Assignment -02

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	EnergyMinimized_Cleaned_2ZJ3_4970_uff_E=725.97	-8.6	0	0
02	EnergyMinimized_Cleaned_2ZJ3_493570_uff_E=317.94	-7.9	0	0
03	EnergyMinimized_Cleaned_2ZJ3_5280343_uff_E=380.43	-7.6	0	0
04	EnergyMinimized_Cleaned_2ZJ3_1130_uff_E=395.86	-6.6	0	0
05	EnergyMinimized_Cleaned_2ZJ3_10281_uff_E=62.47	-6.4	0	0
06	EnergyMinimized_Cleaned_2ZJ3_54670067_uff_E=200.65	-6.4	0	0
07	EnergyMinimized_Cleaned_2ZJ3_10248_uff_E=228.13	-6.1	0	0
08	EnergyMinimized_Cleaned_2ZJ3_5315468_uff_E=179.09	-6.1	0	0
09	EnergyMinimized_Cleaned_2ZJ3_3314_uff_E=169.59	-5.9	0	0
10	EnergyMinimized_Cleaned_2ZJ3_10364_uff_E=78.47	-5.8	0	0

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								Pharmaco kinetics		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
Protopine	4970	CN1CCC2=CC3=C(C=C2C(=O)CC4=C(C1)C5=C(C=C4)OCO5)OCO3	**353.37 g/mol**	**6**	**0**	**3.19**	**-5.38**	**High**	**Yes**	**Yes; 0 violation**	**0 alert**
Riboflavin	493570	CC1=CC2=C(C=C1C)N(C3=NC(=O)NC(=O)C3=N2)C[C@@H]([C@@H]([C@@H](CO)O)O)O	**376.36 g/mol**	**8**	**5**	**1.63**	**-2.62**	**Low**	**No**	**Yes; 0 violation**	**0 alert**
Quercetin	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**
Thiamine	1130	CC1=C(SC=[N+]1CC2=CN=C(N=C2N)C)CCO	**265.35 g/mol**	**3**	**2**	**-1.60**	**-3.30**	**High**	**No**	**Yes; 0 violation**	**0 alert**
Thymoquinone	10281	CC1=CC(=O)C(=CC1=O)C(C)C	**164.20 g/mol**	**2**	**0**	**1.99**	**-2.03**	**High**	**Yes**	**Yes; 0 violation**	**1 alert: quinone_A**
Ascorbic Acid	54670067	C([C@@H]([C@@H]1C(=C(C(=O)O1)O)O)O)O	**176.12 g/mol**	**6**	**4**	**-0.31**	**1.49**	**High**	**No**	**Yes; 0 violation**	**0 alert**
Elemicin	10248	COC1=CC(=CC(=C1OC)OC)CC=C	**208.25 g/mol**	**3**	**0**	**2.89**	**-3.64**	**High**	**Yes**	**Yes; 0 violation**	**0 alert**
(E)-alpha-bisabolene	5315468	CC1=CCC(CC1)/C(=C/CC=C(C)C)/C	**204.35 g/mol**	**0**	**0**	**3.49**	**-4.92**	**Low**	**No**	**Yes; 1 violation**	**0 alert**
Eugenol	3314	COC1=C(C=CC(=C1)CC=C)O	**164.20 g/mol**	**2**	**1**	**2.37**	**-2.79**	**High**	**Yes**	**Yes; 0 violation**	**0 alert**
Carvacrol	10364	CC1=C(C=C(C=C1)C(C)C)O	**150.22 g/mol**	**1**	**1**	**2.24**	**-3.01**	**High**	**Yes**	**Yes; 0 violation**	**0 alert**

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
Protopine	4970	CN1CCC2=CC3=C(C=C2C(=O)CC4=C(C1)C5=C(C=C4)OCO5)OCO3	**Inactive**	**Inactive**	**Inactive**	**Inactive**	**Inactive**
Riboflavin	493570	CC1=CC2=C(C=C1C)N(C3=NC(=O)NC(=O)C3=N2)C[C@@H]([C@@H]([C@@H](CO)O)O)O	**Inactive**	**Inactive**	**Inactive**	**Inactive**	**Inactive**
Quercetin	5280343	C1=CC(=C(C=C1C2=C(C(=O)C3=C(C=C(C=C3O2)O)O)O)O)O	**Inactive**	**Active**	**Inactive**	**Active**	**Inactive**
Thiamine	1130	CC1=C(SC=[N+]1CC2=CN=C(N=C2N)C)CCO	**Inactive**	**Inactive**	**Inactive**	**Inactive**	**Inactive**
Thymoquinone	10281	CC1=CC(=O)C(=CC1=O)C(C)C	**Inactive**	**Inactive**	**Inactive**	**Inactive**	**Inactive**
Ascorbic Acid	54670067	C([C@@H]([C@@H]1C(=C(C(=O)O1)O)O)O)O	**Inactive**	**Inactive**	**Inactive**	**Inactive**	**Inactive**
Elemicin	10248	COC1=CC(=CC(=C1OC)OC)CC=C	**Inactive**	**Active**	**Inactive**	**Active**	**Inactive**
(E)-alpha-bisabolene	5315468	CC1=CCC(CC1)/C(=C/CC=C(C)C)/C	**Inactive**	**Inactive**	**Inactive**	**Inactive**	**Inactive**
Eugenol	3314	COC1=C(C=CC(=C1)CC=C)O	**Inactive**	**Inactive**	**Inactive**	**Inactive**	**Inactive**
Carvacrol	10364	CC1=C(C=C(C=C1)C(C)C)O	**Inactive**	**Inactive**	**Inactive**	**Inactive**	**Inactive**

Task 04: Identify the highest-ranking Protein – ligand complex and input the corresponding figures into the table below.

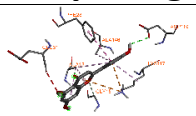
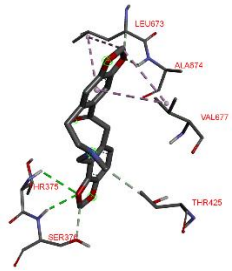
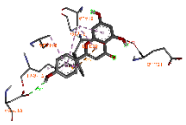
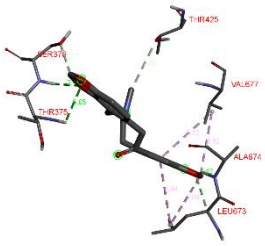
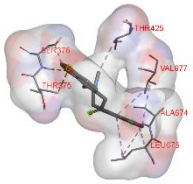
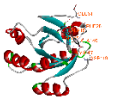
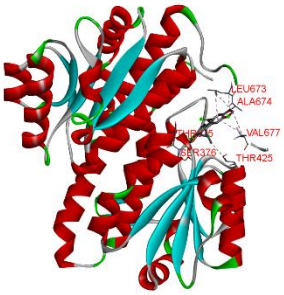
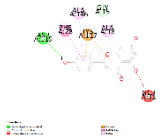
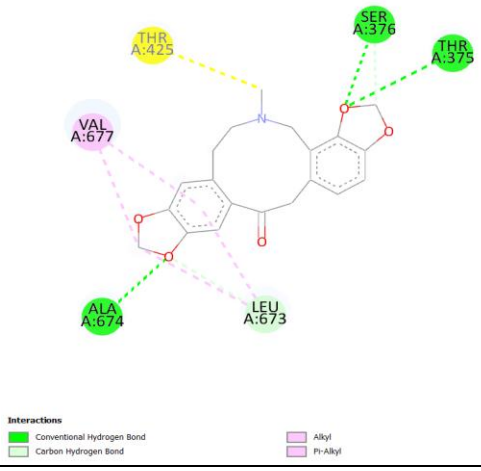
Figure Name	Sample Figure	Input your Docking Figure
Figure 01		
Figure 02		

Figure 03		
Figure 04		
Figure 05		

Task 05: Identify the highest-ranking Protein – ligand complex and input the Interaction details into the table below.

Name	Distance	Category	Types
A:SER17:HN - N:UNK1:O	2.09402	Hydrogen Bond	Conventional Hydrogen Bond
N:UNK1:H - A:ASP119:OD1	2.76343	Hydrogen Bond	Conventional Hydrogen Bond
N:UNK1:H - A:SER17:OG	2.46092	Hydrogen Bond	Conventional Hydrogen Bond
A:GLY15:CA - N:UNK1:O	3.39195	Hydrogen Bond	Carbon Hydrogen Bond
A:LYS117:NZ - N:UNK1	4.76291	Electrostatic	Pi-Cation
A:LYS117:NZ - N:UNK1	4.15331	Electrostatic	Pi-Cation
A:PHE28 - N:UNK1	4.77558	Hydrophobic	Pi-Pi T-shaped
N:UNK1 - A:ALA18	4.61833	Hydrophobic	Pi-Alkyl
N:UNK1 - A:ALA18	4.27778	Hydrophobic	Pi-Alkyl
N:UNK1 - A:ALA18	5.29333	Hydrophobic	Pi-Alkyl
N:UNK1 - A:LYS117	4.1186	Hydrophobic	Pi-Alkyl
N:UNK1 - A:ALA146	4.8247	Hydrophobic	Pi-Alkyl

In the context of protein-ligand docking, the best ligand is usually determined based on the binding affinity (more negative indicates stronger binding) and RMSD values (close to 0 indicates stability in binding poses). From the task 1: Protopine has the most negative binding affinity (-8.6), indicating the strongest interaction with the target protein. It also has RMSD values of 0, showing good binding pose stability.

Based on the task 2: Proto pine appears ideal because: Lipinski has 0 violations, High GI absorption, No BBB permeability issue, 0 alerts in PAINS.

From the toxicity prediction table, Protopine stands out as the best compound as it is Inactive for All Toxicity Categories like Hepatotoxicity, Carcinogenicity, Immunotoxicity, Mutagenicity and Cytotoxicity.

And from the bonds present in the complex it is confirmed that protopine is the best one as it has several strong hydrogen bonds present.