

THE UNIVERSITY OF AUCKLAND

MEDSCI 204 INTRODUCTION TO PHARMACOLOGY & TOXICOLOGY LAB TEST 2009

22nd Oct, 2009

Time allowed: 45 min.

Answer all 40 questions (each question is worth equal marks)
This exam is worth 20% of your final grade.

Instructions

Complete your name and ID information (as per your ID card) and version code (i.e. 00000001) on the SCANTRON MCQ form as instructed **using a pencil** (no entry is required for the STREAM box).

Answer all questions; you have 45 minutes to complete the paper of 40 questions.

There is only one correct answer per question, worth one point.

No points are taken away for an incorrect answer. However, if more than one answer is chosen or it is not clear which answer has been chosen then no points will be awarded.

If you want to change your selection make sure you erase your first answer completely.

CONTINUED

1. With regard to cell signaling, which statement is NOT correct?
 - (a) Paracrine messengers produce a more localized effect than endocrine messengers
 - (b) Although cells may be exposed to many chemical messengers from many sources, cells only respond to a few based on the repertoire of receptors they express
 - (c) Prostaglandins are examples of paracrine messengers produced by the uterus during labour to initiate childbirth
 - (d) Hormones are endocrine messengers that produce the most widespread effect throughout the body
 - (e) None – they are all correct

2. Select the INCORRECT receptor class and example

(a)	Ligand-gated ion channel	Acetylcholine at nicotinic receptors
(b)	G-protein linked	Acetylcholine at muscarinic receptors
(c)	Ligand-gated ion channel	Noradrenaline at alpha and beta receptors
(d)	Tyrosine kinase-linked	Insulin
(e)	Transporters/carriers	Tricyclic antidepressants

3. Which are the following sites in a cell where a drug might act
 - (a) Plasma membrane, mitochondria, nucleus, cytoplasm
 - (b) Plasma membrane, Golgi, mitochondria, nucleus
 - (c) Plasma membrane, vesicles, nucleus, cytoplasm
 - (d) Plasma membrane, centrioles, nucleus, cytoplasm
 - (e) Plasma membrane, Golgi, mitochondria, cytoplasm
4. With regard to the localization of drug targets, which statement is NOT correct?
 - (a) Monoamine oxidase is a drug target that is localized in the cytoplasm
 - (b) If hormones are widely circulated throughout the body, steroid receptors also need to be widely distributed in all cellular compartments including the nucleus and plasma membrane
 - (c) Oestrogen is an example of a steroid hormone that acts on receptors in the nucleus
 - (d) Steroid hormones produce slower intracellular signaling effects because of the requirement for protein synthesis in the cytoplasm
 - (e) Drugs generally need to be lipid soluble to be able to gain access to drug targets in the nucleus and cytoplasm
5. Which of the following statements about G-protein-coupled receptors is FALSE?
 - (a) They typically contain 7 transmembrane helices
 - (b) They can bind ligands via an extracellular ligand binding domain
 - (c) Upon binding to ligand they are translocated to the nucleus
 - (d) They have an intracellular signal transduction domain
 - (e) They can bind ligands in a central pocket of the receptor
6. Generation of cAMP in response to G-protein activation
 - (a) Is a reasonably rapid event that occurs around 10-30 minutes after ligand binding
 - (b) Is an example of cross talk between GPCRs
 - (c) Occurs when heterotrimeric G-proteins are phosphorylated by ATP
 - (d) Is an example of signal amplification through second messenger generation
 - (e) Is a fundamental step in the signal transduction cascade of all GPCRs

7. With respect to GPCR cell signaling, which of the following is CORRECT?
- In the resting state, the α , β and γ G-protein subunits are bound to GTP
 - GPCR signaling is completed when the α -subunit catalyses the transfer of a phosphate molecule to GDP
 - Orphan G-protein receptors are those for whom both ligand and receptor have been identified but there are no other related family members
 - When the G-protein α -subunit is bound to GDP, it associates and activates adenylate cyclase
 - One molecule of adrenaline bound to its receptor is sufficient to generate 100 cAMP molecules
8. Which statement regarding β -adrenoreceptor signaling is INCORRECT?
- The effect enzyme of β -adrenoreceptors is adenylate cyclase
 - β_2 receptors are found predominantly in the heart
 - Salbutamol is an example of a β_2 -receptor agonist
 - β_2 -receptors are found predominantly in smooth muscle of bronchii
 - Propranolol is an example of a competitive antagonist at β adrenoreceptors
9. Which of the following is a mitochondrial enzyme
- Alcohol dehydrogenase
 - Mixed function oxidase
 - Pepsin
 - DNA polymerase
 - Pyruvate dehydrogenase
10. What is the V_{max} of an enzyme
- Maximal rate of reaction
 - Substrate concentration at which reaction rate is maximal
 - Maximally effective enzyme concentration
 - Maximum enzyme velocity
 - Half the K_m
11. Which one of the following changes to enzyme kinetic parameters in response to inhibition is CORRECT?

(a)	Competitive irreversible inhibition	V_{max} no change, K_m increased
(b)	Competitive reversible inhibition	V_{max} no change, K_m increased
(c)	Non-competitive reversible inhibition	V_{max} no change, K_m increased
(d)	Competitive irreversible inhibitor	V_{max} increased, K_m decreased
(e)	Competitive reversible inhibitor	V_{max} decreased, K_m no change

12. Which of the following is NOT an accurate description of how various types of enzyme inhibitors work
- (a) Active-site directed inhibitors bind irreversibly to the active site e.g aspirin
 - (b) Competitive reversible inhibitors bind the active site of the enzyme in a reversible manner e.g captopril
 - (c) Mechanism-based inhibitors are converted to an unstable intermediate which irreversibly binds to the active site e.g clavulanic acid
 - (d) Non-competitive reversible inhibitors interact with a site on the enzyme that is not the active centre or alter the enzyme indirectly e.g paracetamol
 - (e) Mechanism-based inhibitors bind to the active site of the enzyme in a reversible manner e.g ibuprofen

13. Smart-204 is a lipophilic memory-enhancing drug discovered by Ace Therapeutics Inc. Metabolism of Smart-204 is likely to:

	(a)	(b)	(c)	(d)	(e)
Convert it into a water soluble metabolite for excretion	TRUE	FALSE	TRUE	TRUE	TRUE
Make it less water soluble	FALSE	TRUE	TRUE	TRUE	TRUE
Decrease its activity	TRUE	TRUE	FALSE	TRUE	TRUE
Involve both Phase I and Phase reactions	TRUE	TRUE	FALSE	FALSE	TRUE

14. Smart-204 might undergo a Phase I reaction such as

- (a) Glucuronidation
- (b) Acetylation
- (c) Sulphation
- (d) Amino acid conjugation
- (e) Oxidation

15. CYP450 enzymes

- (a) Have a very narrow substrate specificity
- (b) Are found primarily in the cytosol
- (c) Catalyse reactions whose products have a spectral absorbance maxima at 450 nm
- (d) Are enzymes that catalyse many drug oxidation and reduction reactions
- (e) All of the above

16. Which of the following groups is NOT usually a target for conjugation in a Phase I reaction

- (a) (CH₃COO⁻) (acetyl)
- (b) -COOH (carboxylic acid)
- (c) -OH (hydroxyl)
- (d) -NH₂ (amide)
- (e) -SH (sulfhydryl)

17. Which of the following is NOT an outcome of a Phase II metabolism reaction
- Increased water solubility
 - Decreased pharmacological activity
 - Increase in molecular weight
 - Decreased hydrophilicity
 - Enhanced excretion
18. Which of the following statements about glucuronidation reactions is FALSE?
- They always produce more water soluble metabolites
 - They are catalysed by glutathione-S-transferase enzymes
 - They can target amino, hydroxyl and carboxyl groups
 - They always abolish any pharmacological activity
 - They can lead to metabolite excretion in bile
19. In the following table, which metabolic reaction mechanism is NOT correctly aligned with an appropriate substrate example?

	<i>Mechanism</i>	<i>Substrate</i>
(a)	Glucuronidation	Morphine
(b)	Hydroxylation	Codeine
(c)	Amino acid conjugation	Salicylate
(d)	Acetylation	Sulphanilamide
(e)	Sulphation	Oestrone

20. Which of the following is NOT an example of a Phase II metabolizing enzyme
- Amidase
 - Sulphotransferase
 - UDP-glucuronyltransferase
 - Methyl transferase
 - Glutathione S-transferase
21. What is the aim of single dose (acute) toxicity evaluations?
- To estimate how poisonous a drug is in the short term and to determine the mechanism of toxicity
 - To estimate how poisonous a drug is in the long term and to determine the mechanism of toxicity
 - To determine if a drug is toxic or not in the short term
 - To determine if a drug is toxic or not in the long term
 - To estimate how poisonous a drug is to humans in the short term and to determine the mechanism of toxicity
22. Which example of toxicity might be revealed by acute toxicity testing?
- Paracetamol causing hepatic necrosis via a reactive metabolite
 - Rofecoxib causing a heart attack or stroke
 - None of these options are correct
 - Thalidomide causing phocomelia
 - Thalidomide causing malignant neoplasm

23. Which of the following is NOT a typical observation made during general toxicity evaluation?
- (a) Urinalysis
 - (b) Haematology
 - (c) Physical examination
 - (d) Distribution across the placenta
 - (e) Behaviour and condition
24. Which of the following descriptions of toxicological terms is INCORRECT?
- (a) Teratogenicity: ability to cause structure malformations in human reproductive organs
 - (b) Mutagenicity: damage or harm to genes
 - (c) Therapeutic index: the ratio of the amount of a drug required to produce a therapeutic effect and the amount that is toxic in 50% of the population
 - (d) Carcinogenicity: propensity to cause cancer
 - (e) Analogue: a compound similar in activity or structure or from the same family
25. Which of the following statements regarding drug discovery is FALSE?
- (a) None. They are all true
 - (b) Quinine is found in the bark the cinchona tree
 - (c) It may take 5 to 10 years to find a useful candidate molecule after an initial hypothesis
 - (d) The discovery of methicillin was through empirical screening and molecular design
 - (e) Iproniazid was developed after isoniazid was found to elevate mood in patients with tuberculosis
26. Drugs can be discovered and developed through many avenues and approaches. Which one of the following examples is INCORRECT?
- (a) Ranitidine, developed to overcome the anti-androgenic effects of cimetidine
 - (b) Methicillin, a modified form of benzylpenicillin designed to be resistant to enzymatic inactivation/degradation
 - (c) LSD, originally evaluated as an anti-oxytocic drug
 - (d) Penicillin, discovered after mass screening of fungal extracts for antibiotic properties
 - (e) Zidovudine, originally tested as an anti-cancer drug
27. Which of the following statements accurately describes an aspect normally associated with a phase I clinical trial?
- (a) A large number (>2000) subjects are enrolled
 - (b) Pharmacokinetic and pharmacodynamic aspects of the drug are not studied since these have already been determined
 - (c) The participants are young, healthy males and females
 - (d) The biological effects and disposition of the drug are the main area of interest and study
 - (e) The trial is best conducted in the community at large rather than in a hospital setting
28. A new drug is being evaluated in a multicentre study involving 1800 subjects recruited by collaborating GPs from their patient base. What kind of trial is this most likely to be?
- (a) Pre clinical
 - (b) Phase I
 - (c) Phase II
 - (d) Phase III
 - (e) Phase IV

29. Which of the following rows best describes a phase 1 clinical trial for a new chemotherapy agent?

	Less than 200 subjects	Subjects are healthy male volunteers	Trial location
(a)	True	False	Daily visits to hospital
(b)	True	True	Overnight stay in hospital
(c)	False	True	Daily visits to hospital
(d)	True	False	Overnight stay in hospital
(e)	False	True	Overnight stay in hospital

30. Cytokines are regulatory proteins that coordinate cellular responses in physiological systems such as the immune system. Which one of the following is not a cytokine?

- (a) IL-8
- (b) MIP-1 α
- (c) TGF β 2
- (d) TNF α
- (e) HSP90

31. Steroidal anti-inflammatory drugs downregulate:

- (a) Endonucleases
- (b) Neutral endoproteases
- (c) Lipocortin-1
- (d) Endothelin-1
- (e) ACE

32. Choose the FALSE statement regarding NSAIDS:

- (a) Major targets for NSAID toxicity include the GI tract, kidneys and skin
- (b) Low dose aspirin inhibits platelet aggregation via cyclooxygenase
- (c) Nabumetone requires metabolic activation to inhibit COX
- (d) NSAIDS decrease formation of prostaglandins and thromboxane A₂
- (e) Rofecoxib selectively inhibits COX-2, but was withdrawn from the market due to chronic gastrointestinal toxicity

33. Which of the following statements about opioid receptors is correct?

- (a) Opioid receptors exist in four subtypes: μ , δ , κ and ϵ
- (b) All three endogenous opioid peptides bind and activate all opioid receptors equally.
- (c) The main second messenger system utilised by opioid receptor activation is cGMP
- (d) Opioid receptors typically activate G_{i/o} signalling
- (e) Opioids also regulate neurotransmitter release via inhibition of potassium conductance channels and activation of calcium channels

34. Which of the following is NOT a potentially useful target for drugs that affect peptide-mediated transmission?
- (a) Presynaptic reuptake of peptides
 - (b) Peptide synthesis and post-translational modification
 - (c) Peptide transport and storage
 - (d) Post-synaptic actions of peptides
 - (e) Peptide release and activation
35. With respect to opioid receptors
- (a) Opioid receptors mediate increased neurotransmitter release via G-protein activation
 - (b) Endogenous opioids show equal specificity to various opioid receptors
 - (c) Opioid receptors are expressed solely in the central nervous system
 - (d) Endogenous opioid peptide ligands are released both centrally and peripherally
 - (e) Synthetic opiates act as ligands for μ opioid receptors only
36. Which of the following has the highest concentration?
- (a) 1:10 dilution of 1 mM
 - (b) 40 μ M
 - (c) 399 nmol/mL
 - (d) 1:500 dilution of 10 mM
 - (e) 0.004 μ M
37. Which of the following dilution calculations is INCORRECT?
- (a) 10 mL of 10 mM drug, diluted to 25 L, reaches a final concentration of 4000 nM
 - (b) A 1:200 dilution of a 30 mM solution is 150 μ M
 - (c) Taking 50 μ L of a 50 nM solution and adding it to 450 μ L of diluent results in a solution of 5 nM
 - (d) In order to prepare 5 mL of a drug with a final concentration of 10 mM, a student must add 0.5 mL of her stock 100 mM solution to 4.5 mL diluent
 - (e) Making a 1:200 dilution of a 0.05 mM solution will yield a final concentration of 250 μ M
38. A 16 mM solution is diluted 1:40. What is the concentration?
- (a) 0.4 μ mol/L
 - (b) 4000 μ mol/L
 - (c) 4 mM
 - (d) 400 nmol/mL
 - (e) 40 μ mol/mL
39. You need 1200 mL of a 50 mM solution. The drug has a molecular weight of 175 Da. How much drug is needed?
- (a) 0.015 g
 - (b) 150 g
 - (c) 10.5 g
 - (d) 150 mg
 - (e) 1.5 g

40. 1.337 fmol/ μ L is:

- (a) 1337 pM
- (b) 1.337 pM
- (c) 1337 μ M
- (d) 1.337 mM
- (e) 1.337 μ M

END OF TEST