Time: 3 hours **70 marks**

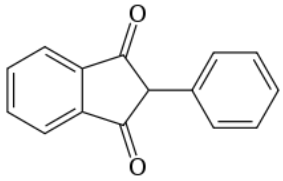
N.B: All questions are compulsory.

Q1] Answer the following questions. **15**

i Name an alkyne containing anticancer agent and indicate its MOA.

ii Give the structure of an anti-herpes agent that is a prodrug.

iii Identify the following structure and indicate its chemical class.



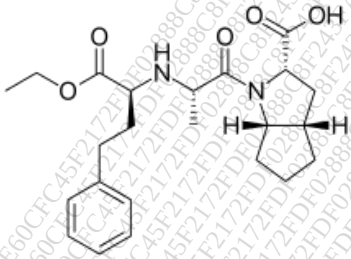
iv Name a naturally obtained drug that inhibits sodium potassium adenosine triphosphatase in the myocardium and indicate its therapeutic use.

v Ethoxazolamide and amiloride belong to ---------- and ---------- mechanistic class respectively.

vi Lidocaine is used as an antiarrhythmic agent and a local anaesthetic. Justify this statement.

vii Give an example of a non-dihydropyridine calcium channel blocker and indicate its therapeutic use. (Structure not needed)

viii Give the structure of the active metabolite of the drug given below and indicate the enzyme that it inhibits.



ix Predict the structure and therapeutic use of the following:

7-chloro-3-methyl-4*H*-1,2,4-benzothiadiazine 1,1-dioxide

x What is abciximab?

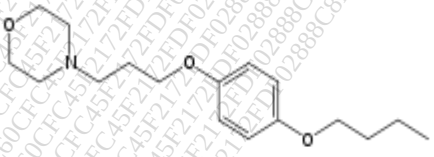
xi Give the name and structure of a cyclopropyl group containing lipid lowering agent.

xii Give the structure of a proton pump inhibitor and indicate its therapeutic use.

xiii What is DPP IV? Give an example of a drug acting on DPP IV.(structure not needed)

xiv Give the structure of a barbituric acid derivative used as a general anaesthetic, indicate the position of its salt form.

xv Identify to which chemical class the following drug belongs and also indicate its use.



Q2] a. Discuss alkylating agents as an important class of anticancer agents. Support your answer with suitable structures in each class. [4]

b. Give reasons for the following. (any two) [4]

i. Nimodipine is used in cerebral vasospasm and ischemia.

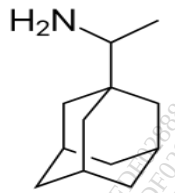
ii. Organic nitrates are used as antianginal agents.

iii. Combination drugs are used in the therapeutic management of HIV infection.

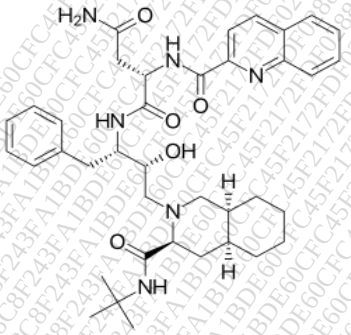
c. Give the synthesis of sotalol indicating the reagents and reaction conditions used. [3]

Q3] a. Classify antiarrhythmic agents on the basis of mechanism of action giving one example with structure from each class. [4]

b. With respect to the structures below, answer the following questions (any four) [4]



A



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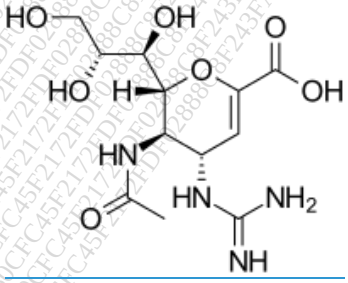
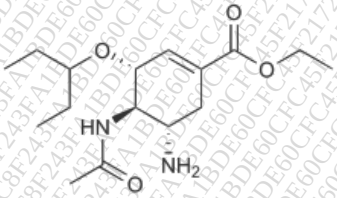
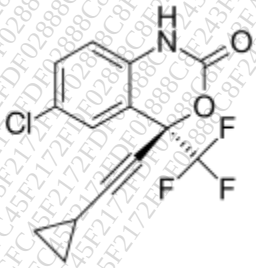


C



D



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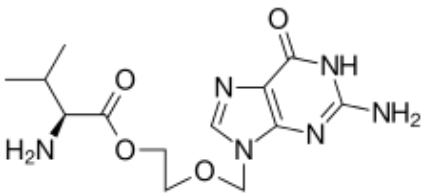


F

i. Identify the drug A, indicate its salt form and use.
ii. What is neuraminidase? Identify and name two NA inhibitors from the above structures and indicate their specific use.
iii. Predict the therapeutic targets (enzymes inhibited) of B and E.
iv. Discuss the structural differences between C and D and indicate their impact on their activity.
v. Identify which of the above are prodrugs. Draw the structures of their active metabolites.

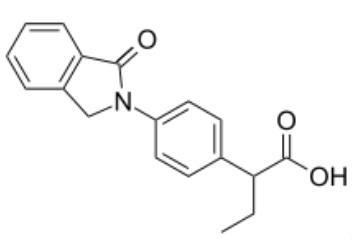
c. Predict the chemical class of the following drugs and indicate their therapeutic use. (Structures needed). [3]

a) Ethacrynic acid b) Furosemide c) Mannitol

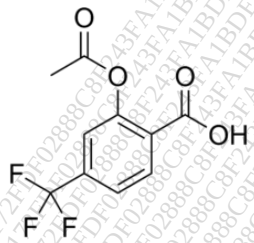
Q4] a. Give the synthesis of acetohexamide indicating the reagents and reaction conditions used. [3]

b. Give the structure of a second generation sulfonyl urea and indicate the functional group responsible for the higher potency of this class. [1]

c. Answer the following questions with respect to the structures given below. [4]



A



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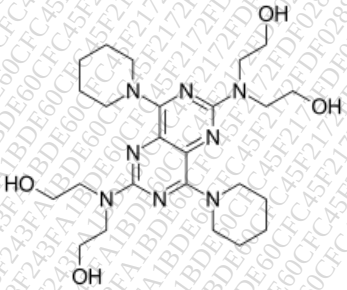

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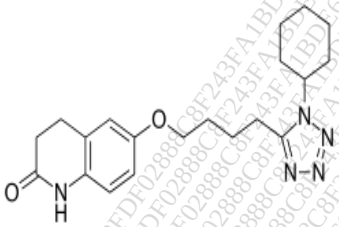
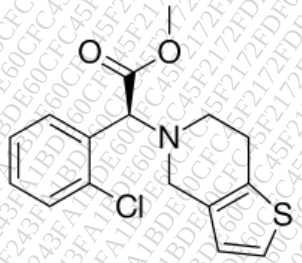
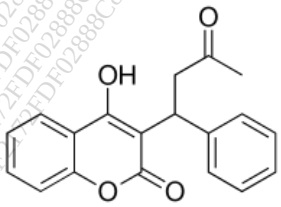


D



E



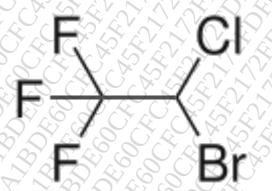
F

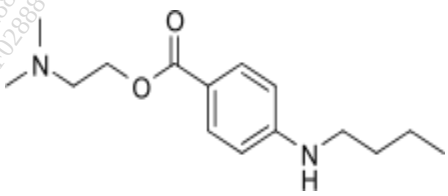
i. Indicate the MOA of drugs A and D.
ii. Identify the generic names of drugs B and E.
iii. Give the name and structure of another drug belonging to the same class as F.
iv. Identify B and name the enzyme inhibited by it.

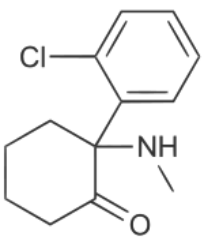
d. Discuss the development of statins as HMG - CoA reductase inhibitors in detail, support your answer with relevant structures. [3]

Q5] a. Discuss the strategy that led to the development of the H2 antagonist cimetidine from histamine. [4]

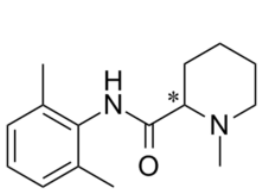
b. Given below are some structures of anaesthetic drugs, answer the following questions with respect to them. (any four) [4]

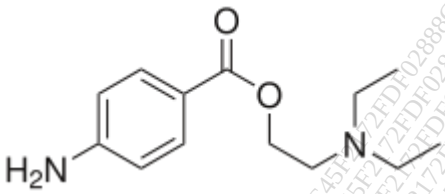






A **B** **C**



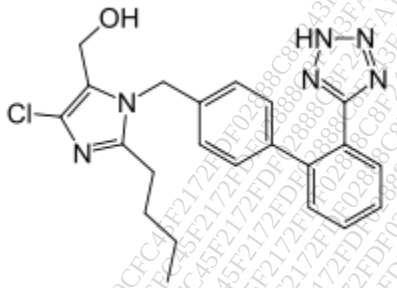


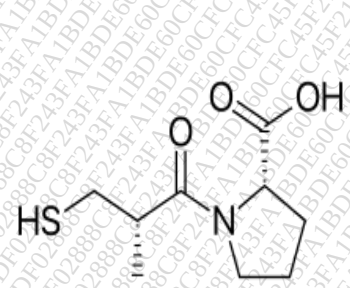
D **E**

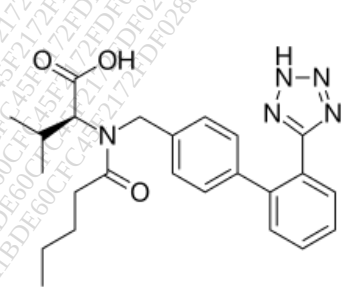
i. Predict the mechanism of action, use of drug C, also identify the chiral centre in C.
ii. Indicate which of the above drugs are weak acids or bases.
iii. Depict the schematic representation of the binding of an ester type local anaesthetic to a receptor site.
iv. Explain why is drug B more potent than drug E.
v. Drug A permeates to a lesser extent into brain in comparison to nitrous oxide. Say T/F, justify your answer.

c. Give the synthesis of chlorthiazide indicating the reagents and reaction conditions used. [3]

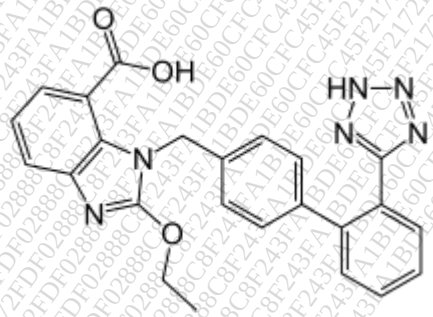
Q6] a. Answer the following questions in the context of the structures given below. [4]

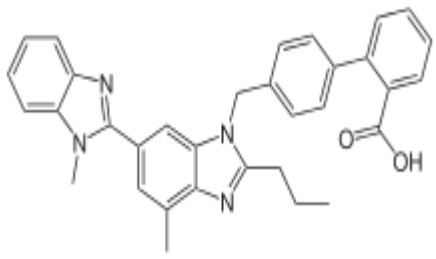






A **B** **C**





D **E**

i. Draw the structure of candesartan cyclohexyl-1-hydroxyethyl carbonate ester.
ii. Give the structure one metabolite of losartan and comment on its activity.
iii. Advantage of having a tetrazole functionality in some of the above structures versus a carboxylic acid group.
iv. Predict the longest acting drug amongst the above drugs and justify your answer.

b. Match the following. [4]

1	Propranolol	A	2-hydroxy-5-[1-hydroxy-2-{(4-phenylbutan-2-yl)}ethyl]benzamide
2	Aliskiren	B	Site 3 diuretic
3	Labetalol	C	Selective α2 blocker
4	Prazosin	D	1-(1-methylethylamino)-3-(1-naphthyloxy)propan-2-ol
5	Indapamide	E	Inhibits the enzyme renin
		F	Site 2 diuretic

c. Discuss the activation of cyclophosphamide indicating the reactions involved. [3]

OR

c. Give the synthesis of chlorambucil indicating the reagents and reaction conditions used.
