UNIVERSITY OF RUHUNA – FACULTY OF ALLIED HEALTH SCIENCES

DEPARTMENT OF PHARMACY

FOURTH BPHARM PART I EXAMINATION – OCTOBER 2019

PH 4112 ADVANCED MEDICINAL CHEMISTRY I (SEQ)

TIME: TWO HOURS

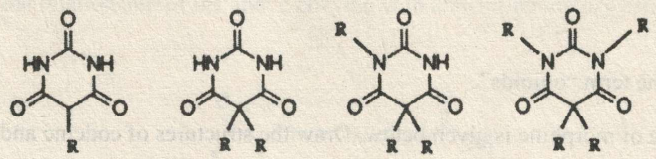
INSTRUCTIONS

- Answer **all** questions in the booklet provided.
- No paper should be removed from the examination hall.
- Do not use any correction fluid.
- Use illustrations where necessary.

01.

1.1 Compare and contrast the use of barbiturate and benzodiazepine classes of drugs as central nervous system depressants. ***(20 marks)***

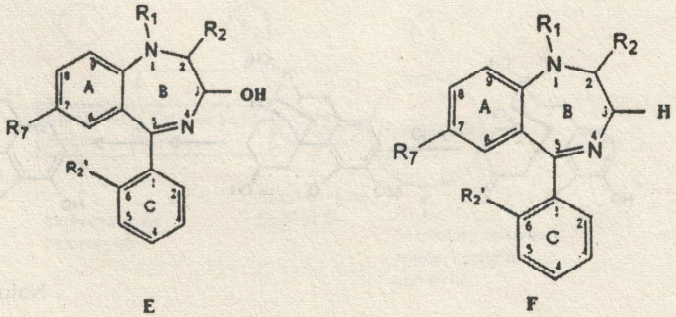
1.2 Considering the structure activity relationship of following barbituric acid derivatives (A-D), identify the molecules with possible hypnotic activity. Give reasons for your answer. ***(30 marks)***



A **B** **C** **D**

1.3 Draw the structures of phenobarbital (5-ethyl-5-phenylbarbituric acid) and metharbital (1-methyl-5,5.diethylbarbituric acid). ***(10 marks)***

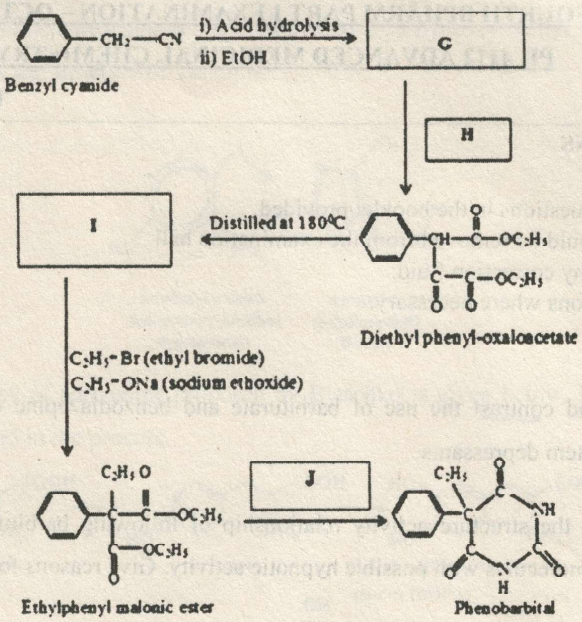
1.4 Drugs E and F shown below are classified as benzodiazepine derivatives. Giving reasons, identify the most suitable molecule to treat anxiety and insomnia separately. ***(20 marks)***



E **F**

1.5 Fill in the blanks (G-J) with the missing reagents/ products in the following synthetic process.

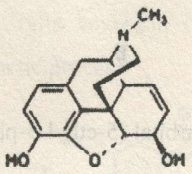
(20 marks)



02.

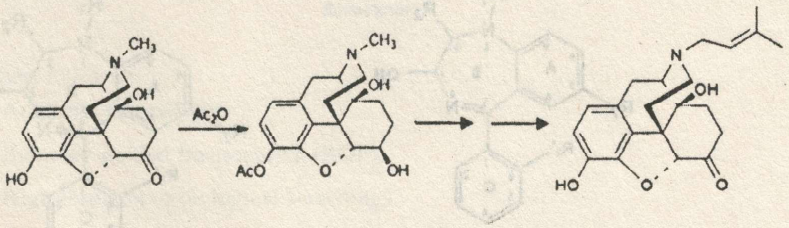
2.1 Define the term "opioids". *(10 marks)*

2.2 Structure of morphine is given below. Draw the structures of codeine and heroin. *(20 marks)*



Morphine

2.3 Write down the complete chemical synthetic process of naloxone using Von-Braun oxidation. First step of the synthesis and the structure of naloxone are given below. *(50 marks)*



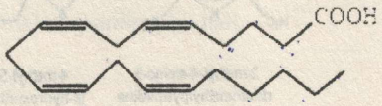
Naloxone

2.4 State the use of acetic anhydride (Ac_2O) in the above synthesis of naloxone. ***(10 marks)***

2.5 "Naloxone is used to prove the mechanism of action of analgesics". Comment on the validity of this statement. ***(10 marks)***

03.

3.1 Chemical structure of arachidonic acid (5.8.11.14-eicosatetraenoic acid) is given below. Draw the structure of eicosapentaenoic acid. ***(15 marks)***



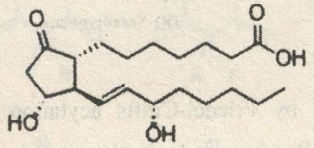
Arachidonic acid

3.2 Answer the following questions using the structure of compound (**K**) given below. ***(30 marks)***

3.2.1 Name the class of chemical mediators to which the compound (**K**) belongs.

3.2.2 State the class of enzyme, which converts the arachidonic acid to compound (**K**).

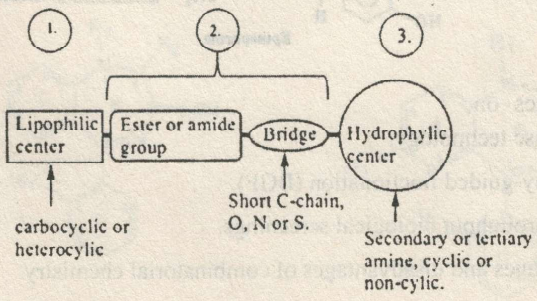
3.2.3 Explain the relationship of the above enzyme with anti-inflammatory drugs.



K

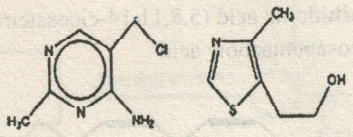
3.3 Explain the mechanism of action of aspirin in relieving inflammation. ***(35 marks)***

3.4 General composition of a local anesthetic is as follows. State the importance of having each part (1-3) in the molecule to produce local anesthetic effect in the body. ***(20 marks)***



04.

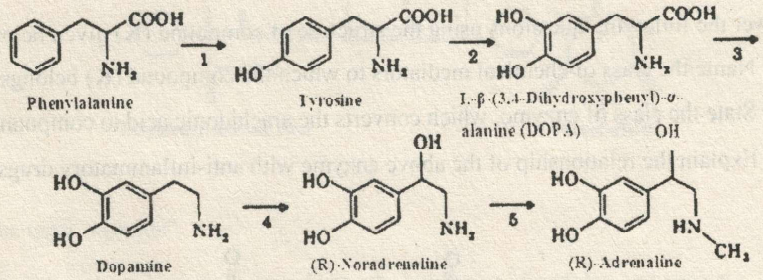
4.1 Thiamine is synthesized by the direct condensation of 2-methyl-4-amino-5-chloromethylpyrimidinehydrochloride and 4-methyl-5-(β-hydroxymethyl)thiazole which are shown below. Draw the structure of Thiamine. ***(10 marks)***



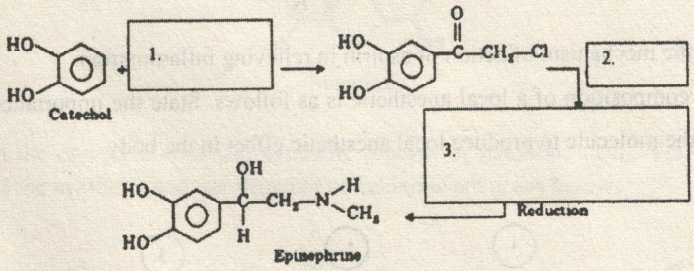
2-methyl-4-amino-5-chloromethylpyrimidine hydrochloride

4-methyl-5-(β-hydroxyethyl) thiazole

4.2 Biosynthetic pathway of adrenaline proposed by Blaschko is given below. Name the respective enzymes 1-5 involved in the process. ***(20 marks)***



4.3 Epinephrine is prepared by Friedel-Crafts acylation of catechol. Write down the missing reagents/products in the following synthetic process. ***(30 marks)***



4.4 Write short notes on ***(40 marks)***

4.4.1 Antisense technology.

4.4.2 Bioassay-guided fractionation (BGF).

4.4.3 High-throughput biological screenings.

4.4.4 Advantages and disadvantages of combinatorial chemistry.

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