**Assignment -02**

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| **Task 01:** Please conduct multiple Protein-Ligand Docking and provide the top 10 results in the following table. | | | | |
|  | Ligand | Binding Affinity | rmsd/ub | rmsd/lb |
| 01 | EN34p\_64945\_uff\_E=805.65 | -9.3 | 0 | 0 |
| 02 | EN34p\_10494\_uff\_E=689.79 | -9.2 | 0 | 0 |
| 03 | EN34p\_1794427\_uff\_E=254.42 | -8.7 | 0 | 0 |
| 04 | EN34p\_5281675\_uff\_E=415.84 | -8.4 | 0 | 0 |
| 05 | EN34p\_5281792\_uff\_E=209.67 | -8.1 | 0 | 0 |
| 06 | EN34p\_5280445\_uff\_E=242.10 | -8.1 | 0 | 0 |
| 07 | EN34p\_5280863\_uff\_E=362.50 | -7.9 | 0 | 0 |
| 08 | EN34p\_5280343\_uff\_E=380.43 | -7.9 | 0 | 0 |
| 09 | EN34p\_72276\_uff\_E=230.94 | -7.7 | 0 | 0 |
| 10 | EN34p\_5280443\_uff\_E=233.26 | -7.6 | 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 |
| [Ursolic acid](https://pubchem.ncbi.nlm.nih.gov/compound/64945) | [64945](https://pubchem.ncbi.nlm.nih.gov/compound/64945) | C[C@@H]1CC[C@@]2(CC[C@@]3(C(=CC[C@H]4[C@]3(CC[C@@H]5[C@@]4(CC[C@@H](C5(C)C)O)C)C)[C@@H]2[C@H]1C)C)C(=O)O | 456.70 g/mol | 3 | 2 | 3.95 | -5.67 | Low | No | Yes; 1 violation: MLOGP>4.15 | 0 alert |
| [OLEANOLIC ACID](https://pubchem.ncbi.nlm.nih.gov/compound/10494) | [10494](https://pubchem.ncbi.nlm.nih.gov/compound/10494) | C[C@]12CC[C@@H](C([C@@H]1CC[C@@]3([C@@H]2CC=C4[C@]3(CC[C@@]5([C@H]4CC(CC5)(C)C)C(=O)O)C)C)(C)C)O | 456.70 g/mol | 3 | 2 | 3.94 | -6.12 | Low | No | Yes; 1 violation: MLOGP>4.15 | 0 alert |
| [CHLOROGENIC ACID](https://pubchem.ncbi.nlm.nih.gov/compound/1794427) | [1794427](https://pubchem.ncbi.nlm.nih.gov/compound/1794427) | C1[C@H]([C@H]([C@@H](C[C@@]1(C(=O)O)O)OC(=O)/C=C/C2=CC(=C(C=C2)O)O)O)O | 456.70 g/mol | 3 | 2 | 3.94 | -6.12 | Low | No | Yes; 1 violation: MLOGP>4.15 | 0 alert |
| [Orientin](https://pubchem.ncbi.nlm.nih.gov/compound/5281675) | [5281675](https://pubchem.ncbi.nlm.nih.gov/compound/5281675) | C1=CC(=C(C=C1C2=CC(=O)C3=C(O2)C(=C(C=C3O)O)[C@H]4[C@@H]([C@H]([C@@H]([C@H](O4)CO)O)O)O)O)O | 448.38 g/mol | 11 | 8 | 1.00 | -1.79 | Low | No | No; 2 violations: NorO>10, NHorOH>5 | 1 alert: catechol\_A |
| [rosmarinic acid](https://pubchem.ncbi.nlm.nih.gov/compound/5281792) | [5281792](https://pubchem.ncbi.nlm.nih.gov/compound/5281792) | C1=CC(=C(C=C1C[C@H](C(=O)O)OC(=O)/C=C/C2=CC(=C(C=C2)O)O)O)O | 360.31 g/mol | 8 | 5 | 1.48 | -2.17 | Low | No | Yes; 0 violation | 1 alert: catechol\_A |
| [luteolin](https://pubchem.ncbi.nlm.nih.gov/compound/5280445) | 5280445 | C1=CC(=C(C=C1C2=CC(=O)C3=C(C=C(C=C3O2)O)O)O)O | 286.24 g/mol | 6 | 4 | 1.86 | -3.82 | High | No | Yes; 0 violation | 1 alert: catechol\_A |
| [kaempferol](https://pubchem.ncbi.nlm.nih.gov/compound/5280863) | [5280863](https://pubchem.ncbi.nlm.nih.gov/compound/5280863) | C1=CC(=CC=C1C2=C(C(=O)C3=C(C=C(C=C3O2)O)O)O)O | 286.24 g/mol | 6 | 4 | 1.70 | -3.82 | High | No | Yes; 0 violation | 0 alert |
| [quercetin](https://pubchem.ncbi.nlm.nih.gov/compound/5280343) | [5280343](https://pubchem.ncbi.nlm.nih.gov/compound/5280343) | C1=CC(=C(C=C1C2=C(C(=O)C3=C(C=C(C=C3O2)O)O)O)O)O | 302.24 g/mol | 7 | 5 | 1.63 | -3.24 | High | No | Yes; 0 violation | 1 alert: catechol\_A |
| [(-)-Epicatechin](https://pubchem.ncbi.nlm.nih.gov/compound/72276) | [72276](https://pubchem.ncbi.nlm.nih.gov/compound/72276) | C1[C@H]([C@H](OC2=CC(=CC(=C21)O)O)C3=CC(=C(C=C3)O)O)O | 290.27 g/mol | 6 | 5 | 1.47 | -2.24 | High | No | Yes; 0 violation | 1 alert: catechol\_A |
| [apigenin](https://pubchem.ncbi.nlm.nih.gov/compound/5280443) | [5280443](https://pubchem.ncbi.nlm.nih.gov/compound/5280443) | C1=CC(=CC=C1C2=CC(=O)C3=C(C=C(C=C3O2)O)O)O | 270.24 g/mol | 5 | 3 | 1.89 | 4.40 | High | No | Yes; 0 violation | 0 alert |

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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 |
| [Ursolic acid](https://pubchem.ncbi.nlm.nih.gov/compound/64945) | [64945](https://pubchem.ncbi.nlm.nih.gov/compound/64945) | C[C@@H]1CC[C@@]2(CC[C@@]3(C(=CC[C@H]4[C@]3(CC[C@@H]5[C@@]4(CC[C@@H](C5(C)C)O)C)C)[C@@H]2[C@H]1C)C)C(=O)O | Active, 0.52 | Active, 0.57 | Active, 0.95 | Inactive, 0.85 | Inactive, 0.99 |
| [OLEANOLIC ACID](https://pubchem.ncbi.nlm.nih.gov/compound/10494) | [10494](https://pubchem.ncbi.nlm.nih.gov/compound/10494) | C[C@]12CC[C@@H](C([C@@H]1CC[C@@]3([C@@H]2CC=C4[C@]3(CC[C@@]5([C@H]4CC(CC5)(C)C)C(=O)O)C)C)(C)C)O | Active, 0.52 | Active, 0.57 | Active, 0.79 | Inactive, 0.85 | Inactive, 0.99 |
| [CHLOROGENIC ACID](https://pubchem.ncbi.nlm.nih.gov/compound/1794427) | [1794427](https://pubchem.ncbi.nlm.nih.gov/compound/1794427) | C1[C@H]([C@H]([C@@H](C[C@@]1(C(=O)O)O)OC(=O)/C=C/C2=CC(=C(C=C2)O)O)O)O | Inactive, 0.72 | Inactive, 0.68 | Active, 0.99 | Inactive, 0.93 | Inactive, 0.80 |
| [Orientin](https://pubchem.ncbi.nlm.nih.gov/compound/5281675) | [5281675](https://pubchem.ncbi.nlm.nih.gov/compound/5281675) | C1=CC(=C(C=C1C2=CC(=O)C3=C(O2)C(=C(C=C3O)O)[C@H]4[C@@H]([C@H]([C@@H]([C@H](O4)CO)O)O)O)O)O | Inactive, 0.81 | Inactive, 0.72 | Active, 0.52 | Active, 0.52 | Inactive, 0.87 |
| [rosmarinic acid](https://pubchem.ncbi.nlm.nih.gov/compound/5281792) | [5281792](https://pubchem.ncbi.nlm.nih.gov/compound/5281792) | C1=CC(=C(C=C1C[C@H](C(=O)O)OC(=O)/C=C/C2=CC(=C(C=C2)O)O)O)O | Inactive, 0.62 | Inactive, 0.66 | Active, 0.93 | Inactive, 0.85 | Inactive, 0.90 |
| [luteolin](https://pubchem.ncbi.nlm.nih.gov/compound/5280445) | 5280445 | C1=CC(=C(C=C1C2=CC(=O)C3=C(C=C(C=C3O2)O)O)O)O | Active, 0.69 | Inactive, 0.62 | Active, 0.96 | Inactive, 0.97 | Inactive, 0.93 |
| [kaempferol](https://pubchem.ncbi.nlm.nih.gov/compound/5280863) | [5280863](https://pubchem.ncbi.nlm.nih.gov/compound/5280863) | C1=CC(=CC=C1C2=C(C(=O)C3=C(C=C(C=C3O2)O)O)O)O | Inactive, 0.68 | Inactive, 0.72 | Inactive, 0.96 | Inactive, 0.52 | Inactive, 0.98 |
| [quercetin](https://pubchem.ncbi.nlm.nih.gov/compound/5280343) | [5280343](https://pubchem.ncbi.nlm.nih.gov/compound/5280343) | C1=CC(=C(C=C1C2=C(C(=O)C3=C(C=C(C=C3O2)O)O)O)O)O | Inactive, 0.69 | Active, 0.68 | Inactive, 0.87 | Active, 0.51 | Inactive, 0.99 |
| [(-)-Epicatechin](https://pubchem.ncbi.nlm.nih.gov/compound/72276) | [72276](https://pubchem.ncbi.nlm.nih.gov/compound/72276) | C1[C@H]([C@H](OC2=CC(=CC(=C21)O)O)C3=CC(=C(C=C3)O)O)O | Inactive, 0.72 | Inactive, 0.51 | Inactive, 0.96 | Inactive, 0.55 | Inactive, 0.84 |
| [apigenin](https://pubchem.ncbi.nlm.nih.gov/compound/5280443) | [5280443](https://pubchem.ncbi.nlm.nih.gov/compound/5280443) | C1=CC(=CC=C1C2=CC(=O)C3=C(C=C(C=C3O2)O)O)O | Inactive, 0.68 | Inactive, 0.62 | Inactive, 0.99 | Inactive, 0.57 | Inactive, 0.87 |

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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** |  |  |
| **Figure 02** | A picture containing sketch, drawing, clipart, cartoon  Description automatically generated |  |
| **Figure 03** | A picture containing cartoon, art  Description automatically generated |  |
| **Figure 04** | A picture containing clipart, illustration, design  Description automatically generated |  |
| **Figure 05** | A picture containing text, diagram, font, screenshot  Description automatically generated |  |

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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 - A:ASP709:OD1 | 2.22512 | Hydrogen Bond | Conventional Hydrogen Bond |
| N:UNK1:C - A:PHE240 | 3.69485 | Hydrophobic | Pi-Sigma |
| N:UNK1:C - A:VAL252 | 4.36188 | Hydrophobic | Alkyl |
| A:LYS122 - N:UNK1 | 5.0335 | Hydrophobic | Alkyl |
| A:VAL252 - N:UNK1 | 5.11543 | Hydrophobic | Alkyl |
| A:ALA707 - N:UNK1 | 4.60727 | Hydrophobic | Alkyl |
| A:ALA707 - N:UNK1 | 5.34871 | Hydrophobic | Alkyl |
| A:PHE240 - N:UNK1 | 5.19991 | Hydrophobic | Pi-Alkyl |
| A:PHE240 - N:UNK1 | 4.5481 | Hydrophobic | Pi-Alkyl |
| A:PHE240 - N:UNK1:C | 4.81697 | Hydrophobic | Pi-Alkyl |
| N:UNK1:H - A:ASP709:OD1 | 2.22512 | Hydrogen Bond | Conventional Hydrogen Bond |
| N:UNK1:C - A:PHE240 | 3.69485 | Hydrophobic | Pi-Sigma |
| N:UNK1:C - A:VAL252 | 4.36188 | Hydrophobic | Alkyl |
| A:LYS122 - N:UNK1 | 5.0335 | Hydrophobic | Alkyl |

Discussion

While the ligand, Ursolic acid (CID:64945) with -9.3 binding affinity has the best score, it shows hepatotoxicity, carcinogenicity, and immunotoxicity concerns. The ligand, OLEANOLIC ACID (CID: 10494) with -8.7 binding affinity has a slightly weaker binding score but demonstrates better toxicity and ADME profiles, making it a more balanced choice.

ADME Properties of OLEANOLIC ACID (CID: 10494)

Molecular Weight: 456.70 g/mol

Number of H-Bond Acceptors: 3

Number of H-Bond Donors: 2

Lipophilicity (iLOGP): 3.94

Water Solubility (Log S - SILICOS-IT): -6.12

GI Absorption: Low

BBB Permeant: No

Lipinski's Rule of Five: Yes (1 violation: MLOGP > 4.15)

PAINS Alert: 0 (No alerts)

Toxicity Profile

Hepatotoxicity: Inactive (0.72); Carcinogenicity: Inactive (0.68); Immunotoxicity: Active (0.99); Mutagenicity: Inactive (0.93); Cytotoxicity: Inactive (0.80)

Conclusion

OLEANOLIC ACID (CID: 10494) with a binding affinity of -8.7 kcal/mol is recommended for further investigation and optimization due to its favorable toxicity profile and acceptable ADME properties.