BSc Degree Examinations 2019-20

Department:
BIOLOGY

Title of Exam:
Pharmacology

Time Allowed:
24 Hours (PLEASE NOTE: Late papers will not be marked)

Time Recommended:
1 hour and 30 minutes

Word limit: Please answer the questions within the line/word limit stated. Content beyond the line/word limit will not be marked.

Allocation of Marks:
Total marks available for this paper: 60
Section A contains interpretation and data handling questions (40 marks).
Section B contains an essay question (one from 2 choices) 20 marks
The marks available for each question are indicated on the paper.

Instructions for Candidates:
All questions should be answered on this question paper using minimum font size Arial 11.
Each question should be answered within the stated line/word limit. Do not adjust the margin width.

Section A: Answer all questions
Section B: Answer either question A or B.
A note on Academic Integrity

We are treating this online examination as a time-limited open assessment, and you are therefore permitted to refer to written and online materials to aid you in your answers.

However, you must ensure that the work you submit is entirely your own, and for the whole time the assessment is live you must not:

- communicate with departmental staff on the topic of the assessment
- communicate with other students on the topic of this assessment.
- seek assistance with the assignment from the academic and/or disability support services, such as the Writing and Language Skills Centre, Maths Skills Centre and/or Disability Services. (The only exception to this will be for those students who have been recommended an exam support worker in a Student Support Plan. If this applies to you, you are advised to contact Disability Services as soon as possible to discuss the necessary arrangements.)
- seek advice or contribution from any third party, including proofreaders, friends, or family members.

We expect, and trust, that all our students will seek to maintain the integrity of the assessment, and of their award, through ensuring that these instructions are strictly followed. Failure to adhere to these requirements will be considered a breach of the Academic Misconduct regulations, where the offences of plagiarism, breach/cheating, collusion and commissioning are relevant - see AM.1.2.1” (Note this supersedes section 7.3 of the Guide to Assessment).
1. Below is the change in plasma concentration ($C_p$) of a newly developed amide local anaesthetic drug immediately following a bolus dose.

![Graph showing plasma concentration over time](image)

a) By what route was this drug most likely administered? Explain your answer.  
   (2 marks, 4 lines)

b) Which compartment model best describes the pharmacokinetic profile of this drug?  
   (1 mark, 1 line)

c) What is the value of $C_0$?  
   (1 mark, 1 line)

d) What is the elimination $t_{1/2}$? Show how you arrived at your answer.  
   (2 marks, 3 lines)

e) Would you recommend a loading dose for this drug? Explain your answer.  
   (2 marks, 3 lines)
2. Below is a Lineweaver Burk plot showing the kinetics of TLR4-MD dimer formation after binding of its ligand LPS. The effect of binding is determined by measuring the % of dimer formation. The black line shows the interaction with LPS alone while the blue line shows LPS with drug Y.

\[ \text{\% Dimer formation} = \frac{1}{1 + \frac{K_d}{[LPS]}} \]

a) What is the binding affinity (Kd) and maximum % dimer formation of LPS alone

(2 marks, 5 lines)

b) Drug Y affects the LPS binding and thus dimer formation. What type of agonist or antagonist describes Drug Y? Explain your answer.

(2 marks, 3 lines)
3. You are investigating two potential receptors (R1 and R2) for Ligand A. To find and characterize the receptor for Ligand A you have generated the following data of cyclic AMP (cAMP) production wherein you measure cAMP production at basal level, after addition of Ligand A, after addition of cAg (a stimulator of cAMP production) and lastly after addition of both cAg and Ligand A to each receptor. Significant changes in cAMP production compared to basal levels are indicated with an asterisk (*).

![cAMP Production Graph]

a) Which of the two receptors are responding to Ligand A? Explain your answer.

(2 marks, 5 lines)

b) Describe what type of receptor Ligand A is binding to? Explain your answer.

(3 marks, 5 lines)
4.  
   a) It is observed that a novel antibiotic is being rapidly cleared in the urine. Devise a strategy to determine the roles of the OATs and/or OCTs in this process, and explain the logic of your strategy.  
      (4 marks, 8 lines)

   b) Outline an approach to slow excretion, justifying your answer with evidence from a current drug.  
      (3 marks, 3 lines)

5.  
   a) Explain the sliding filament theory of muscle contraction  
      (8 marks, 10 lines)

   b) Give an example of a drug that affects muscle contraction, and explain how it interacts with the contractile protein(s)  
      (2 marks, 3 lines)

6. Patients with an autoimmune disease are treated with a prodrug (“Inhibinib”) that reduces immune activation. Inhibinib is converted to a toxic active metabolite (Inhibinib*) by a cytochrome P450 enzyme CYP2JH. The circulating prodrug:drug ratio in a patient cohort is shown below:
a) Explain what the graph shows for groups A and B, and give genetic explanations for this distribution
(4 marks, 8 lines)

b) What are the limitations of treating patients in group A and B with this drug?
(2 marks, 4 lines)

SECTION B: Essay question
Answer either question A or B from this section.

Mark total for this section: 20

A. Epinephrine was used early in the twentieth century to treat asthma but has since been replaced by other drugs such as Salbutamol, which is commonly used in inhalers to treat asthma. Explain key improvements of salbutamol as compared to epinephrine for treating asthma by describing its receptor and signalling, discussing specificity and explaining the relevance of these for drug access, kinetics and side effects (including examples of side effects).

(20 marks, 500 words)

OR

B. Explain the problems posed by ‘first-pass metabolism’ and outline ways in which these can be avoided, illustrating the principles with specific drugs.

(20 marks, 500 words)

End of exam