



UNIVERSITY OF RUHUNA – FACULTY OF MEDICINE

ALLIED HEALTH SCIENCES DEGREE PROGRAMME SECOND BPHARM PART II EXAMINATION – JUNE 2016 PH 2244: MEDICINAL CHEMISTRY & PHARMACOGNOSY IA (SEQ)

TIME: THREE HOURS

INSTRUCTIONS

• Answer all questions.

• Do not use any correction fluid.

Answer questions in the given answer book.

• Marks will be deducted for illegible hand writing.

01. Answer all parts.

1.1

1.1.1. Lipinski's Rule of five is useful in drug design. Explain.

(05 marks)

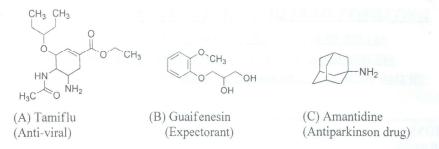
1.1.2. Giving reasons state whether the following drug is considered as satisfactory drug candidate in terms of potential bio-availability and state whether it can be administered orally.

 $\begin{aligned} & \text{Propranalolol C}_{18} \text{H}_{21} \text{NO}_2 \\ & \text{logP=} \ 2.53 \end{aligned}$

(10 marks)

1.1.3. Using the table given below predict the water solubility of the following drugs (A), (B) and (C). State how the water insoluble drugs are formulated. (15 marks)

Functional Group		Molecule with one functional group solubilizes	Molecule with multiple functional groups solubilize	
Alcohol	R-OH	5 or 6 carbons	3 or 4 carbons	
Ether	R-O-R	4 or 5 carbons	2 carbons	
Ketone	R-C(=O)-R	5 or 6 carbons	2 carbons	
Ester	R-C(=O)-OR	6 carbons	3 carbons	
Amine	R-NH ₂	6 or 7 carbons	3 carbons	
Amide R-C(=O)-NH ₂		6 carbons	2 or 3 carbons	



1.2

1.2.1. Explain the term "bioisostere" briefly.

(05 marks)

1.2.2. Although 5-fluorouracil (5-Fu) and uracil are bioisosteres, 5-Fu is used as an anti- cancer drug. Explain. (15 marks)

1.3

1.3.1. **(A)** is an anti-arthritic drug which is quickly excreted in the body compared to that of **(B)**. Explain. *(08 marks)*

$$CI$$
 N
 N
 CH_3
 (A)
 SO_2Me
 CI
 N
 CH_3

- 1.3.2. The following anticonvulsant drug phenytoin used in the treatment of epilepsy, is virtually insoluble in water. Metabolism by cytochrome P450 isoenzymes (CYPs) followed by uridine diphosphate-glucuronosyltransferase (UGT) enzymes produces a metabolite (B) that is highly water soluble. (10 marks)
 - (i) Draw the structures of the intermediate (A) and the final metabolite (B).
 - (ii) State the phases of metabolic reactions that are involved in the formation of (A) and (B).

1.3.3. Name the enzymes involved in the following metabolic transformations and state which phase of metabolic reactions is involved in the reaction (i). (12 marks)

2

1.4. Vitamin E is soluble in fat. It is found in many foods including cereals, meat, eggs, fruits, vegetables. (20 marks)

- 1.4.1. Determine how many possible stereoisomers vitamin E has by placing a star (*) to each chiral centre.
- 1.4.2. How does vitamin E derived from soybeans differ from its synthetic analogue?
- 1.4.3. What additional experiment would clarify the difference between soybean vitamin E and synthetic vitamin E?
- 1.4.4. What do you advise people about taking the synthetic versus plant derived vitamin E?

02.

2.1.

2.1.1. Carryout retrosynthetic analysis to design a synthesis for the following molecule using cyclopentanone and any other necessary conditions. (20 marks)

2.1.2. 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.

3

Br
$$R_3$$
 R_1 R_2 R_3 R_4 R_2 R_3 R_4 R_4 R_5 R_4 R_5 R_4 R_5 R_5 R_4 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)

2.2. The analogues (i, ii, iii and iv) were synthesized on addition and removal of certain groups to the adrenergic agonist lead compound shown below. The following changes in biological activity in determining the structure of the unknown target were observed.

What are the most likely conclusions that can be drawn from following structure activity relationships (SARs).

- 2.2.1. The removal of the Me- group in the lead compound (analogue i) reduced the activity whereas the addition of a cyclopentyl-group (analogue ii) dramatically improved its activity. (10 marks)
- 2.2.2. The addition of a CH₃- group in the lead compound (analogue iii) reduced the activity whereas the addition of an OH- group (analogue iv) improved its activity. (10 marks)
- 2.3. Candoxatril is an ester prodrug for candoxatrilat which inhibits protease enzymes. (20 marks)

- 2.3.1. Write down the chemical structures of the drug and the by- product(s) it would liberate on activation.
- 2.3.2. Give reason(s) why the parent drug cannot be administered orally.

2.4.

2.4.1. The binding of guanine analogue to the active site of purine nucleoside phosphorylase is shown below. The replacement of hydrogen (H) at 8^{th} position of this analogue by an amino group (NH₂) increased the biological activity 100 times. Explain this phenomenon showing the binding of the modified analogue to the above active site.

(15 marks)

2.4.2. Following is the general structure of β -Bromo- β -aryl-ethylamines which shows anti-adrenergic activity. (15 marks)

- i) State the physicochemical properties of this compound which would affect its biological activity.
- ii) Write down the simplified Hansch equation which could be related to the biological activity of this compound.
- iii) State the nature of substituents which could be introduced to improve its biological activity and give an example for each.
- 03. Write short notes on the following.

(20 x5 marks)

- 3.1. Drugs of animal origin.
- 3.2. Classification of surgical fibres.
- 3.3. What is a herb and herbal food.
- 3.4. Identification test for cotton and silk fibers.
- 3.5. Definition of Pharmacognosy

04.

- 4.1. Highlight the important microscopical characters of
 - 4.1.1. Senna leaf powder.

(20 marks)

4.1.2. Datura leaf powder.

(20 marks)

4.2. State the parts of the plant which are used in medicine given below.

(20 marks)

- 4.2.1. Senna
- 4.2.2. Ephidra
- 4.2.3. Rauwolfia
- 4.2.4. Anithum sowa
- 4.3. Explain briefly common adulterants found in marketed samples of bee honey.

(20 marks)

4.4. List ten (10) important crude drugs of family umbeliferae.

(20 marks)

$\downarrow \quad \not \in \quad K_{(5)}C_{(5)}A_{(4)+1}, \ \, \overrightarrow{G}_{(5)}$

5.2. Fill in the blanks using the given table.

(30 marks)

(20 marks)

(20 marks)

A	В	C	D	E	F
Sessile	Dicussate	Climbing	Trailing	Rhizome	Unipinnate
Sheath	Whorled	Epiphytic	Prostrate	Come	Bipinnate
Winged	Spiral	Pneumtophores	Runner	Bulb	Tripinnate

	(i) The category containing Phyllotaxy is			
	(ii) The category containing roots modifications is			
	(iii)The category containing modification of petiole is			
	(iv)The category containing compound leaves is			
	(v) The category containing weak stems is			
	(vi)The category containing underground stems is			
5.3.	Draw diagrams to show the following leaf types.	(10 marks)		
	5.3.1. Even-pinnate compound			
	5.3.2. Odd-pinnate compound			
5.4.	Draw diagrams to show the following ovary positions. (20 (i). Hypogynous			
	(ii).Epigynous			
5.5.	. Give five simple fruit types with example for each. Type of fruit Example	(16 marks)		
06.				
6.1.	. Distinguish between	the second second second		
	6.1.1. simple leaf and compound leaf	(10 marks)		
	6.1.2. stamen and pistil	(10 marks)		
	6.1.3. parietal and axile placentation	(10 marks)		
6.2.	List two common characteristics of families; cucurbitaceae, mal	vacea and amaranthaceae. (18 marks)		
	Family Common characteristic	es		
5.3.	List sub families in family fabaceae.	(12 marks)		

6.4. Briefly explain the economical importance of medicinal plants in family fabaceae.

6.5. Briefly describe the difference between underground stem and root.