BIRLA INSTITUTE OF TECHNOLOGY & SCIENCE
Pilani-333031. Rajasthan
Comprehensive Examination (First Semester 2023-2024)

Course Name: Computer Aided Drug Design Course No: PHA G541
Max. Marks: 30 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) (5x2=10 Marks)

1) Enumerate the significance of choice of bioassay during lead discovery phase of NDD.

2) Write a brief account on Design in Receptor (DiR).

3) Write a note on "threading" method of protein modelling.

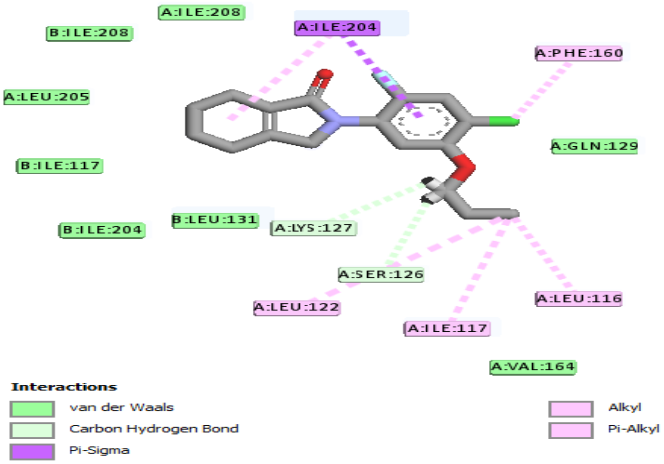
4) Write a note on free Wilson method of 2D QSAR analysis.

5) Write about Retrometabolic Drug Design (RMDD) strategy.

Part-B (Open Book) **(7x3=21 Marks)**

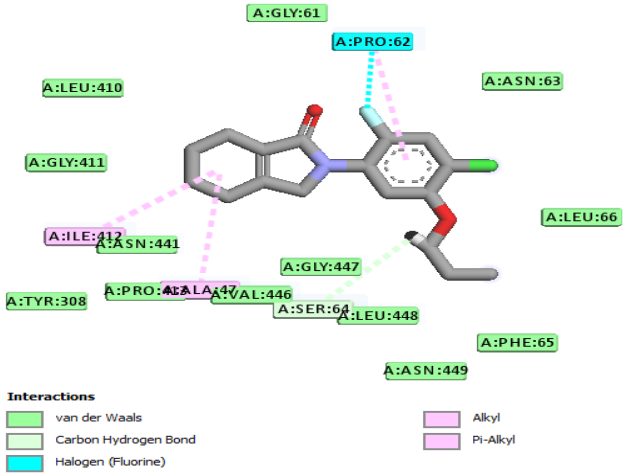
1) Interpret the following *in silico* study results and write your inference / comments.

a)



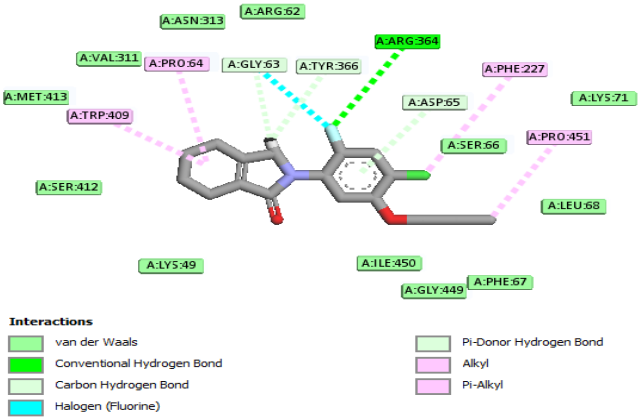
2D Docked interactive pose of **compound A** in the active site of Protoporphyrinogen oxidase of Nicotiana-tabaccum (PDB ID: 1SEZ) with estimated binding free energy of -1.86 Kcal/mol

b)



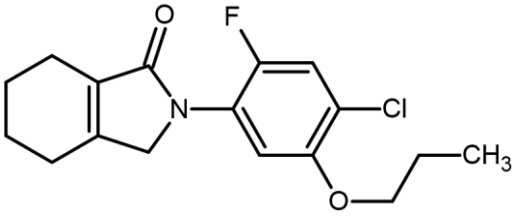
2D Docked interactive pose of **compound A** in the a oxidase of Bacillus Subtilis (PDB ID: 2IVE) with es 4.32 Kcal/mol

c)

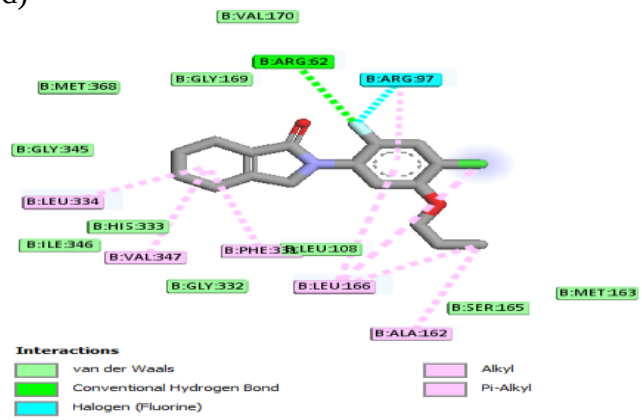


2D Docked interactive pose of **compound A** in the active site of Protoporphyrinogen oxidase of Myxococcus Xanthus (PDB ID: 3I6D) with estimated binding free energy of 6.07 Kcal/mol

Structure of Compound A



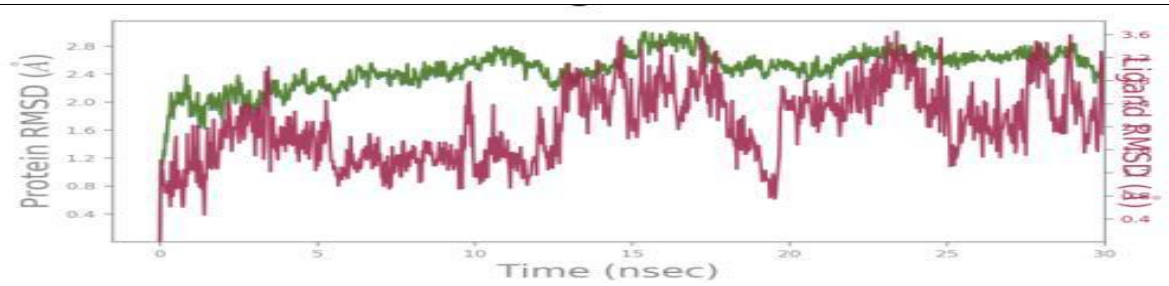
d)



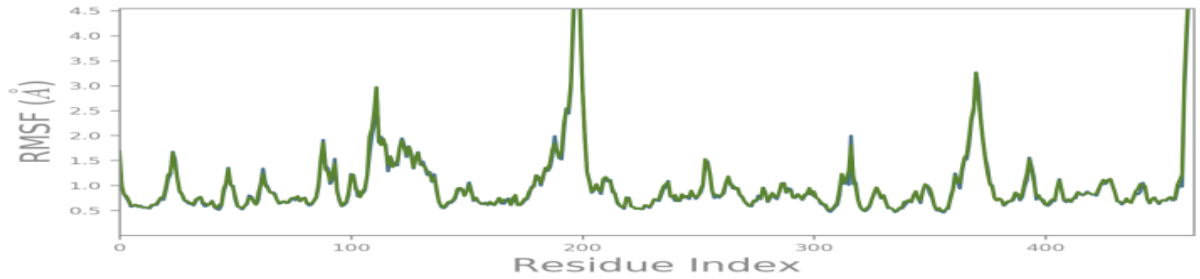
2D Docked interactive pose of **compound A** in the a oxidase of Human (PDB ID: 4IVM) with estimated Kcal/mol

2) Interpret the following *in silico* study results and write your inference / comments.

a)

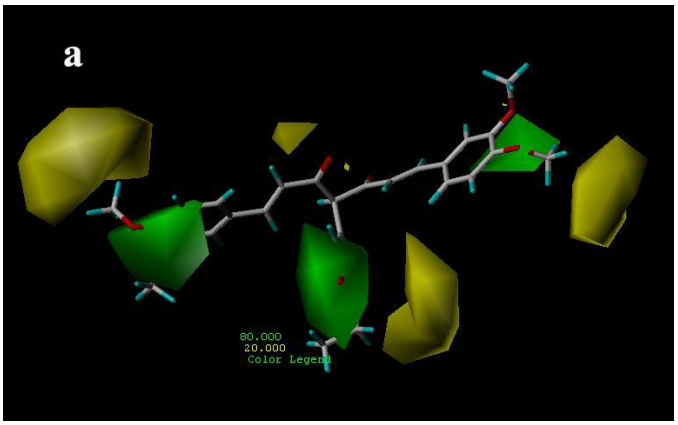


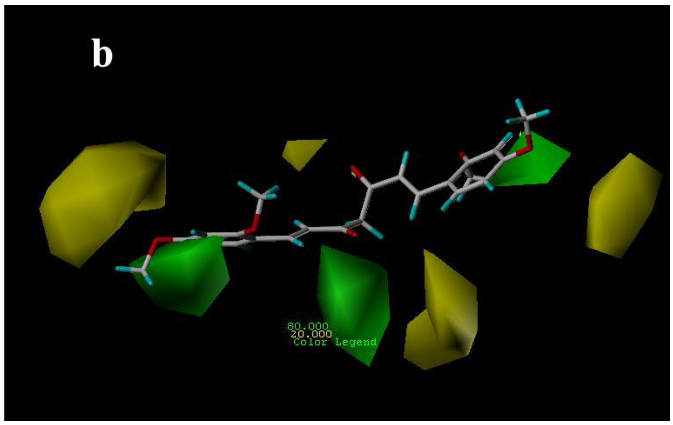
b)

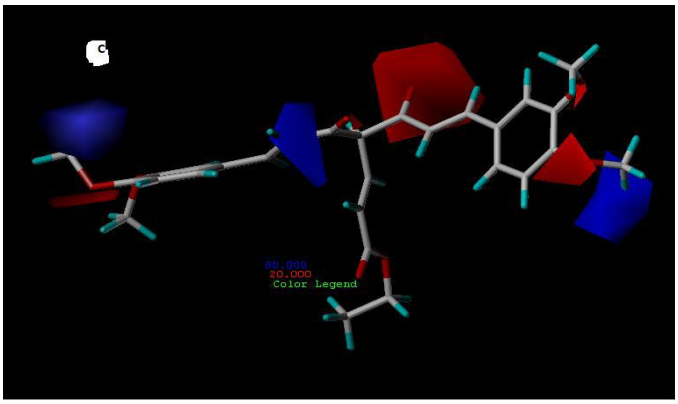


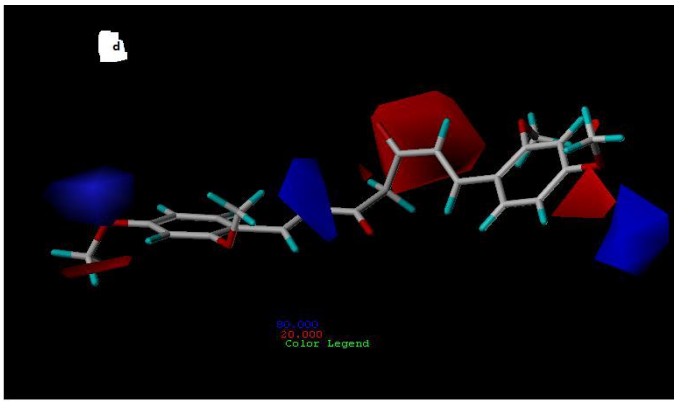
a) RMSD graph of the complex (compound A and Human protoporphirinogen oxidase (PDB: 4IVM); b) RMSF graph of the complex (compound A and Human protoporphirinogen oxidase (PDB: 4IVM)

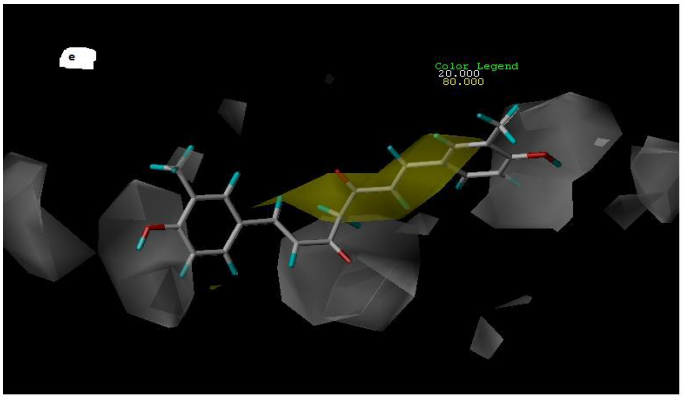
3) Interpret the following 3D QSAR results and write your detailed inferences.

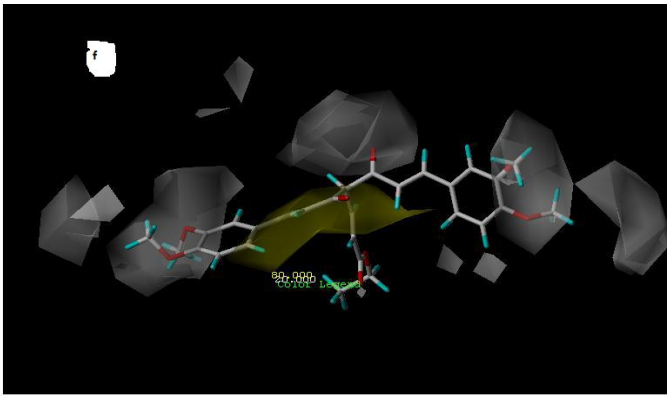


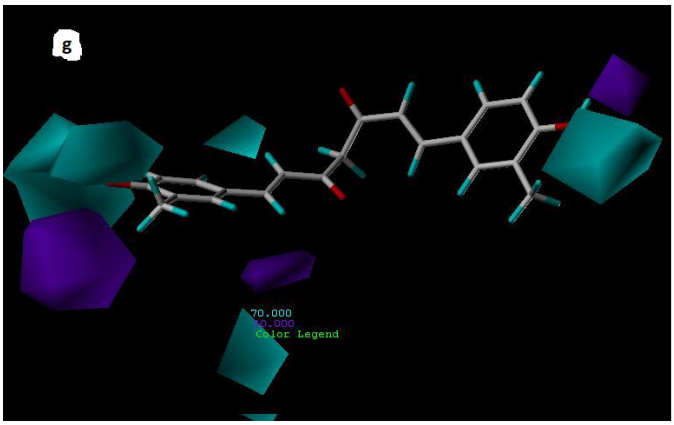


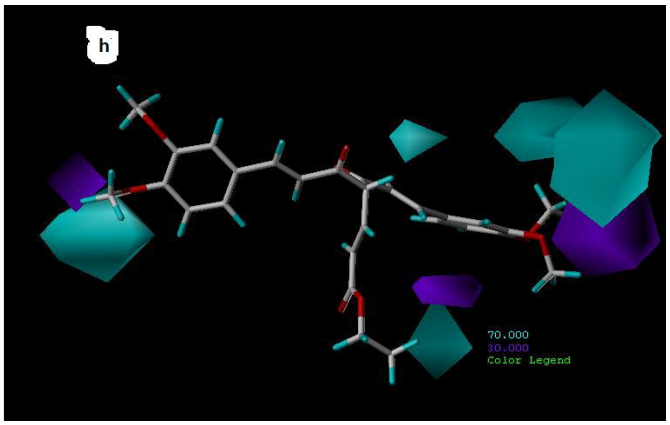


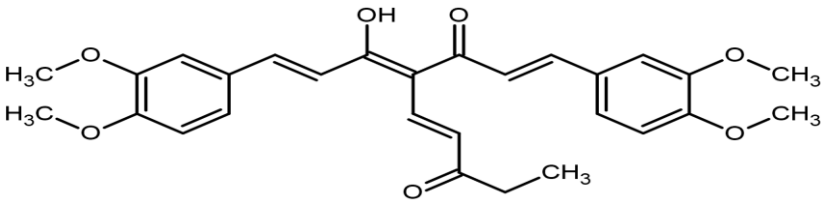
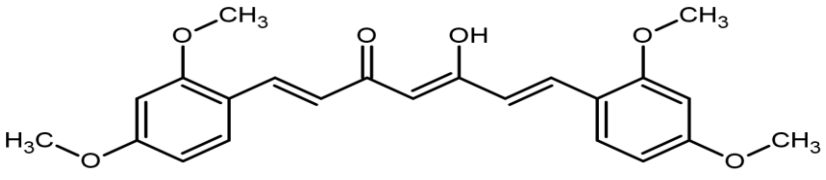
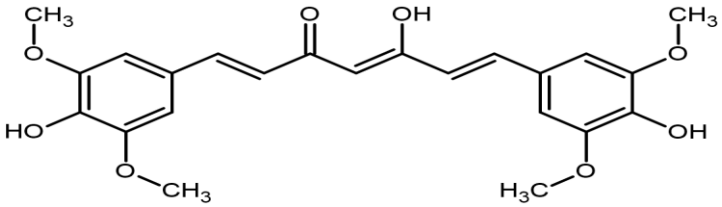










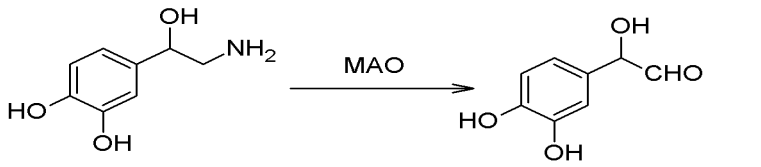
Comp.	Structure
a, c, f, h	
b, d	
e, g	

4) Write your comments regarding the predicted *in silico* parameters for the following compounds.

Comp. No.	Molinspiration							Pre ADMET			Molsoft	
	LogP	MW	n-ON	n-OHNH	Lipinski's Violation	TPSA (Å^2)	% ABS	PPB%	BBB	HIA%	Mol log S (mg/L)	Drug likeness model score
3	2.93	357.39	7	3	0	107.45	71.93	87.61	0.06	91.55	0.56	0.54
6a	**5.46**	463.57	6	3	1	85.31	79.57	100.00	0.09	96.17	0.00	0.08
6c	**5.91**	477.59	6	3	1	85.31	79.57	100.00	0.09	96.27	0.00	0.40
9	2.58	318.37	6	2	0	93.42	76.77	96.47	0.11	97.84	0.19	−0.33
10	3.03	365.42	7	2	0	95.94	75.90	88.94	0.17	98.14	0.26	0.67
11	3.33	366.40	7	1	0	90.14	77.90	95.31	0.22	97.89	0.25	0.78
13	**6.44**	**507.02**	6	1	2	68.00	85.54	100.00	0.08	97.79	0.00	0.35

5) 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)



Norepinephrine Norepinephrine aldehyde

b)

DHF THF

6) What type of work flow will you follow to generate an anti-COVID-19 RdRp target focused library.

7) What are all the strategies will you adopt for the identification of appropriate molecular target for the obtained hit molecule in phenotypic screening against trypanosomiasis?
