Question Paper

Exam Date & Time: 15-May-2023 (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) With respect to the use of NMR for screening ligands , which of the following statement is not true? (1)

- compounds can be tested or screened for their affinity to a macromolecular target
- Relaxation times of ligands bound to a macromolecule are shorter than when they are unbound
- If the drug binds to the protein, its nuclei will have a shorter relaxation time and no NMR spectrum will be detected
- If the drug does not binds to the protein, its nuclei will have a shorter relaxation time and no NMR spectrum will be detected

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

3) Which of the following is not a "Rule of Five" (Ro5) for drug-likeness filter? (1)

- molecular weight less than 500 Da
- number of hydrogen bond donors equal or less than 5
- number of hydrogen bond acceptors less than 10
- calculated Log P more than 5.0

4) What is an allosteric inhibitor? (1)

- inhibitor mimics the substrate, competing for the active site
- inhibitor does not mimics the substrate, competing for the active site
- substrate which binds to the active site
- Inhibitor with binds to the enzyme away from the active site altering the conformation of receptor/enzyme

5) What is the upper Polar Surface Area threshold value for brain penetration of a drug? (1)

90 Å^2

120 Å^2

150 Å^2

60 Å^2

6) Which of the following is not divide and conquer approach for in situ de novo drug design? (1)

fragment-linking

Ligand Morphing

ligand-growing

Lattice based methods

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

When structure of target protein and structure of active ligands against that target is known

When structure of target protein is unknown and structure of active ligands known

When structure of target protein is known and structure of active ligands is unknown

All of the above

8) MM1 force field is applied only to (1)

Saccharides

Hydrocarbons

Nucleotides

Proteins

9) Molecular weight and Partition coefficient as Log P of drug like compoundas per Lipinski Rule of 5 is (1)

100 and 1

300 and 3

700 and 7

500 and 5

10) Ligand based pharmacophore program is called as: (1)

Ligand Scout

SPORES

Pharma Gist

GOLD

11) The most abundant data in bioinformatics consists of the following (1)

Poly Peptides

RNA

Oligo

peptides
DNA

12) A simple molecular mechanics energy equation is given by the sum of (1)

Stretching Energy + Bending Energy +Torsion Energy + Non-Bonded Interaction Energy
Stretching Energy + Bending Energy +Torsion Energy
Bending Energy +Torsion Energy + Non-Bonded Interaction Energy
Stretching Energy +Torsion Energy + Non-Bonded Interaction Energy

13) Relibase provides database and explain search system for handling (1)

protein data
Protein ligand complex data
Carbohydrate data
Nucleotide data

14) Microarray based studies are followed in (1)

Chemoinformatics
Proteomics
Bioinformatics
Combinatorial Chemistry

15) The most popular bioisostere for the carboxylic acid is (1)

Triazole ring system
Thiadiazole ring system
Tetrazole ring system
Thiazole ring system

16) Sterically H and F are quite similar with their (1)

Molecular properties
Vander waals radii
Chemical properties
Physical and functional properties

17) 17α-Oxo-D-homo-1,4 androstadine-3,17-dione is a isoster of Testosterone in following manner (1)

Isosteric replacement of O for C
Isosteric replacement of C for O
Isosteric replacement of N for O
Isosteric replacement of O for N

18) What is Hammett constant? (1)

Measure of acidity of the compound
Measure of oxidizing capacity of the compound
Measure of electronic effect of substituent on the reactivity of the compound

Measure of steric hindrance of the compound

19) Which of the following substituent is electron withdrawing? (1)

$-NH_2$
-OH
-COOH
$-CH_3$

20) What is the significance of positive Pi substituent value? (1)

The substituent has an electron donating effect
The substituent has an electron withdrawing effect
The substituent is neutral
The substituent has steric hindrance effect

II Long Answers

Answer all the questions.

1) Explain Lead optimization and drug development stages in drug discovery and development program (5)

A)

B) Explain lead discovery through CADD (5)

2) What is Force field? Mention the various Force field softwares used along with their applications. List out 3 methods of conformation generations and explain any one of them (5)

A)

B) Mention the 3 data bases and 3 softwares used in Drug discovery. What is Local energy minimam and Global energy minima? (5)

III Short Answers

Answer all the questions.

1) What are the situations/types for pharmacophore search? Briefy explain the fundamental steps involved in the generation of pharmacophore model (5)

2) What is De novo drug design? Explain divide and conquer ligand build up strategies for in situ De novo drug design (5)

3) Write the principle involved in Quantum mechanics. What is Schrodinger equation? When do we apply approximation ? Enlist the various approximations (5)

4) What is HTS and Cobminatorial chemistry? Give their principle and applications in chemoinformatics (5)

5) Explain the steps involved in QSAR studies. Write the equation and explain the co-ordinates for linear relationship between logP and log1/c. (5)

6) Classify bioisosterism giving examples for each class. (5)

7) Explain how bioisosterism allow modification of physicochemical properties of molecules? Give examples (5)

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