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UNIVERSITY OF RUHUNA – FACULTY OF ALLIED HEALTH SCIENCES

DEPARTMENT OF PHARMACY

FOURTH BPHARM PART II EXAMINATION – OCTOBER/NOVEMBER 2022

PH 4213 ADVANCED MEDICINAL CHEMISTRY II – SEQ

TIME: TWO HOURS

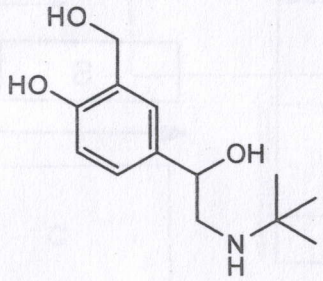
INSTRUCTIONS

- There are **four** questions in **Part A B and C**.
- Answer all questions.
- No paper should be removed from the examination hall.
- Do not use any correction fluid.
- Use illustrations where necessary.

PART A

01.

1.1. The structure of a drug **F** is given below.

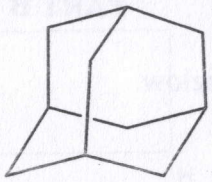


1.1.1. Identify the drug **F**. (***05 marks***)

1.1.2. Write a therapeutic indication and briefly explain the mode of action of drug F. (***15 marks***)

1.1.3. Briefly explain five important structure activity relationships of the drug **F** which are responsible for its pharmacological properties. (***30 marks***)

1.2. The structure of molecule **G** is given below.



1.2.1. Identify the molecule **G**. (***10 marks***)

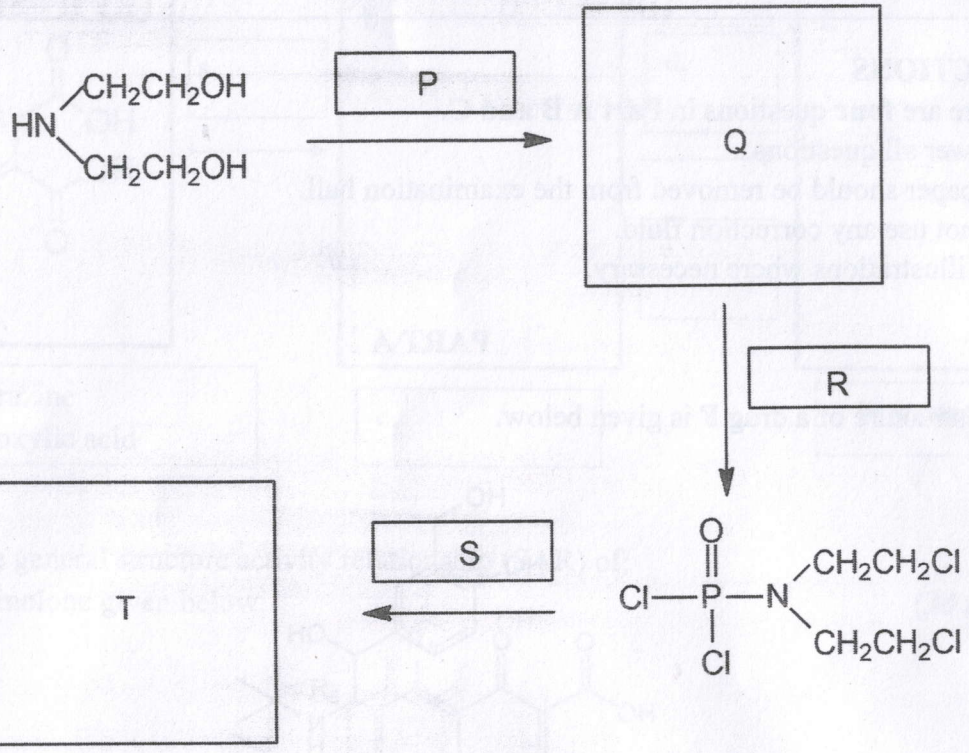
1.2.2. Name two drugs derived from the molecule **G**. (***10 marks***)

1.2.3. Draw the structures of drugs you named in 1.2.2. (***20 marks***)

1.3. Azoles are antifungal agents used to treat many fungal infections. List two types of azoles derivatized drugs giving one example for each. (***10 marks***)

02.

2.1. Synthesis of cyclophosphamide is illustrated below. Identify the missing intermediates/ reagents/product (**P, Q, R, S, T**) and complete the synthetic pathway. (***30 marks***)

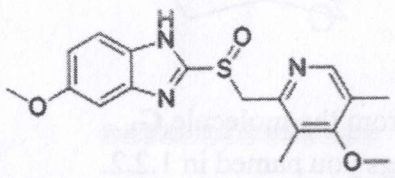


Cyclophosphamide

2.2. "Nitrogen mustards containing aliphatic nitrogen substituents cause serious side effects than nitrogen mustards containing aromatic nitrogen substituents". Briefly explain this statement. (***20 marks***)

PART B

2.3. Structure of omeprazole is given below.



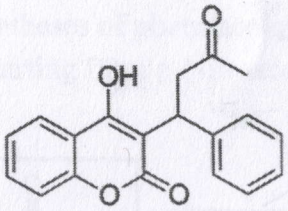
2.3.1. Omeprazole is a racemic mixture of (R) and (S) isomers. Identify the chiral center and draw the (R) and (S) isomers of it. (***20 marks***)

2.3.2. Omeprazole is an irreversible inhibitor of H^+/K^+ ATPase. Under the acidic conditions of parietal cells, omeprazole reacts with cysteine moiety of H^+/K^+ ATPase. Draw detailed mechanism for this inhibition showing the main intermediates. (***30 marks***)

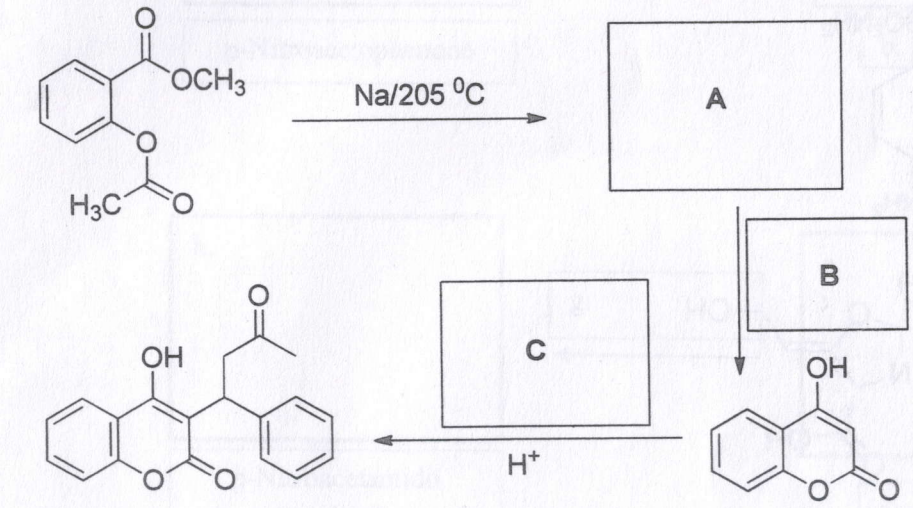
03.

3.1. Draw the chemical structures of two *in vitro* anticoagulants. ***(10 marks)***

3.2. Structure of warfarin is given below. It exists in equilibrium with its cyclic hemi-acetal. Draw the structure of hemi-acetal form of warfarin. ***(10 marks)***

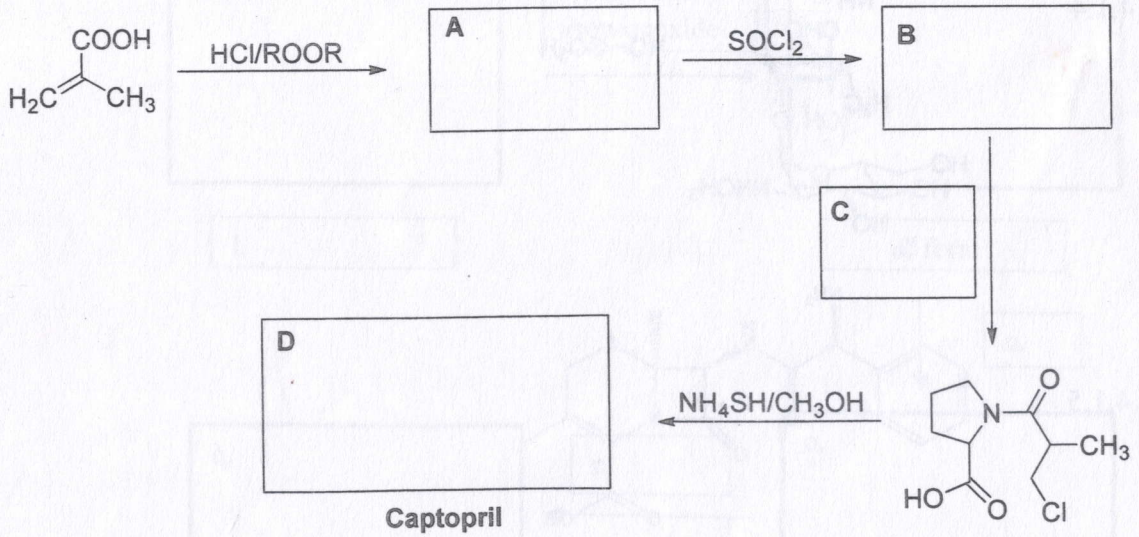


3.3. Complete the following synthesis pathway of warfarin. ***(25 marks)***



3.4. Name three classes of antihypertensive drugs giving one example for each. ***(15 marks)***

3.5. Complete the following synthetic pathway of captopril. ***(40 marks)***



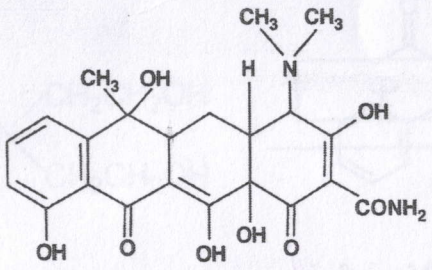
Captopril

PART C

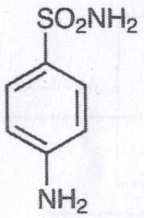
04.

4.1. Write the generic name of the medicines given below which are used in pharmacological treatments. ***(15 marks)***

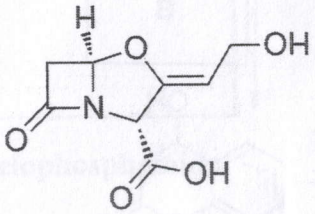
4.1.1



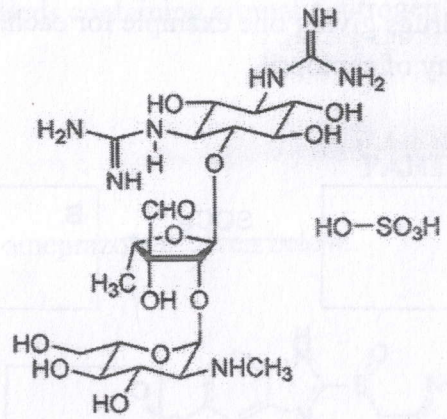
4.1.2



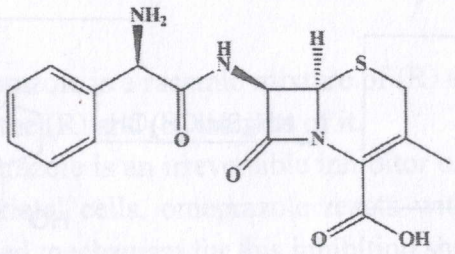
4.1.3



4.1.4



4.1.5



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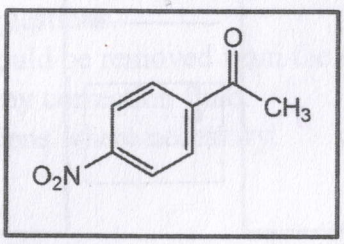
4.2.Complete the following syntheses of pharmacological compounds,

4.2.1. Chloramphenicol starting from p-Nitroacetophenone. **(*20 marks*)**



p-Nitroacetophenone

Bromination/ Br_2

a.

b.

c.

d.

e.

f.

g.

h.

p-Nitroacetamido acetophenone

i.

j.

k.

l.

Aluminum isopropoxide

m.

dl form

n.

o.

dl Form

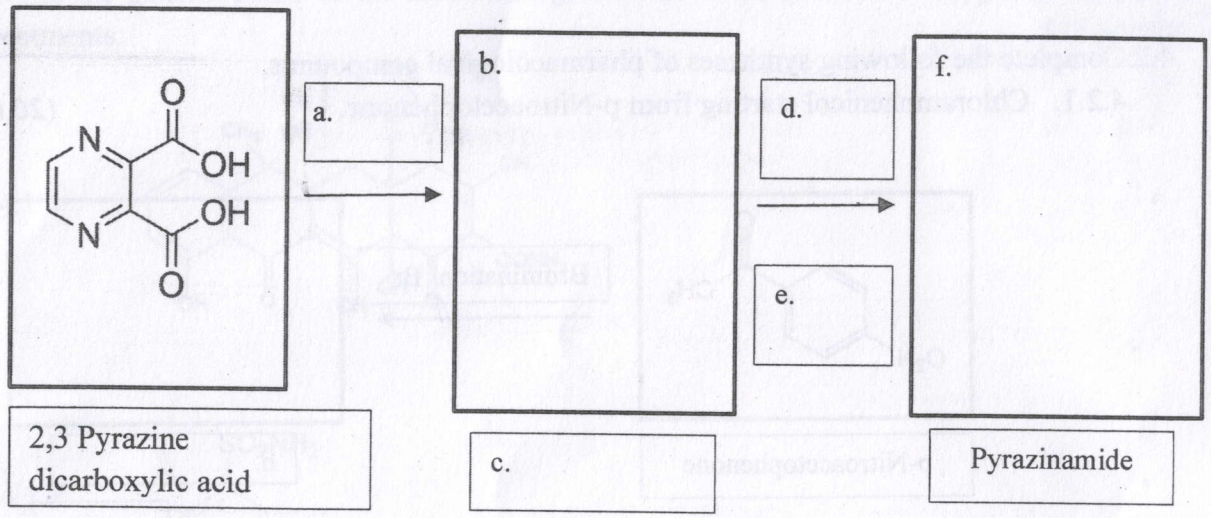
p.

Di-chloro-methyl acetate

q.

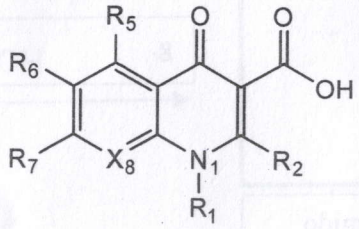
Chloramphenicol

4.2.2. Pyrazinamide starting from 2,3-pyrazine dicarboxylic acid. ***(10 marks)***

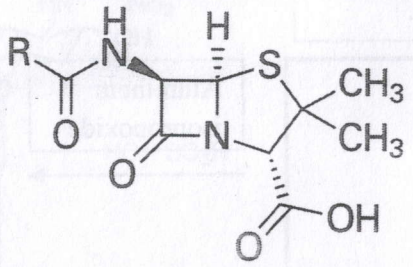


4.3. Discuss the general structure activity relationship (SAR) of:

4.3.1 the quinolone given below. ***(30 marks)***



4.3.2 the pharmacophore given below. ***(25 marks)***



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