Exam Date & Time: 18-Jul-2022 (10:00 AM - 01:00 PM)

MANIPAL ACADEMY OF HIGHER EDUCATION

Computer Aided Drug Design [PCH-BP807ET-S2]

Marks: 75 **Duration: 180 mins.**

I Multiple Choice Questions (MCQs)

Answer all the questions. Section Duration: 30 mins

1) Which of the following statement is not true in identifying a drug target

1)	hitting a target toward the end of a pathway (downstream) causes fewer side effects		2)	hitting a target toward the beginning of a pathway (upstream) causes fewer side effects		3)	Identifying genes whose expression is up- or down-regulated in the disease state		4)	deletion or overexpression of a specific gene in vivo (animals ,mice)		(1)

2) Surface Plasmon resonance for screening ligands involves

1)	Reduction in emission of light		2)	Change in refractive index		3)	Relaxation times of ligands bound to a macromolecule are shorter than when they are unbound		4)	None of the above		(1)

3) Which of the following is not a "Rule of Five" (Ro5) for drug-likeness filter

1)	molecular weight less than 500 Da		2)	number of hydrogen bond donors equal or less than 5		3)	number of hydrogen bond acceptors less than 10		4)	calculated Log P more than 5.0		(1)

4) What is an allosteric inhibitor?

1)	inhibitor mimics the substrate, competing		2)	inhibitor does not mimics the substrate,		3)	substrate which binds to the active		4)	Inhibitor with binds to the enzyme away from the active site altering the		(1)

	for the active site		competing for the active site		site		conformation receptor/enzyme				

5) What is the upper Polar Surface Area threshold value for oral absorption of a drug (1)

1)	80-90 Å2		2)	90-100 Å2		3)	140-150 Å		4)	250-60 Å2	

6) In which of the following cases pharmacophore based approach for virtual screening can be used (1)

1)	When structure of target protein and structure of active ligands against that target is known		2)	When structure of target protein is unknown and structure of active ligands known		3)	When structure of target protein is known and structure of active ligands is unknown		4)	All of the above	

7) Which of the following is not a method used for conformational analysis (1)

1)	Systematic search		2)	Random search		3)	Scaffold hopping		4)	Simulated anncaling/Molecular dynamics	

8) . π-substituent hydrophobicity constant is (1)

1)	Measure of how hydrophobic a substituent is relative to Hydrogen		2)	Measure of hydrophobic substituent constant of unsubstituted chemical species.		3)	Measure of how hydrophobic a Hydrogen is relative to substitution		4)	Measure of hydrophobic constant of an unsubstituted molecule	

9) What does a negative value of σ signify for a substituent? (1)

1)	It is electron withdrawing		2)	It is electron donating		3)	It is neutral		4)	It is hydrophobic	

10) What does MR represent in a QSAR equation? (1)

1)	Molar refractivity is an electronic factor		2)	Molar refractivity is a hydrophobic factor		3)	Molar refractivity is a steric factor		4)	Molar refractivity is a stereoelectronic factor	

11) What does the symbol P represent in a QSAR equation? (1)

1)	pH		2)	Plasma Concentration		3)	Partition coefficient		4)	None of the above	

12) Following is an electronic parameter in QSAR

1)	Dipole moment		2)	Verloop parameter		3)	Mol Ref		4)	Molecular weight		(1)

13) One of the following is not used in QSAR

1)	Molecular connectivity index		2)	Molecular similarity index		3)	Topological polar surface area		4)	Partition coefficient		(1)

14) The most common program for structure drawing is

1)	Dragon		2)	CORINA		3)	UNIPROT		4)	FT map		(1)

15) A simple molecular mechanics energy equation is given by the sum of

1)	Stretching Energy + Bending Energy +Torsion Energy + Non-Bonded interaction energy		2)	Stretching Energy + Bending Energy +Torsion Energy		3)	Bending Energy +Torsion Energy + Non-Bonded Interaction Energy		4)	Stretching Energy +Torsion Energy + Non-Bonded Interaction Energy		(1)

16) Software used to detect presence or absence of water molecule is:

1)	GLIDE		2)	H++		3)	PHASE		4)	JAWS		(1)

17) Chemoinformatics mainly deals with approaches employed for the following:

1)	Chemical, Biological and Biochemical data base concept		2)	Chemical and Biological database concept		3)	Chemical database concept		4)	Biochemical and chemical data base concept		(1)

18) The biggest challenges (protein folding problems) of structural bioinformatics reside in prediction of

1)	Secondary structure from primary structure		2)	Tertiary structure from Primary structure		3)	Tertiary structure from secondary structure		4)	Quaternary structure from secondary structure		(1)

19) Roothan Hall equation follows

1)	Born oppenheimer and Hartree Fock approximation	2)	LCAO and Born oppenheimer approximation	3)	LCAO and Hartree Fock approximation	4)	LCAO, Born oppenheimer and Hartree Fock approximation	(1)

20) MM1 force field is applied only to

1)	Saccharides	2)	Hydrocarbons	3)	Nucleotides	4)	Proteins	(1)

II Long Answers

Answer all the questions.

1) Enlist the various methods used for lead discovery and add a note on lead optimization (5)

A)

B) Explain Lead discovery from existing drugs and serendipity with suitable examples (5)

2) Mention the software used in drug discovery program. Enlist various chemical databases (5)

A)

B) Explain the importance of HTS and Combinatorial chemistry in new Drug discovery (3)

C) How is bioinformatics useful in new drug discovery program? (2)

III Short Answers

Answer all the questions.

1) What are the situations/types for pharmacophore search? Explain divide and conquer ligand build up strategies for in situ De novo drug design (5)

2) Explain in various stages of protein-ligand docking (5)

3) What is Force field? Mention its relevance in molecular mechanics (2)

A)

B) Mention the various Force field softwares used along with their applications and list out 3 methods of conformation generations and explain any one of them (3)

4) Explain the principles and applications of Quantum mechanics (2)

A)

B) What is a pharmacophore? Discuss the importance of pharmacophore concept (3)

5) Explain the parabolic relation between LogP and log 1/C with the help of a graph and write the equation for the parabolic relation. (5)

6) Taking the example of benzoic acid and its derivatives explain π substituent constant (5)

as a parameter in QSAR

7) Explain a case study where alteration of physicochemical properties resulted by bioisosteric replacement (5)

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