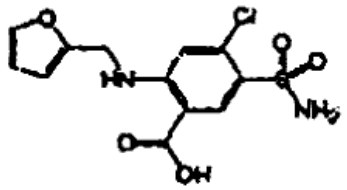
PHARMACEUTICAL CHEMISTRY
SEM – VII – 2015-2016

QP Code : 21796

(3 Hours) [Total Marks : 70

N. B. : (1) All questions are compulsory.

1. Answer the following questions.
   (i) Give an example of an anticancer agent that works as a mitosis inhibitor (no structure) 1
   (ii) Give a drug combination used for antiviral therapy (structures to be given). 2
   (iii) Name the enzyme that is the main target of the cardiac glycosides 1
   (iv) How is quinine and quinidine related stereochemically? 1
   (v) The reaction between p-chlorophenol, acetone, chloroform in the presence of sodium hydroxide is the first step in the synthesis of which drug? 1
   (vi) Identify the following diuretic agent. 1



   (vii) Enalapril is a prodrug. What is the active form of the drug? (structure to be drawn). Which is the enzyme that it inhibits? 2
   (viii) 1-Hydrazinophthalazine hydrochloride is the chemical name of which drug? 1
   (ix) As an antiplatelet drug, aspirin works by inhibiting which enzyme in platelets? 1
   (x) Draw the structure of any drug that has a coumarin ring. Also name the drug. 1
   (xi) Draw the structure of the biguanide moiety 1
   (xii) Give any natural product that is used as a local anaesthetic (structure to be drawn) 1
   (xiii) Name any drug that is used for treatment of breast cancer (structure not to be drawn) 1

2. (i) List agents (structures necessary) that block de novo synthesis of DNA and explain their role in treatment of cancer 4
   (ii) State the important differences in the structures of lovastatin and atorvastatin. What are the important stereochemical attributes that the above mentioned drugs must possess to act as HMG-CoA reductase inhibitors? Give any one active metabolite of lovastatin or rosuvastatin. 3

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(iii) Outline the synthesis of amantadine 3

(iv) Give any drug that has the azide group (structure to be drawn). 1

3. (i) Histamine has two pK_a values of 5.80 and 9.40. Draw the ionized forms of histamine that correspond to these two pK_a values. Also draw the two tautomers of histamine. 2

OR

(i) Give reasons for the nonsedating properties of the second generation H_1 antihistamines. Describe the relationship between fexofenadine and terfenadine. 2

(ii) Show what happens to omeprazole in a strongly acidic environment and explain how this is related to its mechanism of action. 2

(iii) The following are the chemical names of drugs used for treatment of cardiac arrhythmia. Draw their structures and state to which class they belong (answer any two). 2

a. 4-Amino-N-((2-diethylamino)ethyl)benzamide

b. (RS)-1-(1-Methylethylamino)-3-(1-naphthyloxy)propan-2-ol

c. N-o-Bromobenzyl-N-ethyl-N,N-dimethylammonium tosylate

d. N-(2,6-Dimethylphenyl)alaninamide

(iv) Name (no structures) any two sugars that are part of the structures of the cardiac glycosides. 1

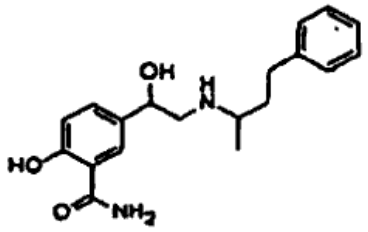
(v) State which of the following statements for the sulfonyl ureas as oral hypoglycemic agents are true or false. Correct those that are false. 4

a. The alkyl group on the nitrogen of the urea moiety may be methyl or ethyl for good activity.

b. At the *para* position of the aromatic ring, groups like methyl, acetyl, β-arylcarboxyamidoethyl are tolerated.

c. Sulfonylureas are strongly acidic with pk_a values of 1 to 2.

4. (i) Following is the structure of labetalol. Mark the structural feature that is responsible for it's α-blocking activity. Also mark out the chiral centres in the molecule. Is there any relationship between the stereochemistry at these centres and its α/β-blocking activity? 4



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(ii) What is the effect of aliskiren on the RAS pathway? 1

(iii) Outline the synthesis of acetazolamide or furosemide 3

(iv) Give one point of difference between a general and a local anesthetic. 1

OR

(iv) Local anesthetic activity generally decreases with increasing lipid solubility. True or false? 1

(v) Give reasons for the enhanced chemical stability of lidocaine over benzocaine (structures of both molecules to be drawn) 2

5. (i) Outline the synthesis of chlorambucil or cyclophosphamide. 4

(ii) What do the antiviral drugs rimantadine and oseltamivir have in common? (no structures to be drawn) 2

(iii) Draw the structure of ganciclovir sodium, clearly showing the attachment of sodium to the ganciclovir moiety. 1

(iv) Briefly outline the role of the P2Y receptor in platelet aggregation. Give one molecule that is an antagonist of this receptor. Name the heterocyclic ring in the molecule. 3

(v) The heterocyclic ring- thiazole- is present in which two H_2 receptor antagonists? 1

6. (i) With regard to the SAR of thiazide diuretics, state which statement is true or false. Correct those that are false. 4

a. An electron releasing group is necessary at the 6 position.

b. Removal of the sulphonamide group at position 7 gives little or no diuretic activity.

c. Saturation of the double bond at the 3-4 position increases the diuretic action more than 10 fold.

d. Substitution with a lipophilic group at position 3 gives a marked increase in diuretic potency.

(ii) Outline the synthesis of captopril. 3

(iii) In the 1,4-dihydropyridine class of calcium channel blockers, explain the role of the substituents at the 2/6 positions and the substituents at the 3/5 positions. 2

OR

(iii) Explain the role of cAMP and cGMP in smooth muscle contraction/ relaxation 2

(iv) Show clearly how the nitrogen mustards destroy DNA in human cells. 2
