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UNIVERSITY OF RUHUNA – FACULTY OF ALLIED HEALTH SCIENCES

DEPARTMENT OF PHARMACY

SECOND BPHARM PART II EXAMINATION – DECEMBER 2017/JANUARY 2018

PH 2244 MEDICINAL CHEMISTRY AND PHARMACOGNOSY IA (SEQ)

TIME: THREE HOURS

INSTRUCTIONS

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

PART A

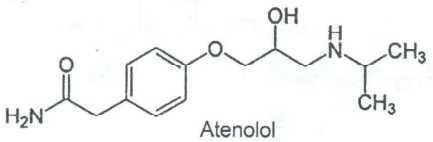
1. Answer all the parts.

1.1

1.1.1. Define the terms partition coefficient (P) and logP. (***08 marks***)

1.1.2. State **three** occasions where logP is important in drug design. (***12 marks***)

1.2 Indicate the lipophilic and hydrophilic sites of the following 'beta-blocker' atenolol.

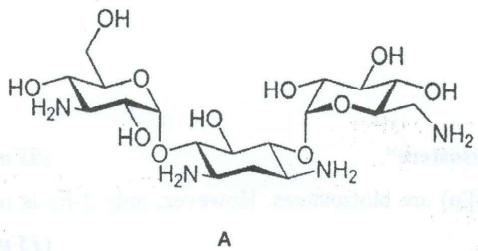


Atenolol

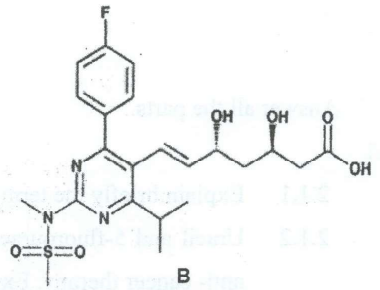
(***10 marks***)

1.3 Lipinski's *Rule of five* is useful in drug design. Explain. (***10 marks***)

1.4 Following drugs A ($C_{18}H_{36}N_4O_{11}$, MW 484, Log P -6.3) and B ($C_{22}H_{28}FN_3O_6S$, MW 491, LogP 1.92) are used as an antibiotic for variety of infections and as an anti-cholesterol agent respectively. State the number of hydrogen bond donors and hydrogen bond acceptors present in these drugs and state whether they could be administered orally.



A



B

(***15 marks***)

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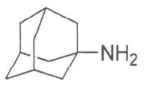
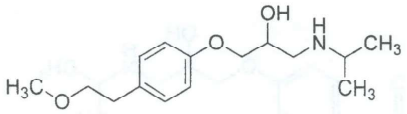
1.5 Using the table given below, predict the water solubility of the following drugs A, B and C. Give reasons for your answer.

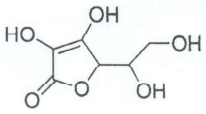
Functional Group		Molecule with one functional group solubilizes	Molecule with multiple functional groups solubilize
Alcohol	R-OH	5 or 6 carbons	3 or 4 carbons
Ether	R-O-R	4 or 5 carbons	2 carbons
Ketone	R-C(=O)-R	5 or 6 carbons	2 carbons
Ester	R-C(=O)-OR	6 carbons	3 carbons
Amine	$R\text{-}NH_2$	6 or 7 carbons	3 carbons



A



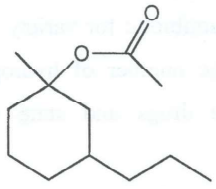
B



C

(*20 marks*)

1.6 Use retrosynthetic analysis to design a synthesis for the following compound using cyclohex-2-enone and any other necessary conditions.



(*25 marks*)

2. Answer all the parts.

2.1

2.1.1 Explain briefly the term "**bioisostere**". (*05 marks*)

2.1.2 Uracil and 5-fluorouracil (5-Fu) are bioisosteres. However, only 5-Fu is used in anti- cancer therapy. Explain. (*15 marks*)

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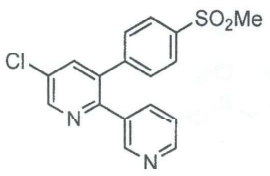
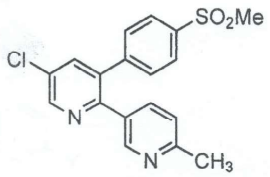
2.2

2.2.1 Anti-arthritic drug (**B**) is quickly metabolized and excreted in the body compared to **(A).** Explain. ***(10 marks)***



(A)

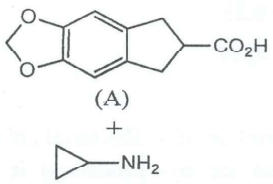


(B)

2.2.2 State the phase and the enzyme involved in the above metabolic reaction.

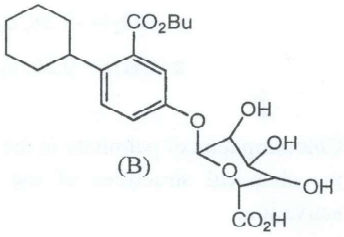
(05 marks)

2.2.3 Predict the structures of the compounds that produce the following metabolites (A) and (B) (work backwards from metabolite to compound). Show the steps (not detailed mechanism) and suggest enzymes and the phases involved.



(A)

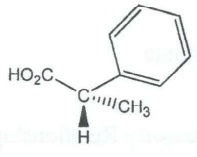
+



(B)

(05 marks)

2.3 The popular non-steroidal anti-inflammatory drug (NSAID), ibuprofen is sold as the racemic mixture. Its eutomer shown exhibits the anti-inflamatory activity by inhibiting the enzyme cyclooxygenase. The distomer does not show any analgesic activity, but in vivo it becomes active. Explain this observation assigning the stereochemistry to the structure shown.



Eutomer of Ibuprofen

(10 marks)

2.4

2.4.1 Explain how the following physicochemical properties of a drug molecule are quantified for QSAR study. ***(10 marks)***

2.4.1.1 Lipophilicity.

2.4.1.2 Electronic effect of a substituent.

2.4.1.3 Steric characteristics.

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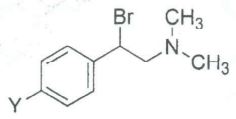
2.4.2 A Hansch analysis was carried out on a series of β- halo- arylamines that demonstrated anti-adrenergic activity. The following Hansch equation was derived from the study.

$$\text{Log } 1/C = 1.22\pi - 1.59\sigma + 7.89$$



2.4.2.1 Based on the above Hansch equation, state the physicochemical properties of the β- halo- amines that showed an impact on their adrenergic activity?

(***05 marks***)

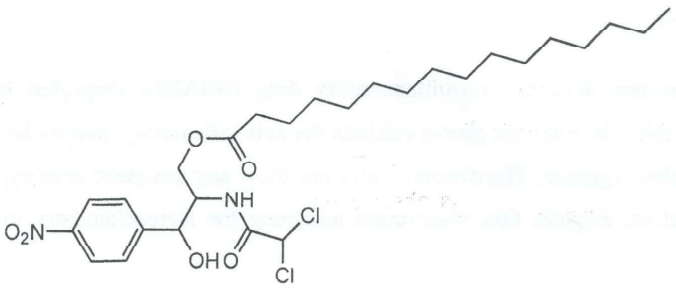
2.4.2.2 Use the above derived Hansch equation and the following data to predict whether a 4- nitro(Y) analogue will give better activity than a 4- methyl(Y) substituted analogue.

$\pi\ (NO_2) = -0.28$, $\sigma_p(NO_2) = 0.23$

$\pi\ (CH_3)) = 0.56$, $\sigma_p(CH_3) = -0.17$

(***10 marks***)

2.5 Chloramphenicol palmitate is the ester- prodrug of antibacterial chloramphenicol. State the chemical structures of the drug and the by- product(s) it would liberate on activation.



Chloramphenicol palmitate

(***10 marks***)

2.6 Some steps of the Structure Activity Relationship (SAR) carried out on the lead (I) in the development of the antifungal agent, Nevirapineare shown in the scheme given below. The IC_{50} (μM) values of structures (I), (II) and Nevirapine for their antifungal activity have been found to be 3.9, 0.31 and 0.015 respectively. Explain. (***15 marks***)

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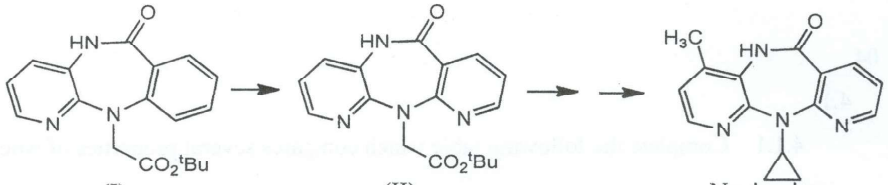

(I) (II) Nevirapine

IC_{50}= 3.9μM IC_{50}= 0.31μM IC_{50}= 0.015μM

PART B

03.

3.1 Ayurveda medicine is considered as one of the oldest types of medicine practiced in the world. Answer the following questions in relation to Ayurveda.

3.1.1 What are the **three** elements that regulate body functions? (***05 marks***)

3.1.2 Briefly explain **five** types of Ayurvedic formulations giving **two** examples for each.

(***30 marks***)

3.2

3.2.1 How would you define a crude drug? (***10 marks***)

3.2.2 Briefly summarize the differences between organized and unorganized drugs.

(***25 marks***)

3.2.3 Briefly explain **ten** standards that are applied to maintain the quality of crude drugs. (***30 marks***)

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04.

4.1

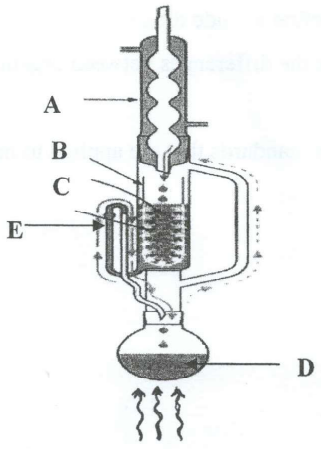
4.1.1 Complete the following table which compares several properties of wool and silk.

(***36 marks***)

Test	Wool	Silk
Burn in flame		
Millon's reagent		
Warm 5% KOH		
Conc. HCl		
CuOxam		
Sulphoprotein test		

4.1.2 Silk fibers are obtained from several species of order Lepidoptera. Explain briefly the steps involved in the preparation of silk giving emphasis to the species involved in the process. (***20 marks***)

4.2 Following picture displays an apparatus involved in the hot continuous extraction of natural products.



4.2.1 Identify the apparatus. (***05 marks***)

4.2.2 Label the parts **A-E**. (***10 marks***)

4.2.3 Briefly describe the process involved in this setup. (***15 marks***)

4.2.4 What are the limitations of this process? (***04 marks***)

4.3 Animal products are involved in the pharmaceutical industry for the manufacture of different pharmaceuticals. Indicate the source of the following animal products and their pharmaceutical uses. ***(10 marks)***

4.3.1 Shellac

4.3.2 Cod liver oil

PART C

5.

5.1 Briefly describe the given floral formula: ⚥ * K (8) C (5+3) A∞, G (5) ***(10 marks)***

5.2 Fill in the blanks using the given table. ***(12 marks)***

A	B	C	D	E	F
Spike	Epigynous	Spatulate	Trailing	Pulvinus	Pod
Spadix	Perigynous	Reniform	Prostrate	Elongated	Capsule
Raceme	Hypogynous	Linear	Runner	Sessile	Silique

5.2.1 The category containing **leaf shapes** is ....

5.2.2 The category containing **ovary positions** is ....

5.2.3 The category containing modification of leaf petioles is ....

5.2.4 The category containing **dehiscent dry fruits** is ....

5.2.5 The category containing **weak stems** is ....

5.2.6 The category containing **inflorescence** types is..

5.3 Draw diagrams to show the following types. ***(20 marks)***

5.3.1 Corymb inflorescence

5.3.2 Umbel inflorescence

5.3.3 Palmately compound leaf

5.3.4 Even-bipinnate leaf

5.4 Distinguish between

5.4.1 a pod type fruit and a silique type fruit. ***(06 marks)***

5.4.2 alternate and opposite phyllotaxy. ***(06 marks)***

5.4.3 rhizome and come modified stems. ***(06 marks)***

5.5 List **two** common characteristics of families; Euphorbiaceae and Acanthaceae. ***(10 marks)***

5.6 List **two** main types of calcium oxalate crystals occurring in monocotyledons. ***(10 marks)***

5.7 Briefly describe the use of calcium oxalate crystals in plant characterization. ***(10 marks)***

5.8 Briefly explain the economical importance of medicinal plants in family cucurbitaceae. ***(10 marks)***

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6.

6.1 Name **one** morphological trait that is used to establish the plants belonging to the following plant families. ***(20 marks)***

6.1.1 Malvaceae .....

6.1.2 Fabaceae .....

6.1.3 Amaranthaceae .....

6.1.4 Araceae .....

6.1.5 Rutaceae .....

6.2

6.2.1 Give **five** different methods that can be used in drug evaluation. ***(20 marks)***

6.2.2 Briefly describe organoleptic techniques used in drug evaluation. ***(30 marks)***

6.3 Describe in sequence, the important steps of collecting and processing a plant sample for a herbarium specimen. ***(30 marks)***

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