THE UNIVERSITY OF AUCKLAND

MEDSCI 204
INTRODUCTION TO PHARMACOLOGY & TOXICOLOGY
MID-SEMESTER TEST 2009

15th September, 2009

Time allowed: 45 min.

Answer all 40 questions (each question is worth equal marks)
This exam is worth 10% 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.

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1. Which of the following is an example of a drug derived from a flowering plant?

   (a) acetylsalicylic acid
   (b) penicillin
   (c) testosterone
   (d) digitalis
   (e) cyclosporine

2. The actions of a number of important drugs have been discovered by accident. Which one of the following is NOT an example of this?

   (a) Lithium, discovered as a result of an experiment aimed at investigating the effects of uric acid on behaviour
   (b) Sildenafil, discovered during studies of anti-hypertensive agents in medical students
   (c) Cisplatin, discovered through experiments on the effects of electrical currents on bacterial growth
   (d) Celecoxib, discovered during routine drug screening of potential SSRIs
   (e) Cyclosporin, discovered when a failed anti-mycotic fungal extract was fortuitously fed into a general screening programme

3. With respect to receptors, which of the following is an example of poor selectivity?

   (a) Fenoterol targeting β2 receptors in the lungs, but also causing tachycardia via β1 receptors in the heart
   (b) NSAIDs targeting COX-2, but also causing stomach ulcers via inhibition of COX-1
   (c) Antihistamines targeting peripheral H1 receptors, but also causing sedation via H1 receptors in the brain
   (d) Phenoxybenzamine targeting α1 adrenoceptors, but also causing unwanted effects by antagonising histamine receptors
   (e) All of the available options are correct

4. Which of the following is a measure of the response that can be expected from a given drug?

   (a) Efficacy
   (b) Affinity
   (c) Responsiveness
   (d) Potency
   (e) Specificity

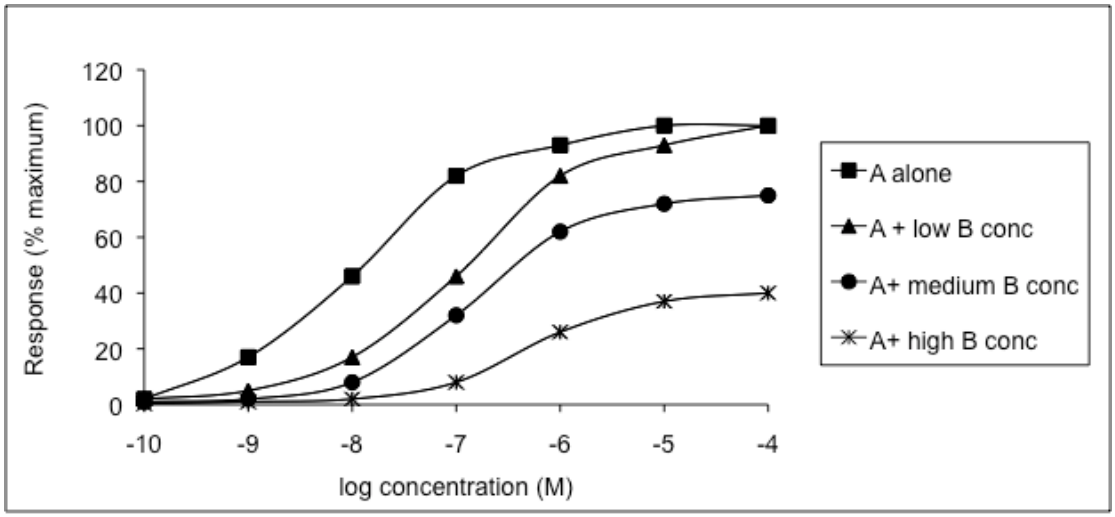
5. The value EC50 (or IC50) can be defined from the results of a competitive ligand binding assay. Below are some EC50 values of competitor molecules ability to displace 3H-Drug X binding from the Drug X receptor:

Drug	EC50
A	0.1 mM
B	2000 nM
C	2.5 mM
D	100 pM
X	1.0 nM

   Which drug has the highest affinity for the Drug X receptor?

   (a) Drug A
   (b) Drug B
   (c) Drug C
   (d) Drug D
   (e) Drug X

6. The following graph contains concentration-response curves for compound A alone and in the presence of various concentrations of compound B.



Compound B is most likely to be:

(a) an inverse agonist
(b) a competitive, reversible antagonist
(c) a competitive, irreversible antagonist
(d) a non-competitive antagonist
(e) a physiological antagonist

7. With regard to pharmacodynamic concepts, which statement is CORRECT?

(a) A partial agonist is a drug which binds to a receptor without stimulating it
(b) Drug A is said to be more potent than drug B, if drug A's maximal effect is greater than that of drug B
(c) The maximal response of an agonist in the presence of increasing concentrations of a non-competitive antagonist remains unchanged
(d) Drug A is said to be more efficacious than drug B, if drug A produces its maximum effect at lower concentration than drug B
(e) The maximal response of an agonist in the presence of increasing concentrations of a competitive irreversible antagonist will decrease

8. For agonist and antagonist drugs, which is correct in terms of action at receptors?

(a) Agonists have affinity but no efficacy
(b) Agonists have efficacy but no affinity
(c) Antagonists have affinity but no efficacy
(d) Antagonists have efficacy but no affinity
(e) A partial agonist has no affinity and no efficacy

9. Which type of receptor is likely to produce the most rapid response?

(a) Catalytic
(b) Metabotropic
(c) Ionotropic
(d) Nuclear
(e) It's impossible to tell

10. Which of the following descriptions relating to G-protein-coupled receptors (GPCRs) is FALSE?

(a) Many neurotransmitters, such as noradrenaline, are ligands for GPCRs
(b) GPCRs provide ligand selectivity and signal amplification
(c) All GPCRs signal via modulation of intracellular cAMP or cGMP levels
(d) GPCRs share common structural elements such as the number of transmembrane-spanning helices
(e) Activation of a GPCR by ligand results in changes in second messenger release within seconds

11. Which of the following statements about ligand-activated ion channels is FALSE?

(a) They typically require two ligand molecules for activation
(b) They are often composed of 5 subunits surrounding a central pore
(c) They transmit their effects within milliseconds
(d) Acetylcholine, GABA and glutamate are all ion channel ligands
(e) None of the above

12. With respect to receptor regulation, what is the most likely process to occur following prolonged/chronic administration of an antagonist?

(a) Desensitisation
(b) Down regulation
(c) Production of 3rd messengers (e.g. Fos)
(d) Up regulation
(e) Production of 2nd messengers (e.g. cAMP)

13. Which of the following is an example of a drug interaction with a carrier protein?

(a) Inhibition by ibuprofen of COX-mediated prostaglandin transport
(b) Blockade of the calcium transporter by nifedipine
(c) Alpha2 adrenergic blockade by yohimbine
(d) Fluoxetine blockade of serotin/5HT uptake
(e) None of the above

14. Which is the most important mechanism for drug movement across biological membranes:

(a) facilitated diffusion
(b) passive diffusion
(c) active transport
(d) endocytosis
(e) filtration

15. Which is the main organ involved in the elimination of lipid soluble drugs:

(a) kidney
(b) lungs
(c) pancreas
(d) liver
(e) stomach

16. Which mechanism might be expected to have the least impact on the duration and intensity of drug action after an oral dose of a water soluble drug:

(a) excretion
(b) metabolism
(c) absorption
(d) bioavailability
(e) sequestration

17. If you wished to have precise control of the amount of drug getting into the bloodstream, which route would be preferred:

(a) intramuscular
(b) subcutaneous
(c) sublingual
(d) intravenous
(e) oral administration

18. Which mechanism is the most important in producing the increased bioavailability observed when some drugs are taken orally with grapefruit juice:

(a) inhibition of CYP enzymes in gut/liver
(b) increase in gut transit time
(c) decrease in degradation by gut microorganisms
(d) inhibition of gut proteases and lipases
(e) decrease in gut transit time

19. A small lipid and water soluble compound (such as ethanol) would be expected to have an approximate volume of distribution in a 70 kg male of:

(a) 28 L (the intracellular fluid)
(b) 3 L (the plasma)
(c) 14 L (the extracellular fluid)
(d) 42 L (total body water)
(e) 5.5 L (the blood volume)

20. Which one would be <u>least likely</u> to influence the rate of absorption into the blood stream of an orally ingested drug:

(a) anticholinergic drugs
(b) antibiotics
(c) diarrhoea
(d) hunger
(e) renal disease

21. Which statement is FALSE. Drug metabolism:

(a) usually makes the drug less active
(b) usually makes the drug more susceptible to Phase 2 enzymes
(c) usually produces toxic metabolites
(d) usually involves the CYP enzymes
(e) can take place in the liver

22. Which statement is FALSE. Phase 2 metabolism:

(a) always requires Phase 1 metabolism before it can take place
(b) makes the drug molecule more amenable to active transport
(c) increases the molecular weight of the drug
(d) usually makes the drug more water soluble
(e) usually makes the drug more amenable for excretion

23. Which one of the following is <u>not</u> a Phase 2 reaction:

(a) glucuronidation
(b) sulphation
(c) hydrolysis
(d) acetylation
(e) methylation

24. Which statement is FALSE. Induction of drug metabolism:

(a) usually results in an exaggerated drug response
(b) increases to a peak over 3-5 days of exposure
(c) often results in therapeutic failure
(d) decreases over 1-3 weeks after the inducing agent is removed
(e) none of the above

25. Which statement is CORRECT. The major reason for the inter-individual variability in patient response to a standard dose of a drug is:

(a) absorption
(b) distribution
(c) metabolism
(d) excretion
(e) dissolution

26. Which statement is FALSE. The renal excretion of a drug:

(a) increases with increasing age
(b) increases with pregnancy
(c) increases with increased urinary flow rate
(d) decreases with heart failure
(e) increases with decreased urinary flow rate

27. If 1 mg of a drug given i.v. gave an AUC = 10 ug.h/ml and 10 mg p.o. gave an AUC = 5ug.h/ml, what would the % p.o. bioavailability for this drug:

(a) 0.5
(b) 1.0
(c) 5.0
(d) 50.0
(e) 10.0

28. The half-life of a drug could be potentially decreased by:

(a) renal disease
(b) liver failure
(c) heart failure
(d) enzyme induction
(e) all of the above

29. A drug has a volume of distribution of 20 L/kg and a clearance of 2 L/h/kg, how long would it take to get to steady state using a constant rate infusion:

(a) 2.8 h
(b) 7 h
(c) 28 h
(d) 70 h
(e) 40 h

30. If you wished to get to a steady state concentration more rapidly. Would you:

(a) increase the rate of the infusion
(b) give a loading dose
(c) give an inhibiting agent to decrease metabolism
(d) give an agent to increase the rate of onset of drug effect
(e) none of the above

31. With regard to neurotransmission in the autonomic nervous system, which of the following is INCORRECT?

(a) acetylcholine is the primary transmitter released by pre-ganglionic neurons
(b) post-ganglionic neurons of the sympathetic nervous system release noradrenaline
(c) in general, the actions of a transmitter are terminated by enzymatic degradation or reuptake of the transmitter into the nerve terminal
(d) the parasympathetic nervous system is associated with "rest and digest" functions
(e) the parasympathetic nervous system is associated with "fight or flight" responses

32. With regard to signaling in the ANS, which of the following is INCORRECT?

(a) the autonomic nervous system uses both homotropic and heterotropic neuromodulation to control neurotransmitter release
(b) cotransmission is the release of several neurotransmitters from a single nerve terminal but they all act on the same postsynaptic receptor
(c) neuromodulators are chemicals that can influence neurotransmitter release without participating directly as a transmitter
(d) presynaptic and postsynaptic receptors at cholinergic and noradrenergic synapses can be distinguished pharmacologically
(e) ATP and Neuropeptide Y are also NANC neurotransmitters

33. Cholinergic neurotransmission can be regulated by:

(a) presynaptic M2 receptors that serve to inhibit acetylcholine release
(b) presynaptic nicotinic receptors that serve to inhibit acetylcholine release
(c) rapid uptake of acetylcholine into the nerve terminal
(d) changing the availability of acetylcoA and glucose
(e) the rate of acetylcholine breakdown once it has been taken up by the vesicular transporter

34. With regard to cholinergic neurotransmissin, which of the following is INCORRECT?

(a) all nicotinic receptors are ionotropic receptors
(b) nicotinic receptors are not useful as drug targets because of their widespread distribution
(c) choline acetyltransferase (ChAT) terminates the action of acetylcholine by breaking it down at the synpase
(d) the muscarinic receptors (M1-M5) are all are G-protein coupled receptors
(e) nicotinic receptors are blocked by competitive antagonists as well as agonists that produce sustained depolarization at the postsynaptic membrane

35. Cholinergic agonists

(a) stimulate an increase in heart rate
(b) produce relaxation of smooth muscles in the gastrointestinal tract
(c) are also known as sympathomimetics
(d) have widespread effects including stimulation of GI tract activity and increased secretion from sweat and salivary glands and slowing heart rate
(e) can be used for treating glaucoma because it dilates the pupils of the eye

36. With respect to noradrenergic transmission

(a) termination of NA action occurs primarily via reuptake into the nerve terminal rather than degradation at the synapse
(b) the norepinephrine transporter (Uptake 1) and vesicular monoamine transporter (VMAT) function to terminate the actions of NA
(c) NA binds to postsynaptic receptors but not to presynaptic receptors
(d) Nicotine is an antagonist at nicotinic receptors
(e) Noradrenaline is an agonist for alpha but not beta-noradrenergic receptors

37. On the same topic, which of the following statements is INCORRECT?

(a) subtype selectivity is important for drugs acting at adrenoreceptors in order to prevent unwanted side-effects
(b) synthesis of noradrenaline follows a common pathway to that of adrenaline
(c) drugs that act as agonists at post-synpatic adrenoreceptors could be referred to as direct-acting sympathomimetics
(d) reserpine blocks the transport of NA into vesicles leadng to NA accumulation and breakdown in the cytoplasm
(e) preventing storage of NA in synaptic vesicles will have no effect on NA neurotransmission

38. Which is NOT an accurate description with respect to actions at B-adrenergic receptors?

(a) non-selective B-antagonists are useful for treating cardiovascular problems such as heart failure as it has a dual effect in causing relaxation of bronchial smooth muscle
(b) salbutamol is a B2 agonist used as a broncodilator for the treatment of asthma
(c) B1 agonists have major effects on the heart and increase contractility and heart rate
(d) B3 receptor specific agonists could potentially be developed as anti-obesity drugs
(e) atenolol is a B1-selective antagonist used for treating hypertension and cardiovascular problems

39. A phase 2 trial is likely to be

(a) performed on >2000 patients
(b) performed on subjects with a wide range of conditions in addition to the target disease
(c) performed in multiple centers
(d) placebo controlled
(e) none of the above

40. In a clinical trial of a cholesterol-lowering drug, which of the following could NOT be accurately described as a surrogate endpoint?

(a) death or hospitalization through myocardial infarction
(b) concentration of the drug in recipients circulation
(c) serum HDL/LDL ratio
(d) serum cholesterol concentration
(e) none of the above

END OF TEST