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UNIVERSITY OF RUHUNA – FACULTY OF ALLIED HEALTH SCIENCES

DEPARTMENT OF PHARMACY

SECOND BPHARM PART II EXAMINATION – DECEMBER 2018/JANUARY 2019

PH 2244 MEDICINAL CHEMISTRY AND PHARMACOGNOSY IA (SEQ)

TIME: THREE HOURS

INSTRUCTIONS

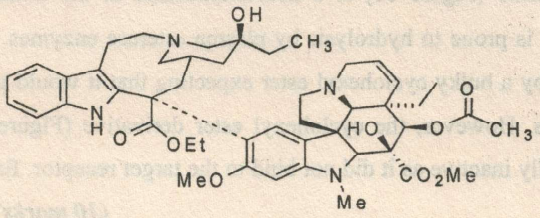
- There are Six (**06**) questions in the Parts A, B, C and D of SEQ paper.
- Answer each part in the booklet given.
- No paper should be removed from the examination hall.
- Do not use any correction fluid.
- Use illustrations where necessary.

01.

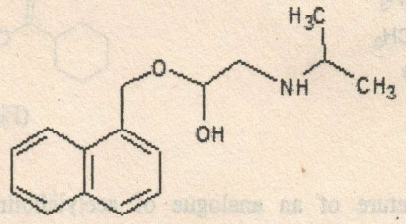
1.1. Describe the rule that is used to predict the oral bioavailability of the drugs. ***(10 marks)***

1.2. Which of the following drugs (A and B) would be expected to have a better bioavailability? Give reasons for your answer. ***(20 marks)***

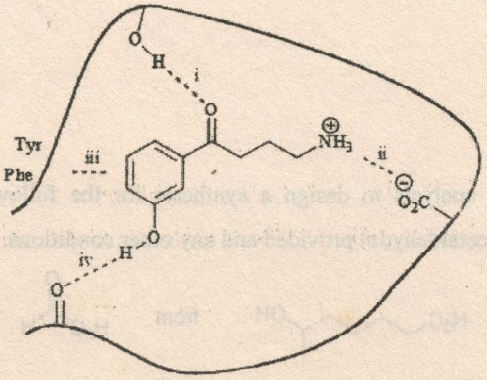
Drug A ($C_{47}H_{62}N_4O_9$; logP 6.05)



Drug B ($C_{16}H_{21}NO_2$; logP 2.53)



1.3. Consider the following molecule bound to a binding site. Identify the binding interactions taking place at i, ii, iii and iv. ***(10 marks)***



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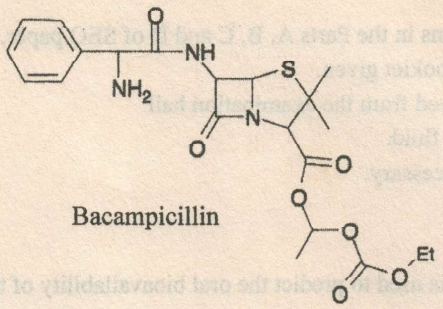
1.4. Bacampicillin is the ester- prodrug of the antibacterial Ampicillin.

1.4.1. State the chemical structures of the drug and the by- product(s) it would liberate on activation. (***15 marks***)

1.4.2. State the enzyme involved in the liberation of this drug in vivo. (***05 marks***)

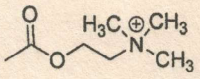
1.4.3. State **two** advantages and **two** disadvantages of using this prodrug. (***10 marks***)



Bacampicillin

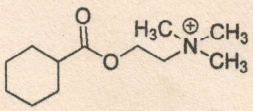
1.5.

1.5.1. Acetylcholine (Figure 01) is a neurotransmitter in the autonomic nervous system (ANS). It is prone to hydrolysis by plasma esterase enzymes. This methyl ester was replaced by a bulky cyclohexyl ester expecting that it would probably be resistant to hydrolysis. However, the cyclohexyl ester derivative (Figure 02) was found to be biologically inactive as it did not bind to the target receptor. Explain this observation. (***10 marks***)



Acetylcholine

(Figure 01)



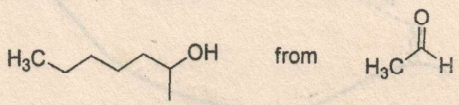
(Figure 02)

1.5.2. Draw the structure of an analogue of acetylcholine having similar biological activity to acetylcholine, but with a longer half-life. Explain the reason for longer half-life. (***10 marks***)

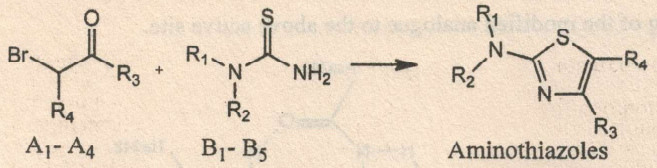
1.6. How does a 'Serendipitous drug' differ from a 'Me too drug'. Give **one** example for each type. (***10 marks***)

02.

2.1. Use retrosynthetic analysis to design a synthesis for the following molecule using the starting material (acetaldehyde) provided and any other conditions. (***20 marks***)



2.2. Following combinatorial synthesis of Aminothiazole library from ketones (A_1 – A_4) and thioureas (B_1- B_5) including fanetizole [$R_1 = Ph(CH_2)_3$; $R_2 = H$; $R_3 = Ph$; $R_4 = H$] a known anti-inflammatory agent is given by the following reaction.



A_1- A_4 B_1- B_5 Aminothiazoles

State how many analogues of Aminothiazoles can be prepared using the above combinatorial synthesis and show all the possible library of compounds that can be prepared. ***(10 marks)***

2.3. Draw the structures of the reactant molecules of the following metabolites in the presence of the following enzymes. State phase of the metabolic reaction involved in each reaction.

(20 marks)

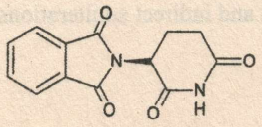
a) ..... Peptidase (Hydrolysis) H_3CH_2C O OH + $(CH_3)_2NH$ Phase .....

b) ..... (Oxidation) UDP Glucuronate UDP HO_2C HO HO $OCH_2CH_2CH_3$ OH Phase .....

c) ..... Cytochrome P_{450} (Oxidation) H_3CH_2C NH H_3C Phase .....

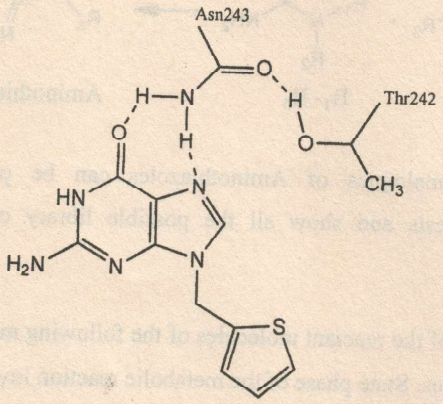
d) ..... Cytochrome P_{450} (Oxidation) H_3CH_2C OH Phase .....

2.4. Thalidomide has the properties that made it useful as a sedative and an emetic drug. However, when the pure (R)- enantiomer was given as a drug to treat the morning sickness in pregnant women, thousands of children were born worldwide with malformed limbs.

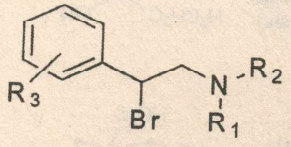


Explain briefly, the role of stereochemistry in the above disaster giving the structure of the undesired enantiomer. ***(15 marks)***

2.5. The binding of guanine analogue to the active site of purine nucleoside phosphorylases shown below. The replacement of hydrogen (H) at 8th position of this analogue by an amino group (NH_2) increased the biological activity 100 times. Explain this phenomenon showing the binding of the modified analogue to the above active site. ***(15 marks)***



2.6. Following is the general structure of β-Bromo-β-aryl-ethylamines which shows anti-adrenergic activity.



2.6.1. State the physicochemical properties of this compound which would affect its biological activity. ***(05 marks)***

2.6.2. Write down the simplified Hansch equation which could be related to the biological activity of this compound. ***(05 marks)***

2.6.3. State the nature of substituents which could be introduced to improve its biological activity and give an example for each. ***(10 marks)***

03.

3.1 Define the term "crude drug". ***(10 marks)***

3.2 Write short accounts on alphabetical classification and pharmacological classification of crude drugs. ***(30 marks)***

3.3. Explain briefly, the factors affecting ~~on~~ the production of crude drugs. ***(30 marks)***

3.4 State the different types of direct and indirect adulterations of drugs. ***(30 marks)***

04.

4.1 Following questions are based on surgical sutures.

4.1.1. What is meant by a surgical suture? ***(10 marks)***

4.1.2. List the **three** main types of sutures used in surgery and indicate their sources. ***(20 marks)***

4.1.3. List **four** properties of surgical sutures. (*20 marks*)

4.2 Terrestrial and marine creatures are considered as important sources of natural products.

4.2.1. Identify the animal shown in the **Figure 1**. (*05 marks*)

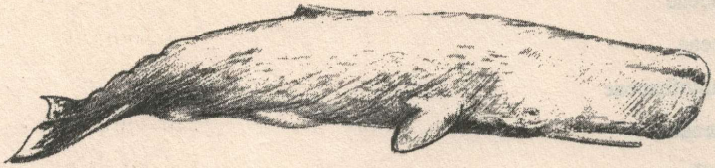


Figure 1

4.2.2. What is the name given for the product obtained from this animal? (*05 marks*)

4.2.3. What is the principle constituent of the product you mentioned in 4.2.2? (*05 marks*)

4.2.4. Name the current source of the product you mentioned in 4.2.2. (*05 marks*)

4.3 **Figure 2** illustrates a stage in the extraction of natural products.

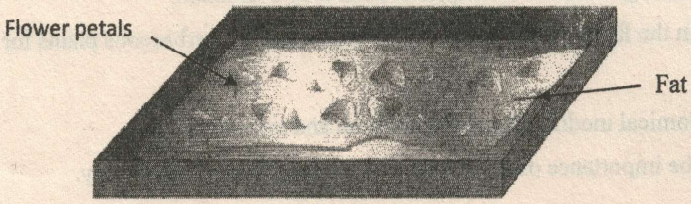


Figure 2

4.3.1. Identify the method. (*05 marks*)

4.3.2. What is the type of natural product extracted by this method? (*05 marks*)

4.3.3. Briefly explain the advantage of using this method for the extraction of the natural product you mentioned in 4.3.2 over other conventional methods for the extraction of natural products. (*10 marks*)

4.3.4. Name **two** products produced using this method and indicate the major difference in the manufacturing procedure. (*10 marks*)

05.

5.1. Name **two** main types of inflorescence. (*10 marks*)

5.2. Differentiate corymb, cyme and umbel using illustrations. (*15 marks*)

5.3. List types of underground stem modifications with examples. (*20 marks*)

Type of underground stem	Example
1.	
2.	
3.	
4.	

5.4. Draw line diagrams for the followings. (*10 marks*)

5.4.1. Pinnately lobbed simple Leaf

5.4.2. Reticulate leaf venation

5.4.3. Serrate leaf margin

5.4.4. Trifoliate compound leaf

5.5. Name **two** characteristics to identify following plant families. ***(25 marks)***

5.5.1. Fabaceae

5.5.2. Araceae

5.5.3. Amaranthaceae

5.5.4. Rutaceae

5.5.5. Acanthaceae

5.6. List **five** medicinally important plants in family Cucurbitaceae. ***(10 marks)***

5.7. List the **five** most important information that should be included in the herbarium label. ***(10 marks)***

06.

6.1. Briefly describe organoleptic techniques used in drug evaluation. ***(20 marks)***

6.2. Briefly explain the factors to be considered when collecting herbaceous plants for herbarium preparation. ***(30 marks)***

6.3. Compare anatomical modifications of dicot stem and monocot stem. ***(20 marks)***

6.4. Briefly describe importance of calcium oxalate crystals in plant taxonomy. ***(30 marks)***

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