Answers

Chapter 15

Exercises

1 intramuscular / into muscles

intravenous / into veins

subcutaneous / into fat

The fastest will be intravenous as the drug can be transported quickly all over the body in the bloodstream.

2 Tolerance occurs when repeated doses of a drug result in smaller physiological effects. It is potentially dangerous because increasing doses of the drug are used in response and this might get close to or exceed the toxic level.

3 **(a)** Lethal doses can be determined for animals; in humans the upper limit is the toxic dose.

(b) Bioavailability, side-effects, possibility of tolerance and addiction of the drug; age, sex, diet and weight of patient.

(c) Low therapeutic index means a low margin of safety, so small changes in dosage may produce adverse side-effects.

4 Method of administration of drug, solubility (in water and lipid) and functional group activity.

5 **(a)** 84.94%

(b) melting point determination: melting point of asprin is 138–140°C

6 Increase its solubility in water by converting to sodium salt.

7 **(a)** Mild analgesic blocks transmission of impulses at site of injury, not in the brain; anticoagulant acts to prevent coagulation / thickening of the blood and so reduces risk of coronary disease.

(b) Alcohol has synergistic effect with other drugs; can cause stomach bleeding with aspirin.

8 **(a)** R—$C_9H_{11}N_2O_4S$

(b) At the R group. Modification prevents the binding of the penicillinase enzyme and so maintains the action of the drug / prevents resistant bacteria rendering it inactive.

(c) Beta-lactam ring undergoes cleavage and binds irreversibly to the transpeptidase enzyme in bacteria. This inactivates the enzyme, which interrupts the synthesis of bacterial cell walls.

9 Overuse of antibiotics in animal stocks / food chain; over-prescription; failure of patients to complete treatment regimen.

10 **(a)** The functional groups in common are ether linkage (–C–O–C–), tertiary amine linkage (R–N(R′) – R″), alkene (–C=C–) and a benzene ring.

(b) main effect: pain relief

side-effect: constipation

11 Diamorphine has two ester groups in place of two –OH groups in morphine. The less polar diamorphine is more soluble in lipids and so crosses the blood–brain barrier more easily, and enters the brain where it blocks the perception of pain.

12 In favour: strongest pain killer known; the only effective analgesic against extreme pain.

Against: addictive drug; leads to dependence and serious side-effects.

13 H_2-receptor antagonists: block the binding of histamine, which prevents the reactions leading to stomach acid secretion.

Proton-pump inhibitors: directly prevent the release of acid into the stomach lumen.

14 **(a)** $Mg(OH)_2 + 2HCl \rightarrow MgCl_2 + 2H_2O$

$Al(OH)_3 + 3HCl \rightarrow AlCl_3 + 3H_2O$

(b) $Al(OH)_3$ reacts with H^+ in a mole ratio of 1:3

$Mg(OH)_2$ reacts with H^+ in a mole ratio of 1:2

So 0.1 mol $Al(OH)_3$ will neutralize the greater amount.

(c) KOH is a strong alkali so would be dangerous for body cells; it is corrosive and would upset the stomach pH.

15 **(a)** pH changes from 5.12 to 5.11 (assuming no volume change on mixing).

(b) No change in pH on dilution of buffer.

16 Viruses lack a cellular structure and so are difficult to target. Antibiotics specifically interfere with bacterial cell walls or internal structures. Viruses replicate inside host cells and so treatment may involve killing host cells.

17 Subunits in hemagglutinin (H) and neuraminidase (N) can mutate and mix and match, so forming different strains. These change the specific nature of the glycoprotein–host interactions, and alter the body's immune response. This is why it is possible to suffer from flu several times during a lifetime.

18 Tamiflu and Relenza do not prevent the flu virus from entering cells, but act to stop it from being released from the host cells. So if the infection is not stopped early, too many new viral particles may have already been released.

19 Challenges: antiretroviral costs, distribution and availability; patient compliance to regimen and multiple drug treatments; sociocultural issues.

Successes: new and more effective antivirals that can be used in combination; better screening of HIV-positive; controlling infection through drugs.

20 **(a)** Bark of Pacific yew tree. Harvesting has depleted the trees which grow slowly.

(b) Taxol has 11 chiral carbon atoms, giving rise to a very large number of possible stereoisomers. At many stages in its synthesis, different enantiomers could be produced, which may have different physiological properties, so these steps need to be controlled by chiral auxiliaries.

21 A chiral auxiliary is itself an enantiomer which bonds to the reacting molecule to create the stereochemical environment necessary to follow a certain pathway. The reaction then takes place, forming the desired enantiomer and the chiral auxiliary is then removed.

Different enantiomers may have different biological effects, some of which may be harmful. An example are the genetic deformities caused by the (*S*)-enantiomer of the drug thalidomide in the racemic mixture.

22 **(a)** $^{90}_{39}Y \rightarrow {}^{90}_{40}Zr + {}^{0}_{-1}\beta$

(b) 23 g

23 6.12 hours

24 **(a)** Half-life is 6 hours – long enough for diagnosis but decays quickly.

Radiation is gamma rays used for detection, and low-energy electrons which minimize radiation dose. The isotope is chemically able to bond to various biomolecules.

(b) Strong beta emitters that also emit gamma radiation to enable imaging.

25 **(a)** Targeted alpha therapy uses alpha emitters attached to carriers such as antibodies, which specifically target certain cells.

(b) Very high ionizing density and so a high probability of killing cells along their track.

Short range and so minimize unwanted irradiation of normal tissue surrounding the targeted cancer cells.

26 B – immiscible liquids

27 **(a)** An ideal solution contains fully miscible components. Each component exerts the same vapour pressure in the mixture, according to its relative concentration, as it does when pure. The intermolecular forces between the particles of the different components are the same as those between the particles in the pure substances.

(b) Boiling point of a mixture decreases with increasing height in a fractionating column as the mixture becomes enriched in the more volatile component.

28 **(a)** 2850–3090 cm^{-1} is characteristic of the C—H bond

3200–3600 cm^{-1} is characteristic of the O—H bond

(b) The peak at 2850–3100 cm^{-1} is used to characterize ethanol in the presence of water vapour.

(c) Propanone also contains C—H bonds, which give the same characteristic band at 2950 cm^{-1} as ethanol.

29 **(a)** molecular ion at m/z = 194

(b) C—H in methyl groups: 2850–3090 cm^{-1}

C=O: 1700–1750 cm^{-1} (two different peaks)

(c) four peaks, relative areas 3:3:3:1

(d) amine, amide, alkene

30 Solvents cause problems of disposal. Organic solvents can be incinerated, causing release of pollutants, greenhouse gases and toxins. Solvents can contaminate ground water and soil. Some solvents can be hazardous to health of workers.

31 Protective shoe-covers, clothing, gloves, paper towels and contaminated implements. Interim storage in sealed containers for radioactivity to decay, before conventional disposal.

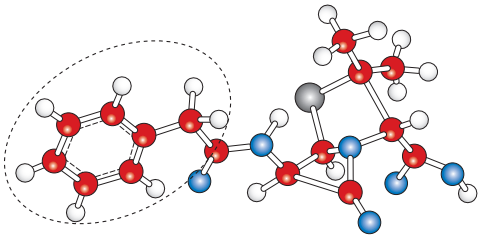
32 The success of antibiotics in treating disease has led to their widespread use, and in some cases over-use. Exposure of bacteria to antibiotics increases the spread of resistant strains. Antibiotic resistance renders some antibiotics ineffective, especially with multiply resistant strains, e.g. MRSA.

33 Patient compliance refers to the importance of patients following medical instructions, in particular to completing the course of an antibiotic treatment. This helps prevent the spread of antibiotic-resistant bacteria.

34 Green Chemistry principles seek to reduce toxic emissions and waste substances in the manufacture of drugs. This includes reduction in the amount of solvent used, the adoption of synthesis pathways with shorter routes, the replacement of inorganic catalysts with enzymes and the recycling of waste.

Practice questions

For advice on how to interpret the marking below please see Chapter 1.

1 **(a)**  [1]

No mark if circle includes CO or just O.

*Award **[1]** if it includes 7 C atoms but misses out on attached H atoms*

(b) overprescription can lead to allergic reaction

may wipe-out harmless/helpful/beneficial bacteria (in the alimentary canal)/destroyed bacteria may be replaced by more harmful bacteria

(may pass on genetic) resistance/immunity

***[1]** each for any two.*

modify R group/side chain to change penicillin effectiveness / form penicillin that is more resistant to penicillinase enzyme [3 max]

2 chiral auxiliaries are enantiomers/optically active

auxiliary creates stereochemical condition necessary to follow a certain pathway / is used to manufacture one enantiomer (so avoids need to separate a racemic mixture)

attaches/connects itself to non-chiral molecule / makes it optically active

only desired/one enantiomer/molecule formed (and chiral auxiliary removed) [2 max]

3 **(a)** $Al(OH)_3 + 3HCl \rightarrow AlCl_3 + 3H_2O$ / $Mg(OH)_2 + 2HCl \rightarrow MgCl_2 + 2H_2O$ [1]

Accept ionic equations.

(b) less effect **and** (magnesium hydroxide) 2/0.2 mol OH^- ions available as compared to (aluminium hydroxide) 3/0.3 mol OH^- ions for neutralization / neutralizes 2H^+/0.2 mol acid as compared to 3H^+/0.3 mol acid [1]

Do not accept aluminium hydroxide can neutralize more acid.

4 **(a)** viruses do not have cell/cellular structure

viruses do not have nucleus

viruses do not have cell wall

viruses do not have cytoplasm [2]

Accept opposite statements for bacteria.

(b) stops virus replication

Accept reproduction / multiplication.

becomes part of DNA of virus / alters virus DNA / blocks polymerase which builds DNA

changes the cell membrane that inhibits the entry of virus into the cells

prevents viruses from leaving the cell (after reproducing) [2 max]

(c) HIV mutates (rapidly)

Accept AIDS mutates

HIV metabolism linked to that of host cell / HIV uses host cell / drugs harm host cell as well as HIV / difficult to target HIV without damaging host cell

HIV destroys helper cells of the immune system [2 max]

5 **(a)** fast delivery / *OWTTE* [1]

(b) diamorphine has (2) ester/acetyl/$COOCH_3$ groups instead of hydroxyl/OH groups

diamorphine is less polar/non-polar [2]

6 if concentration is too high it will have harmful side effects / determination of the lethal dose (to 50% of the population / *OWTTE*

if concentration is too low it has little or no beneficial effect / determination of the effective dose / dose which has a noticeable effect (on 50% of the population) / *OWTTE*

therapeutic window is the range between these doses / range over which a drug can be safely administered / ratio of LD_{50}:ED_{50}

for minor ailments a large window is desirable, for serious conditions a smaller window may be acceptable / *OWTTE*

(therapeutic window) depends on the drug/age/sex/weight

a small therapeutic window means that an overdose is a high risk / *OWTTE* [4 max]

7 **(a)** amine

ether

alkene

benzene ring [2 max]

Do not allow arene.

Allow phenyl (ring or group) or benzene.

Allow structural representation of functional group instead of name (e.g. C=C instead of alkene).

(b) phenol / alcohol / hydroxyl (group) [1]

Allow OH.

(c) (di)esterification / condensation / (di) acetylation [1]

8 **(a)** penicillins interfere with the enzymes that bacteria need to make cell walls / interfere with formation of bacterial cell walls / *OWTTE*

the increased osmotic pressure causes the bacterium to die / the bacterial cells absorb too much water and burst / *OWTTE* [2]

(b) resistance to penicillinase enzyme / more resistance to bacteria breaking it down / effective against bacteria that are resistant (to penicillin G)

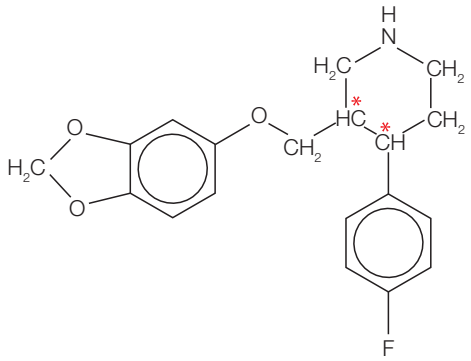
resistance to breakdown by stomach acid (so can be taken orally / *OWTTE* [2]

(c) amide group / —CONH— / peptide

ring is strained /

ring breaks easily so (the two fragments similar to cysteine and valine) then bond(s) covalently to the enzyme that synthesizes the bacterium cell wall (so blocking its action) [3]

9 **(a)**



[2]

Award [1] for each correctly placed asterisk.

(b) different enantiomers can cause different (physiological) effects in the body

thalidomide – one isomer prevented morning sickness, the other caused fetal abnormalities / ibuprofen – one isomer is more effective than the other / DOPA – one isomer helps manage Parkinson disease, the other has no physiological effects [2]

Accept other correct examples.

(c) chiral auxiliaries are themselves chiral

attach to the non-chiral molecule (to enable the desired enantiomer to be formed)

after the desired enantiomer is formed the chiral auxiliary is removed/recycled [2 max]

(d) **(i)** it turns the (relatively non-polar) molecule into an ionic/polar species

it increases its solubility in aqueous solutions / facilitates distribution around the body [2]

(ii) (secondary) amine group / non-bonding pair of electrons on (electronegative) N atom [1]

10 **(a)** C [1]

(b) A / B/ A **and** B [1]

(c) A [1]

11 **(a)** intravenous / into veins

transported/pumped via blood (to various parts of the body) [2]

(b) intramuscular/intermuscular/into muscles **and** subcutaneous/into fat [1]

(c) inhalation/breathing it in [1]

12 **(a)** **(i)** *Oxidation:*

$C_2H_5OH + H_2O \rightarrow CH_3COOH + 4H^+ + 4e^-$

Reduction:

$Cr_2O_7^{-2} + 14H^+ + 6e^- \rightarrow 2Cr^{3+} + 7H_2O$

Accept balanced equation with molecular formulas.

*If both equations are wrong, award **[1]** for $C_2H_5OH \rightarrow CH_3COOH$ and $Cr_2O_7^{2-} \rightarrow 2Cr^{3+}$.*

*If correct equations are used but oxidation and reduction reversed, award **[1]**.*

(ii) orange to green [1]

(b) peak at 2950 cm^{-1} / absorption occurs due to C—H bonds in ethanol

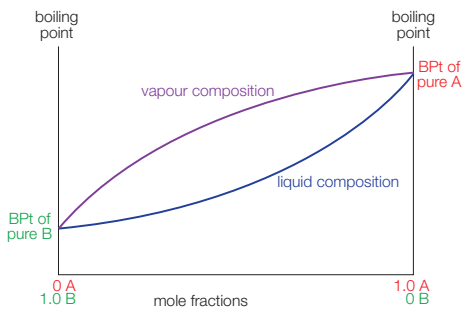
No mark for absorption due to just ethanol, or O—H bond in ethanol (water vapour in breath also contributes).

intensity / height to peak / absorption / amount of transmittance depends on amount of ethanol / compare absorption to standard / reference/control sample / sample containing no alcohol [2]

13 **(a)** shorter half-life means the body is exposed to radiation for a shorter time [1]

(b) $^{131}_{53}I \rightarrow {}^{131}_{54}Xe + {}^{0}_{-1}\beta + {}^{0}_{0}\gamma$ [1]

14 **(a)**



[3]

(b) as vapour rises up the column, it cools, condenses and falls back down. It is re-boiled by ascending vapour in a repeating cycle until vapour exits the top of the column [3]

15 obtained from needles of Pacific yew tree / obtained from fungus / fermentation process

avoids production of waste / hazardous by-products / (fermentation) avoids use of solvents / reagents / resources used renewable [2]

Challenge yourself

1 Two top C atoms in beta lactam ring: sp^3

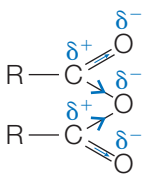
Lower C atom in beta lactam ring: sp^2

C in COOH group: sp^2

All other C atoms: sp^3

lower C atom in beta lactam ring (amide carbon): sp^2

2 Ethanoic anhydride is more susceptible to nucleophilic attack due to two electron-withdrawing carbonyl groups:



This enables it to react more vigorously than CH_3COOH with the —OH groups in morphine.

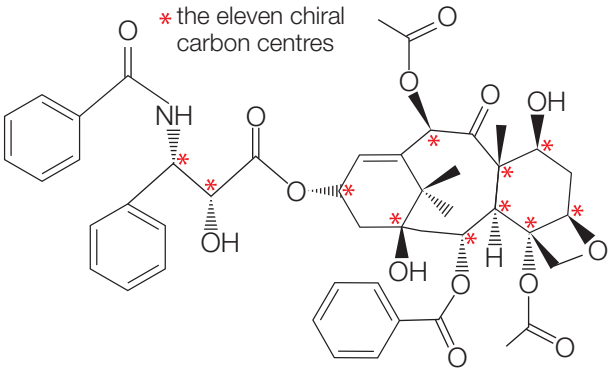
3 Na_2CO_3 and $NaHCO_3$ contain the conjugate bases CO_3^{2-} and HCO_3^- of weak acids. They are able to hydrolyse water and release OH^- ions:

$CO_3^{2-}(aq) + H_2O(l) \rightleftharpoons HCO_3^-(aq) + OH^-(aq)$

$HCO_3^-(aq) + H_2O(l) \rightleftharpoons H_2CO_3(aq) + OH^-(aq)$

4 Neuraminidase inhibitors compete with the substrate sialic acid for binding to the enzyme neuraminidase. They have a chemical structure similar to the substrate and so bind in the same way at the active site of the enzyme.

5 Red asterisks mark the position of chiral carbon atoms.



6 K_2CO_3 dissolves readily in water, but not easily in ethanol as it is less polar. The presence of the ions in water reduces the solubility of the ethanol, so it forms a separate layer on top of the water. This process is used in biochemistry to precipitate proteins from solution.