

BIO484 (M) 2019/2020

UNIVERSITY OF ESWATINI

FACULTY OF SCIENCE AND ENGINEERING

DEPARTMENT OF BIOLOGICAL SCIENCES

MAIN EXAMINATION PAPER 2019/2020

COURSE CODE: BIO484

TITLE OF PAPER: DRUG METABOLISM AND TOXICOLOGY

TIME ALLOWED: THREE (3) HOURS

INSTRUCTIONS: NUMBERS IN BRACKETS DENOTE THE NUMBER OF MARKS

THIS PAPER COMPRISES OF **THREE SECTIONS**. SECTION A COMPRISES OF 11 QUESTIONS (15 MARKS). SECTION B COMPRISES OF 4 QUESTIONS (60 MARKS). ANSWER ALL QUESTIONS IN SECTIONS A AND B. SECTION C HAS TWO QUESTIONS. ANSWER ONLY ONE QUESTION FROM SECTION C (25 MARKS).

**CLEARLY INDICATE THE SECTION AND QUESTION NUMBER ON YOUR ANSWER PAPER.**

**CALCULATORS MAY BE TAKEN INTO THE EXAMINATION.**

**DO NOT OPEN THIS PAPER UNTIL PERMISSION HAS BEEN GRANTED BY THE CHIEF INVIGILATOR**

## Section A

Total marks available: 15

There are eleven (11) questions in this section. Answer ALL the questions in this section

AQ1: Which one of the following is an example of a toxin [1]

- a) Digoxin from the foxglove plant
- b) Benzene from gasoline
- c) Ascorbic acid from a canning factory
- d) All of the above
- e) None of the above

AQ2: LADME stands for [1]

- a) Liberation, adhesion, distribution, metabolism, excretion
- b) Longevity, adhesion, distribution, metabolism, elimination
- c) Longevity, absorption, digestion, metabolism, emancipation
- d) Liberation, absorption, distribution, metabolism, excretion
- e) Liberation, absorption, dissolution, modification, elimination

AQ3: After 78mg of a drug is administered to a patient intravenously the plasma concentration was found to be 4g/L. The volume of distribution of this drug is [2]

- a) 19.5L
- b) 51.3L
- c) 0.05L
- d) 0.0195L
- e) 1950L

AQ4: When doing a bioavailability study on 'newdrugzavir', you calculate the following information area under the curve for buccal tablet, oral capsule and IV formulations are 21.5-, 13.9- and 25.7- units square, respectively. Peak plasma concentrations for each formulation was 48mg/L, 27mg/L and 103mg/L, respectively. The bioavailability of buccal newdrugzavir? [2]

- a) 2.23%
- b) 84%
- c) 45%
- d) 21%
- e) 25%

AQ5: Which of the following statements is a principle of drug-receptor interactions? [1]

- a) A drug exerts a qualitative effect at the receptor site
- b) Free and bound drugs can exert an effect at the receptor site
- c) Forces must be present to attract and hold a drug in contact with a receptor
- d) All of the above
- e) None of the above

AQ6: The dose-response relationship is [1]

- a) Relationship between dose and effect on the individual level
- b) Best described by the 'all or nothing' effect
- c) usually linear for toxic chemicals
- d) All of the above
- e) None of the above

- AQ7: A substance that is described as teratogenic is damaging to the [1]
- a) Lungs
  - b) Eyes
  - c) Pancreas
  - d) Foetus
  - e) Gut

- AQ8: When administering first aid to a patient bitten by a rhinokaals snake, it is important to [1]
- a) Apply a tourniquet below the bite site
  - b) Make an incision at the bite site and suck the venom out
  - c) Urinate on the bite site
  - d) Elevate the limb above the heart
  - e) None of the above

AQ9: A doctor from Mankhayane Government Hospital calls your toxicology department for some advice. She has a patient who was been bitten about 3 hours by a green mamba whilst walking from her homestead to the river to wash her clothes. The patient has no particular symptoms but there are two small 'dots' on her ankle. The patient did not bring the snake with her. What advice would you give the doctor? [2]

- a) Immediately intubate the patient and start 5 vials of polyvalent antivenom
- b) Immediately start fluids and give adrenaline
- c) Send the patient to theatre for venom removal
- d) All of the above
- e) None of the above

- AQ10: Toxicogenomics is [1]
- a) Is the study of formulating toxic substances into therapeutic dosage forms
  - b) Investigates the effects of toxic substances on gene expression and protein activity
  - c) The study of how a substance gets into the body and what happens to it in the body
  - d) The dynamic interactions of a toxicant with a biological target and its biological effects
  - e) The mechanism of mode of action of toxicants

AQ11: At the intervarsity games, all gold medal winners are tested for doping. Your forensic toxicology lab has been awarded the tender to run all the tests. The following report is an excerpt from the winner of the men's 200m sprint.

Test name	Result	Cut off level
Amphetamines	200ng/ml	1000ng/ml
Cocaine metabolites	305ng/ml	300ng/ml
Marijuana metabolites	10ng/ml	50ng/ml
Opiates	450ng/ml	300ng/ml

Based on the figures in the table above, the results show the winner of the men's 200m sprint [2]

- a) Passed the doping test and is the rightful gold medalist
- b) Should be stripped of the gold medal as they failed the doping test, because the marijuana and amphetamine levels were elevated
- c) Should keep the gold medal despite failing the doping test for marijuana and cocaine
- d) Should be stripped of the gold medal as they failed the doping test, because the cocaine and opiates levels were elevated
- e) Should be stripped of the gold medal as they failed all the tests

## Section B

Total marks available: 60

There are four (4) questions in this section. Answer ALL the questions in this section

BQ1: Majaha is a 20-year-old male and weighs 72kg. He was admitted to Mbabane Government Hospital after falling unconscious. Blood samples were sent for analysis, and Majaha was found to have very elevated levels of cyp450. The toxicology report has come back negative for any heavy metal poisoning or other known toxins. His records show that last week he saw his regular doctor in Nhlanguano, who prescribed Majaha a course of Fabulousillin 150mg three times a day for 2 weeks, to treat an ear infection. Two days ago, Majaha had a minor accident at work where his hand was injured. He was treated by another doctor in Manzini for the cuts to his hand. The doctor in Manzini prescribed Majaha Superbacyclin 100mg once daily for 5 days.

	ED50	LD50	Fraction bound	$K_D$	pKa	Route of elimination
Fabulousillin	0.25mg/kg	2mg/kg	95%	5 $\mu$ M	5.3	Liver
Superbacyclin	0.3mg/kg	15mg/kg	80%	3nM	8.5	Kidney

- Explain the difference between  $EC_{50}$  and  $LD_{50}$ . [5]
- Briefly describe the role of Cyp450 in the body and the likely reason(s) it is elevated in Majaha. [5]
- Assuming a bioavailability of 0.8, calculate the estimated amount of unbound Fabulousillin that would have been present in Majaha's plasma before his accident. [3]
- Did the doctor in Nhlanguano prescribe the correct dose of Fabulousillin for Majaha? Explain your answer. [3]
- Assuming a bioavailability of 0.3, calculate the estimated amount of unbound Superbacyclin in Majaha's plasma. [3]
- Which drug do you expect to have the greater volume of distribution? Explain your answer. [3]
- Which drug do you expect to be best absorbed in the stomach? Explain your answer. [2]
- Explain what you think are the most probable cause(s) of Majaha's clinical presentations. In your answer, explain how you could confirm your suspicions. [11]
- The doctor wants to acidify Majaha's urine. Do you think this is a good idea and what will be the effect on each drug if Majaha's urine is acidified? [5]

BQ2: List FIVE factors that can affect the absorption of a xenobiotic. [5]

BQ3: Provide an overview of how xenobiotics are metabolized in the body. [10]

BQ4: Outline the key differences between agonists, partial agonists and antagonists. [5]

## Section C

Total marks available: 25

There are two questions in this section. Answer only ONE question

CQ1: Explain the toxicology of at least TWO animal venoms and the benefits their venoms can provide to humans. [25]

OR

CQ2: You are working at the National Poisons Centre and have received a call from a cattle farmer who has noticed her cows have started to become disorientated. Local villagers have also reported large numbers of dead fish and birds too, and several people – mostly slender elderly and infants - have been admitted to the local hospital with generalized rash, jaundice and disorientation / confusion. A few patients are in critical condition and are being looked after in intensive care, with more patients presenting with similar symptoms at the hospital every day. Plasma samples taken from the dead cows and the admitted patients find high levels of “Mambanite” – a toxic chemical produced as a by-product of one of the drugs produced by the new pharmaceutical industry 10km upstream of where the cattle farmer and her village. Mambanite is a lipid-soluble substance, pH 6.2, and has a MW 200Da. It readily forms liposomes when it comes into contact with water, has a low affinity to plasma proteins and does not easily chelate.

Based on the information above, and your expertise in toxicology, explain the toxicokinetics of Mambanite. [25]

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ADDITIONAL INFORMATION

Henderson-Hasselbalch Equation

$$\text{Acids: } pH - pKa = \log \frac{\textit{nontionised}}{\textit{ionised}}$$

$$\text{Bases: } pH - pKa = \log \frac{\textit{ionised}}{\textit{nontionised}}$$

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END OF EXAMINATION