BIRLA INSTITUTE OF TECHNOLOGY AND SCIENCE, PILANI

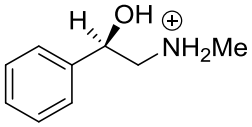
First Semester 2023-2024 MIDSEM EXAMINATION (Close Book)

Course No: CHEM F335 Course Title: Organic Chemistry and Drug Design

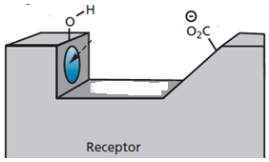
Max. Marks: 60 **Date: 11-10-2023** **Time: 90 min**

Q1. (a) Explain the distinction between a binding site and a binding region. **3**

(b) Schematically explain the binding of a chemical messenger to a protein receptor. Illustrate the binding of the given neurotransmitter to a binding site of receptor **6**

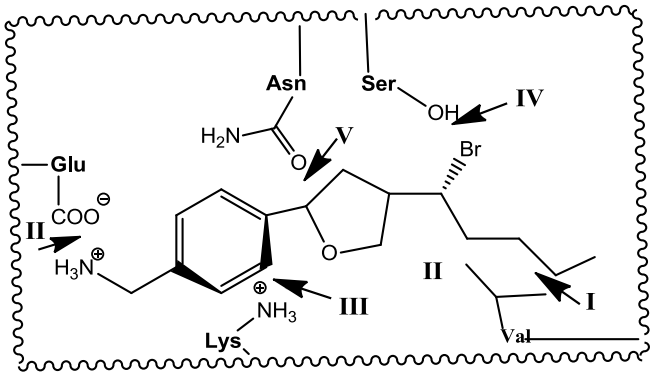


Neurotransmitter



(c) Briefly explain, (i) Dipole-dipole and ion-dipole interactions (ii) Prodrugs **4**

(d) Indicate what drug–receptor interactions are involved at every arrow shown in the figure below. More than one kind of interaction is possible for each letter. **5**



I _____

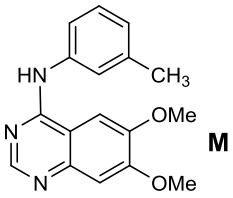
II _____

III _____

IV _____

V _____

(e) 4-Anilinoquinazoline **M** had useful *in vitro* activity but its *in vivo* activity was hampered as it gets rapidly metabolized by cytochrome P450 to produce two metabolites. Identify the structures of metabolites and modified structure which is resistance to metabolism. **4**

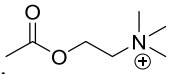


M

Q2 (**a**) Identify the intermolecular/intramolecular that are possible for the side chain of Phenylalanine and Serine **3**

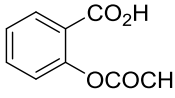
(b) What is the one letter code for the polypeptide, Glu-Leu-Pro-Asp-Gly-Thr **3**

(c) Acetylcholine is the substrate for the enzyme acetylcholinesterase. Suggest what short of binding interactions could be involved in holding acetylcholine to the active site **4**



acetylcholine

Q3. **(a)** Describe Lipinski's rule of five. Verify the Lipinski's rule of five for the following drug molecule. **4**



(Log P = 2.44

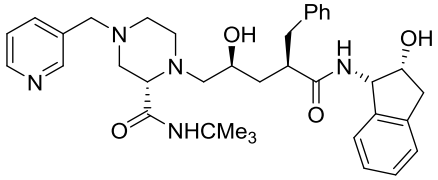
(b) A lead compound has a mono-substituted aromatic ring present as part of its structure. An analogue was synthesized containing a para chloro substituent which had approximately the same activity. It was decided to synthesize an analogue bearing a methyl group at the para position. This showed increased activity. What analogue would you prepare next and why? **4**

(c) Calculate the log P value for ***p***-methylphenol (Values of π for a range of substituents) **3**

Group	CH3	*t*- Bu	OH	OCH_3	CF_3	Cl	Br	F
π (aliphatic substituents)	0.50	1.68	−1.16	0.47	1.07	0.39	0.60	−0.17
π (aromatic substituents)	0.52	1.68	−0.67	−0.02	1.16	0.71	0.86	0.14

(d) Phenols are antiseptics. Hansch analysis carried out on a series of phenols with the general structure **A** (p-RC_6H_4OH) yielded the Hansch equation $\log 1/C = 1.5\ \Pi - 0.2\ \sigma + 2.3$ (n = 23, s = 0.13, r = 0.87) **5** What is (I) the significance of the terms n, s and r, (ii) the relative significance of the lipophilicity and electronic distribution of a phenol of type **A** on its activity and (iii) the effect of replacing the R group of **A** by a more polar group?

(**e**) Write the metabolites of antiviral agent given below **4**



Q4. (a) Write the target and mechanism of action for chlormethine [$MeN(CH_2CH_2Cl)_2$]. Why chlormethine is too reactive to survive the oral route? Design an analogue of chlormethine with reduced side effects. **5**

(b) Lineweaver-Burk plots are extremely useful in determining the nature of inhibition. Draw Lineweaver-Burk plots with and without competitive inhibitors present **3**