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MASINDE MULIRO UNIVERSITY OF SCIENCE AND TECHNOLOGY

UNIVERSITY EXAMINATIONS 2021/2022 ACADEMIC YEAR

THIRD YEAR SPECIAL/SUPPLEMENTARY EXAMINATION

FOR THE DEGREE OF

BACHELOR OF SCIENCE (CHEMISTRY)

COURSE CODE: **SCH 334E**

COURSE TITLE: **MEDICINAL CHEMISTRY**

DATE: FRIDAY, 29TH JULY 2022 **TIME: 8:00 – 10:00 AM**

INSTRUCTIONS

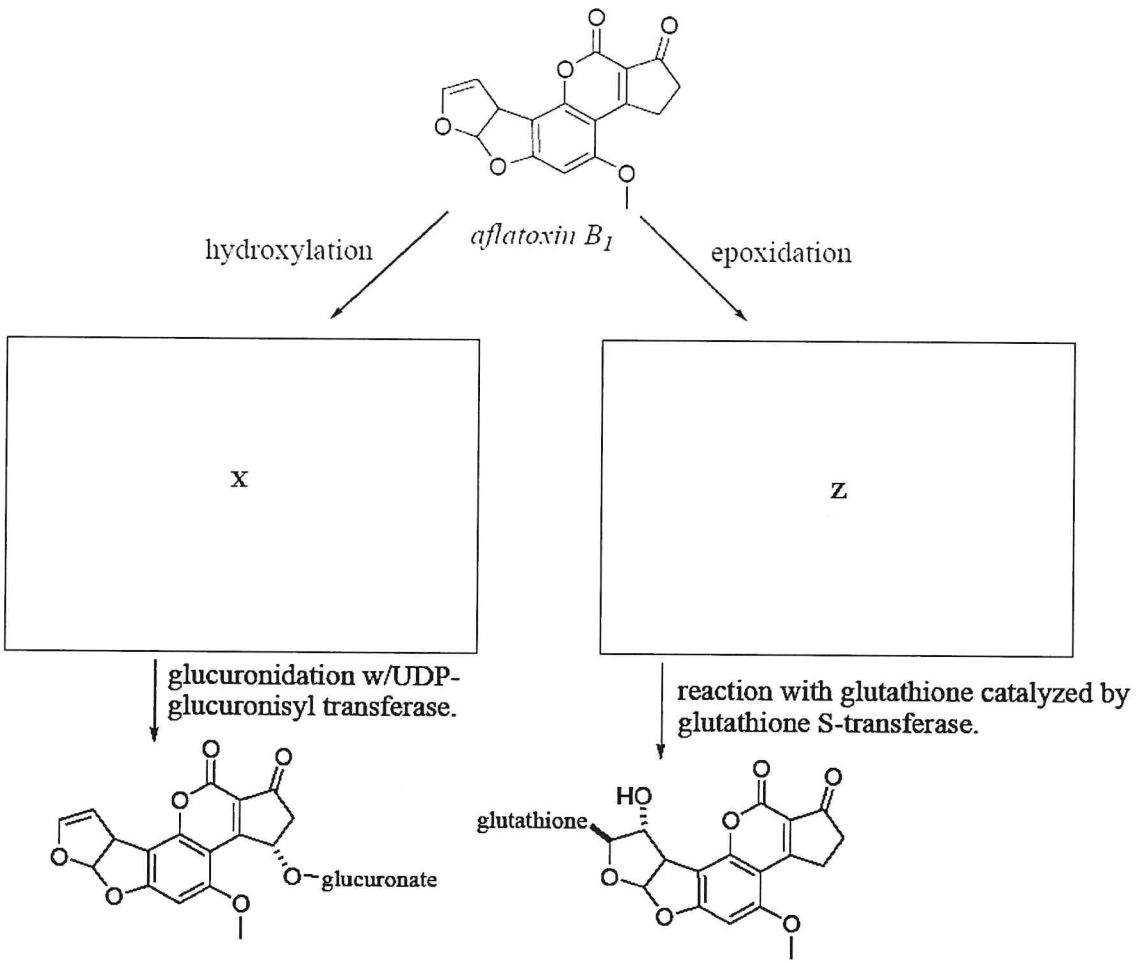
- *Answer **ALL** Questions*

Q1. (a) Medicinal chemistry concerns the discovery, the development, the identification and the interpretation of the mode of action of biologically active compounds at the molecular level. Explain the three key stages a lead compound undergoes from the beginning up to when it is declared clinically fit for use as a medicine. *[3 marks]*

(b) Giving a relevant example or illustration in each case, what is the broad classification? criteria of drugs as known today? *[5 marks]*

(c) Explain any three (3) different routes of drug administration. *[3 marks]*

(d) Hydrophobic molecules that are foreign to the body are usually metabolized along two general pathways. Both of these are amongst the pathways we discussed in drug metabolism lectures. One of the most potent carcinogens, aflatoxin B1, a fungal toxin, is processed in these two different ways as shown in the scheme below. Unfortunately, one pathway creates the lethal form of aflatoxin B1 that leads to its carcinogenic properties.



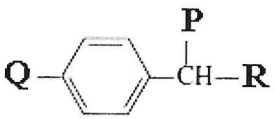
(i) Draw the structure of the intermediate metabolic products in the two boxes marked **X** and **Z**. *[3 marks]*

(ii) What type of enzyme probably catalyzes the first set of reactions (hydroxylation and epoxidation)? *[1 mark]*

(iii) Which phase of metabolic reactions is represented in the second set of transformations (reaction with glucuronic acid and glutathione)? *[2 marks]*

(iv) What is the body's primary goal in the series of metabolic reactions shown above? *[2 marks]*

Q2. (a) Complete the chemical structure given below of the pain-relieving drug Ibuprofen on the basis of the fact that ibuprofen is a carboxylic acid that has the molecular formula $C_{13}H_{18}O_2$, **Q** is an isobutyl group, and **P** is a methyl group. *[2 marks]*



(b) Mandelonitrile may be obtained from peach flowers. Derive its structure from the template in Q2 (a) given that **Q** is hydrogen, **P** is the functional group that characterizes alcohols, and **R** characterizes nitriles. *[2 marks]*

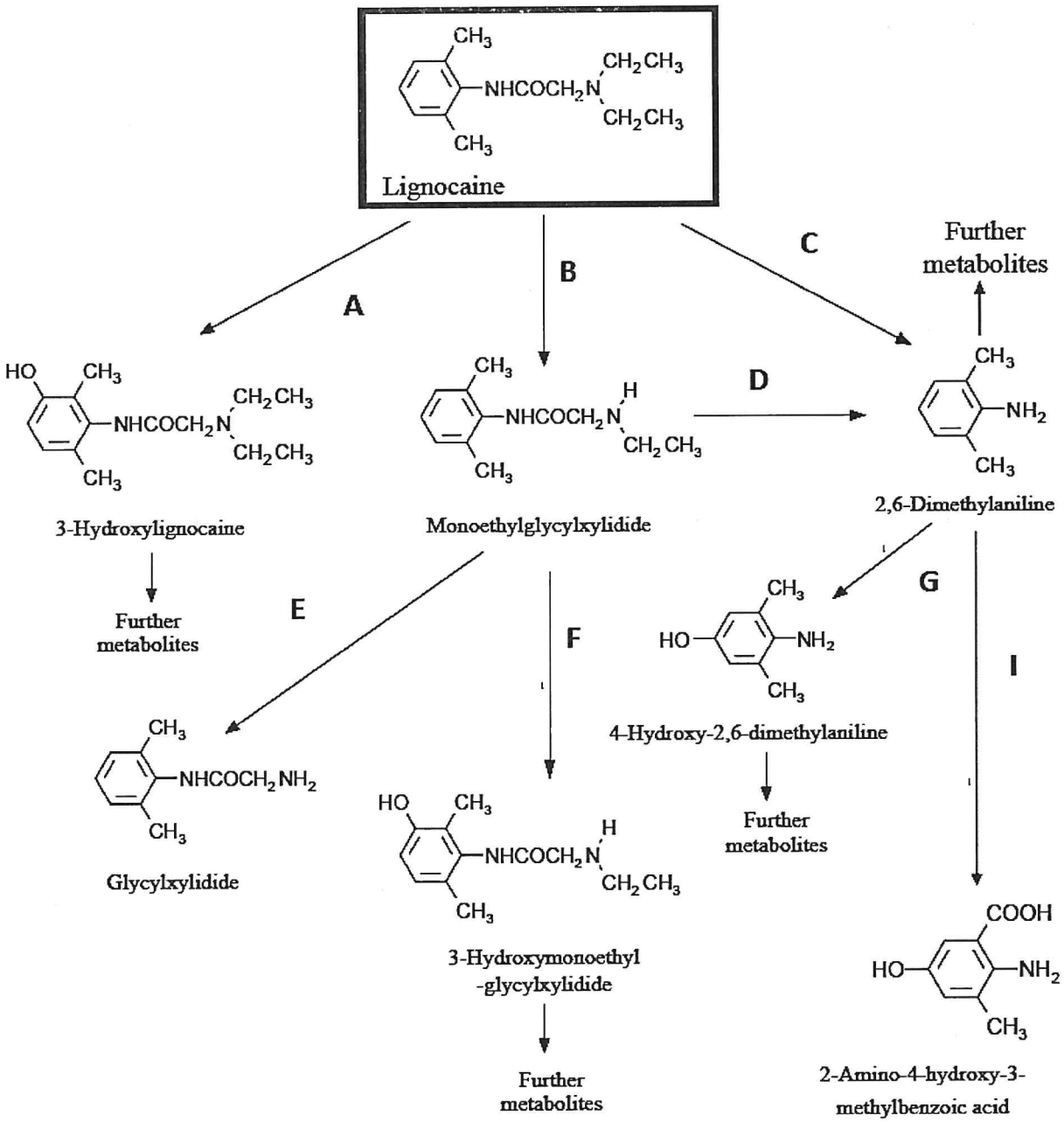
(c) List four (4) types of drug-receptors giving at least one(1) example in each case. *[8 marks]*

(d) Drug-receptor interactions may be described as agonist or antagonist. Explain? *[4 marks]*

(e) Outline the type of chemical interactions drugs may have with receptors. *[5 marks]*

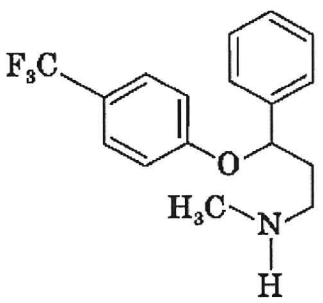
Q3. (a) Explain what you understand by the abbreviations ADME and QSAR in medicinal chemistry. *[8 marks]*

(b) Drug metabolism is the biotransformation of a drug along its ADME process into other compounds (metabolites) that are usually more water soluble than their parent drug and are excreted in the urine. Given below is an outline of the known metabolic pathways of the local anaesthetic lignocaine. Study the outline carefully and answer the following question.



Identify the classes of chemical reactions marked **A – I.** (For example, substitution, reduction, oxidation, dealkylation, alkylation etc.) *[7 marks]*

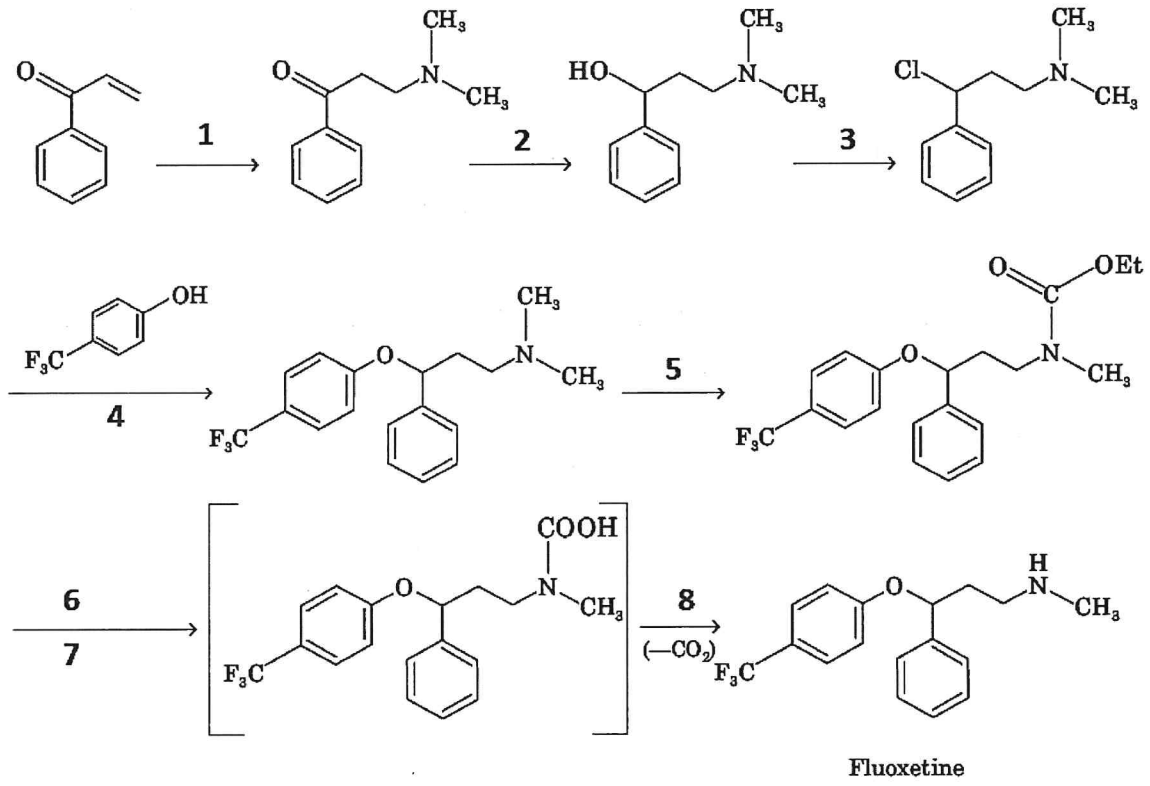
Q4. Shown alongside is the chemical structure of Fluoxetine (N-methyl-3-phenyl-3-(ptrifluoromethyl)-phenoxy-propylamine), a widely used antidepressant drug. Study the structure carefully and answer the following questions.



(a) What the chemical class of Fluoxetine? *[1 mark]*

(b) Propose a proprietary name of Fluoxetine? *[1 mark]*

(c) Below is a outline for the synthesis of fluoxetine. Identify the missing reagents and or reactions marked **1-8**. *[9 marks]*



(d) Considering the chemical structure of Fluoxetine, explain four (4) key physicochemical factors that may greatly influence its antidepressant pharmacological activity. *[4 marks]*