KENYATTA UNIVERSITY

EXAMINATION FOR THE DEGREE OF BACHELOR OF PHARMACY

(BPharm Level III)

PPC 310: PHARMACEUTICAL CHEMISTRY I

1ST SEMESTER 2022/2023 **TIME: 3 HOURS**

INSTRUCTIONS:

1. **The paper consists of THREE Sections ; A, B and C**
2. **Answer All Questions**
3. **Answer Section A, B and C in separate Booklets**

SECTION A: PHYSICOCHEMICAL PROPERTIES OF DRUGS

1. Based on the structures of the drugs presented in figure (1), answer the following questions:
   (a). Classify the drug molecules as acidic or basic drugs (5 marks)
   (b). Using equations, illustrate the ionization of the drug molecules (5 marks)
   (c). Explain where in the gastrointestinal tract aspirin and ephedrine will be absorbed into the bloodstream most quickly. (4 marks)

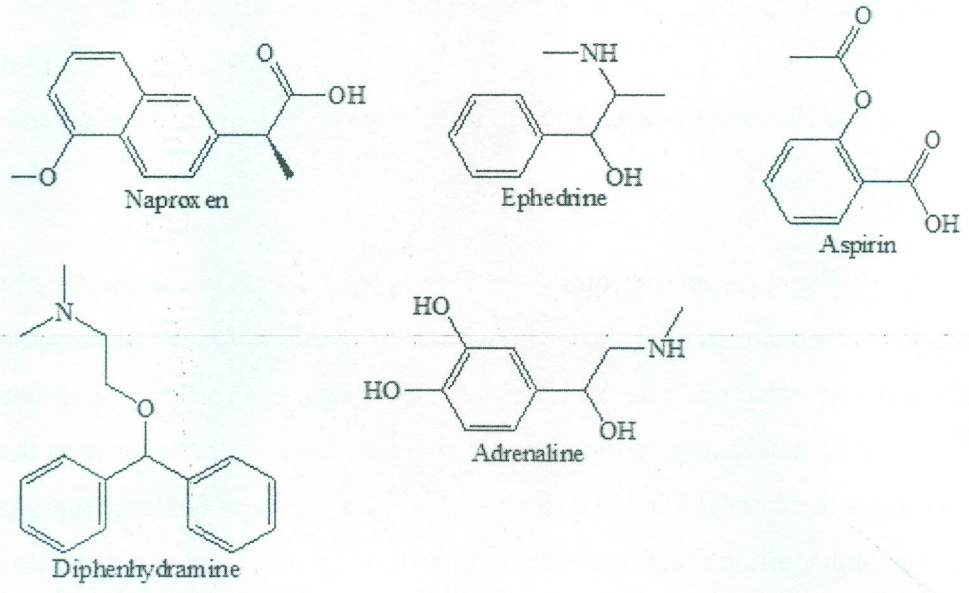

Figure 1: Drug Molecules

2. Explain the importance of the following functional groups in the action of a drug molecule.
   (a). Chelating agents (2 marks)
   (b). Halogens (2 marks)
   (c). Acylating agents (2 marks)
3. (a) Using equations, illustrate the difference between partition and distribution coefficients (4 marks)
   (b) Explain how lipophilicity influence pharmacokinetic properties of a drug. (6 marks)
4. Using a real drug example, explain the role of stereochemistry in the pharmacological action of drugs. (5 marks)
5. Highlight Lipinski's Rule of Five for oral drugs. (5 marks)

SECTION B: DRUG DEVELOPMENT AND DESIGN

1. Differentiate between the following as used in drug design:
   (a). Isosterism and bioisosterism (2 marks)
   (b). SAR and QSAR as used in drug design (2 marks)

2. During an SAR investigation, identify an alternative halogen containing group that could be used in place of chlorine. Give one reason for the use of this group. (3 marks)
3. Explain the significance of target specificity and selectivity in drug design and development. (5 marks)

4. Pharmacy Students' research group were developing a new anti-cancer drug by designing inhibitors of indoleamine-2,3-dioxygenase (IDO) enzyme. One lead compound has the naphthoquinone structure (X, Y=H) shown in Figure 2. The proposed mode of IDO inhibition involves binding of the ketone oxygen in the naphthoquinone to the heme iron atom at the active site of IDO. To test the proposed mode of binding, the group decided to make naphthaquinone analogues in order to modify the electronic nature of the ketone oxygen.

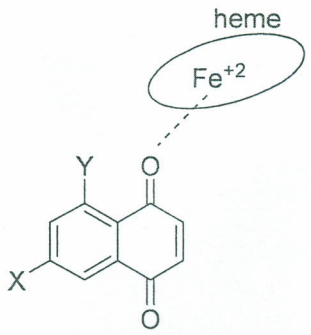

Figure 2: Naphthaquinone structure bound to Fe^{2+} at IDO active site

(a). By explaining your answer, for each case, draw one possible structure of an analogue with a group at X position that would make the ketone oxygen more:

(i). Electron rich (4 marks)

(ii). Electron poor (4 marks)

(b). Changing substituents at position Y might afford similar electronic changes, however conclusions about the electronic effects of substituents at Y would be less certain. Explain this observation. (3 marks)

5. Using a relevant example in each case, discuss three reasons for the utility of prodrugs in drug design. (9 marks)
6. Discuss four effects of bioisosteric replacements on a drug molecule (8 marks)

SECTION C: PRINCIPLES OF DRUG QUALITY CONTROL

1. (a) With regard to pharmaceutical industry, distinguish between:

(i). Good manufacturing practices and Good laboratory practices (4marks)

(ii). Quality control and Quality assurance (4marks).

(b) Give the significance of the following in drug quality control:

(i). Proper sampling in analysis (2 marks)

(ii). Validation of analytical method. (2marks).

2. (a) Describe two official specifications that guide the assessment of quality of a pharmaceutical product. (2marks)

(b) Outline:

(i) Three ways through which impurities can be introduced in a pharmaceutical product during manufacturing (3marks)

(ii) The procedure for controlling moisture level in a pharmaceutical product. (3marks)

(c) Explain the principle, on which the levels of the following impurities are controlled in drug products,

(i) Chloride (2marks)

(ii) Heavy metals (2marks)

(d) Give the most likely reason for controlling levels of each impurity in question 2(c) above (2marks)

3. (a) With regard to pharmaceutical analysis, distinguish between:

(i) Procedure and protocol (4marks)

(ii) Robustness and ruggedness of an analytical technique. (4 marks)

(b) Describe a validated *in vitro* method for predicting the bioavailability of a new drug. (3marks)

(c) Using a specific example, explain the role of standards in analysis. (3marks)