

BIO484 (M) 2021

UNIVERSITY OF ESWATINI
FACULTY OF SCIENCE AND ENGINEERING
DEPARTMENT OF BIOLOGICAL SCIENCES
MAIN EXAMINATION PAPER 2021

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.

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Section A

Total marks available: 15

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

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- AQ1: An antagonist is a xenobiotic that: [1]
- a) Has affinity and efficacy
 - b) Has no affinity and no efficacy
 - c) Has affinity and no efficacy
 - d) Has efficacy and no affinity
 - e) Has affinity and reverse efficacy
- AQ2: Which one of the following is an example of a toxin [1]
- a) Mercury from fluorescent lightbulbs
 - b) Glycoalkaloids in potatoes
 - c) Citric acid from a food factory
 - d) All of the above
 - e) None of the above
- AQ3: Which of the following statements is a principle of toxicology? [1]
- a) A drug exerts a qualitative effect at the receptor site
 - b) Chemicals in the same class cause different human health effects
 - c) All entry sites have the same absorption and distribution rates
 - d) All exposures are poisonings
 - e) None of the above
- AQ4: After 60mg of a drug is administered to a patient intravenously the plasma concentration was found to be 74ng/L. The volume of distribution of this drug is [2]
- a) 1.23ml
 - b) 1.23L
 - c) 0.81L
 - d) 811L
 - e) 1233L
- AQ5: When doing a bioavailability study on 'randomicillin', you calculate the following: peak plasma concentrations for vaginal tablet, oral capsule and IV formulations was 76mg/L, 24mg/L and 99mg/L, respectively. Area under the curve for each formulation was 15.8-, 10.5- and 32.9- units square, respectively. What is the bioavailability of oral randomicillin? [2]
- a) 24%
 - b) 32%
 - c) 44%
 - d) 48%
 - e) 77%
- AQ6: The dose-response relationship is [1]
- a) best described by the 'all or nothing' effect
 - b) the relationship between dose and effect on the individual level
 - c) usually linear for toxic chemicals
 - d) the relationship between dose and effect at the population level
 - e) None of the above

AQ7: A substance that is described as ototoxic is damaging to the [1]

- a) Eyes
- b) Nose
- c) Ears
- d) Foetus
- e) Gut

AQ8: When administering first aid to a patient bitten by a spotted bush 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: Relative efficacy is best described using: [1]

- a) An inverse agonist and a full agonist
- b) A partial agonist and a full agonist
- c) A reversible competitive antagonist and a full agonist
- d) An irreversible competitive antagonist and a full agonist
- e) None of the above

AQ10: Toxicogenomics is [1]

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

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
Cocaine metabolites	312ng/ml	300ng/ml
Anabolic androgenic steroids	0ng/ml	0ng/ml
Adrenaline	12ng/ml	10mcg/ml
Beta-2-agonists (formoterol)	38ng/ml	0.04mg/ml
Opiates	450ng/ml	1mg/ml

Based on the figures in the table above, the results show the winner of the men's 200m sprint [3]

- 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 cocaine levels were elevated
- c) Should be stripped of the gold medal as they failed the doping test, because the cocaine and opiates levels were elevated
- d) Should be stripped of the gold medal as they failed the doping test, because the adrenaline, cocaine and formoterol
- 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: Mcebisi is a 29-year-old male and weighs 83kg. He was admitted to Lubombo Referral Hospital after falling unconscious. Blood samples were sent for analysis, and Mcebisi was found to have very elevated levels of CYP2D6. The toxicology report has come back negative for any heavy metal poisoning or other known toxins. His records show that 7 days ago he saw his regular clinician in Lomahasha, who prescribed Mcebisi a pain killer "Painaway" 600mg three times a day for upto 2 weeks, to treat his backache. Two days ago, Mcebisi had saw another doctor in Manzini for a cut to his leg following an accident at work. The doctor in Manzini prescribed Mcebisi "staphycyclin" 1.25g once daily for 5 days.

	ED50	LD50	Fraction bound	Bioavailability	t _{1/2}	K _D	pKa	Route of elimination
Painaway	2.5mg/kg	10mg/kg	97%	0.73	240min	3μM	7.3	Kidney
Staphycyclin	0.3mg/kg	15mg/kg	82%	0.65	16hours	9nM	6.8	Liver

- a) Calculate the dose (in mg/kg) for each of the two drugs prescribed to Mcebisi. [2]
- b) Are the two drugs prescribed for Mcebisi within the therapeutic window? Explain your answer. [5]
- c) Which drug do you expect to have the greater volume of distribution? Explain your answer. [3]
- d) Did the clinician in Lomahasha prescribe the correct dose of Painaway for Mcebisi? Explain your answer and show all your calculations. [10]
- e) Calculate the estimated amount of unbound Staphycyclin that would have been present in Mcebisi's plasma before his accident. [3]
- f) Which drug do you expect to be best absorbed in the stomach? Explain your answer. [2]
- g) Explain what you think are the most probable cause(s) of Mcebisi's clinical presentations. In your answer, explain how you could confirm your suspicions. [10]
- h) The doctor wants to acidify Mcebisi's urine. Do you think this is a good idea and what will be the effect on each drug if Mcebisi's urine is acidified? Explain your answer. [5]

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

BQ3: Explain how xenobiotics can cause neurotoxicity. Your answer should include at least one diagram and an example of a xenobiotic that causes neurotoxicity. [10]

BQ4: Outline the key differences between competitive and non-competitive antagonists. [5]

Section C

Total marks available: 25

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

CQ1: You are working at the National Poisons Centre and have received a call from a local resident who has noticed large numbers of dead marabou storks and fish in the local area. In the past 5 days, you have also received calls from clinicians at the local hospital requesting toxicology analysis of patients (from neonates to adults to elderly) admitted with generalized pain and jaundice. Some patients are in intensive care, with more patients presenting with similar symptoms at the hospital every day. Plasma samples taken from these patients have identified high levels of "Magugafite" – a

toxic chemical used by the road industry to seal roads after laying down the tar. Magugafite is a highly lipophilic, pH 7.2, and has a MW 300Da. It has a both a high affinity to plasma and tissue proteins and easily chelates with cationic compounds.

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

OR

CQ2: Explain the toxicology of at least **ONE** xenobiotic that causes teratogenicity and **ONE** xenobiotic that causes nephrotoxicity. Your answer should include at least one diagram and an example of a xenobiotic that causes neurotoxicity. [25]

ADDITIONAL INFORMATION

Henderson-Hasselbalch Equation

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

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

END OF EXAMINATION