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UNIVERSITY OF RUHUNA – FACULTY OF ALLIED HEALTH SCIENCES

DEPARTMENT OF PHARMACY

SECOND BPHARM PART II EXAMINATION-AUGUST 2022

PH 2244 MEDICINAL CHEMISTRY AND PHARMACOGNOSY IA – SEQ

TIME: THREE HOURS

INSTRUCTIONS

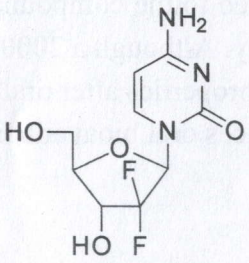
- There are six questions in part **A**, **B**, **C** and **D** of this SEQ paper.
- Answer all questions.
- No paper should be removed from the examination hall.
- Do not use any correction fluid.
- Use illustrations where necessary.

PART A

1.

1.1

1.1.1 The anticancer compound gemcitabine is found to have a logP value of -1.4. If its solubility in water is 0.24 *mol dm*$^{-3}$, what is its solubility in n-octanol? (***10 marks***)



Gemcitabine

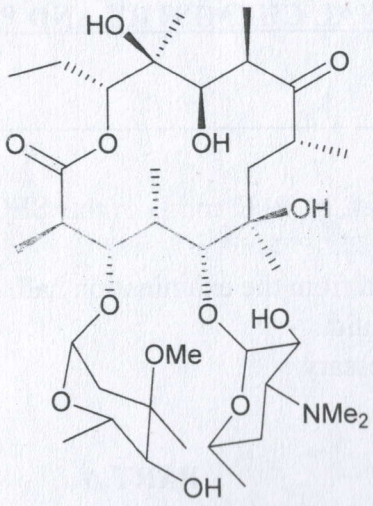
1.1.2 The calculated logP values of several HMG-CoA reductase inhibitors are given in the table below:

Drug	clogP
Atrovastatin	4.13
Fuvastatin	3.62
Lovastatin	4.07
Pitavastatin	3.45
Pravastatin	1.44
Rosuvastatin	0.42

1.1.2.1 Arrange them in the order of increasing hydrophobicity (the most hydrophilic to the most liphophilic). (***10 marks***)

1.1.2.2 Which of these drugs is most likely to be excreted (a) renally and (b) hepatically? (***10 marks***)

1.2 Using Lipinski's rules, estimate whether erythromycin ($C_{37}H_{67}NO_{13}$, logP= -0.14) is expected to show good oral bioavailability. (***15 marks***)

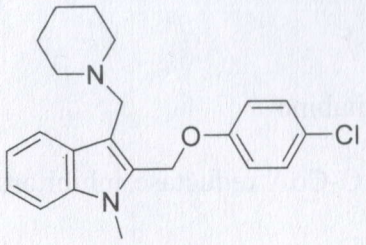


Erythromycin

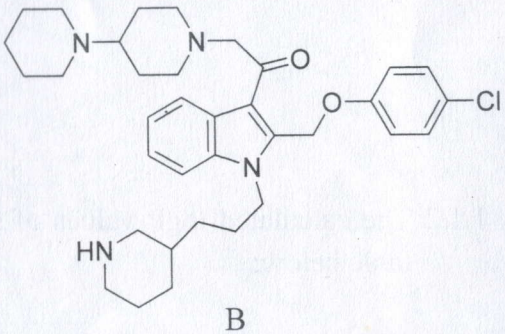
1.3 Lead identification and optimization is a crucial step in the drug discovery process.

1.3.1 What is a lead compound in drug development or design process? (***05 marks***)

1.3.2 The lead compound **A** ($C_{22}H_{25}ClN_2O$, logP = 5.7) which is a neuropeptide Y Y1 antagonist, was modified to the compound **B** ($C_{35}H_{47}ClN_4O_2$, logP = 7.3) in a structural optimization for activity. Although a 2000-fold increase in potency was achieved from **B**, it had poor absorption properties after oral dozing. Considering the Lipinki's rule, explain why this drug experiences oral bioavailability problems compared to **A.** (***20 marks***)

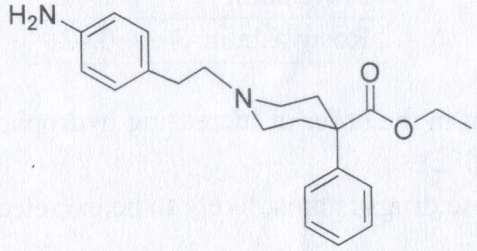


A



B

1.4 Water solubility of a drug can be predicted by either empirical or analytical approach. Aniledrine which is a narcotic pain reliever has the structure shown below:



Aniledrine

1.4.1 Predict the water solubility of this drug using:

1.4.1.1 Lemke's empirical approach based on the solubilizing potential of various functional groups, versus the number of carbon atoms. (Refer table 1) ***(10 marks)***

1.4.1.2 The fragment values (analytical approach) according to the equation, $\log P = \Sigma\pi(\text{fragments})$ (Refer table 2) [Hint: it is considered that water soluble if calculated $\log P < +0.5$]. ***(10 marks)***

1.4.2 If aniledrine is not water soluble, what would you do to increase its solubility? ***(10 marks)***

Table 1: Water solubilization of functional groups

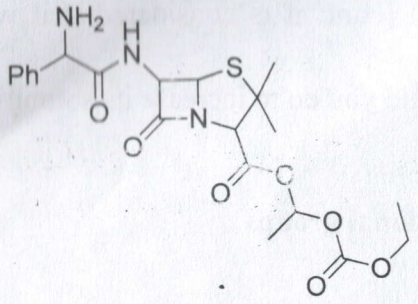
Functional group	Monofunctional compound	Polyfunctional compound
Alcohol	5-6 carbons	3-4 carbons
Phenol	6-7	3-4
Ether	4-5	2
Aldehyde	4-5	2
Ketone	5-6	2
Amine	6-7	3
Carboxylic acid	5-6	3
Ester	6	3
Amide	6	2-3
1 charge		20-30

Table 2: Hydrophilic-lipophilic values (π) of organic fragments

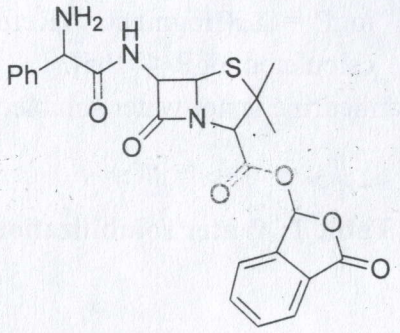
Fragment	π value
C (each aliphatic)	+0.5
Phenyl	+2.0
Cl	+0.5
S	0.0
O (hydroxyl, ether)	-1.0
N (amine)	-1.0
O=C-O (carboxyl)	-0.7
O=C-O (amide, imide)	-0.7
IMHB (Intra molecular hydrogen bonding)	+0.65

2.

2.1 Ampicillin remains the penicillin of choice for many infections because of its oral activity and good potency against Gram-negative bacteria. A number of prodrugs has been developed in attempts to improve pharmacodynamic characteristics and two of them, bacampicillin and talampicillin are shown below:



Bacampicillin



Talampicillin

2.1.1 Propose a mechanism of how these prodrugs are converted to the respective active drug. State the specific enzyme that is involved. (***25 marks***)

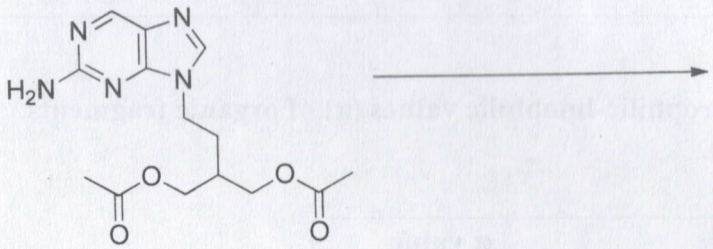
2.1.2 What by-product(s) would it liberate, besides the drug on activation? (***10 marks***)

2.2

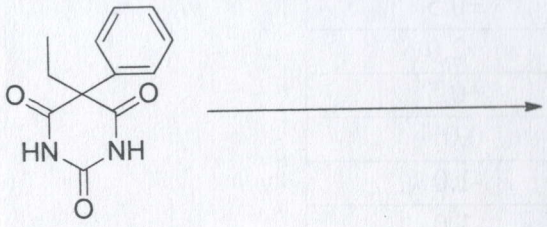
2.2.1 What is the difference between phase I and phase II in drug metabolism? (***10 marks***)

2.2.2 Propose structures for the phase I active metabolites and by products (if any) of each of the following drugs. (***30 marks***)

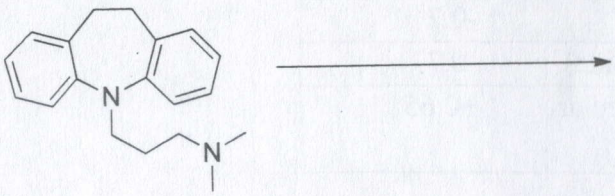
2.2.2.1



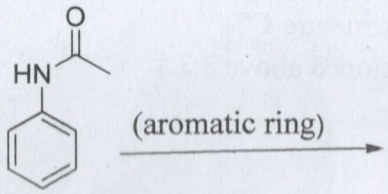
2.2.2.2



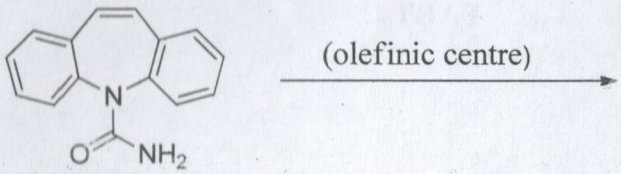
2.2.2.3



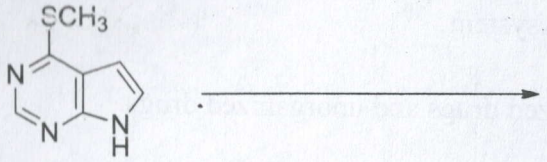
2.2.2.4



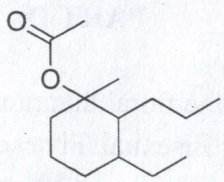
2.2.2.5



2.2.2.6



2.3 Use a retrosynthetic analysis to design a synthetic route for the following molecule. (***25 marks***)



PART B

3.

3.1 Adulteration is one of the main challenges in herbal drug industry.

3.1.1 Define the term adulteration. (***10 marks***)

3.1.2 Substitution with exhausted drug is one of the types of intentional herbal drug adulteration. Briefly explain this statement. (***20 marks***)

3.1.3 Write a common adulterant of following authentic drugs. (***15 marks***)

3.1.3.1 Senna plant

3.1.3.2 Bees wax

3.1.3.3 Olive oil

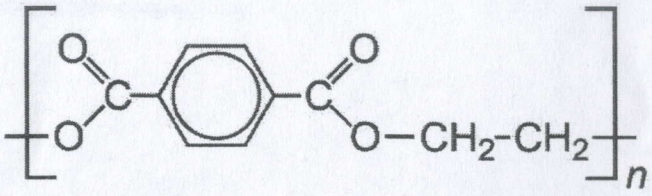
3.2 Purified honey has valuable health benefits.

3.2.1 Briefly explain the steps involved in honey production. (***15 marks***)

3.2.2 State two medicinal uses of purified honey. (***10 marks***)

3.3 Following structure **C** represents one of the synthetic fibers.

Structure C



3.3.1 What is the synthetic fiber represent by the structure **C**? (***05 marks***)

3.3.2 List two uses of the synthetic fiber you mentioned above 3.3.1. (***10 marks***)

3.4 List three functions of surgical dressings. (***15 marks***)

PART C

4.

4.1 Define the term crude drug. (***10 marks***)

4.2 Briefly explain the different classification systems of crude drugs. Mention advantages and disadvantages of each classification system. (***40 marks***)

4.3 List the differences between organized drugs and unorganized drugs. (***20 marks***)

4.4 Giving examples, explain briefly how the environmental factors affect the production of crude drugs. (***30 marks***)

PART D

5.

5.1 Write the floral formula and draw the floral diagram for the following description.
Flower is actinomorphic (regular). Bisexual. Five sepals aestivation imbricate, free. Five petals twisted, connected. Androecium consists of 10 stamens, 9 stamens large and one is small. Inferior ovary consists of five carpals and they are syncarpous. Parietal placentation.
(***30 marks***)

5.2 Briefly describe types of inflorescences with examples. (***40 marks***)

5.3 Write short notes on types of stomata in plants. (***30 marks***)

6.

6.1 Briefly describe the factors to be considered in herbarium sampling. (***40 marks***)

6.2 List four most important facts to be included when labeling a herbarium specimen.
(***20 marks***)

6.3 Briefly describe advantages and disadvantages of crude drug evaluation using organoleptic properties. (***40 marks***)

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