BIRLA INSTITUTE OF TECHNOLOGY & SCIENCE
Comprehensive Examination (First Semester 2022-2023)

Course Name: Computer Aided Drug Design Course No: PHA G541
Max. Marks: 35 Time: 180 Min

Note: Give your precise answers for both Part-A and Part-B in a separate answer sheets with appropriate illustrations and examples wherever applicable.
Write answers for sub-division in all one place together.

Part-A (Closed Book) 15 Marks

1) a) Explain about the risk mitigation strategies in academic pre-clinical drug discovery.
b) Write the applications and limitations of Pharmacophore modeling. **(2x2.5=5)**

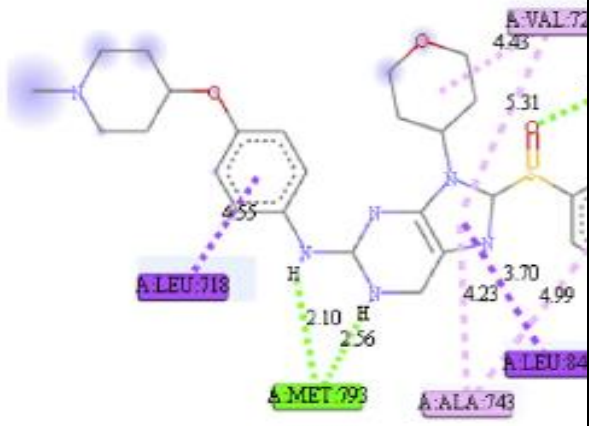
2) a) Explain about the available methods of 2D QSAR. Write the strategies for the selection of descriptors in 2D QSAR. **(2x2.5=5)**
b) Write the significance of pre-systemic metabolism, protein binding in drug discovery.

3) a) Explain about the integrated target / physiology-based drug discovery approach. **(2x2.5=5)**
b) Write a brief account on filtering strategies adopted during LBDD in the case of DD for unknown target.

Part-B (Open Book) **(5x4=20 Marks)**

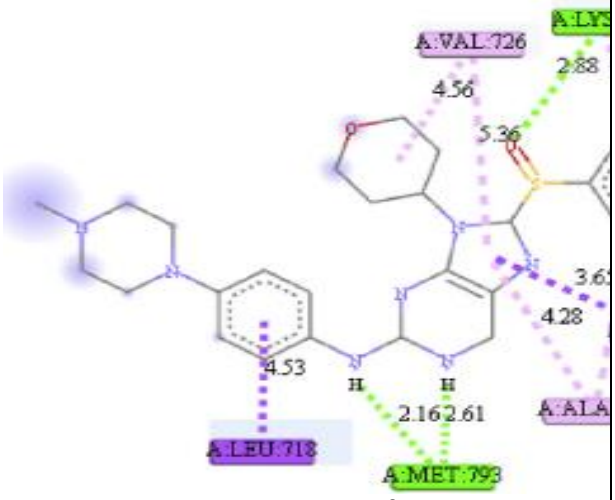
1) Interpret the following docking results and write your comments,

a)



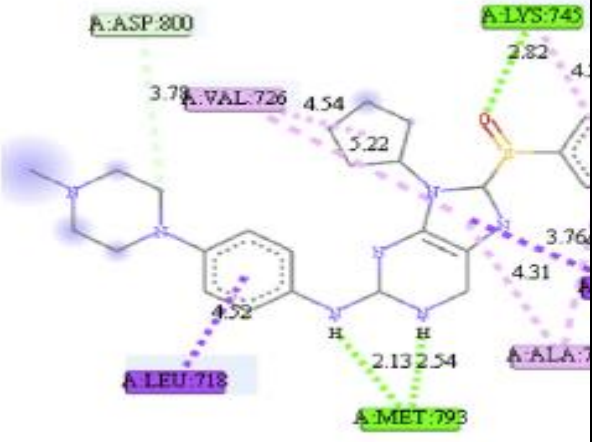
2D Docked interactive pose of **compound A** in the active site of in the active site of EGFR-TK (PDB ID: 4ZAU with estimated binding free energy of -10.40 Kcal/mol

b)



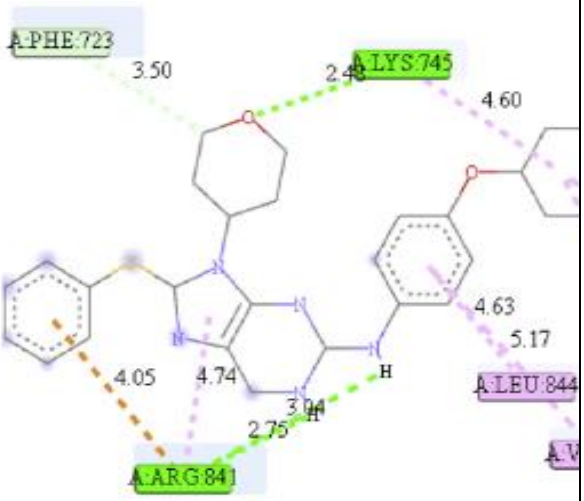
2D Docked interactive pose of **compound B** in the active site of in the active site of EGFR-TK (PDB ID: 4ZAU with estimated binding free energy of -10.30 Kcal/mol

c)



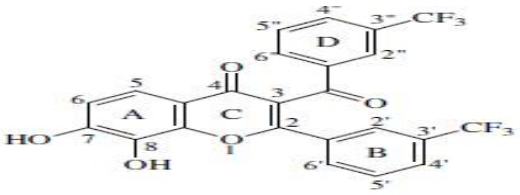
2D Docked interactive pose of **compound C** in the active site of in the active site of EGFR-TK (PDB ID: 4ZAU with estimated binding free energy of -10.20 Kcal/mol

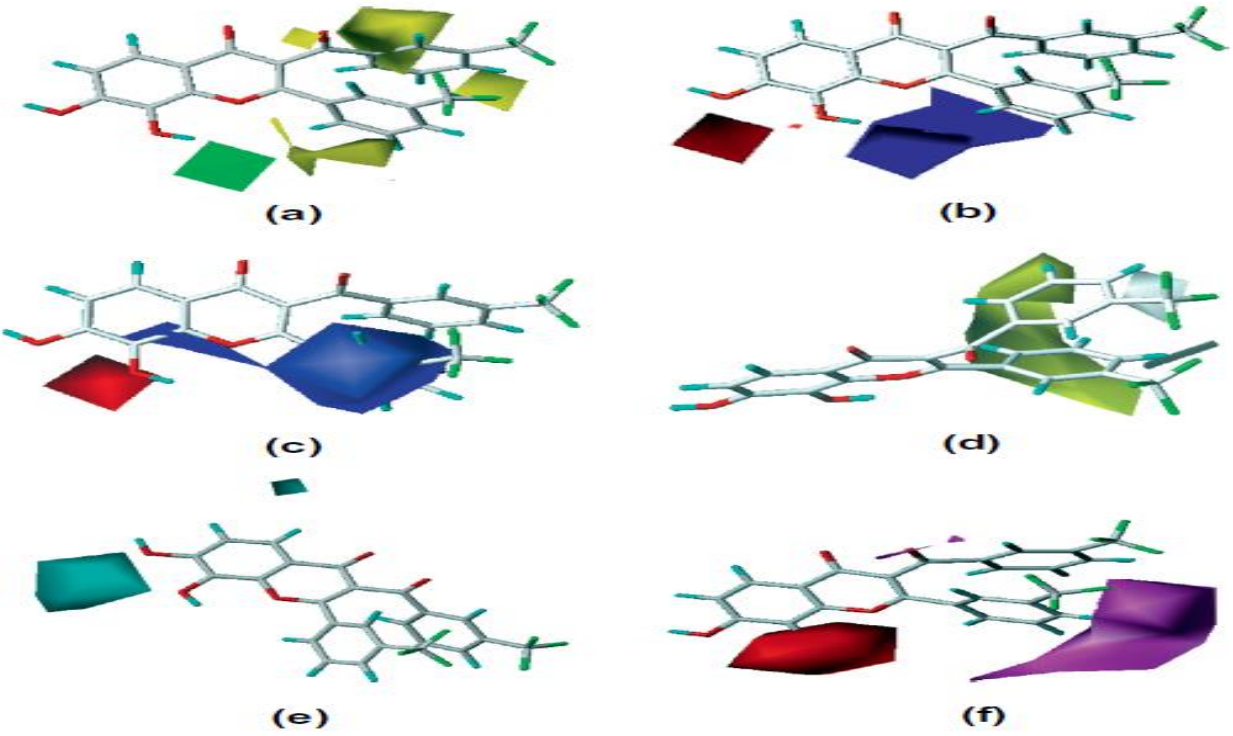
d)



2D Docked interactive pose of **compound D** in the active site of in the active site of EGFR-TK (PDB ID: 4ZAU with estimated binding free energy of -10.10 Kcal/mol

2) Interpret the following 3D QSAR results and write your detailed inferences





3) Write your comments regarding the predicted drug likeness score obtained using Molinspiration server for the following compounds.

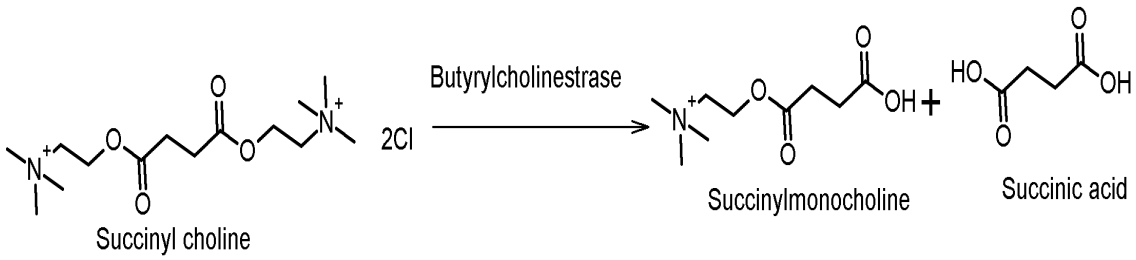
Entry	MW	*n*-ON	*n*-OHNH	logP(o/w)	*n*-rotb	MV	TPSA	%Abs	n violation
Rule	< 500	< 10	< 5	< 5	≤10	,500	< 160	100%	≤1
4a	421.47	9	1	2.14	4	367.36	91.29	77.50	0
4b	435.50	9	1	2.59	4	383.92	91.29	77.50	0
4c	451.49	10	1	2.20	5	392.91	100.52	74.32	0
4d	465.52	10	1	2.57	6	409.71	100.52	74.32	0
4e	497.57	9	1	3.94	5	438.77	91.29	77.50	0
4f	439.46	9	1	2.30	4	372.30	91.29	77.50	0
4g	455.91	9	1	2.79	4	380.90	91.29	77.50	0
4h	455.91	9	1	2.82	4	380.90	91.29	77.50	0
4i	500.36	9	1	2.92	4	385.25	91.29	77.50	1
4j	500.36	9	1	2.95	4	385.25	91.29	77.50	1
4k	547.36	9	1	3.22	4	391.35	91.29	77.50	1
4l	466.46	12	1	2.08	5	390.70	137.11	61.70	1
4m	466.46	12	1	2.10	5	390.70	137.11	61.70	1
4n	446.48	10	1	1.90	4	384.22	115.08	69.30	0

4a–n

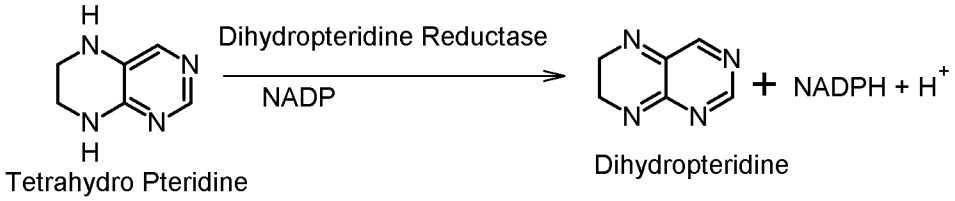
Comp. Code	**R**	**Comp. Code**	**R**
4a	H	4h	4-Cl
4b	4-CH_3	4i	3-Br
4c	4-OCH_3	4j	4-Br
4d	4-OC_2H_5	4k	4-I
4e	4-C_6H_5	4l	3-NO_2
4f	4-F	4m	4-NO_2
4g	3-Cl	4n	4-CN

4) How will you design a potential lead for the inhibition of the following enzymes. Write the appropriate category of application of the developed lead.

a)



b)



5) How will you access the stability of ligand-target complex and write the roadmap for the same.
