W1-2-60-1-6

JOMO KENYATTA UNIVERSITY
OF
AGRICULTURE AND TECHNOLOGY
UNIVERSITY EXAMINATIONS 2025/2026

END OF SEMESTER EXAMINATIONS FOR THE DEGREE OF MASTER OF SCIENCE IN PHARMACY

TPS 3109: PHARMACOLOGY AND TOXICOLOGY

DATE: NOVEMBER 2025 **TIME: 3 HOURS**

INSTRUCTIONS: ANSWER ANY FOUR QUESTIONS

QUESTION ONE (25 MARKS)

a) Differentiate between full agonists, partial agonists, antagonists, and inverse agonists. Give a clinical example for each. **3 Marks**

b) Using Warfarin as a case study, explain the importance of the therapeutic index (TI) and describe how pharmacogenetics influences patient response. **4 Marks**

c) Explain how drug lipophilicity and ionization influence absorption, using aspirin as an example. **3 marks**

d) Explain the Two-State Model of receptor activation. **3 marks**

Using an example, discuss the concept of spare receptors. **2 marks**

e) Describe the major types of drug–receptor binding interactions. **3 marks**

Explain, using aspirin, how the type of binding determines both therapeutic and toxicological effects. **2 marks**

f) Compare and contrast buprenorphine and naloxone in terms of efficacy, affinity, and clinical application. **5 marks**

QUESTION TWO (25 MARKS)

a) i. Briefly describe the structural features of GPCRs. **3 marks**

ii. Explain how these features relate to GPCR functions in signal transduction. **2 marks**

b) Using case studies, compare the therapeutic application of Gs-linked and Gi-linked GPCRs, highlighting both clinical benefits and risks. **5 marks**

c) Differentiate between drug efficacy and drug effectiveness. **2 marks**

List two in vitro and two in vivo methods used in preclinical evaluation of drug efficacy. **2 marks**

Explain the difference between pharmacological assays and bioassays. **2 marks**

What is pharmacovigilance and why is it important in drug effectiveness evaluation? **2 marks**

d Trastuzumab targets the HER2 receptor in breast cancer. Preclinical studies showed tumor regression in HER2+ xenograft models, and clinical trials demonstrated improved survival in HER2+ patients. However, post-marketing surveillance revealed risks of cardiotoxicity.

i. What biomarker is essential before prescribing trastuzumab **1 mark**

ii. Why was pharmacovigilance crucial in this case? **1 mark**

e Rofecoxib, a COX-2 inhibitor, showed fewer GI side effects than traditional NSAIDs. Despite strong preclinical and clinical data, it was withdrawn after post-marketing studies revealed cardiovascular risks.

i. Which stage of drug evaluation detected the cardiovascular risks? **1 mark**

ii. What does this case teach about the limitations of clinical trials? **1 mark**

f Imatinib targets the BCR-ABL fusion protein in chronic myeloid leukemia (CML). It is only effective in patients with the Philadelphia chromosome mutation.

i.Why is imatinib an example of precision medicine? **2 marks**

ii.How do emerging techniques such as genomics improve drug evaluation? **1 mark**

QUESTION THREE (25 MARKS)

a) Explain the principle *"the dose makes the poison"* and illustrate your answer with reference to acetaminophen toxicity. **5 marks**

b) Describe the mechanism of toxicity of organophosphate pesticides and outline the pharmacological management of poisoning. **5 marks**

c) Discuss the role of oxidative stress in toxicology with reference to carbon tetrachloride (CCl_4) toxicity. **4 marks**

d) A 32-year-old man is found unresponsive with pinpoint pupils, shallow breathing (RR 6/min), and oxygen saturation of 80%.

i. Identify the toxidrome present. **1 marks**

ii. State the mechanism of toxicity for this condition.) **1 mark**

iii. Outline the immediate management, including the antidote of choice. **2 marks**

e) A 25-year-old woman ingests 15 g of acetaminophen in a suicide attempt.

i. Explain why the patient may initially be asymptomatic. **1 mark**

ii. Describe the toxic metabolite responsible for hepatotoxicity. **1 marks**

iii. State the antidote used, its mechanism of action, and the optimal time window for administration. **1 mark**

f) A farmer collapses after spraying pesticides. He has profuse salivation, sweating, bradycardia, diarrhea, and muscle fasciculations.

i. Which enzyme is inhibited in this poisoning? **1 mark**

ii. Name two characteristic clinical signs of muscarinic excess. **2 marks**

iii. Outline the immediate management, including two specific antidotes. **1 mark**

QUESTION FOUR (25 MARKS)

a) i) List four properties of toxins that make them suitable for removal by hemodialysis. **3 marks**

ii) Give two examples of toxins commonly treated with hemodialysis. **1 marks**

iii) State one reason why hemodialysis is ineffective in digoxin overdose. **1 marks**

b) Compare hemodialysis and hemoperfusion in terms of:

i) Mechanism of action. **2 marks**

ii) Type of toxins effectively removed. **2 marks**

iii) One limitation of hemoperfusion. **1 mark**

c) Discuss chelation therapy by:

i. Explaining the principle behind chelation. **2 marks**

ii. Match the following chelators with their primary use: **3 marks**

d) A 40-year-old man presents with confusion, blurred vision, and severe metabolic acidosis after drinking illicit alcohol.

i) Identify the toxic metabolite responsible for his symptoms. **1 mark**

ii) Name two antidotes that block its formation. **3 marks**

iii) Which extracorporeal technique is most effective in clearing methanol and its metabolites **1 mark**

e) A 3-year-old girl ingests 20 iron tablets and presents with abdominal pain, vomiting blood, shock, and metabolic acidosis.

i) Which lab test confirms toxicity? **1 mark**

ii) Which antidote should be administered? **2 marks**

iii) What unique urine finding is expected after treatment? **2 marks**

QUESTION FIVE (25 MARKS)

a) Explain the key goals of pharmacogenomics and discuss how these goals are applied in personalized medicine. **5 marks**

b) A 65-year-old man with atrial fibrillation on warfarin develops severe gum bleeding. His genotyping reveals CYP2C9*3 allele and VKORC1 -1639 G>A polymorphism.

i. Explain the role of CYP2C9 polymorphism in this case. **3 marks**

ii. Explain the role of VKORC1 mutation. **3 marks**

iii. Suggest a pharmacogenomic approach for safe therapy. **3 marks**

c) Discuss Phase I and Phase II enzyme polymorphisms in drug metabolism, giving one clinical example for each. **5 marks**

d) A 40-year-old HIV patient develops fever, rash, abdominal pain, and malaise 12 days after starting abacavir.

i. Which genetic marker is implicated? **2 marks**

ii. Explain the mechanism of this reaction. **2 marks**

iii. What is the clinical recommendation? **2 marks**

QUESTION SIX (25 MARKS)

a) Explain the pharmacological advantages of nanomedicine in oncology and illustrate with the example of pegylated liposomal doxorubicin (PLD). **5 marks**

b) population in Western Kenya is exposed to high levels of arsenic in drinking water. Describe the mechanism of arsenic toxicity and propose a three-pronged strategy to mitigate its effects. **5 marks**

c) Discuss how AI and organoid technologies are transforming drug safety evaluation, giving an example from antiviral drug development. **5 marks**

d) Explain the role of pharmacogenomics in preventing abacavir hypersensitivity, including the mechanism and clinical implications. **5 marks**

e) Evaluate the potential long-term risks of nanomedicine and discuss how pharmacologists and toxicologists can mitigate these risks. **5 marks**

THE END