KENYATTA UNIVERSITY

EXAMINATION FOR THE DEGREE OF BACHELOR OF PHARMACY

PPC 520: PHARMACEUTICAL CHEMISTRY V

2ND TRIMESTER 2021/2022 TIME: 3 HRS

INSTRUCTIONS

1. The paper consists of three sections; A, B and C
2. Answer all questions
3. Answer sections A, B and C in separate booklets

## SECTION A: PHARMACODYNAMIC AGENTS I

### Part 1: Multiple Choice Questions (10 marks)

1. Which of the following statements about NSAIDs is true?
   A. Most NSAIDs are weak acids
   B. Most NSAIDs are metabolized by the liver into inactive metabolites
   C. Oxicams tend to have the longest half-lives of all NSAIDs
   D. All of the above

2. Paracetamol is an NSAID with a comparatively low anti-inflammatory effect compared to other NSAIDs.
   A. True
   B. False

3. *P*-hydroxy acetanilide is_____.
   A. Paracetamol
   B. Acetaminophen
   C. A & B
   D. None of the above

4. Which of the following drugs is a phenyl acetic acid derivative?

   A. Ibuprofen
   B. Paracetamol
   C. Diclofenac
   D. Phenacetin

5. Indomethacin contain_____heterocycle.

   A. Pyrrole
   B. Indole
   C. Indene
   D. Oxazole

6. Which of the following statements is true about acarbose?

   A. It is metabolized solely in the GI tract by intestinal bacteria forming sulfate, methyl and glucuronide conjugates.
   B. About 34% of the intestinal metabolites are absorbed and excreted through the kidneys.
   C. An active metabolite is formed by the cleavage of one glucose molecule.
   D. All of the above

7. Which of the following drugs is an enolic acid derivative?

   A. Mefenamic acid
   B. Diclofenac
   C. Piroxicam
   D. Celecoxib

8. Phenylbutazone belongs to_____class of NSAIDs

   A. Anthranilates
   B. Oxicams
   C. Phenylpyrazolones
   D. Anilides

9. Choose the correct classification of the antigout agents

   A. Colchicum alkaloid –NSAIDs-Uricosuric Agents-Urate synthesis inhibitors
   B. Urate synthesis inhibitors-Colchicine –NSAIDs-Uricosuric agents
   C. Allupurinol-Colchicum alkaloid–NSAIDs-Urate synthesis inhibitors
   D. Colchicum alkaloid –Phenylbutazone-Uricosuric Agents-Urate synthesis inhibitors

10. Choose the correct classification of sulfonylureas

A. First generation: Glyburide; Second generation: Tolbutamide; Third generation: Glimepiride
B. First generation: Tolbutamide; Second generation: Glyburide; Third generation: Glimepiride
C. First generation: Glimepiride; Second generation: Glyburide; Third generation: Tolazamide
D. First generation: Glimepiride; Second generation: Tolbutamide Third generation: Glyburide

**Part 2: Short Answer Questions**

1. Outline five SARs of colchicum alkaloids using Figure 1. (5 marks)

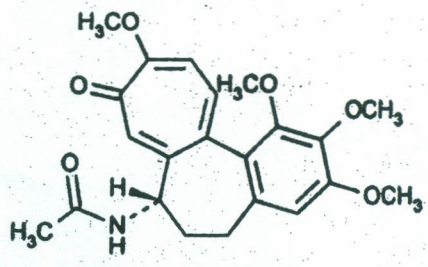


**Figure 1:** Chemical Structure of Colchicine

2. Discuss metabolism of biguanides. (5 marks)
3. Categorize the following insulin preparations to short acting, intermediate acting and long actions: (5 marks)

   Regular, Insulin detemir, Isophane (NPH), Protamine zinc, Lispro, Lente, Ultra Lente, Insulin zinc, Biphasic insulin aspart, Insulin glargine.

4. Regarding glitazones:
   (i). Describe two structural features (2 marks)
   (ii). Explain three SARs (3 marks)

**Part 3: Essay Question**

1. Regarding muscle relaxants:
   (a). Discuss their classification. (5 marks)
   (b). Discuss the SAR of baclofen (Figure 2). (5 marks)

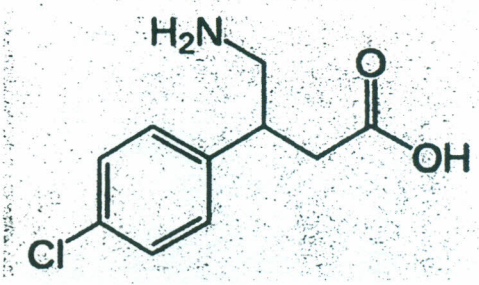


**Figure 2:** Chemical Structure of Baclofen

## SECTION B: PHARMACODYNAMIC AGENTS II

**Part 1: Multiple Choice Questions** (10 marks)

1. Chlorpheniramine structure has the following number of asymmetric centers:
   A. 1
   B. 2
   C. 4
   D. 0
   E. 3

2. Which of the following statement is true regarding the SAR of alkylamine antihistamine drugs?
   A. E- and Z- isomers in alkanes show differences in activity
   B. Z-isomers are less potent than E-isomers of alkenes
   C. Z-isomers are inactive
   D. S-enantiomers are inactive
   E. None of the above

3. Which of the following antihistaminic drugs does not have a pyridyl moiety in its structure?
   A. Clemastine
   B. Doxylamine
   C. Desloratadine
   D. Acrivastine
   E. Bepotastine

4. The correct sequence for True (T) and False (F) for the given statements relating to the SAR of class ethanolamine ethers antihistamines is:
   i. Compounds with *p*-Cl-Ph and 2-pyridyl aryl groups include carbinoxamine, which is a potent anti-histamine drug.
   ii. 8-chlorotheophyllinate salt of diphenhydramine is used for treatment of rhinitis.

iii. Doxylamine has an amino group at the carbon alpha to the ether function.
iv. An additional carbon atom between oxygen and nitrogen produces clemastine which has lower sedative properties.

A. TTFF
B. TFTF
C. TFFT
D. FTFF
E. FFFF

5. Diphenhydramine can be synthesized by the reaction of benzhydryl bromide with?
   A. 2-aminobenzoic acid
   B. 4-aminobenzoic acid
   C. Butanoic acid
   D. 2-dimethylaminoethanol
   E. 2-diaminoethanoic acid

6. Match the following vitamins with the corresponding disease arising from their deficiencies:

| | |
|---|---|
| i. Niacin | A. Beriberi |
| ii. Thiamine | B. Pellagra |
| iii. Pantothenic acid | C. Anaemia |
| iv. Cyanocobalamin | D. Paresthesia |

   A. i-D, ii-A, iii-C, iv-B
   B. i-A, ii-B, iii-C, iv-D
   C. i-A, ii-D, iii-B, iv-C
   D. i-B, ii-A, iii-D, iv-C
   E. i-B, ii-C, iii-A, iv-D

7. Which one of the following drugs and its classification is correct?
   A. Bepotastine: Ethanolamine ether $H_1$ antihistamine
   B. Metoclopramide: Gastrointestinal protectant
   C. Ranitidine: Proton pump inhibitor
   D. Acrivastine: Topical antihistamine
   E. None of the above

8. Cyclizine has actions on:
   A. Vomiting center

B. Cholinergic receptors
C. Muscarinic receptors
D. All the above
E. None of the above

9. The following are metabolites of histamine except:

A. N-methylimidazole acetic acid
B. 3-methylhistamine
C. Imidazole acetic acid riboside
D. 4-methylhistamine
E. Imidazole acetic acid

10. Which of the following regarding binding of antihistamines to $H_1$ receptors is correct?

A. Antihistamines bind to the receptor via similar $H_1$ receptor residues as histamine.
B. $Asn^{107}$ is a common binding residue for both antihistamines and histamine.
C. $Phe^{432}$ and $Trp^{158}$ are critical binding residues for $H_1$-selective antihistamines.
D. Hydrophilic receptor sites are the most critical for antihistamine binding.
E. Most antihistamines are inverse antagonists that bind to an inactive form of the receptor.

**Part 2: Short Answer Questions**

1. Describe the limit test for peroxides in all-trans-retinol. (3 marks)

2. Outline the assay of vitamin C (Figure 1) by titration. (3 marks)

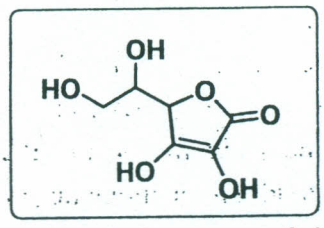


**Figure 1:** Chemical structure of vitamin C

3. Explain the mode of action of cromolyn sodium. (4 marks)

4. Regarding the class of compounds represented by Figure 2:

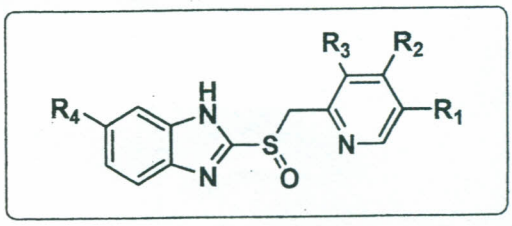


**Figure 2**

(a). Identify the class of agents represented by the chemical structure. (1 mark)

(b). Name six drug examples belonging to this class. (3 marks)

(c). Outline the metabolism of the prototype drug for this class. (6 marks)

**Part 3: Essay Question**

1. With suitable drug examples, discuss $H_2$-selective antihistamines under the following:

   (a). Structure-activity relationships. (5 marks)

   (b). Binding to histamine $H_2$ receptor. (5 marks)

## SECTION C: HORMONAL AGENTS

**Part 1: Multiple Choice Questions** (10 marks)

1. Steroids have sterol nucleus _____

   A. with two alkyl chain attached to the ring D of cholesterol
   B. with two $CH_3$ between C and D ring and A and B ring of cholesterol
   C. without $CH_3$ between C ring and D ring of cholesterol
   D. but lack the alkyl chain attached to the ring D of cholesterol

2. Match the following with respect to the SAR of drug prednisolone-

| | |
|---|---|
| i. Introduction of 17-alpha-hydroxy group | A. Increases the activity of drug |
| ii. Double bond at C-1 position | B. Decreases the activity of drug |
| | C. Increases the activity of drug |
| | D. Decreases the activity of drug |

   A. i-A, ii-C
   B. i-A, ii-D
   C. i-B, ii-C
   D. i-B, ii-D

3. The number of chiral centrers in the structure of ethinylestradiol is _____.

A. 1
B. 3
C. 5
D. 7

4. Which amongst the following statements is/are incorrect relating to the SAR of ethinylestradiol?

I. Oxygen at C11 is not important for the activity.
II. Introduction of 17-alpha-hydroxy group increases the activity.
III. Introduction of 17-alpha-hydroxy group decreases the activity

A. I & III
B. I & II
C. I only
D. All statements are correct

5. Match the drugs with the correct classification.

| | |
|---|---|
| i. Prednisolone | A. Selective estrogen receptor down regulators |
| ii. Ethinylestradiol | B. Estrogens |
| iii. Tamoxifen | C. Glucocorticoids |
| iv. Fulvestrant | D. Selective estrogen receptor modulator |

A. i-B, ii-D, iii-C, iv-A
B. i-B, ii-A, iii-C, iv-D
C. i-D, ii-A, iii-C, iv-B
D. i-C, ii-B, iii-A, iv-D

6. The following are chemical classifications of hormones except

A. Steroid hormones
B. Amino-acid based hormones
C. Glucose containing hormones
D. Protein based hormones

7. Water-soluble hormones have a short .....

A. Chain of amino acids
B. Activation time
C. Half life
D. Molecule

8. Which of the following is the major point of regulation on the pathway to cholesterol?
   A. Thiolase
   B. HMG Co-A synthase
   C. HMG Co-A reductase
   D. Pyruvate kinase

9. Which of the following hormones is a polypeptide?
   A. Estrogen
   B. Insulin
   C. Androgen
   D. Epinephrine

10. Which is the first intermediate in cholesterol synthesis?
   A. Mevalonate
   B. Isoprene
   C. Ethylene
   D. Squalene

**Part 2: Short Answer Questions**

1. Describe two structural features that are responsible for the activity of the following peptide hormones:
   (a). Calcitonin (2 marks)
   (b). Thyroliberin (2 marks)
   (c). Iodothyronines (2 marks)

2. Explain the significance of stereochemistry in the design of peptide hormonal agents. (3 marks)

3. Explain the significance of the biosynthetic pathways of steroid hormones in the design of hormonal agents for the treatment breast cancer. Illustrate your answer using a relevant drug. (5 marks)

4. Describe three SARs of estrogens (6 marks)

**Part 3: Essay Question**

1. Using relevant drug structures, discuss five SARs of iodothyronines. (10 marks)