TECHNICAL UNIVERSITY OF MOMBASA

FACULTY OF APPLIED AND HEALTH SCIENCES

DEPARTMENT OF PURE & APPLIED SCIENCES

UNIVERSITY EXAMINATION FOR:

BTAC

ACH 4402: MEDICINAL CHEMISTRY II

END OF SEMESTER EXAMINATION

SERIES: APRIL 2016

TIME: 2 HOURS

DATE: 9th May 2016

Instructions to Candidates

You should have the following for this examination

-Answer Booklet, examination pass and student ID

This paper consists of **FIVE** questions. Attempt question ONE (Compulsory) and any other TWO questions.

Do not write on the question paper.

Question ONE:

a) Define the following terms as used in medicinal chemistry.

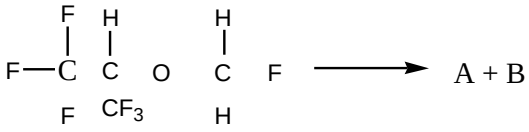
i. Anticonvulsant and antiepileptic drugs (AEDs)

ii. Cholinergic and anticholinergic drugs.

iii. Sympathomimetics and sympatholytics,

iv. sedative–hypnotics and antipsychotics (4 marks)

b) Sevoflurane is a general anesthetic that reacts with desiccated carbon dioxide adsorbents, to produce compounds (A and B) with known toxicity.



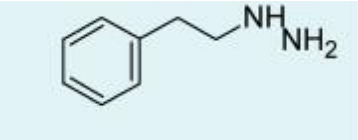
Sevoflurane

i. Draw the structures of compounds A and B (2 mks)

ii. The degree to which sevoflurane breaks down is influenced by three factors. Name the three factors (3 mks)

c) Antidepressant therapy usually implies therapy directed against major depressive disorders of the unipolar type and is centered on three groups of chemical agents. Name these groups (3 mks)

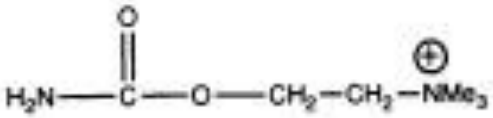
d) Phenelzine sulfate, an effective antidepressant agent irreversibly inactivates the enzyme or its cofactor via irreversible inhibition.



Phenelzine sulfate

i. Why do we say that phenelzine is irreversible (2 mks)
ii. Discuss the biotransformation of phenelzine to the active species in irreversible inhibition (5 mks)

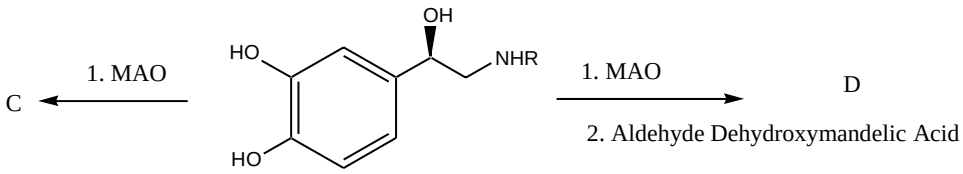
e) Carbachol is a long acting cholinergic agent. It is certainly stable to hydrolysis and is the right size to fit the cholinergic receptor.



Carbachol

i. Explain why carbachol is resistant to hydrolysis more than acetylcholine (3 mks)
ii. Explain why even after a hydrophobic methyl group has been replaced with a polar NH_2 group, carbachol does fit the cholinergic receptor and is active (2 mks)
iii. Give reasons as to why Carbachol though a long acting cholinergic agent is used locally and cannot be ingested (2 mks)

f) In the metabolism of catecholamines (CAs), monoamine oxidase (MAOs) oxidatively deaminate CAs to their corresponding aldehydes, which are rapidly oxidized to the corresponding acid by the enzyme aldehyde dehydrogenase (AD). In some circumstances, the aldehyde is reduced to the glycol by aldehyde reductase (AR). Propose structures of compounds C and D formed from the metabolism of CAs (3 mks)



Question TWO:

a) In the structure activity relationship (SAR) of anesthetics, the chemical structure is related to the activity of the drug molecule.

i. Discuss the potency of alkanes, cycloalkanes, and aromatic hydrocarbons in relation to the anesthetic activity (6 mks)

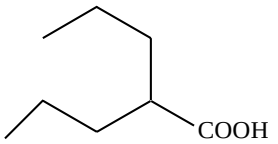
ii. Explain the reason for the reduced activity of the anesthetic compounds beyond their cut-off number (2 mks)

iii. Discuss the effect of halogenation on anesthetics (3 mks)

b) At cellular level, three basic mechanisms are believed to contribute to the antiepileptic action of the currently marketed anticonvulsants. State the three mechanisms of action of anticonvulsants (3 mks)

c) State four possible causes of epilepsy and convulsions (4 mks)

4. Valproic Acid (VPA) is an established AED with a simple chemical structure but an unusually broad spectrum of action. It is generally well tolerated, but its use is limited by two rare but significant toxic side effects (hepatotoxicity and teratogenicity).



Valproic Acid (VPA)

Identify two possible reactive metabolites of VPA that are responsible for this observation (2 mks)

Question THREE

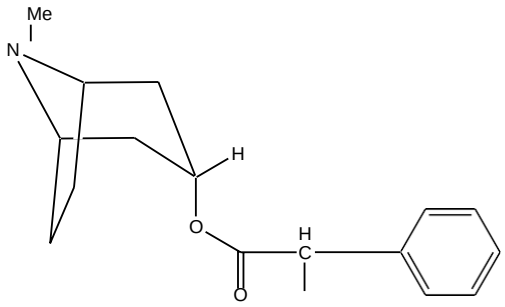
a) Differentiate between nucleotides and nucleosides (2 mks.

b) Explain in details the biosynthesis of acetylcholine at synapses involving acetylcholine as the neurotransmitter (7 mks).

c) Explain why it is not feasible to give a patient more acetylcholine if there is lack of acetylcholine acting at a certain part of the body (3 mks).

d) Antidepressant therapy usually implies therapy directed against major depressive disorders of the unipolar type and is centered on three groups of chemical agents. Name these three groups (3 mks).

e) Atropine is an antagonist of the cholinergic receptor. It can bind to and block the receptor. Explain the SAR of Atropine and the cholinergic receptor that makes this possible. (5 mks)



Atropine

Question FOUR

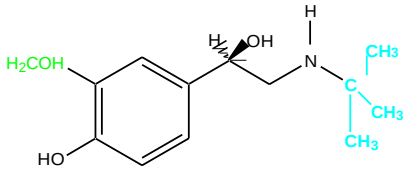
a) To which class of compounds do adrenaline, noradrenaline and dopamine belong? (1 mk)

b) Name the natural chemical messenger for the following receptors

i. Adrenaline receptor (1 mk)

ii. GABA receptors (1 mk)

c) Salbutamol is an important clinical agent. The coloured groups are modifications that distinguish the molecule from adrenaline or noradrenaline.

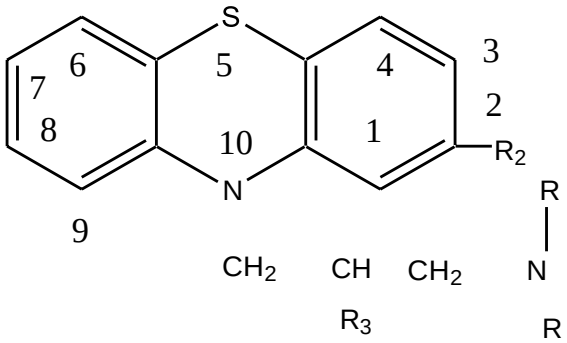


Salbutamol

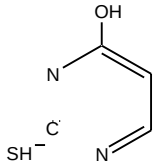
i. What role does the t-butyl group play? (2 mks)

ii. Why was the hydroxymethylene group introduced? (3 mks)

d) Phenothiazine is an antipsychotic agent. The best position for substitution is the 2-position. Activity increases (with some exceptions) as electron-withdrawing ability of the 2-substituent increases. Explain why. (4 mks).



e) 2-Thioimidazole derivatives are antithyroid agents whose mechanism of action is by prevention of the iodination of the precursors of thyroxine and triiodothyronine.



These compounds are absorbed well after oral administration and excreted in the urine. However, they are tautomeric compounds. Draw three tautomeric compounds of 2-thioimidazole (3 mks)

f) The mechanisms of action of all antithyroid agents are similar. State the mechanism of action (1mk)

g) Discuss the four stages of general anesthesia (4 mks)

Question FIVE

a) Define the following terms as used in medicinal chemistry

i. Antihyperlipidermic agents (1 mk)
ii. Hyperlipidemia (1 mk)
iii. Hyperthyroidism (1 mk)
iv. Nucleotides and Nucleosides (2 mks)

b) What is the disadvantage of using adrenaline as an adrenergic agonist (2 mks)

c) Lipids are transported in the body by both exogenous and endogenous pathways. Differentiate between the two pathways (4mks)

d) There are two mechanism of action of inhaled anesthetics.

i. Discuss the Meyer Overton Theory (4 mks)
ii. The misgivings of the theory (2 mks)
iii. Name the second theory and its hypothesis (3 mks)