**Assignment -02**

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| **Task 01:** Please conduct multiple Protein-Ligand Docking and provide the top 10 results in the following table. | | | | |
|  | Ligands | Binding Affinity | Rmsd/ub | Rmsd/ib |
| 01 | Gingerenone A | -7.7 | 0 | 0 |
| 02 | Gingerenone B | -7.5 | 0 | 0 |
| 03 | Isogingerenone B | -7.4 | 0 | 0 |
| 04 | Zingiberene | -7 | 0 | 0 |
| 05 | Sesquisabinene | -6.3 | 0 | 0 |
| 06 | alpha-Phellandrene | -6.2 | 0 | 0 |
| 07 | Zingerone | -6.1 | 0 | 0 |
| 08 | Gingerdiol | -6 | 0 | 0 |
| 09 | Zingiberenol | -5.9 | 0 | 0 |
| 10 | Eugenol | -5.9 | 0 | 0 |

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| **Task 02:** Please perform ADME analysis on the 10 compounds obtained from the Protein-Ligand Docking and provide the results in the table below. | | | | | | | | | | | |
| **ADME Analysis** | | | | | | | | Pharmacokinetics |  | Drug likeness | Medicinal Chemistry |
| Name | CID ID | Canonical SMILES | Molecular weight | Num. H-bond acceptors | Num. H-bond donors | Lipophilicity (iLOGP) | Water Solubility (Log S (SILICOS-IT)) | GI absorption | BBB permeant | Lipinski | PAINS |
| Gingerenone A | 5281775 | COc1cc(CC/C=C/C(=O)CCc2ccc(c(c2)OC)O)ccc1O | 356.41 | 5 | 2 | 3.6 | -4.15 Moderately soluble | High | Yes | 0 | 0 |
| Gingerenone B | 5317592 | COc1cc(CCC(=O)/C=C/CCc2cc(OC)c(c(c2)OC)O)ccc1O | 386.44 | 6 | 2 | 3.7 | -4.24 | High | No | 0 | 0 |
| Isogingerenone B | 5318568 | COc1cc(CC/C=C/C(=O)CCc2cc(OC)c(c(c2)OC)O)ccc1O | 386.44 | 6 | 2 | 3.77 | -4.24 | High | No | 0 | 0 |
| Zingiberene | 92776 | CC(=CCC[C@@H]([C@H]1CC=C(C=C1)C)C)C | 204.35 | 0 | 0 | 3.63 | -4.1 | Low | No | 1 | 0 |
| Sesquisabinene | 25147318 | CC(=CCCC(C12CCC(=C)C2C1)C)C | 204.35 | 0 | 0 | 3.63 | -4.02 | Low | No | 1 | 0 |
| alpha-Phellandrene | 7460 | CC1=CCC(C=C1)C(C)C | 136.23 | 0 | 0 | 2.64 | -2.64 | Low | Yes | 0 | 0 |
| Zingerone | 31211 | COc1cc(CCC(=O)C)ccc1O | 194.23 | 3 | 1 | 2.09 | -1.8 | High | Yes | 0 | 0 |
| Gingerdiol | 11369949 | CCCCC[C@@H](C[C@@H](CCc1ccc(c(c1)OC)O)O)O | 296.4 | 4 | 3 | 3.38 | -3.29 | High | Yes | 0 | 0 |
| Zingiberenol | 13213649 | CC(=CCCC(C1CCC(C=C1)(C)O)C)C | 222.37 | 1 | 1 | 3.41 | -3.64 | High | Yes | 0 | 0 |
| Eugenol | 3314 | C=CCc1ccc(c(c1)OC)O | 164.2 | 2 | 1 | 2.37 | -2.46 | High | Yes | 0 | 0 |

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| **Task 03:** Perform Toxicity Prediction on the 10 compounds obtained from the Protein-Ligand Docking and provide the results in the table below. | | | | | | | | |
| **Toxicity Prediction** | | | | | | | | |
| Name | CID ID | Canonical SMILES | Hepatotoxicity | | Carcinogenicity | Immunotoxicity | Mutagenicity | Cytotoxicity |
| Gingerenone A | 5281775 | COc1cc(CC/C=C/C(=O)CCc2ccc(c(c2)OC)O)ccc1O | Inactive | Inactive | | Inactive | Inactive | Inactive |
| Gingerenone B | 5317592 | COc1cc(CCC(=O)/C=C/CCc2cc(OC)c(c(c2)OC)O)ccc1O | Inactive | Inactive | | **Active** | Inactive | Inactive |
| Isogingerenone B | 5318568 | COc1cc(CC/C=C/C(=O)CCc2cc(OC)c(c(c2)OC)O)ccc1O | Inactive | Inactive | | **Active** | Inactive | Inactive |
| Zingiberene | 92776 | CC(=CCC[C@@H]([C@H]1CC=C(C=C1)C)C)C | Inactive | Inactive | | Inactive | Inactive | Inactive |
| Sesquisabinene | 25147318 | CC(=CCCC(C12CCC(=C)C2C1)C)C | Inactive | Inactive | | **Active** | Inactive | Inactive |
| alpha-Phellandrene | 7460 | CC1=CCC(C=C1)C(C)C | Inactive | Inactive | | Inactive | Inactive | Inactive |
| Zingerone | 31211 | COc1cc(CCC(=O)C)ccc1O | Inactive | Inactive | | Inactive | Inactive | Inactive |
| Gingerdiol | 11369949 | CCCCC[C@@H](C[C@@H](CCc1ccc(c(c1)OC)O)O)O | Inactive | Inactive | | **Active** | Inactive | Inactive |
| Zingiberenol | 13213649 | CC(=CCCC(C1CCC(C=C1)(C)O)C)C | Inactive | Inactive | | **Active** | Inactive | Inactive |
| Eugenol | 3314 | C=CCc1ccc(c(c1)OC)O | Inactive | Inactive | | Inactive | Inactive | Inactive |

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| **Task 04:** Identify the highest-ranking Protein – ligand complex and input the corresponding figures into the table below. | | |
| **Figure Name** | **Sample Figure** | **Input your Docking Figure** |
| **Figure 01** |  | **C:\Users\Mehedul IT\Desktop\2222\PyRx_AutoDock4\Macromolecules\EC2fs9\f1.png** |
| **Figure 02** | A picture containing sketch, drawing, clipart, cartoon  Description automatically generated | **C:\Users\Mehedul IT\Desktop\2222\PyRx_AutoDock4\Macromolecules\EC2fs9\f2.png** |
| **Figure 03** | A picture containing cartoon, art  Description automatically generated | **C:\Users\Mehedul IT\Desktop\2222\PyRx_AutoDock4\Macromolecules\EC2fs9\f3.png** |
| **Figure 04** | A picture containing clipart, illustration, design  Description automatically generated | **C:\Users\Mehedul IT\Desktop\2222\PyRx_AutoDock4\Macromolecules\EC2fs9\f4.png** |
| **Figure 05** | A picture containing text, diagram, font, screenshot  Description automatically generated | **C:\Users\Mehedul IT\Desktop\2222\PyRx_AutoDock4\Macromolecules\EC2fs9\f5.png** |

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| **Task 05:** Identify the highest-ranking Protein – ligand complex and input the Interaction details into the table below. | | | |
| Name | Distance | Category | Types |
| N:UNK1:H - B:TRP141:O | 2.69878 | Hydrogen Bond | Conventional Hydrogen Bond |
| A:TYR74:HH - N:UNK1:O | 2.12193 | Hydrogen Bond | Conventional Hydrogen Bond |
| B:TYR37B:OH - N:UNK1:O | 2.96994 | Hydrogen Bond | Conventional Hydrogen Bond |
| B:LEU151:HN - N:UNK1:O | 2.69115 | Hydrogen Bond | Conventional Hydrogen Bond |
| N:UNK1:C - A:ASP143:OD1 | 3.77614 | Hydrogen Bond | Carbon Hydrogen Bond |
| N:UNK1:C - A:ARG150 | 4.26051 | Hydrophobic | Alkyl |
| N:UNK1:C - B:ARG150 | 4.54133 | Hydrophobic | Alkyl |
| N:UNK1 - B:ARG150 | 4.34098 | Hydrophobic | Pi-Alkyl |
| B:PHE153 - N:UNK1 | 4.65375 | Hydrophobic | Pi-Alkyl |
| N:UNK1:H - B:TRP141:O | 2.69878 | Hydrogen Bond | Conventional Hydrogen Bond |
| A:TYR74:HH - N:UNK1:O | 2.12193 | Hydrogen Bond | Conventional Hydrogen Bond |
| B:TYR37B:OH - N:UNK1:O | 2.96994 | Hydrogen Bond | Conventional Hydrogen Bond |
| B:LEU151:HN - N:UNK1:O | 2.69115 | Hydrogen Bond | Conventional Hydrogen Bond |
| N:UNK1:C - A:ASP143:OD1 | 3.77614 | Hydrogen Bond | Carbon Hydrogen Bond |
| N:UNK1:C - A:ARG150 | 4.26051 | Hydrophobic | Alkyl |

Result interpretation

I initially selected the disease (pneumonia) and the target protein (C4A) that causes it. The protein was then retrieved from the Protein Data Bank. Next, I got 25 chemicals from the plant (Zingiber officinale) that have anti-therapeutic properties against pneumonia from PubChem. Next, I use Open Babel and Discovery Studio Visualizer to prepare the protein and ligand.   
I then carried out multiple docking using PyRx. The docking results were then displayed in Table 1, which shows the top ten results from multiple docking. Gingerenone A has the highest binding affinity, -7.7, according to the table.

Next, I used SwissADME to do an ADME analysis of the top ten compounds, and the results are displayed in Table 2. Gingerenone A had the best result, as seen in Table 1.   
  
I then used Protox3 to analyze the toxicity of those ten chemicals, and the results are displayed in Table 3. In terms of hepatotoxicity, carcinogenicity, immunotoxicity, mutagenicity, and cytotoxicity, all ten of those substances shown inactivity. Since Table 2 indicates that Gingerenone A has the best ADME analysis result and Table 3 indicates that it is inactive in all toxicity analyses, I once more selected Gingerenone A for drug design.   
  
I used PyMOL to generate the protein-ligand (Gingerenone A\_5281775) complex after selecting Gingerenone A based on Tables 1, 2, and 3.

Using Discovery Studio Visualizer, I created five figures. I displayed the results in Table 4 and the specifics of the protein-ligand interaction in Table 5.  
  
Following the preceding discussion, I ultimately decided to employ the C4A \_Gingerenone A complex for the development of a medication to treat pneumonia since Gingerenone A exhibits the best results across all analyses, as shown in Tables 1, 2, 3, 4, and 5.