The South African Pharmacy Council

PROFESSIONAL EXAMINATION OF COUNCIL IN TERMS OF THE PHARMACY ACT, 1974 (ACT 53 OF 1974)

APPLIED PHARMACEUTICS AND PHARMACEUTICAL CHEMISTRY EXAMINATION

2020 PRACTICE PAPER

TIME ALLOWED: Three (3) hours

MAXIMUM MARKS: 40

PASS MARK: 20

APPLIED PHARMACEUTICAL CHEMISTRY: SECTION A

EXAMINER: Prof L Du Toit

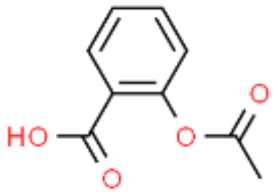
MODERATOR: Prof J Petzer

NO. OF PAGES: 11

CANDIDATES PLEASE NOTE:

(a) Ensure that you have the correct question paper for your examination.
(b) Ensure that all your details as requested on the cover page are filled in correctly.
(c) There is 15 minutes reading time for this paper.
(d) Do not commence writing until you are told to do so.
(e) The marks allocated to each question must be borne in mind when answering.
(f) All multiple choice questions are worth one mark.
(g) There is no negative marking for incorrect answers.
(h) There is only one correct answer per multiple choice question, therefore select only one option per question.
(i) Questions can be answered in any given order within the given time.
(j) All questions must be answered.
(k) **Section A: Pharmaceutical Chemistry** and **Section B Pharmaceutics** *Mark the answers for each question clearly.* Please ensure that all your details as requested on the cover page are filled in correctly.

1. As a Regulatory Affairs Pharmacist at an international pharmaceutical company, you are required to report on the physicochemical properties of a pharmaceutical product incorporating aspirin in the dossier that you are preparing. What is the pK_a value of aspirin?



(a) 0.5
(b) 10.5
(c) 7.5
(d) 3.5

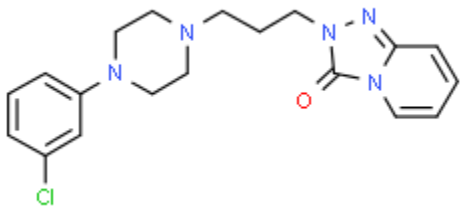
2. Considering your answer to Question 1, if aspirin is exposed to a gastric pH of 1.5, what fraction of the drug is in the unionised form?

(a) 1%
(b) 9%
(c) 90.9%
(d) 99%

3. In the equation: $HF + H_2O \rightarrow H_3O^+ + F^-$

(a) H_2O is a base and HF is its conjugate acid
(b) H_2O is an acid and HF is the conjugate base
(c) HF is an acid and F^- is its conjugate base
(d) HF is a base and H_3O^+ is its conjugate acid

4. What would the ionisation state of the tetracyclic antidepressant trazodone (pKa = 6.52) be at normal physiological pH (7.4)?



(a) Mainly neutral
(b) Mainly anionic
(c) Mainly cationic
(d) Zwitterionic

5. Which of the following is equal to the pK_a of a weak acidic drug?

(a) Its relative molecular mass
(b) The pK_b of its conjugate base
(c) The pH of a solution containing equal amounts of the acid and its conjugate base
(d) The equilibrium concentration of its conjugate base

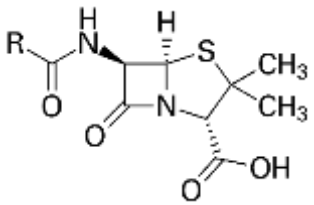
6. An aqueous solution containing a concentration of 2.5×10^{-8} mol.L^{-1} OH^- ions will have a pH of:

(a) 6.40
(b) 6.42
(c) 7.40
(d) 7.60

7. A buffer solution contains ethanoic (acetic) acid and its conjugate base; the pK_a of ethanoic acid is 4.74. At what pH does the solution most effectively buffer?

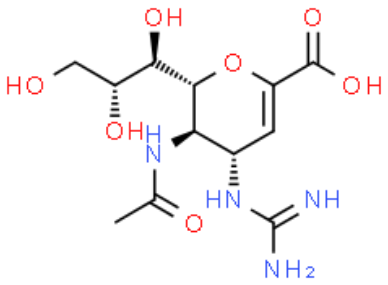
(a) 3.0
(b) 4.0
(c) 5.0
(d) 6.0

8. Stability of the natural penicillins is a challenge. Which of the following chemical modifications is used to overcome the acid instability of penicillins (general structure shown below)?



(a) Introduction of an electronegative oxygen group into the C7-amide side chain
(b) Introduction of moiety which mimics a longer section of the bacterial peptidoglycan chain
(c) Addition of functional groups to the C7-amide side chain which introduce steric hindrance
(d) Substitution of methylene hydrogens of the side chain with a carboxylic acid group

9. Zanamivir is used for the treatment of influenza A and B infections. How many stereocentres does the drug molecule possess?



(a) 1
(b) 3
(c) 5
(d) 7

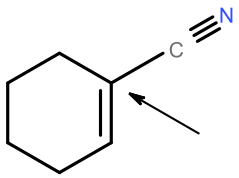
10. The route of administration of zanamivir is determined by the specific physicochemical properties of its structure (i.e. high polarity). Identify the preferred route of administration:

(a) Oral
(b) Intravenous
(c) Intranasal
(d) Topical

11. Which of the following functional groups is most likely to participate in a dipole-dipole interaction?

(a) Aromatic ring
(b) Ketone
(c) Alcohol
(d) Alkene

12. What is the hybridisation of the indicated atom in the following molecule?

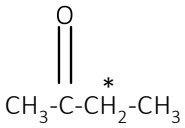


(a) sp^3 hybridised
(b) sp^2 hybridised
(c) sp hybridised
(d) Both sp^2 and sp^3 hybridised

13. The hybridisation of the central carbon in $CH_3C{\equiv}N$ and the bond angle CCN are:

(a) sp^2, 180°
(b) sp, 180°
(c) sp^2, 120°.
(d) sp^3, 109°

14. What is the multiplicity that is expected in the proton NMR spectrum for the hydrogen atoms marked by an asterisk in the following compound?



(a) Singlet
(b) Triplet
(c) Quartet
(d) Septet

15. Sodium nitroprusside, an inorganic pharmaceutical, has a formula $Na_2[Fe(CN)_5NO]$. The charge of the CN (cyano) is -1, and the charge of the NO (nitrosyl) is +1. The respective charge of the complex ion and coordination number for iron is:

(a) +2, +1
(b) -2, +2
(c) +2, +2
(d) -2, +3

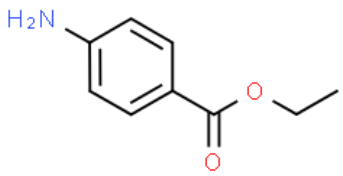
16. The fingerprint region for drug molecule identification in an infrared spectrum covers the range:

(a) 4000-2750 cm^{-1}
(b) 2750-2000 cm^{-1}
(c) 2000-1500 cm^{-1}
(d) 1500-750 cm^{-1}

17. The carbonyl stretch of a saturated ester group results in an IR band in the region of:

(a) 750 cm^{-1}
(b) 1750 cm^{-1}
(c) 2500 cm^{-1}
(d) 3500 cm^{-1}

18. Following physicochemical analysis of benzocaine via magnetic resonance of the CH_2 protons, the following is observed:



(a) A doublet at 3.5 ppm
(b) A doublet at 1 ppm
(c) A quartet at 3.5 ppm
(d) A quartet at 1 ppm

19. Which of the following techniques would furnish the greatest amount of information to be used in determining the structure of an unknown compound?

(a) UV spectroscopy
(b) Mass spectrometry
(c) ^{1}H NMR
(d) IR spectroscopy

20. Given that the specific absorbance A (1%, 1 cm) of aceclofenac (in methanol solution, at 275 nm) is 330 $dL.g^{-1}.cm^{-1}$, what will be the concentration of the drug present in a sample with an absorbance of 0.33 (measured at 275 nm in a 2 mm path cell)?

(a) 0.005 $g.mL^{-1}$
(b) 0.005% $^{w}/_{v}$
(c) 0.001 $g.mL^{-1}$
(d) 0.001% $^{w}/_{v}$

21. The molarity of a 30% ($^{m}/_{v}$) calcium chloride (mw = 110.98g/mol) solution is:

(a) 0.0027M
(b) 2.70M
(c) 0.27M
(d) None of the above

22. In preparing a medicines registration dossier for a pharmaceutical product, you as the Pharmacist note that the drug compound has an aqueous solubility of 200mg/mL. Its solubility therefore falls in the range of being:

(a) Freely soluble
(b) Soluble
(c) Sparingly soluble
(d) None of the above

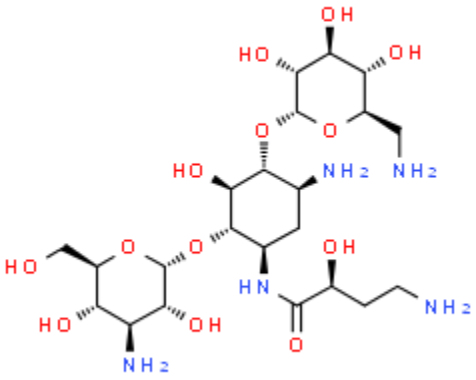
23. An unknown amount (in grams) of the antifungal miconazole (mw = 416.129 g/mol) was dissolved in 50 mL of solvent to form a solution with a concentration of 0.001 M. As the responsible Pharmacist in the manufacturing facility, you were requested to determine the mass of miconazole used to form this solution:

(a) 0.0416 g
(b) 0.0208 g
(c) 0.0042 g
(d) 0.0021 g

24. As a Pharmacist, you are required to prepare 3.00 L of a 0.250 M solution of potassium permanganate ($KMnO_4$, Mw = 158.034g/mol) for cleaning of wounds. What mass of $KMnO_4$ is required to prepare the solution?

(a) 158 g
(b) 238 g
(c) 138 g
(d) 119 g

25. The antibiotic amikacin is predicted to have a low oral bioavailability due to the fact that:



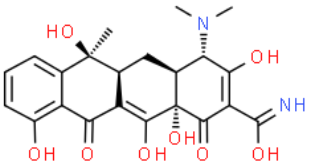
(a) It has too many rings
(b) It has a molecular mass <500
(c) It has no charged groups
(d) It has too many hydrogen bond acceptor and donor groups

26. As a Pharmacist, knowledge of drug stability is important. Natural tetracyclines have a tertiary benzylic group at C6 which allows for acid-catalysed dehydration involving the C5a hydrogen resulting in a naphthalene derivative - the C5a,6 anhydrotetracycline, which is deeper in colour and inactive. Which tetracycline below does not undergo this dehydration?

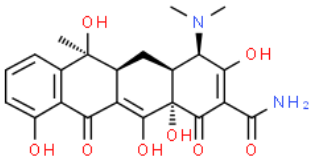
(a) Tetracycline
(b) Minocycline
(c) Demeclocycline
(d) Oxytetracycline

27. The antibiotic molecules, tetracycline and epi-tetracycline, can be considered to be:

Tetracycline

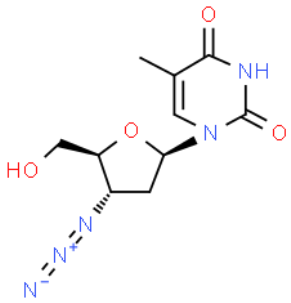


Epi-tetracycline



(a) Diastereomers
(b) Drug and pro-drug, respectively
(c) Enantiomers
(d) Equally active

28. The antiretroviral drug zidovudine is a:

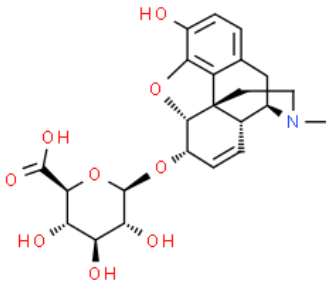


(a) Purine nucleoside analogue
(b) Purine nucleotide analogue
(c) Pyrimidine nucleoside analogue
(d) Pyrimidine nucleotide analogue

29. When a patient who is treated with the anticoagulant drug warfarin is subsequently administered the drug rifampicin, the administered dose of warfarin has to be increased in order to achieve the same anticoagulant effect. This is most likely necessary because:

(a) Rifampicin is highly chemically reactive and destroys the warfarin
(b) Rifampicin causes increased absorption of the warfarin
(c) Rifampicin induces the enzyme that metabolises the warfarin
(d) Rifampicin inhibits the enzyme that metabolises the warfarin

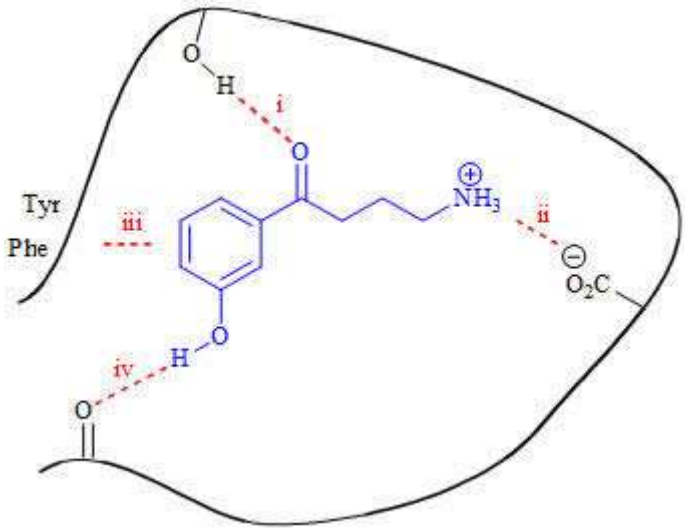
30. The metabolism and biotransformation of drug compounds are important considerations for Pharmacists. The opioid derivative below is the product of:



(a) O-demethylation of codeine followed by glucuronidation at position 6

(b) N-demethylation of codeine followed by glucuronidation at position 3
(c) O-demethylation of morphine followed by glucuronidation at position 6
(d) N-demethylation of morphine followed by glucuronidation at position

31. Consider the molecule below bound to a binding site. Identify the binding interactions taking place at i and iv:



(a) Hydrogen bonds
(b) Ionic bonds
(c) Van der Waals interactions
(d) Induced dipole-dipole interactions

32. With reference to Question 31 above, identify the interactions taking place at iii:

(a) Hydrogen bonds
(b) Ionic bonds
(c) Van der Waals interactions
(d) Induced dipole-dipole interactions

33. What is the term used for small molecules that bind to different regions of a binding site?

(a) Epimers
(b) Isomers
(c) Isotopes
(d) Epitopes

34. Which of the following drugs was not isolated from a natural source?

(a) Quinine
(b) Morphine
(c) Isoniazid
(d) Artemisinin

35. Which source has been particularly fruitful in identifying novel antitumour agents such as bryostatins and dolostatins?

(a) Marine sources
(b) Venoms and toxins
(c) Combinatorial chemistry
(d) Animals

36. What is meant by a lead compound in medicinal chemistry?

(a) A drug containing the element lead.
(b) A leading drug in a particular area of medicine
(c) A compound that acts as the starting point for drug design and development
(d) A drug which is normally the first to be prescribed for a particular ailment

37. The macrolides are a group of antibioitics. They are orally administered but are chemically unstable in acid due to internal cyclic ketal formation leading to inactivity. These ketal derivatives are associated with gastrointestinal cramping. There is a chemical and a pharmaceutical formulatory approach to this challenge. The chemical approach involves the design of a macrolide derivative that lacks the C6 hydroxyl group. An example of a macrolide with this composition is:

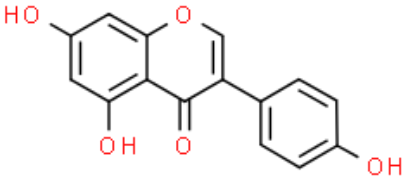
(a) Erythromycin
(b) Oleandomycin
(c) Clarithromycin
(d) Clindamycin

38. With reference to Question 37 above, what formulatory approach can be most effectively used to overcome this instability?

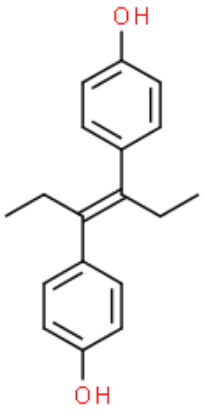
(a) Liquid oral system
(b) IV administration
(c) Slow-release tablet
(d) Enteric coated tablet

39. You have been employed at an innovative Pharmaceutical company: XY Innovations. As your first task you have been instructed to develop a novel dosage form for delivery of an active pharmaceutical ingredient (API) with oestrogenic activity. You have been provided with four compounds as potential APIs for consideration (structures i-iv). Identify the compound where the *trans*-isomer is used for the treatment of breast cancer?

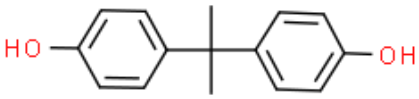
(i)



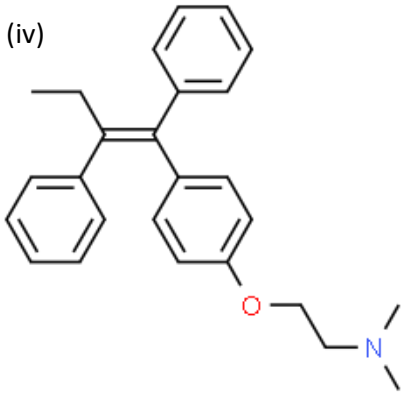
(ii)



(iii)



(iv)



(a) i
(b) ii
(c) iii
(d) iv

40. With reference to Question 37 above, which compound is a phytoestrogen that is available in certain over-the-counter preparations?

(a) i
(b) ii
(c) iii
(d) iv