KENYATTA UNIVERSITY

EXAMINATION FOR THE DEGREE OF BACHELOR OF PHARMACY

(BPharm Level III)

PPC 310: PHARMACEUTICAL CHEMISTRY I

3RD TRIMESTER 2021/2022 TIME: 3 HOURS

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: PHYSICOCHEMICAL PROPERTIES OF DRUGS

1. The ability of a chemical compound to elicit a pharmacologic effect is related to the influence of its various physicochemical properties. Explain this statement using the following properties:
   (a). Acidity and basicity (4 marks)
   (b). Solubility (4 marks)
   (c). Protein binding (3 marks)
   (d). Molecular size (3 marks)
2. Explain the importance of the following functional groups in a drug molecule
   (a). Hydrocarbons (3 marks)
   (b). Alcohols (2 marks)
   (c). Aromatic hydrocarbons (3 marks)
3. Regarding logP of a drug molecule:
   (a). Describe its role in the therapeutic effect of a drug (3 marks)
   (b). Calculate logP value for *m*-chlorobenzamide (3 marks)

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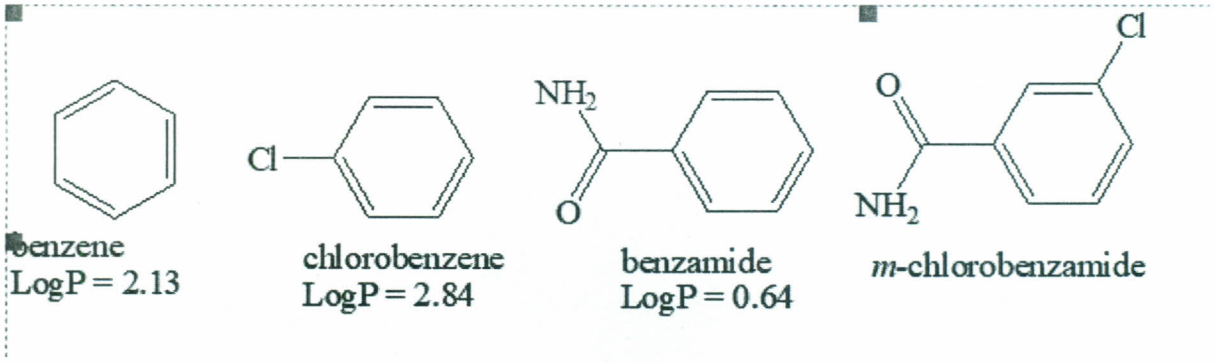

benzene
LogP = 2.13

chlorobenzene
LogP = 2.84

benzamide
LogP = 0.64

m-chlorobenzamide

4. Illustrate how the following steric factors influence the pharmacological activity of a drug:
   (a). Geometrical and optical isomerism (4 marks)
   (b). Conformational isomerism (4 marks)
   (c). Isosterism and bioisosterism (4 marks)

SECTION B: DRUG DEVELOPMENT AND DESIGN

1. Explain the meaning of the terms as used in drug design: (4 marks)
   (a). Lead compound
   (b). Prodrug
   (c). Pharmacophore
   (d). Analogue
2. Identify four approaches that may lead to the discovery of a lead compound in drug design and development. Give one example of a drug discovered through each identified approach. (8 marks)
3. Using relevant drug examples, describe how each of the following concepts are utilized in drug design
   (a). Steric shields (3 marks)
   (b). Metabolic blockers (3 marks)
   (c). Stereo-electronic modification (3 marks)
   (d). Conformational blockers (3 marks)
4. Explain how you would apply the principles of rigidification to structure **A** shown in Figure 1 in order to improve its pharmacological properties. Draw two specific examples of resulting rigidified structures. (5 marks)

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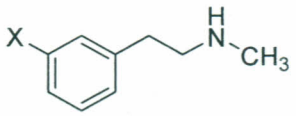

Figure 1: Structure A

5. The oral bioavailability of the antiviral drug acyclovir (whose structure is shown in Figure 2) is only 15–30%. Explain why this may be the case and how the bioavailability of this drug could be increased. (5 marks)

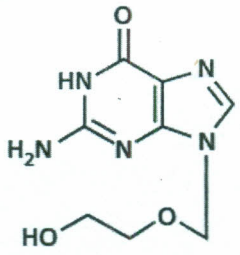

Figure 2: Structure of acyclovir

6. Using a relevant example in each case, discuss three reasons for the utility of prodrugs in drug design. (6 marks)

SECTION C: PRINCIPLES OF DRUG QUALITY CONTROL

1. Define the following terms:
   (a). Disintegration test. (1 mark)
   (b). Sulphated ash. (1 mark)
   (c). Quality assurance. (1 mark)
   (d). Quality control. (1 mark)
2. Outline the procedure for quantifying the amount of phenytoin in phenytoin sodium raw material. (4 marks)
3. Using suitable drug examples, explain the following chemical processes as sources of impurities in pharmaceutical substances:
   (a). Oxidation. (3 marks)
   (b). Hydrolysis. (3 marks)
4. Discuss the semi-quantitative limit test of arsenic in pharmaceutical substances. (6 marks)
5. Regarding quality control tests on a batch of chlorpromazine hydrochloride tablets, use the information provided below to answer the questions that follow:
   - Manufacturer's label claim: Each tablet contains chlorpromazine hydrochloride 25 mg.

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- During the uniformity of weight test, the following tablet weights (mg) were obtained: 110; 108; 100, 111; 105; 103; 106; 104; 99; 102; 101; 108; 112; 102; 103; 110; 107; 87; 110; and 112.
- Six tablets were subjected to dissolution test under the following USP conditions:
  - Dissolution medium: 0.1 M hydrochloric acid solution (500 mL) using apparatus 1 set at 50 revolutions per minute for 30 minutes.
  - Standard solution: About 10 mg of USP chlorpromazine hydrochloride reference standard was dissolved in 200 mL of the medium. Its purity was 98%.
  - Sample solution: A filtered portion of the tablet solution under test.
  - Instrumental conditions: Absorbances of the standard and sample solutions were measured using an ultraviolet-visible (UV-Vis) spectrophotometer set at 254 nm.
  - Tolerances: Not less than 80% of the labeled amount of chlorpromazine hydrochloride is dissolved.
  - Results:

	Standard A (9.80 mg)	**Standard B (10.20 mg)**	**Tablets**					
			1	**2**	**3**	**4**	**5**	**6**
Absorbance	0.501	0.524	0.480	0.460	0.400	0.450	0.410	0.420

(a). State the type of weighing balance that was used to weigh the reference standard. (1 mark)

(b). Describe the category of reference standard that was used in the dissolution test. (2 marks)

(c). Determine the uniformity of weight and make a conclusion based on the British Pharmacopoeia (BP 2021) specifications (Deviation limit ± 7.5%) for uniformity of weight. (6 marks)

(d). Explain how you would prepare a stock solution of three liters (3.0 L) of 0.1 M hydrochloric acid from concentrated HCl (36% w/w, density = 1.18 g/mL).(4 marks)

(e). Calculate the percentage of the labeled amount of chlorpromazine hydrochloride dissolved for each of the six tablets. (7 marks)

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