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: 9 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) Epilepsy is the most prevalent neurological disorder affecting more than 0.5% of the world's population.

i. Identify two components that characterize epilepsy and seizures. (2 mks)

ii. There are many possible causes of epilepsy. Name five of these causes. (5 mks)

b) Propose a process by which acetylcholine can be prepared in the laboratory. (3 mks)

c) The early inhaled anesthetics like sevoflurane suffered from stability problems, leading to explosions and operating room fires.

i. State the causes of the sporadic fires and explosions. (2 mks)

ii. Explain how the problem of stability and flammability was addressed. (2 mks)

d) Define five characteristics of an ideal inhaled anaesthetic. (5 mks)

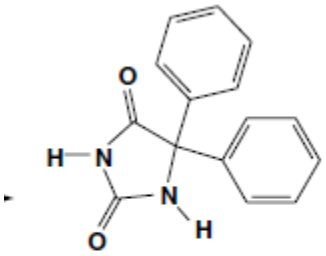
e) In the structure activity relationship (SAR) of anesthetics, the chemical structure is related to the activity of the drug molecule. State which one is a more potent anesthetic stating clearly the reason for your answer.

i. Alkanes and cycloalkanes, and aromatic hydrocarbons in relation to the anesthetic activity. (3 mks)

ii. Alkanes and n-alkanol series. (3 mks)

iii. Explain why cyclooctane shows no anesthetic activity in rat. (2 mks)

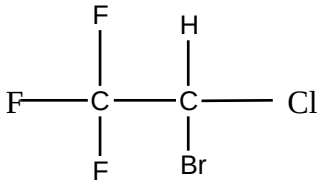
f) Phenytoin, is a prime example of an effective anticonvulsant acting through the VGSC (Voltage-gated sodium channels). It is administered as a pro-drug Fosphenytoin. Discuss the transformation of Fosphenytoin to Phenytoin. (3 mks)



Phenytoin

Question TWO:

a) Halothane is an anaesthetic compound and undergoes both reductive and oxidative processes with up to 20% of the dose undergoing metabolism.



Halothane

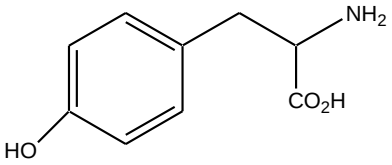
i. Draw compounds A and B formed after reductive and oxidative processes. (2 mks)

ii. One of the metabolites is electrophilic and can form covalent bonds with proteins leading to immune responses and halothane hepatitis upon subsequent halothane exposure. Identify and name the metabolite. (2 mks)

b) State the mechanism of action of most currently available anticonvulsant and antiepileptic drugs (AED). (2 mks)

c) Differentiate between parasympathetic and sympathetic nerves. (4 mks)

d) The first step in Catecholamine (CA) biosynthesis is the 3'-hydroxylation of the amino acid L-tyrosine to form compound C by tyrosine hydroxylase (TH, tyrosine-3-monooxygenase). Draw compound C. (1 mk)

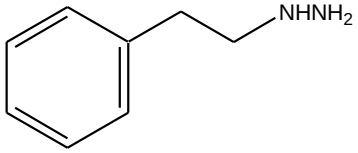


Tyrosine Hydroxylase (TH) → C

L-Tyrosine

e) Explain why solutions of catecholamines (CAs) drugs are often stabilized by the addition of an antioxidant (reducing agent) such as ascorbic acid or sodium bisulfite (3 mks)

f) Nardil, an effective antidepressant agent inactivates the enzyme or its cofactor irreversibly via irreversible inhibition.



Nardil

i. Discuss the transformation of Nardil to the active species. (4 mks)
ii. Why do we say that Nardil is irreversible? (2 mks)

Question THREE

a) Discuss the relationship between Acetylcholine structure and activity relationships (SAR), with respect to receptor binding. (10 mks)

b) Recent opinion has moved away from the classical view of the cholinergic receptor, Explain why. (5mks)

c) 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)

Question FOUR

a) Explain why when choosing an anesthetic for a particular patient the following parameters have to be put into consideration.

i. Potency. (2 mks)
ii. Solubility. (2 mks)
iii. Stability. (2 mks)

b) Central nervous system (CNS) depressants are drugs that can be used to slow down or "depress" the functions of the CNS. There are three different groups of drugs used as CNS depressants.

i. Name the three different groups. (3 mks)
ii. Describe the usage and classification of antipsychotic drugs. (3 mks)

iii. Name two neurotransmitters involved in the peripheral nervous system. (2 mks)
iv. Name three Adrenergic neurotransmitters (NTs) acting on adrenergic receptors. (3 mks)

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

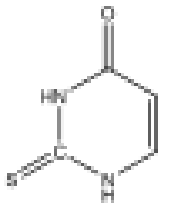
Question FIVE

a) Define the following terms as used in medicinal chemistry

i. Anticonvulsant and antiepileptic drugs (AEDs). (1 mk)
ii. Cholinergic and anticholinergic drugs. (1 mk)
iii. Bioisostere (1 mk)
iv. Sympathomimetics and sympatholytics. (1 mk)
v. Sedative–hypnotics and antipsychotics. (1 mk)

b) Explain why bethanechol is more stable and selective than acetylcholine and its analogues. (6 mks)

c) 2-Thioimidazole derivatives are antihyperlipidemic 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)



2-Thiouracil

d) Explain why Epinephrine (E) and norepinephrine (NE) are orally inactive and have short durations of action. (3 mks)

e) Explain why

i. Most benzodiazepines are well absorbed from the gastrointestinal tract. (2 mks)
ii. Benzodiazepines with a 3-hydroxyl group tend to be absorbed more slowly. (1 mks)