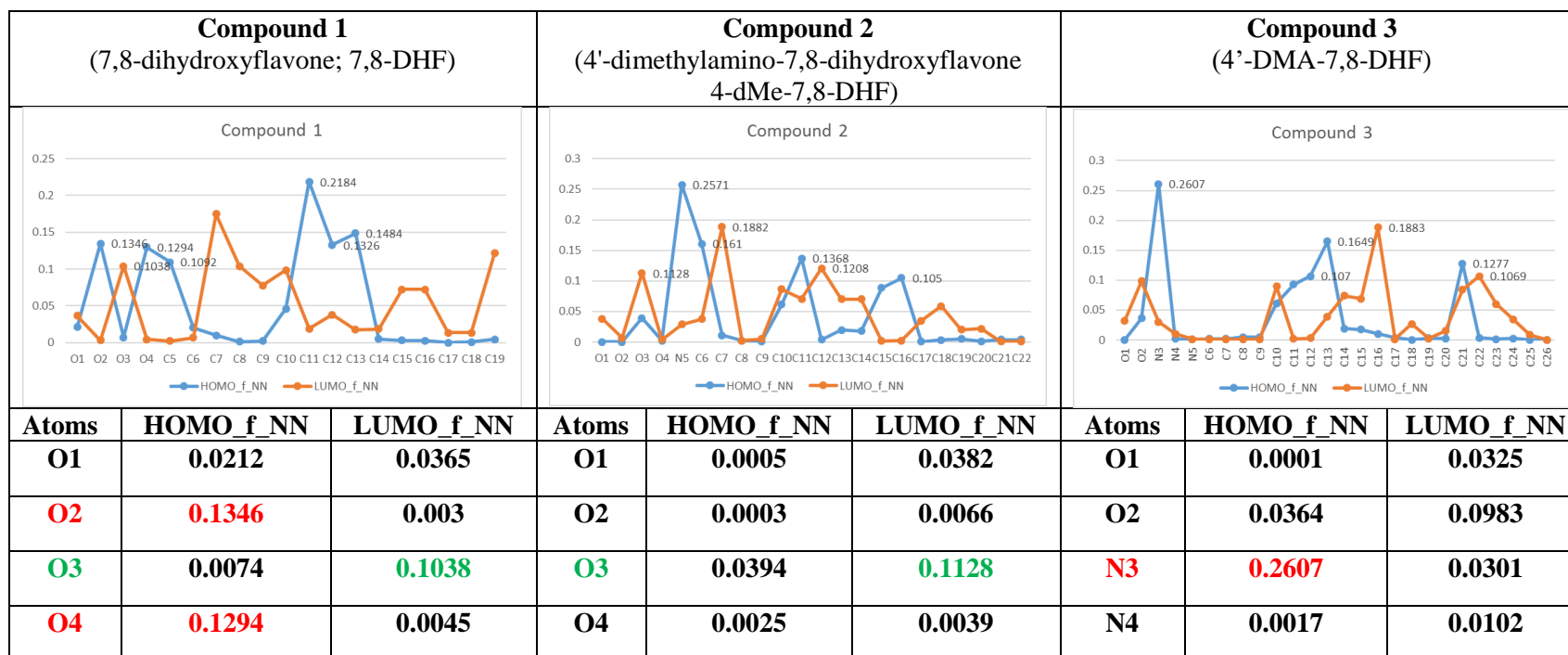
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## SUPPORTING INFORMATION

**Table 1. (a)** The absolute values of reactivity HOMO-LUMO Fukui indices (hartrees) of all six flavonoid analogues calculated at DFT B3LYP 6-311G\* levels of theory and the corresponding Fukui plots which emphasize the significant atoms within the molecule



|            |               |               |            |               |               |            |               |               |
|------------|---------------|---------------|------------|---------------|---------------|------------|---------------|---------------|
| <b>C5</b>  | <b>0.1092</b> | <b>0.0021</b> | <b>N5</b>  | <b>0.2571</b> | <b>0.029</b>  | <b>N5</b>  | <b>0.0009</b> | <b>0.0016</b> |
| <b>C6</b>  | <b>0.0203</b> | <b>0.0066</b> | <b>C6</b>  | <b>0.161</b>  | <b>0.0376</b> | <b>C6</b>  | <b>0.0019</b> | <b>0.0006</b> |
| <b>C7</b>  | <b>0.0101</b> | <b>0.1746</b> | <b>C7</b>  | <b>0.0111</b> | <b>0.1882</b> | <b>C7</b>  | <b>0.0018</b> | <b>0.0006</b> |
| <b>C8</b>  | <b>0.0013</b> | <b>0.1038</b> | <b>C8</b>  | <b>0.0027</b> | <b>0.0024</b> | <b>C8</b>  | <b>0.0046</b> | <b>0.0009</b> |
| <b>C9</b>  | <b>0.0024</b> | <b>0.0777</b> | <b>C9</b>  | <b>0.0016</b> | <b>0.0051</b> | <b>C9</b>  | <b>0.0047</b> | <b>0.0009</b> |
| <b>C10</b> | <b>0.046</b>  | <b>0.0984</b> | <b>C10</b> | <b>0.0614</b> | <b>0.0863</b> | <b>C10</b> | <b>0.0615</b> | <b>0.0895</b> |
| <b>C11</b> | <b>0.2184</b> | <b>0.0189</b> | <b>C11</b> | <b>0.1368</b> | <b>0.071</b>  | <b>C11</b> | <b>0.0926</b> | <b>0.002</b>  |
| <b>C12</b> | <b>0.1326</b> | <b>0.038</b>  | <b>C12</b> | <b>0.0042</b> | <b>0.1208</b> | <b>C12</b> | <b>0.107</b>  | <b>0.0028</b> |
| <b>C13</b> | <b>0.1484</b> | <b>0.0178</b> | <b>C13</b> | <b>0.0201</b> | <b>0.0702</b> | <b>C13</b> | <b>0.1649</b> | <b>0.0389</b> |
| <b>C14</b> | <b>0.005</b>  | <b>0.0184</b> | <b>C14</b> | <b>0.0182</b> | <b>0.07</b>   | <b>C14</b> | <b>0.0194</b> | <b>0.0738</b> |
| <b>C15</b> | <b>0.0032</b> | <b>0.0721</b> | <b>C15</b> | <b>0.0887</b> | <b>0.0021</b> | <b>C15</b> | <b>0.0177</b> | <b>0.0692</b> |
| <b>C16</b> | <b>0.0025</b> | <b>0.0721</b> | <b>C16</b> | <b>0.105</b>  | <b>0.0024</b> | <b>C16</b> | <b>0.0103</b> | <b>0.1883</b> |
| <b>C17</b> | <b>0.0002</b> | <b>0.0137</b> | <b>C17</b> | <b>0.0006</b> | <b>0.0348</b> | <b>C17</b> | <b>0.0038</b> | <b>0.0013</b> |
| <b>C18</b> | <b>0.0009</b> | <b>0.0137</b> | <b>C18</b> | <b>0.0038</b> | <b>0.059</b>  | <b>C18</b> | <b>0.0001</b> | <b>0.0271</b> |
| <b>C19</b> | <b>0.0043</b> | <b>0.1215</b> | <b>C19</b> | <b>0.0051</b> | <b>0.0206</b> | <b>C19</b> | <b>0.0029</b> | <b>0.0026</b> |
| <b>H20</b> | <b>0.0002</b> | <b>0.0007</b> | <b>C20</b> | <b>0.0016</b> | <b>0.0219</b> | <b>C20</b> | <b>0.0027</b> | <b>0.0152</b> |
| <b>H21</b> | <b>0.0005</b> | <b>0.0002</b> | <b>C21</b> | <b>0.004</b>  | <b>0.0009</b> | <b>C21</b> | <b>0.1277</b> | <b>0.0842</b> |
| <b>H22</b> | <b>0</b>      | <b>0.0001</b> | <b>C22</b> | <b>0.0041</b> | <b>0.0009</b> | <b>C22</b> | <b>0.0039</b> | <b>0.1069</b> |
| <b>H23</b> | <b>0.0001</b> | <b>0.0004</b> | <b>H23</b> | <b>0.0004</b> | <b>0.0003</b> | <b>C23</b> | <b>0.0013</b> | <b>0.0599</b> |
| <b>H24</b> | <b>0</b>      | <b>0.0003</b> | <b>H24</b> | <b>0.0001</b> | <b>0.0004</b> | <b>C24</b> | <b>0.0026</b> | <b>0.0349</b> |
| <b>H25</b> | <b>0</b>      | <b>0.0002</b> | <b>H25</b> | <b>0.0001</b> | <b>0.0004</b> | <b>C25</b> | <b>0.0002</b> | <b>0.0084</b> |

|            |               |               |            |               |               |            |               |               |
|------------|---------------|---------------|------------|---------------|---------------|------------|---------------|---------------|
| <b>H26</b> | <b>0</b>      | <b>0.0001</b> | <b>H26</b> | <b>0.0004</b> | <b>0</b>      | <b>C26</b> | <b>0</b>      | <b>0.0004</b> |
| <b>H27</b> | <b>0</b>      | <b>0.0007</b> | <b>H27</b> | <b>0.0004</b> | <b>0</b>      | <b>H27</b> | <b>0</b>      | <b>0.0001</b> |
| <b>H28</b> | <b>0.0011</b> | <b>0.0001</b> | <b>H28</b> | <b>0</b>      | <b>0.0003</b> | <b>H28</b> | <b>0.0006</b> | <b>0.0006</b> |
|            |               |               | <b>H29</b> | <b>0</b>      | <b>0.0001</b> | <b>H29</b> | <b>0</b>      | <b>0.0001</b> |
|            |               |               | <b>H30</b> | <b>0</b>      | <b>0</b>      | <b>H30</b> | <b>0.0006</b> | <b>0.0006</b> |
|            |               |               | <b>H31</b> | <b>0.0168</b> | <b>0.0033</b> | <b>H31</b> | <b>0.0199</b> | <b>0.0039</b> |
|            |               |               | <b>H32</b> | <b>0.0177</b> | <b>0.0035</b> | <b>H32</b> | <b>0.0132</b> | <b>0.0031</b> |
|            |               |               | <b>H33</b> | <b>0</b>      | <b>0</b>      | <b>H33</b> | <b>0.0199</b> | <b>0.0038</b> |
|            |               |               | <b>H34</b> | <b>0.0175</b> | <b>0.0036</b> | <b>H34</b> | <b>0.0132</b> | <b>0.003</b>  |
|            |               |               | <b>H35</b> | <b>0.0169</b> | <b>0.0034</b> | <b>H35</b> | <b>0.0004</b> | <b>0</b>      |
|            |               |               | <b>H36</b> | <b>0</b>      | <b>0</b>      | <b>H36</b> | <b>0.0004</b> | <b>0</b>      |
|            |               |               | <b>H37</b> | <b>0</b>      | <b>0</b>      | <b>H37</b> | <b>0.0001</b> | <b>0.0004</b> |
|            |               |               |            |               |               | <b>H38</b> | <b>0.0001</b> | <b>0.0004</b> |
|            |               |               |            |               |               | <b>H39</b> | <b>0.0004</b> | <b>0.0004</b> |
|            |               |               |            |               |               | <b>H40</b> | <b>0</b>      | <b>0.0003</b> |
|            |               |               |            |               |               | <b>H41</b> | <b>0</b>      | <b>0.0002</b> |
|            |               |               |            |               |               | <b>H42</b> | <b>0</b>      | <b>0.0001</b> |
|            |               |               |            |               |               | <b>H43</b> | <b>0</b>      | <b>0.0009</b> |
|            |               |               |            |               |               | <b>H44</b> | <b>0</b>      | <b>0.0009</b> |
|            |               |               |            |               |               | <b>H45</b> | <b>0</b>      | <b>0</b>      |

\*the red color of the HOMO values and the green color of the LUMO values indicates the significant atoms within the molecule

**Table 1. (b)** The absolute values of reactivity HOMO-LUMO Fukui indices (hartrees) of all six flavonoid analogues calculated at DFT B3LYP 6-311G\* levels of theory and the corresponding Fukui plots which emphasize the significant atoms within the molecule

| Compound 4<br>(quercetin; Qu) |           |           | Compound 5<br>(chrysin; 5,7-DHF) |           |           | Compound 6<br>(7,8-dihydroxy-2-phenyl-1H-quinolin-4-one;<br>7,8-DNF) |           |           |
|-------------------------------|-----------|-----------|----------------------------------|-----------|-----------|--|-----------|-----------|
|                               |           |           |                                  |           |           |  |           |           |
| Atoms                         | HOMO_f_NN | LUMO_f_NN | Atoms                            | HOMO_f_NN | LUMO_f_NN | Atoms  | HOMO_f_NN | LUMO_f_NN |
| O1                            | 0.0526    | 0.0442    | O1                               | 0.0413    | 0.0445    | O1   | 0.0631    | 0.0067    |
| O2                            | 0.094     | 0.0087    | O2                               | 0.1608    | 0.0122    | O2   | 0.1242    | 0.077     |
| O3                            | 0.0686    | 0.0171    | O3                               | 0         | 0.0942    | O3   | 0.0087    | 0.0016    |
| O4                            | 0.0176    | 0.1225    | O4                               | 0.0223    | 0.005     | N4   | 0.1848    | 0.042     |
| O5                            | 0.0147    | 0.009     | C5                               | 0.0934    | 0.009     | C5   | 0.0511    | 0.0017    |
| O6                            | 0.0099    | 0.0002    | C6                               | 0.0262    | 0.0074    | C6   | 0.016     | 0.0033    |
| O7                            | 0.0351    | 0.0181    | C7                               | 0.0188    | 0.1912    | C7   | 0.0264    | 0.1482    |
| C8                            | 0.0294    | 0.0058    | C8                               | 0.0014    | 0.122     | C8   | 0.0061    | 0.0794    |
| C9                            | 0.0048    | 0.017     | C9                               | 0.0049    | 0.0663    | C9   | 0.224     | 0.0799    |
| C10                           | 0.087     | 0.1645    | C10                              | 0.0974    | 0.0351    | C10  | 0.0018    | 0.104     |
| C11                           | 0.0411    | 0.0472    | C11                              | 0.089     | 0.0856    | C11  | 0.1182    | 0.0404    |

|            |               |               |            |               |               |            |               |               |
|------------|---------------|---------------|------------|---------------|---------------|------------|---------------|---------------|
| <b>C12</b> | <b>0.1501</b> | <b>0.0602</b> | <b>C12</b> | <b>0.2988</b> | <b>0.0091</b> | <b>C12</b> | <b>0.0701</b> | <b>0.0497</b> |
| <b>C13</b> | <b>0.0052</b> | <b>0.1704</b> | <b>C13</b> | <b>0.0267</b> | <b>0.0203</b> | <b>C13</b> | <b>0.0208</b> | <b>0.0093</b> |
| <b>C14</b> | <b>0.0498</b> | <b>0.0524</b> | <b>C14</b> | <b>0.0936</b> | <b>0.0093</b> | <b>C14</b> | <b>0.0678</b> | <b>0.0364</b> |
| <b>C15</b> | <b>0.1476</b> | <b>0.0092</b> | <b>C15</b> | <b>0.0065</b> | <b>0.0736</b> | <b>C15</b> | <b>0.0036</b> | <b>0.0652</b> |
| <b>C16</b> | <b>0.0205</b> | <b>0.0379</b> | <b>C16</b> | <b>0.0047</b> | <b>0.0733</b> | <b>C16</b> | <b>0.0033</b> | <b>0.0753</b> |
| <b>C17</b> | <b>0.0084</b> | <b>0.0665</b> | <b>C17</b> | <b>0.0003</b> | <b>0.0108</b> | <b>C17</b> | <b>0.0002</b> | <b>0.0239</b> |
| <b>C18</b> | <b>0.0414</b> | <b>0.0069</b> | <b>C18</b> | <b>0.0022</b> | <b>0.0122</b> | <b>C18</b> | <b>0.0007</b> | <b>0.0163</b> |
| <b>C19</b> | <b>0.034</b>  | <b>0.0535</b> | <b>C19</b> | <b>0.0088</b> | <b>0.1166</b> | <b>C19</b> | <b>0.0039</b> | <b>0.1363</b> |
| <b>C20</b> | <b>0.021</b>  | <b>0.0025</b> | <b>H20</b> | <b>0.0003</b> | <b>0.0006</b> | <b>H20</b> | <b>0.002</b>  | <b>0.0005</b> |
| <b>C21</b> | <b>0.0129</b> | <b>0.0068</b> | <b>H21</b> | <b>0.001</b>  | <b>0</b>      | <b>H21</b> | <b>0.0008</b> | <b>0.0004</b> |
| <b>C22</b> | <b>0.0498</b> | <b>0.0776</b> | <b>H22</b> | <b>0.0003</b> | <b>0.0001</b> | <b>H22</b> | <b>0.0003</b> | <b>0.0002</b> |
| <b>H23</b> | <b>0.0005</b> | <b>0</b>      | <b>H23</b> | <b>0.0002</b> | <b>0.0004</b> | <b>H23</b> | <b>0.0003</b> | <b>0.0002</b> |
| <b>H24</b> | <b>0</b>      | <b>0.0008</b> | <b>H24</b> | <b>0</b>      | <b>0.0003</b> | <b>H24</b> | <b>0.0007</b> | <b>0.0003</b> |
| <b>H25</b> | <b>0.0002</b> | <b>0</b>      | <b>H25</b> | <b>0</b>      | <b>0.0001</b> | <b>H25</b> | <b>0.0005</b> | <b>0.0005</b> |
| <b>H26</b> | <b>0.0001</b> | <b>0.0002</b> | <b>H26</b> | <b>0</b>      | <b>0.0001</b> | <b>H26</b> | <b>0</b>      | <b>0.0002</b> |
| <b>H27</b> | <b>0.0002</b> | <b>0.0001</b> | <b>H27</b> | <b>0</b>      | <b>0.0006</b> | <b>H27</b> | <b>0</b>      | <b>0.0002</b> |
| <b>H28</b> | <b>0.0025</b> | <b>0.0005</b> | <b>H28</b> | <b>0.0008</b> | <b>0</b>      | <b>H28</b> | <b>0.0001</b> | <b>0.0008</b> |
| <b>H29</b> | <b>0.0003</b> | <b>0</b>      | <b>H29</b> | <b>0.0002</b> | <b>0</b>      | <b>H29</b> | <b>0.0004</b> | <b>0</b>      |
| <b>H30</b> | <b>0.0001</b> | <b>0.0001</b> |            |               |               | <b>H30</b> | <b>0.0001</b> | <b>0</b>      |
| <b>H31</b> | <b>0.0001</b> | <b>0</b>      |            |               |               |            |               |               |

\*the red color of the HOMO values and the green color of the LUMO values indicates the significant atoms within the molecule