KIBABII UNIVERSITY

UNIVERSITY EXAMINATIONS
2021/2022 ACADEMIC YEAR

THIRD YEAR FIRST SEMESTER
MAIN EXAMINATIONS

FOR THE DEGREE OF BSC (CHEMISTRY)

COURSE CODE: SCH 317

COURSE TITLE: BIOORGANIC AND MEDICINAL CHEMISTRY

DATE: 23/05/2022 **TIME: 9:00AM-11:00AM**

INSTRUCTIONS TO CANDIDATES
Time: 2 Hours

Answer question ONE and any other TWO of the remaining

QUESTION ONE [30 MARKS]

a) Define the following terms as used in medicinal chemistry **[5 marks]**

i. Pharmacodynamics

ii. Structure activity relationship

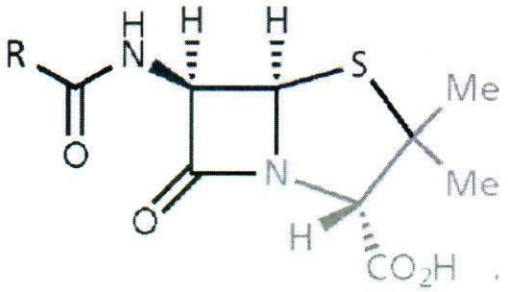
iii. Drug targets

iv. Holoenzyme

v. Nucleotide

b) Mention fives factors that affect biotransformation of drug in the body **[5 marks]**

c) The structure of penicillin is give below



i. From the structure above, name the amino acid penicillin is biosynthesized from **[2 marks]**

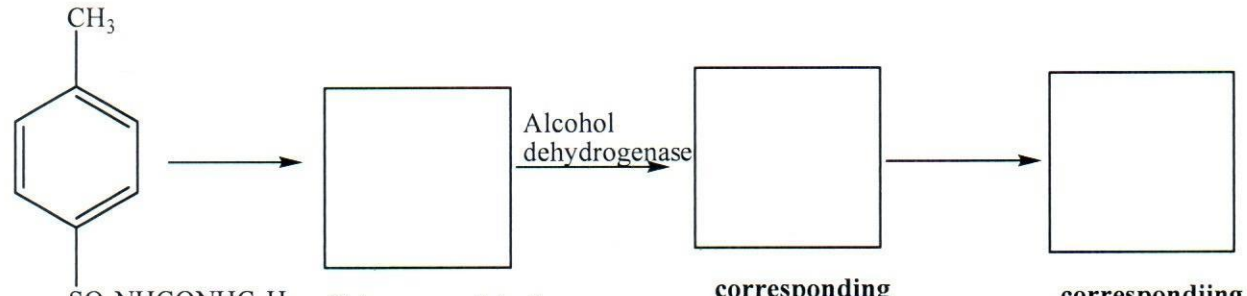
ii. State five features are important for penicillin activity **[5 marks]**

d) Drug target is a molecule in the body, that is essential to a particular disease process and that could be addressed by a drug to produce a desired therapeutic effect. Name three protein drug targets **[3 marks]**

e) With aid of diagram, explain how desolvation assist in drug-target interactions **[3 marks]**

f) Pharmacokinetic processes are represented by the acronym ADME. Name and briefly explain these processes **[4 marks]**

g) The following represents oxidation of benzylic carbon atoms during Phase I, name the missing metabolites **[3 marks]**



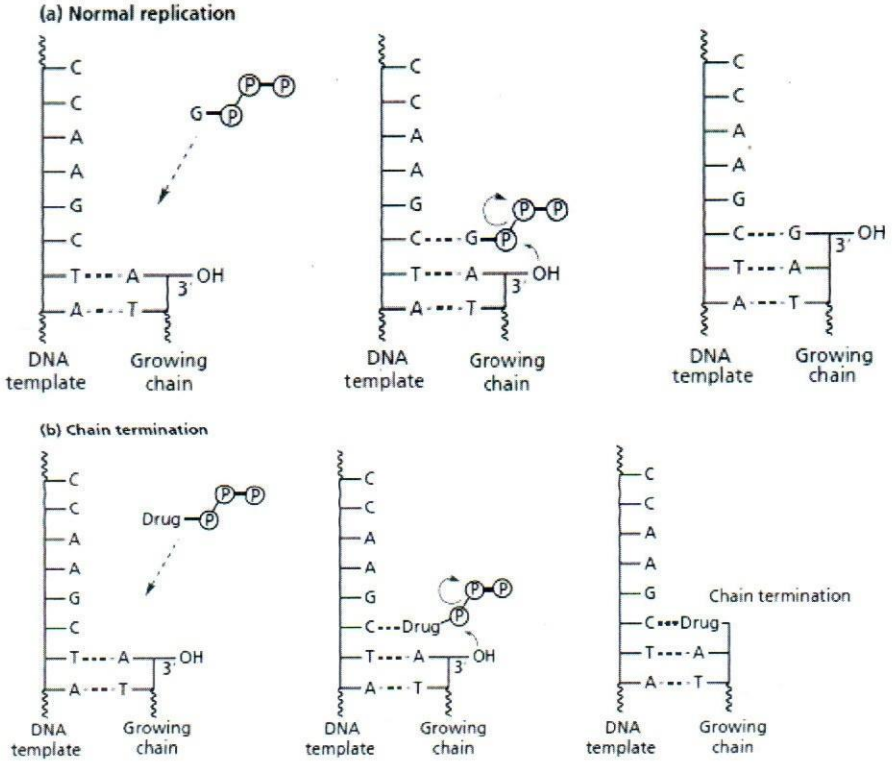
QUESTION TWO [20 MARKS]

a) Drug targets are macromolecules while drugs are generally much smaller than their targets. Drugs interact with their targets by binding to binding site which typically involve intermolecular bonds

i. Define intermolecular bonds **[1 mark]**

ii. Discuss with relevant diagrams how drugs interacts with active sites by ***electrostatic, induce dipole*** and ***dipole-dipole*** interactions **[9 marks]**

b) The figure below illustrated mechanism of action of drug which target nucleic acid



(a) The normal replication mechanism. (b) A drug acting as a chain terminator. (Ⓟ = Phosphate)

Explain the mechanism of action of the drug **[10 marks]**

QUESTION THREE [20 MARKS]

a) With aid of a diagram, briefly explain induced fit model of enzyme action **[4 marks]**

b) One of the processing involved in Phase II metabolism is glucuronide conjugation.

i. Name four functional groups that many be used for glucuronide conjugation **[2 marks]**

ii. In details explain glucuronide formation **[4 marks]**

c) Explain the following terms as used in enzyme as drug target **[5 marks]**

i. Irreversible enzyme inhibitor

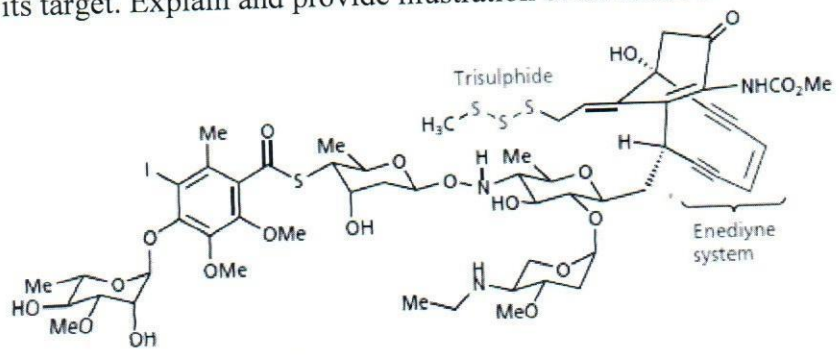
ii. Natural substrate

iii. Allosteric binding site

iv. Uncompetitive inhibitor

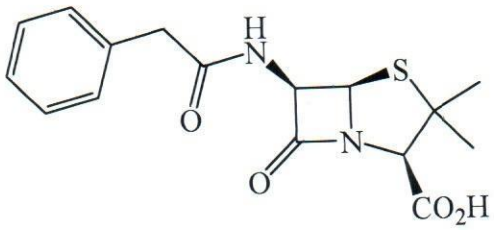
v. Transition state analogue

d) Podophyllotoxins (calicheamicin γ) shown below is anticancer drug that interact with DNA as its target. Explain and provide illustration of its mode of action **[5 marks]**

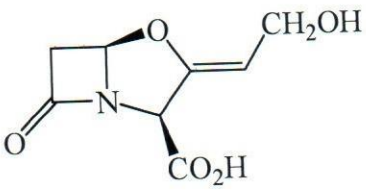


QUESTION FOUR [20 MARKS]

a) 'Suicide substrates are *bona fide* visitors to an enzyme's active site that become stubborn squatters once they have arrived' Provide illustration of this statement using a suicide substrate *clavulanic acid,* used clinically in antibacterial medications to inhibit the bacterial β-lactamase enzyme in comparison to the mode of action of penicillin G. **[6 marks]**



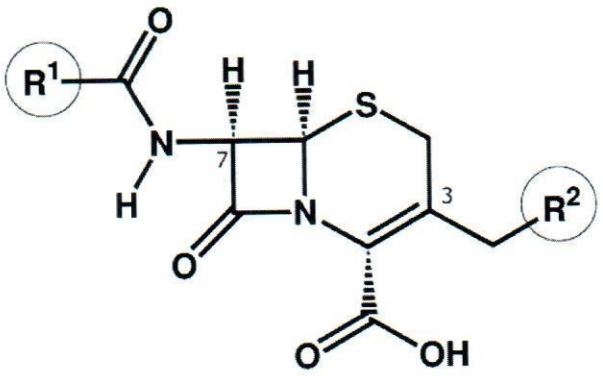
Penicillin G



Clavulanic acid

b) Provide simple procedure on how you would carry out esterification of alcohol and acyl chloride using the principle of combinatorial chemistry **[4 marks]**

c) Cephalosporins are antibacterial agents which inhibit bacterial cell wall synthesis. The nucleus of cephalosporin is given below



i. Explain important parts of cephalosporin essential for its activity **[10 marks]**