Supplementary materials

In silico approach: Biological activities prediction of nординatin derivatives as anticancer agent in cAMP pathway inhibitors

Muhammad Ikhlas Abdjan\textsuperscript{a}, Nanik Siti Aminah\textsuperscript{a*}, Imam Siswanto\textsuperscript{a}, Tin Myo Thant\textsuperscript{b,c}, Alfinda Novi Kristanti\textsuperscript{a}, Yoshiaki Takaya\textsuperscript{d}

\textsuperscript{a}Departement of Chemistry, Faculty of Science and Technology, Universitas Airlangga, Surabaya 60115, Indonesia. E-mail: nanik-s-a@fst.unair.ac.id

\textsuperscript{b}Posdocot fellow Department of Chemistry, Faculty of Science and Technology, Universitas Airlangga, Komplek Kampus C, Jl. Mulyorejo, Surabaya, Indonesia. 60115

\textsuperscript{c}Department of Chemistry, Mandalar Degree College, Mandalay, Myanmar

\textsuperscript{d}Faculty of Pharmacy, Meijo University, 150 Yagotoyama, Tempaku, Nagoya, 468-8503 Japan
Fig. S1. Types of interactions in each complex of the candidate-receptor: (A) PS-1, (B) PS-2, (C) PS-3, (D) PS-5, (E) PS-7, and (F) PS-9.
Fig. S2. The residual energy decomposition plotted along with the simulation over the last 20 ns of each complex.
Fig. S3. Lifetime H-bond of each complex
**Fig. S4** The suitable physicochemical space for oral bioavailability prediction (A) PS-1, (B) PS-2, (C) PS-3, (D) PS-5, (E) PS-7, and (F) PS-9
<table>
<thead>
<tr>
<th>Parameters</th>
<th>PS-1</th>
<th>PS-2</th>
<th>PS-3</th>
<th>PS-5</th>
<th>PS-7</th>
<th>PS-9</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Absorption</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Water Solubility (log mol/L)</td>
<td>-6.31</td>
<td>-6.15</td>
<td>-5.95</td>
<td>-5.97</td>
<td>-6.31</td>
<td>-6.30</td>
</tr>
<tr>
<td>Caco-2 Permeability (log Papp in $10^{-6}$ cm/s)</td>
<td>1.30</td>
<td>1.24</td>
<td>1.19</td>
<td>0.83</td>
<td>1.21</td>
<td>1.21</td>
</tr>
<tr>
<td>Intestinal Absorption-Human (%) Absorbed</td>
<td>90.56</td>
<td>93.83</td>
<td>95.38</td>
<td>100</td>
<td>95.15</td>
<td>92.22</td>
</tr>
<tr>
<td>Skin Permeability (Log Kp)</td>
<td>-2.74</td>
<td>-2.74</td>
<td>-2.74</td>
<td>-2.73</td>
<td>-2.73</td>
<td>-2.74</td>
</tr>
<tr>
<td>P-glycoprotein substrate</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td><strong>Distribution</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>VDss-Human (log L/Kg)</td>
<td>-0.06</td>
<td>-0.06</td>
<td>-0.04</td>
<td>-0.48</td>
<td>-0.15</td>
<td>0.01</td>
</tr>
<tr>
<td>Fraction Unbound-Human (Fu)</td>
<td>0.01</td>
<td>0.03</td>
<td>0.04</td>
<td>0.04</td>
<td>0.05</td>
<td>0.02</td>
</tr>
<tr>
<td>BBB Permeability (log BB)</td>
<td>-0.25</td>
<td>-0.26</td>
<td>-0.26</td>
<td>-1.08</td>
<td>-0.41</td>
<td>-0.26</td>
</tr>
<tr>
<td><strong>Metabolism</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CYP2D6 Substrate</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td>CYP1A2 Inhibitor</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td>CYP2D6 Inhibitor</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td><strong>Excretion</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total Clearance (log mL/min/Kg)</td>
<td>-0.36</td>
<td>-0.02</td>
<td>-0.09</td>
<td>0.13</td>
<td>0.36</td>
<td>0.08</td>
</tr>
<tr>
<td>Renal OCT2 Substrate</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td><strong>Toxicity</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>AMES Toxicity</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td>Max. Tolerated Dose-Human (log mg/Kg/day)</td>
<td>0.53</td>
<td>0.54</td>
<td>0.59</td>
<td>0.39</td>
<td>0.56</td>
<td>0.61</td>
</tr>
<tr>
<td>hERG I Inhibitor</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td>Oral Rat Acute Toxicity-LD50 (mol/Kg)</td>
<td>3.46</td>
<td>3.21</td>
<td>2.97</td>
<td>2.54</td>
<td>2.72</td>
<td>3.20</td>
</tr>
<tr>
<td>Oral Rat Chronic Toxicity-LOAEL (log mg/Kg_bw/day)</td>
<td>0.71</td>
<td>1.21</td>
<td>1.49</td>
<td>1.33</td>
<td>1.45</td>
<td>1.11</td>
</tr>
<tr>
<td>Hepatotoxicity</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td>Skin Sensitisation</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>No</td>
</tr>
</tbody>
</table>