KENYATTA UNIVERSITY

EXAMINATION FOR THE DEGREE OF BACHELOR OF PHARMACY

PPC 510: PHARMACEUTICAL CHEMISTRY V

1ST TRIMESTER 2020/2021 **TIME: 3 HOURS**

INSTRUCTIONS:

- **The paper consists of three sections; A, B and C**
- **Answer all questions**
- **Answer sections A, B and C in separate booklets**

SECTION A: CENTRAL NERVOUS SYSTEM AGENTS

1. Regarding analgesics:

   (a). Draw the chemical structure of morphine. (3marks)

   (b). Outline three structural changes that resulted in morphine analogues with enhanced analgesic activity. (3 marks)

   (c). Outline three structural changes that resulted in morphine analogues with reduced analgesic activity. (3 marks)

   (d). Using chemical structures, illustrate two metabolic pathways for morphine. (4 marks)

2. Use the general structure (figure 1) below to answer the following questions:

   (a). Identify the class of drugs it represents. (1 mark)

   (b). Identify three drug examples in the class named in 2(a) above and state their clinical uses. (6 marks)

   (c). Outline four structure activity relationships (SAR) for this class of drugs. (8 marks)

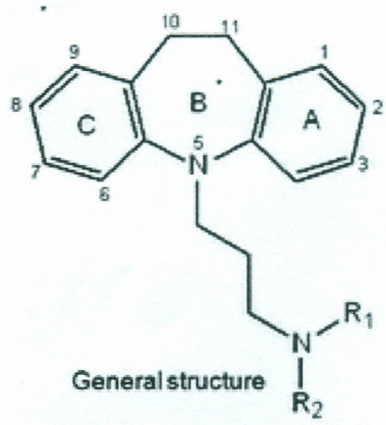

Figure :

3. (a) Identify the class of drugs represented by figure 2 below. (1 mark)

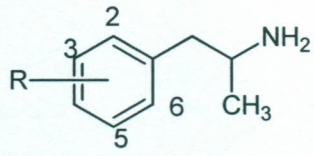

Figure 2:

(b) State the clinical use of one drug in the class named in 3(a) above. (2 marks)

(c) Illustrate two metabolic reactions undergone by drugs in this class. (2 marks)

(d) Illustrate the preparation of a water soluble salt of one drug in this class. (1 mark)

(c) Outline three structure activity relationships (SAR) for this class of drugs. (6 marks)

SECTION B: AUTONOMIC DRUGS

1. For each of the following adrenergic drug classes, name **one** drug example and **one** disease indication. (4 marks)
   a) α_1-adrenoceptor agonists
   b) α_2-adrenoceptor agonists
   c) α_1-adrenoceptor blockers
   d) β_2-adrenoceptor agonists

2. Explain the chemical instability of aqueous solution of pilocarpine (**figure 3**) in an environment of basic pH. (4 marks)

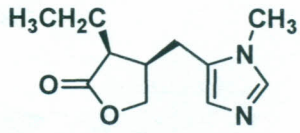

Figure 3: Chemical structure of pilocarpine

3. Using appropriate chemical structures and schematic reaction mechanism, explain the mode of action of phenoxybenzamine (**figure 4**) in alleviating the symptoms of pheochromocytoma. (5 marks)

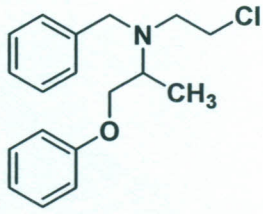

Figure 4: Chemical structure of phenoxybenzamine

4. Outline the reaction scheme for the chemical synthesis of carbachol chloride (**figure 5**) from 2-chloroethanol. (5 marks)

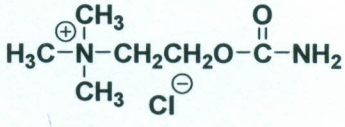

Figure 5: Chemical structure of carbachol chloride

5. Using suitable chemical structures of the main metabolites and naming the enzymes involved, describe the metabolism of norepinephrine (**figure 6**). (8 marks)

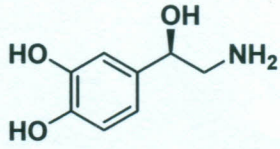

Figure 6: Chemical structure of norepinephrine

6. Regarding acetylcholine (**figure 7**):

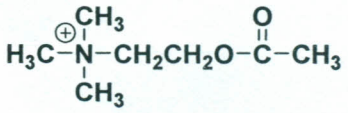

Figure 7: Chemical structure of acetylcholine

a) Explain why it is a very poor therapeutic agent. (3 marks)

b) Name its active conformational isomer. (1 mark)

c) Using suitable drug examples, discuss the structure-activity relationship (SAR) associated with its analogs as muscarinic receptor agonists. (10 marks)

SECTION C: CARDIOVASCULAR DRUGS

1. Describe three structural features of the following
   a. Angiotensin converting enzyme inhibitors (3 marks)
   b. Cardiac glycosides (3 marks)
   c. β - Adrenoceptor antagonists (3 marks)
2. Describe the strategy that was used in the design of the following drugs
   a. Indanedione from coumarins (2 marks)
   b. Tocainide from lidocaine (2 marks)
3. Explain the importance of *para*-substitution of aryl group in aryoxypropanolamines (3marks)
4. Figure 8 shows the structure of encainide. Use it to answer the following questions.

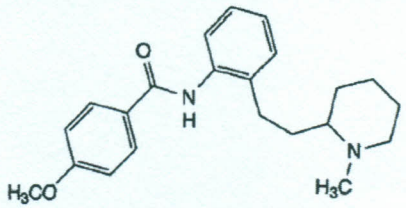

Figure 8: structure of encainide

   a. Describe its mechanism of action. (2 marks)
   b. Describe three SARs of the drug. (6 marks)
   c. Draw the structures of two of its metabolites which display anti-arrhythmic activity. (4 marks)

5. Discuss three SARs of the following

   a. Thiazide diuretics. (6 marks)

   b. Heterocyclic sulfonamide carbonic anhydrase inhibitors. (6 marks)