11A Extraction, purification and identification of medicinal molecules

STUDY DESIGN DOT POINTS

- extraction and purification of natural plant compounds as possible active ingredients for medicines, using solvent extraction and distillation
- identification of the structure and functional groups of organic molecules that are medicines
- significance of isomers and the identification of chiral centres (carbon atom surrounded by four different groups) in the effectiveness of medicines

11A — 11B

- 4.2.12.1 Solvent extraction and distillation of natural plant compounds
- 4.2.13.1 Medicinal organic molecules
- 4.2.14.1 Chirality

ESSENTIAL PRIOR KNOWLEDGE

- Polarity
- Partial charges

7A Benzene
7A Isomers
10F Instrumental techniques
See questions Xx-Xx.


Image: lv-olga/shutterstock.com

How can oil from this tree fight infection?

The tea tree is a plant native to Australia that has been used as a medicine by Aboriginal and Torres Strait Islander Peoples for thousands of years. In this lesson, we will investigate how **medicinal molecules** are extracted from plants and subsequently purified, exploring some important plant-sourced medicines from Australia and around the world. The significance of structure, functional groups, and chirality to medicinal molecules will also be explored.

KEY TERMS AND DEFINITIONS

Achiral compound compound with a superimposable mirror image
Active ingredient component of a substance or mixture that produces a chemical or biological effect
Chiral centre carbon atom in a compound attached to four unique chemical environments
Chiral compound compound with a non-superimposable mirror image
Immiscible describes a set of liquids that do not mix with each other
Medicinal molecule compound with healing properties
Optical isomers two non-superimposable mirror images of the same compound
Racemate an approximately 50/50 mixture of a chiral compound's two optical isomers, which does not rotate polarised light in a specific direction
Simple distillation method of separating compounds based on a difference in boiling points, by continual evaporation and recondensation
Solvent extraction method of separating compounds based on a difference in solubility in two solvents
Steam distillation distillation by injection of water vapour to lower the boiling point of substances and hence minimise decomposition

Solvent extraction and distillation of natural plant compounds 4.2.12.1

For thousands of years, humans have used plants as a source of medicinal compounds. Various laboratory techniques can be employed to extract and purify these compounds for analysis and subsequent medicinal use.

What medicinal molecules are extracted from plants?

Tea tree oil

Tea tree oil is a mixture extracted from the tea tree (*Melaleuca alternifolia*), which is native to Australia. Aboriginal and Torres Strait Islander Peoples have traditionally used tea tree oil as a medicine for treating insect bites and superficial wounds. The major component and possible **active ingredient** in tea tree oil is terpinen-4-ol (figure 1).

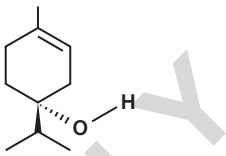


Figure 1 Structure of terpinen-4-ol, a major component of tea tree oil

Emu bush extract

Eremophila alternifolia is a species of emu bush (figure 2), another plant native to Australia which grows primarily in south-western Australia. Its leaves have been dried and used by Aboriginal and Torres Strait Islander Peoples to treat septic wounds, among other ailments associated with infection. As will be explored later in this lesson, modern analytical techniques have been applied to determine and isolate the potential active ingredients in this plant.

Image: alybaba/shutterstock.com

Figure 2 Emu bush

Paclitaxel

Paclitaxel, commonly sold as Taxol© (figure 3) is listed as an essential medicine by the World Health Organisation for its effectiveness in treating breast cancer, ovarian cancer, lung cancer, and others. Notably, it is almost exclusively obtained by extraction from the Pacific Yew Tree (*Taxus brevifolia*), which is native to North America.

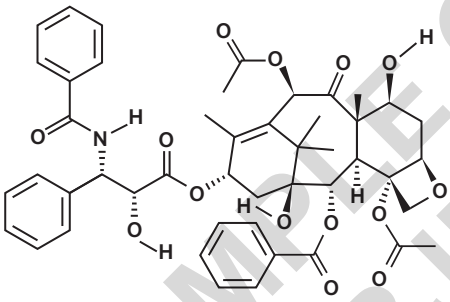


Figure 3 Structure of paclitaxel

Paclitaxel's success initially led to concerns surrounding the sustainability of yew forests, since extraction from the bark kills the tree. However, scientists have since developed methods of extracting a reactive compound that can be made into paclitaxel from the needles of Pacific and European yew trees (figure 4), hence keeping the tree alive.

Image: OlgaLo/shutterstock.com

Figure 4 Pacific yew tree needles

How are medicinal molecules extracted from plants?

As discussed in lesson 10E, 'like dissolves like': polar solvents dissolve polar solutes, whereas non-polar solvents dissolve non-polar solutes. This principle can be employed to separate desired compounds from impurities based on differences in polarity, in a process called **solvent extraction** or liquid-liquid extraction.

In this process, the initial mixture, containing the product we wish to extract and some impurities, is dissolved in a given solvent. Another solvent **immiscible** with the first is then added to the system, and the vessel is agitated (shaken).
As a result, the two immiscible solvents come in contact with each other, and any solutes that are more soluble in the new solvent (compared with in the initial one) will partition (transfer) to the new solvent. Table 1 shows some common solvents used in solvent extraction.

USEFUL TIP

In representations of larger molecules, thick triangle-shaped lines ('wedges') are often used to represent bonds 'coming out of the page', whereas striped triangle-shaped lines ('dashes') are used to represent bonds 'going into the page'. These are used to show the molecule's 3D shape on a 2D page.

USEFUL TIP

Polarity is largely relative, meaning compounds are best described as more or less polar than other compounds, rather than 'absolutely polar' or 'absolutely non-polar'.

Table 1 Common solvents and their polarities

Solvent	Polarity
Hexane	Very non-polar
Acetone (propanone)	Quite non-polar
DMSO (dimethylsulfoxide)	Somewhat polar, somewhat non-polar
Ethanol	Quite polar
Water	Quite polar

Figure 5 represents an example of solvent extraction. In this example, a mixture containing a desired product that is less polar and impurities that are more polar is initially dissolved in a non-polar solvent (e.g. hexane). A polar solvent (e.g. water) is added, and upon shaking, the polar impurities dissolve in this polar solvent, whilst the less polar desired product remains in the non-polar solvent. Since the two solvents are immiscible, they are then separated by opening the separating funnel tap, and the desired product can then be extracted via evaporation of the solvent.

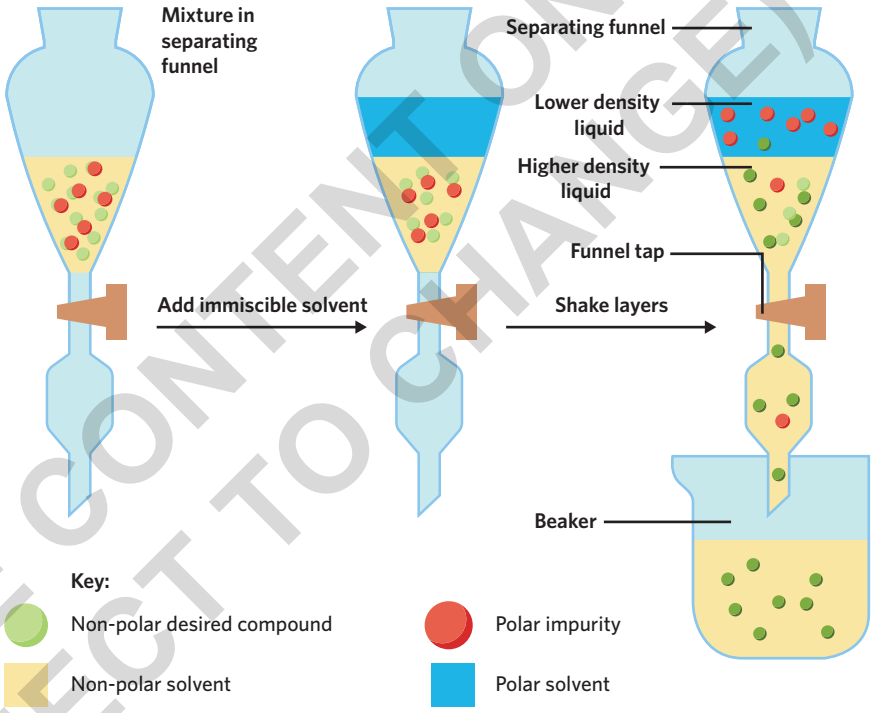


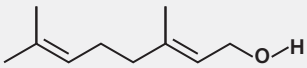
Figure 5 Example of solvent extraction

One of the primary uses of solvent extraction is to isolate oils from mixtures. Since oils contain long hydrocarbon chains and are hence largely non-polar, they dissolve well in non-polar solvents, and so can be separated from more polar impurities. To determine the optimal solvents to use for extraction, it is necessary to be able to identify the polar and non-polar regions of a molecule, and hence its overall polarity.

However, solvent extraction has its limitations. The process can be slow, and requires large volumes of solvents at an industrial scale. Solvent extraction is also ineffective at removing impurities with a similar polarity to the desired compound as they will likely dissolve to a similar extent in a given solvent, preventing them from being separated.

WORKED EXAMPLE 1

A cosmetics brand is looking to use solvent extraction to extract the compound geraniol (shown below), from roses. Would geraniol dissolve better in a more polar or non-polar solvent?



What information is presented in the question?

The structural formula of geraniol.

What is the question asking us to do?

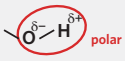
Determine whether geraniol would dissolve better in a polar or non-polar solvent.

What strategies do we need in order to answer the question?

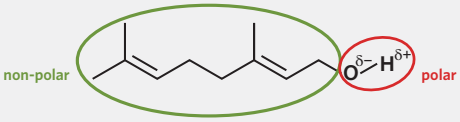
1. Identify any polar regions in the molecule.
2. Compare the relative size of the polar and non-polar regions of the molecule.
3. Assess the overall polarity of the molecule.

Answer

Since oxygen is significantly more electronegative than hydrogen, a polar bond exists between –O and –H in this compound. This forms a polar region around the hydroxyl group, shown in red.



The rest of the molecule consists only of carbon and hydrogen atoms (which have similar electronegativity), and so is considered non-polar, shown in green.



Since the polar (green) region appears much larger than the non-polar (red) region, geraniol is predominantly non-polar. Since 'like dissolves like', geraniol will hence likely dissolve better in a non-polar solvent than a polar solvent.

How are medicinal molecules purified after extraction?

As mentioned, the product of solvent extraction is often highly impure. To further purify this extract, a common method used is distillation, which involves the separation of liquids based on a difference in their boiling points.

Simple distillation can be used to separate two substances (usually liquids) with significantly different boiling points. This process, shown in figure 6, works by heating the mixture until the substance with the lower boiling point vaporises, transporting these vapours to a separate chamber, and then recondensing them, hence separating the two liquids. For example, simple distillation can be used to separate a mixture of water and ethanol, which is used to prevent skin infections. Since ethanol has a lower boiling point than water (78 °C vs. 100 °C), it can be vaporised at a lower temperature, separated from water, and recondensed. When heating fuels like ethanol, a heating mantle must be used (instead of a Bunsen burner) to minimise risk of explosion.

USEFUL TIP

Anti-bumping granules (also known as boiling chips) are added to the distillation mixture to distribute heat more evenly, producing smaller bubbles when the mixture boils and hence reducing the risk of explosion.

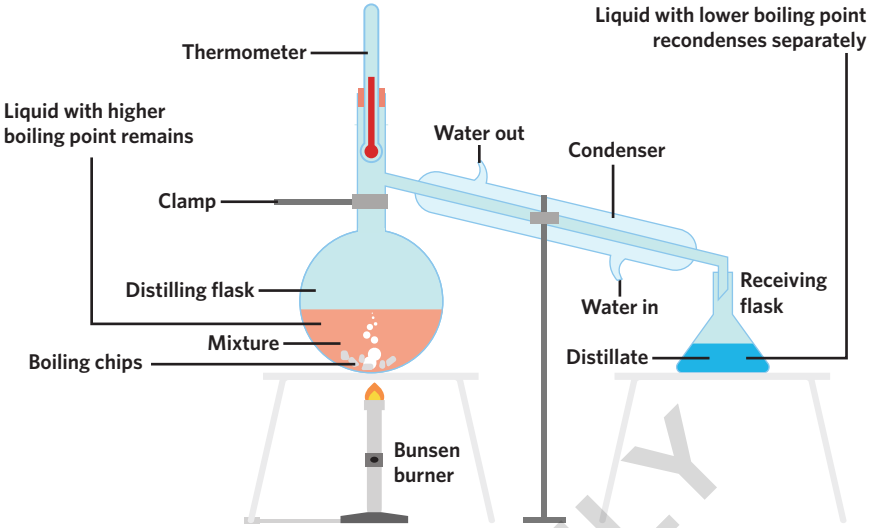


Figure 6 Simple distillation apparatus

However, some molecules are heat-sensitive, meaning that the high temperatures required for vaporisation can damage the structure of the molecule (a type of chemical decomposition). This is particularly true for compounds with high boiling points, such as oils, as simple distillation can alter their structure and hinder their medicinal properties.

As a result, a much more commonly used method for purifying compounds from plants is **steam distillation** (figure 7). In this process, water vapour:

- is pumped through the distillation apparatus
- reduces the temperature required to vaporise the substances in the mixture
- minimises decomposition of heat-sensitive compounds
- therefore preserves the desired product.

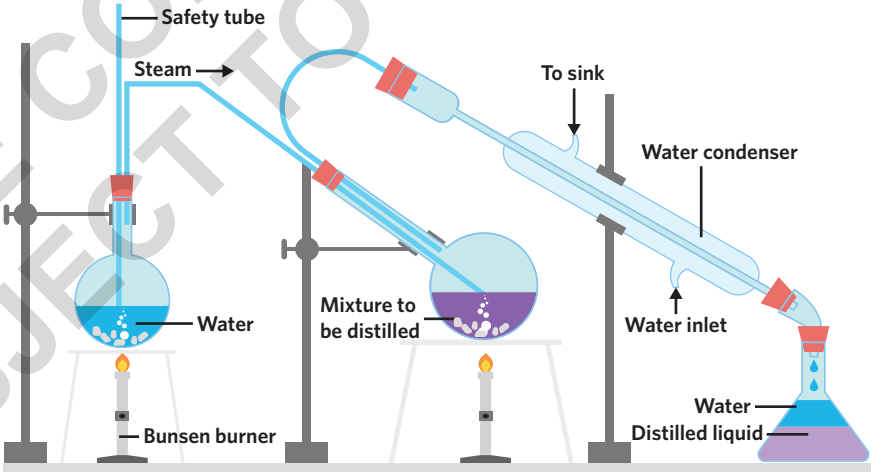


Figure 7 Steam distillation apparatus

Although boiling point is the lowest temperature at which a substance is present entirely in gaseous form, at lower temperatures, a portion of the substance is present as a gas. As a result of this, in the distillation process, a percentage of the substance with the higher boiling point will be vaporised and recondensed alongside the other, meaning that the product of distillation is never entirely pure. Accordingly, the distillation process is usually repeated many times to maximise the purity of the product, as outlined in figure 8.

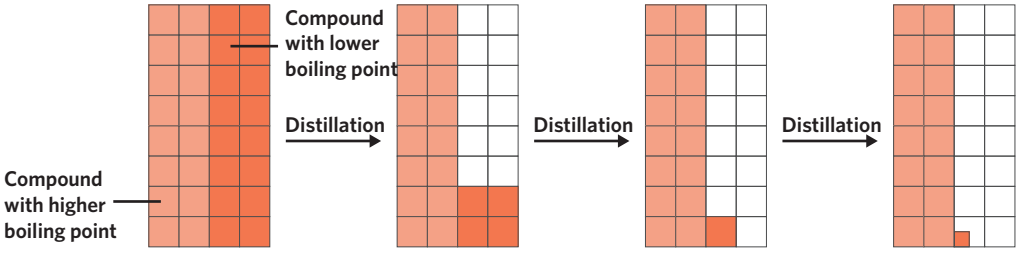


Figure 8 Representation of distillation, where three quarters of the remaining undesired compound is distilled at each stage

PROGRESS QUESTIONS

Question 1

An appropriate pair of solvents for use in solvent extraction is

A. heptane and hexane.

B. heptane and water.

C. water and methanol.

D. deionised water and seawater.

Question 2

Which is the most appropriate technique for separating hexane and octane?

A. Distillation

B. Decomposition

C. Solvent extraction

D. Isolation

Question 3

Why is steam distillation preferable to simple distillation for purifying oils?

A. Oils have high boiling points.

B. Oils are heat-sensitive.

C. Steam distillation prevents decomposition of oils.

D. All of the above

Medicinal organic molecules 4.2.13.1

A medicine is any substance that can be used to treat or cure an ailment. Many of the instrumental techniques studied in chapter 10 can be applied to medicines, enabling their structures and functional groups to be determined.

How can we identify medicinal molecules?

Whilst some medicines have been used and considered effective for thousands of years, it is only with the development of advanced analytical techniques that scientists have been able to determine the exact composition of active ingredients within medicines, and thus research exactly what makes these medicines effective. The analytical methods explored in chapter 10 can be employed for this.

This process can be explored through the case study of the emu bush, *Eremophila alternifolia*. Firstly, a mixture containing potential active ingredients is extracted from plants using solvent extraction (among other methods). Scientists predict potential compounds present in the mixture using chemical tests and prior knowledge. These potential compounds are then analysed using high-performance liquid chromatography (HPLC), and their respective chromatograms are compared to qualitatively determine which compounds are present in the mixture.

The chromatogram obtained for the emu bush extract is shown in figure 9.

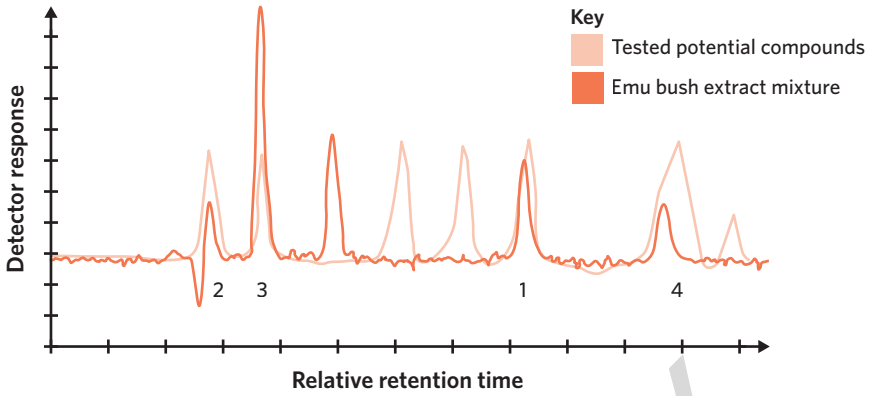


Figure 9 Sample HPLC chromatogram for emu bush extract and a number of potential compounds

Following this, the peak areas of the constituent compounds can be compared to quantitatively determine the relative percentage of each compound in the mixture. Finally, mass spectroscopy (MS), infrared spectroscopy (IR), and nuclear magnetic resonance spectroscopy (^{1}H-NMR and ^{13}C-NMR) are used to determine the functional groups and exact structures of the compounds present. Figure 10 displays the structures of each investigated potential active ingredient present in the emu bush extract.

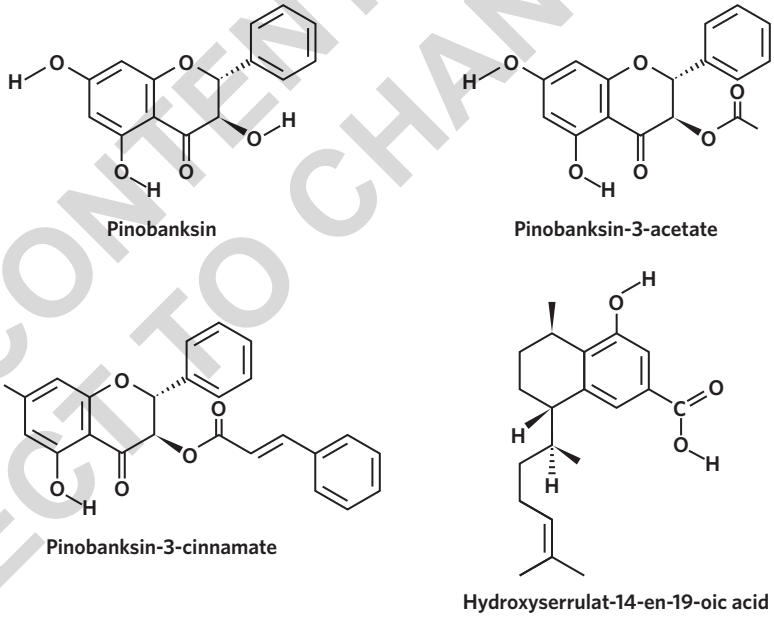


Figure 10 Structures of potential active ingredients in emu bush extract

As will be further discussed in lesson 11B, medicines often work by binding to specific receptors in the body. Medicinal molecules must have the correct structure and properties to align with these receptors and maximise electrostatic interactions. For example, if a medicinal molecule needs to bind to a positively charged receptor in the body, it should contain partially negatively-charged functional groups positioned to optimally bind to this receptor and fit the 3D shape of the receptor. This is illustrated in figure 11.

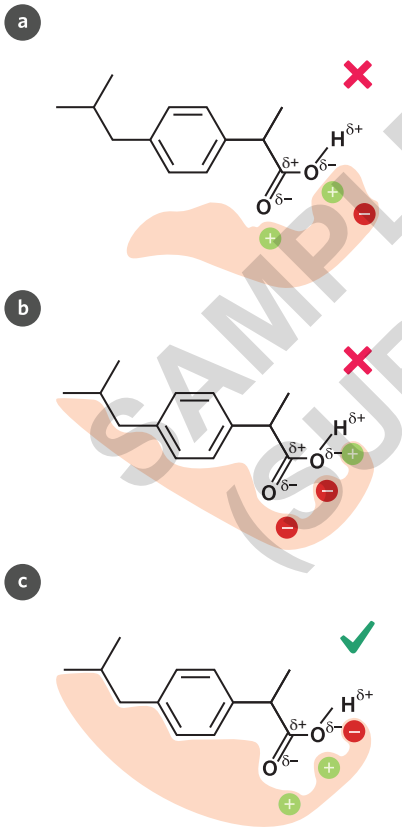


Figure 11 An ibuprofen molecule: **(a)** failing to bind to a receptor which is of unsuitable shape; **(b)** failing to bind to a receptor which has sites of unsuitable charge; and **(c)** binding to a receptor with the correct shape and charged sites

Although there is no 'universal' marker of medicinal molecules, many medicinal compounds:

- are relatively large molecules
- contain polar groups
- contain rings.

Rings may be saturated, with only single bonds between carbon atoms, or aromatic (like benzene, explored in lesson 7A), commonly represented with either alternating double and single bonds between carbon atoms or as a circle. Rings give these molecules lots of flat surfaces, which provide plenty of sticking points to receptors, and are also easily modifiable, so when developing medicines, chemists can add functional groups to help bind to specific receptors. Polar groups are also very important, as they enable some medicines to dissolve and be absorbed by our bodies and hence act on the desired receptors. An example of a medicinal molecule's 3D structure is shown in figure 12.

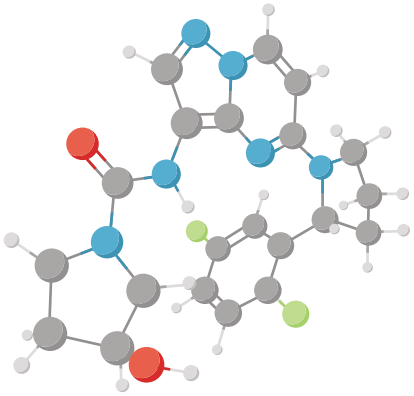


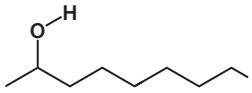
Figure 12 Ball-and-stick model of larotrectinib, an anti-cancer medicine with multiple polar groups and rings

PROGRESS QUESTIONS

Question 4

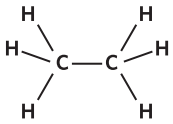
Which of the following structures is most likely to be a medicinal molecule?

A.

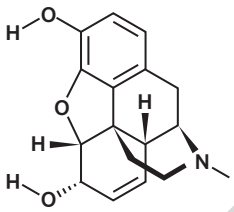


B.

C.

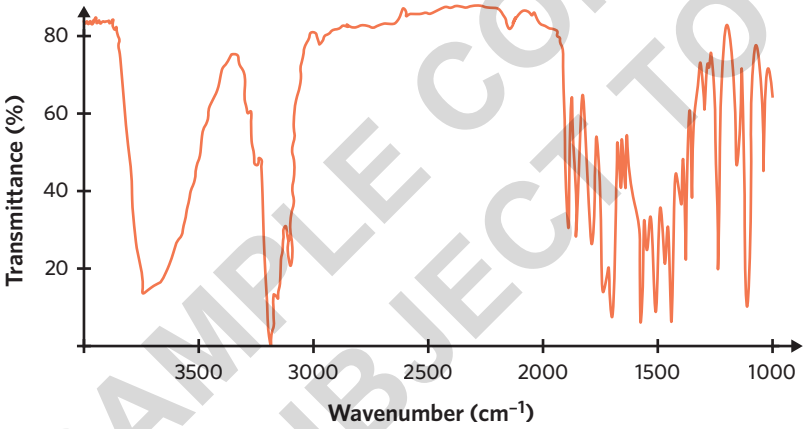


D.



Question 5

The following is an IR spectrum obtained for thymol, a plant compound noted for its antiseptic properties.



Which of the given groups is most likely to be present in thymol?

A. $-C{=}O$

B. $-NH_3$

C. $-OH$

D. $-COOH$

Chirality 4.2.14.1

Chirality is a property exhibited by some chemical compounds that is particularly important to the effectiveness of many medicinal molecules.

What is chirality?

Chiral compounds are compounds whose mirror image is not superimposable on the original compound. In other words, if an image of a chiral compound were mirrored and placed on top of the original image, the images would not align. Conversely, superimposable compounds (i.e. compounds that align with their mirror image) are described as **achiral compounds**. This concept is demonstrated through non-chemical objects in figure 13.

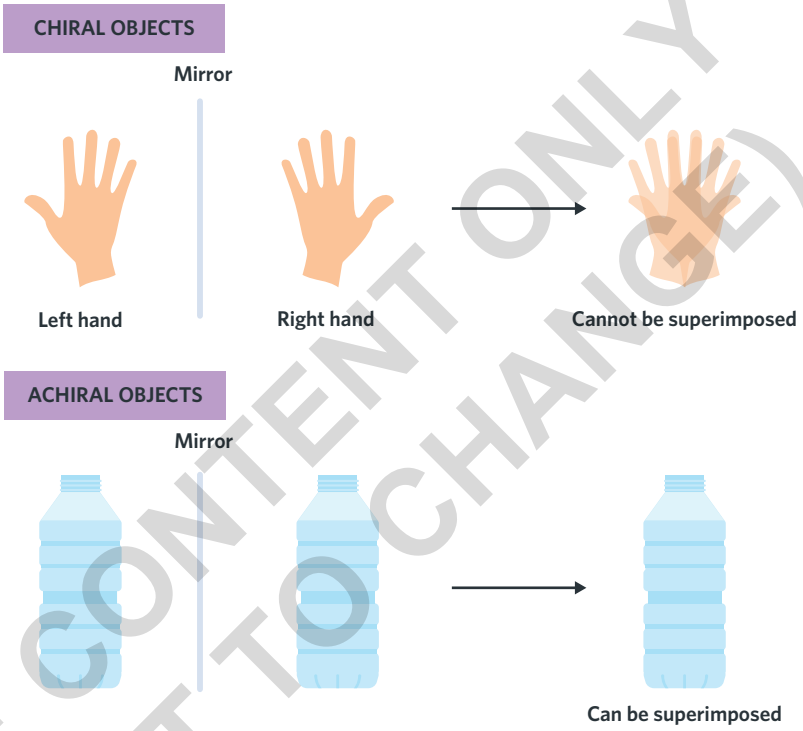


Figure 13 Chiral vs. achiral objects

Two isomers of a (chiral) molecule that are non-superimposable mirror images of each other are known as **optical isomers**, a type of stereoisomers (molecules with the same sequence of atoms but in a different spatial arrangement). For example, the green and red molecules shown in figure 14 are each other's mirror image, but are not superimposable on each other, making them optical isomers.

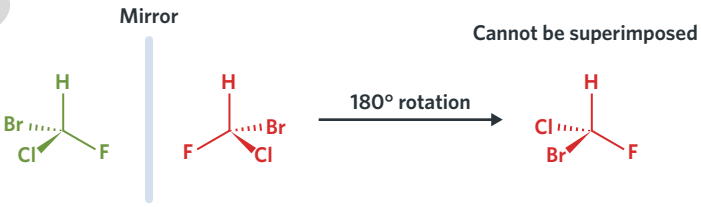


Figure 14 Non-superimposable mirror images of bromochlorofluoromethane

KEEN TO INVESTIGATE?

1 **How do different sugars rotate polarised light in different directions?**
Search YouTube:
Optical rotation of sugars – chirality

USEFUL TIP

Optical isomers are called 'optical' since they rotate polarised light in opposite directions (clockwise or anticlockwise).[1]

All chiral molecules contain at least one **chiral centre**, which is an atom covalently bonded to four different groups. In the context of organic compounds, a chiral centre is most frequently a carbon atom, often referred to as a chiral carbon. When identifying chiral centres, it is vital to look for an atom attached to four different environments, and not just a carbon atom attached to four atoms. The general representation of a chiral carbon is shown in figure 15.

Figure 15 General representation of a chiral carbon, where C* is the chiral carbon, and R, R′, R″, and R‴ represent different environments

MISCONCEPTION

'Chiral centres are always carbon atoms.'

Although chiral centres are almost always carbon atoms, atoms such as nitrogen, phosphorus, and sulfur can also be chiral centres in rarer cases. For example, the narcolepsy medicine modafinil is chiral around a sulfur atom.

For example, to determine whether halothane (figure 16), a once-commonly used general anaesthetic, is chiral, first we need to assess whether either of the two carbon atoms are chiral centres.

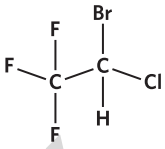


Figure 16 Structural formula of 2-bromo-2-chloro-1,1,1-trifluoroethane, commonly known as halothane

Figure 17a shows the four environments attached to C_1, which are −F, −F, −F, and −CBrClH. Since these are not all different (three are fluorine atoms) C_1 is not a chiral carbon. Figure 17b shows the four environments attached to C_2, which are −Br, −Cl, −H, and $-CF_3$. Since these are all different, C_2 is a chiral centre.

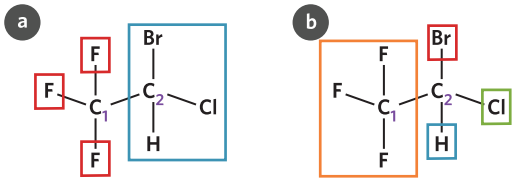


Figure 17 **(a)** Environments attached to C_1 and **(b)** environments attached to C_2.

This means that the structural formula shown for halothane is non-superimposable on its mirror image, and so halothane is a chiral compound centred at C_2. These two optical isomers of halothane, *S*-halothane and *R*-halothane are shown in figure 18.

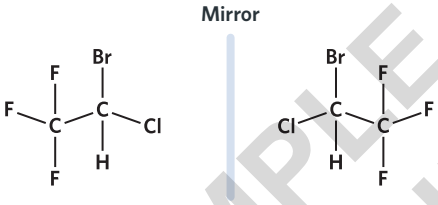


Figure 18 The two optical isomers of halothane; note that the two are mirror images of each other, yet one cannot be superimposed on the other, no matter which way it is rotated.

USEFUL TIP

Pairs of optical isomers may be labelled in different ways, including *S*– and *R*–, *L*– and *D*–, + and –, left-handed and right-handed, or clockwise and anticlockwise. These abbreviations are beyond the scope of the study design.[2]

KEEN TO INVESTIGATE?

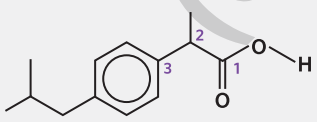
[2] **How are optical isomers named?**
Search: Naming enantiomers

USEFUL TIP

Any carbon atom with a double or triple bond coming from it (including carbon atoms in aromatic rings) cannot be a chiral centre, so can be discounted straight away when searching for chiral centres.

WORKED EXAMPLE 2

Ibuprofen is a chiral molecule used as an anti-inflammatory medication to treat pain and fever. Which of carbon atoms 1, 2, and 3 is a chiral centre?



What information is presented in the question?

The skeletal formula of ibuprofen.

Ibuprofen is a chiral molecule.

Three candidate carbon atoms for a chiral centre.

What is the question asking us to do?

Determine which of the carbon atoms labelled 1, 2, and 3 is a chiral centre.

Continues →

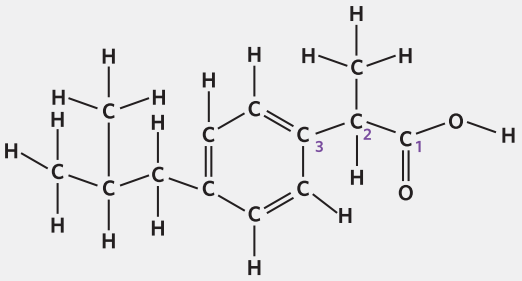
What strategies do we need in order to answer the question?

1. Draw the full structural formula of the molecule from the skeletal formula.
2. Identify the environments attached to each of the three possible carbon atoms.
3. Assess which of the three carbon atoms has four different environments attached to it.

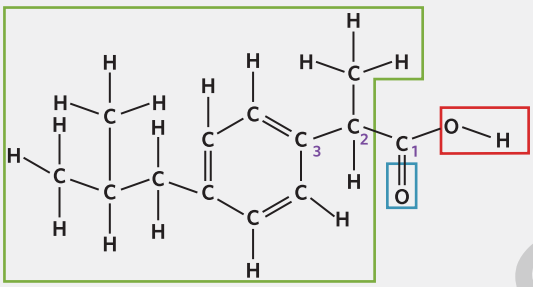
Answer

Recall that the hexagon around a continuous circle represents a six-carbon aromatic ring (like benzene). Since any carbon atom within an aromatic ring is never a chiral centre (as it is attached to a maximum of three unique environments), it is acceptable to represent an aromatic ring with alternating double and single bonds between carbon atoms for chiral centre identification.

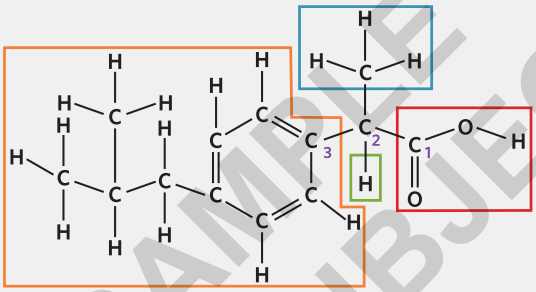
To identify chiral centres, first draw the full structural formula from the skeletal structure given.



Then, identify the environments attached to each of the three possible carbons, starting from carbon atom 1.

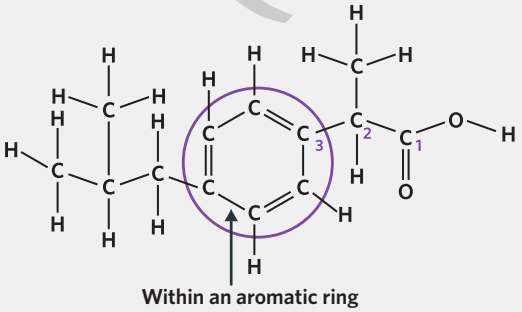


Due to the =O double bond, only three environments are attached to carbon atom 1, meaning carbon 1 is not attached to four different groups and, hence, cannot be a chiral centre. Next, consider carbon atom 2.



In this case, the four environments attached to carbon atom 2 (−H, $-CH_3$, −COOH, and −R, where R represents the remainder of the molecule) are all different, so carbon atom 2 is a chiral centre.

Lastly, consider carbon atom 3.



Since carbon atom 3 is within an aromatic ring, it is attached to a maximum of three environments and hence is not a chiral centre. Therefore, carbon atom 2 is a chiral centre, whereas carbon atoms 1 and 3 are not chiral centres.

Molecules may also have multiple chiral centres. In these cases, further steps are required to determine whether the molecule is chiral. In general, if a molecule with multiple chiral centres has a plane of symmetry (figure 19a), it is not chiral (it is achiral), as its mirror image is superimposable; if a molecule with multiple chiral centres has no plane of symmetry, it is chiral (figure 19b).

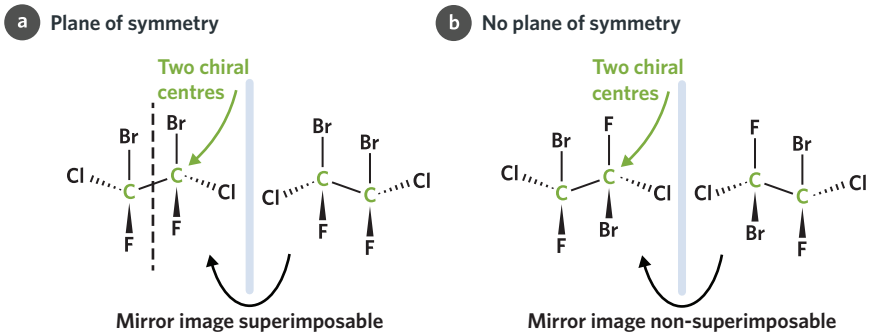
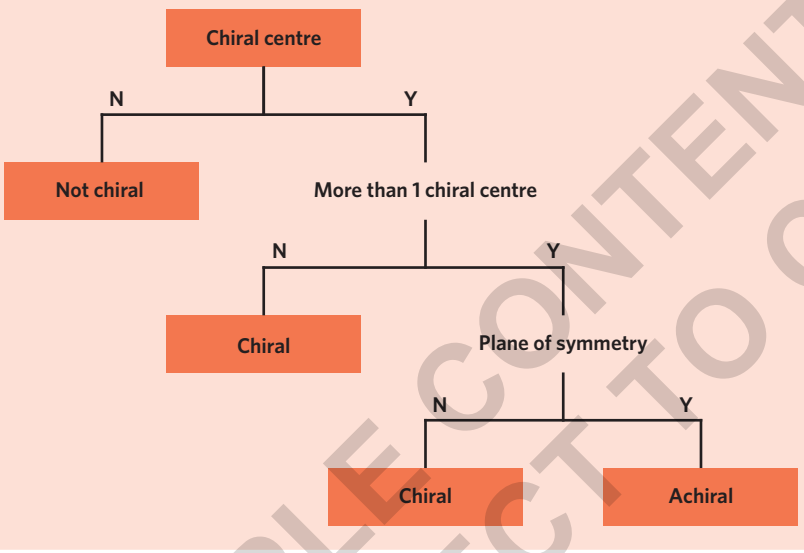


Figure 19 **(a)** Achiral and **(b)** chiral molecule with multiple chiral centres

STRATEGY

To determine if a molecule is chiral, use the following flowchart:



USEFUL TIP

All chiral molecules have at least one chiral centre; all molecules with exactly one chiral centre are chiral; but not all molecules with multiple chiral centres are chiral. In this way, chiral centres and chiral molecules are analogous to polar bonds and polar molecules respectively.

Why are optical isomers vital to the effectiveness of medicinal molecules?

Although optical isomers exhibit primarily the same physical properties, they may interact with other complex chemicals, such as those in our bodies, in vastly contrasting ways. For example, one optical isomer of a drug may have medicinal properties, yet the other optical isomer may have no effect at all, as demonstrated in figure 20.

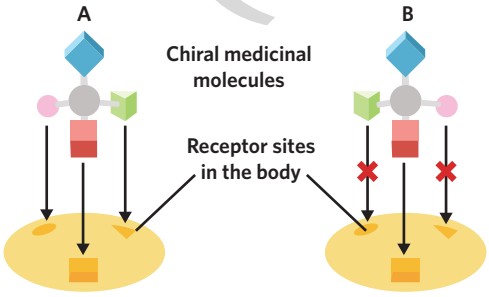


Figure 20 Optical isomer A binds to the receptor in the body, whereas optical isomer B does not.

KEEN TO INVESTIGATE?

[3] How did thalidomide's optical isomerism cause thousands of deaths and deformities?
Search YouTube:
Thalidomide: The Chemistry Mistake

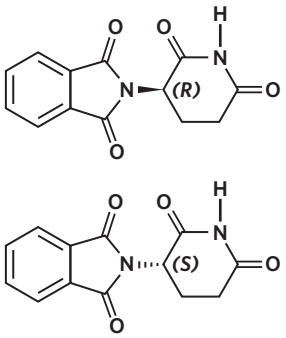


Figure 21 The two optical isomers of thalidomide; **(S)** (left) and **(R)** (right) denote the direction each optical isomer rotates a plane of polarised light.

An infamous example of this is the case of the medicine thalidomide (figure 21); its *R*- optical isomer is a safe and effective sedative, whereas its *S*- optical isomer causes tragic birth defects when administered to pregnant people.[3]

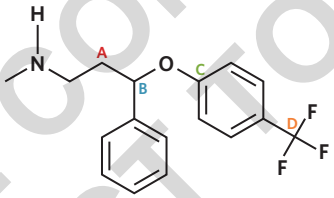
Optical isomers interact differently with the body because, as discussed, medicinal molecules must have a specific 3D shape and electrostatic interactions to bind with the desired receptors; the optical isomer of the medicine has a mirrored 3D shape and is thus unlikely to bind to the desired receptors. Instead, it may even bind to other receptors, often to negative effect. To draw an analogy, hands are optical isomers, as are gloves; a left glove generally fits a left hand well, yet wearing a right glove on a left hand will cause a very different (and likely uncomfortable) interaction. The same is true for many medicinal molecules: their two optical isomers may interact very differently with optically active receptors in the body.

As a result, it is often vital for pharmaceutical companies to select and isolate a specific optical isomer when producing medications, in order to ensure that the medicine acts as intended. To determine which optical isomer is present, we can test which direction the molecule rotates polarised light. However, many synthesis reactions of medicinal compounds produce a **racemate** or racemic mixture, a roughly 50/50 mixture of a compound's two optical isomers which is optically inactive (it does not rotate polarised light in a specific direction). Separation of a racemate is not always feasible, and this is a common cause of failure for potential medicines. Many medicines even 're-racemise' under biological conditions, meaning that the isolation of one optical isomer in the production process does not guarantee the safety or efficacy of the final product.

PROGRESS QUESTIONS

Question 6

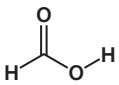
Which of the carbons shown is a chiral centre?

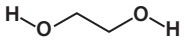


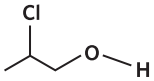
A. Carbon atom A
B. Carbon atom B
C. Carbon atom C
D. Carbon atom D

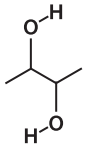
Question 7

Which of the following molecules is chiral?

A.


B.


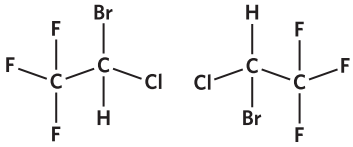
C.


D.


Continues →

Question 8

The two structures shown represent



A. structural isomers.

B. optical isomers.

C. the same compound.

D. neither isomers nor the same compound.

Question 9

Optical isomers of a medicine

A. bind with all receptors in the same way.

B. have identical physical properties.

C. always bind to different receptors from each other.

D. cannot always be separated from each other.

Theory summary

- The active ingredient in medicines is the compound that produces the desired effect on our body. For some medicines, the active ingredient is extracted from plants.
- Solvent extraction separates the desired compound from the source based on differing respective solubilities in two different, immiscible solvents.
- Once the desired compound has been extracted, it can be purified using distillation, a process in which the substance is heated and impurities are removed according to their different boiling points.
- Instrumental techniques – primarily HPLC, MS, IR, ^{1}H-NMR and ^{13}C-NMR – can be used to determine the structures of medicinal molecules and the typical functional groups present.
- Chiral molecules have a non-superimposable mirror image, and these two mirror images are referred to as optical isomers.
- A pair of optical isomers can be distinguished from each other by the direction in which they rotate a plane of polarised light.
- Often, two optical isomers of the same molecule have vastly different medicinal properties and degrees of effectiveness and safety, meaning that optical isomer selection is vital to the development and production of medicines.

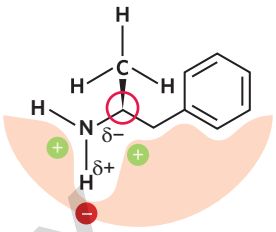
11A Questions

Mild Medium Spicy

Deconstructed

Use the following information to answer questions 10–12.

Dextroamphetamine is a medicinal compound used to treat ADHD (attention deficit hyperactivity disorder). The diagram shown is a simplified representation of the binding of dextroamphetamine to a receptor in the body.



Question 10 (1 MARK)

The carbon circled in the structural formula above is attached to

A. one unique environment.

B. two unique environments.

C. three unique environments.

D. four unique environments.

Question 11 (1 MARK)

Dextroamphetamine is

A. chiral, because its mirror image is superimposable.

B. chiral, because it contains exactly one chiral centre.

C. achiral, because it contains no chiral centres.

D. achiral, because it contains multiple chiral centres yet has a plane of symmetry.

Question 12 (3 MARKS)

Explain, with the aid of a diagram, whether optical isomerism could affect the ability of the compound to bind to this receptor in the body, and hence its effectiveness.

Exam-style

Question 13 (6 MARKS)

Tea tree leaves and the oil within them have been used by Aboriginal and Torres Strait Islander Peoples for thousands of years as a medicine to treat coughs and colds.

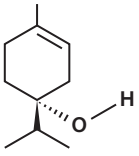
a. Explain briefly how 4 MARKS

i. tea tree oil could be extracted and purified (note: tea tree oil is sensitive to high temperatures).

ii. the compounds present in tea tree oil could be determined.

iii. the structures and functional groups of these compounds could be identified.

b. The major compound and potential active ingredient present in tea tree oil is terpinen-4-ol. 2 MARKS

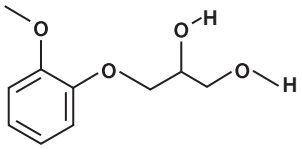


i. Identify the chiral centre in terpinen-4-ol.

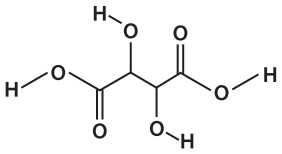
ii. Explain briefly how chirality can affect the effectiveness of medicinal molecules.

Question 14 (6 MARKS)

Guaifenesin and tartaric acid are two important compounds in cough medicines.



Guaifenesin



Tartaric acid

a. Identify the chiral centre(s) in: (2 MARKS)

i. Guaifenesin

ii. Tartaric acid

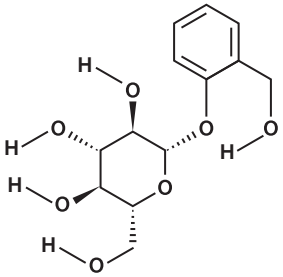
b. Identify and explain whether these molecules are chiral: (4 MARKS)

i. Guaifenesin

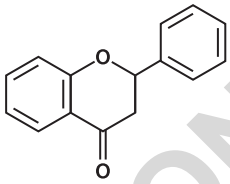
ii. Tartaric acid

Question 15 (5 MARKS)

Aspirin is a commonly prescribed painkiller which can be derived from salicin (shown below) in willow tree extract.



Salicin



Flavone

Another compound present in willow tree extract is flavone.

The boiling points of these compounds are given in the table below.

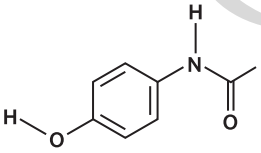
Compound	Melting point (°C)	Boiling point (°C)
Salicin	207	549
Flavone	97	367

a. Explain how solvent extraction could be used to isolate salicin from flavone, identifying particular solvents. 3 MARKS

b. Distillation can then be used to separate salicin from flavone. To what temperature should this mixture be heated to undertake distillation? Justify. 2 MARKS

Question 16 (8 MARKS)

Paracetamol is a medicine widely used to treat headaches and reduce fever. Its structure is shown.



a. Identify partial charges on any polar components in the molecule. 3 MARKS

b. Draw a diagram of a receptor to which paracetamol could bind, considering shape and electrostatic attractions. 2 MARKS

c. Is paracetamol chiral? Justify your answer. 2 MARKS

d. Predict whether the pictured molecule's mirror image would likely bind differently to a receptor in the body. 1 MARK

Key science skills

Question 17 🌶🌶 (5 MARKS)

Tony is seeking to use steam distillation to extract the compound eucalyptol from eucalyptus leaves he has collected. Assume that all other compounds in eucalyptus leaves have a higher boiling point than eucalyptol.

a. There are a number of environmental factors that Tony must take into consideration 2 MARKS

i. Give one environmental factor regarding collection of leaves that Tony should consider.

ii. Give one environmental factor regarding steam distillation itself that Tony should consider.

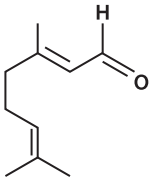
b. Outline a list of experimental method steps for Tony to use in his experiment. 3 MARKS

FROM LESSONS 12B & 12E

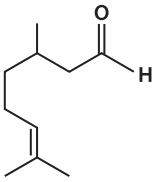
Questions from multiple lessons

Question 18 🌶🌶🌶 (7 MARKS)

Citral and citronellal are compounds present in oil extracted from lemon myrtle, a native Australian plant. These compounds have shown promising effectiveness as an insect repellent.



Citral

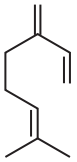


Citronellal

a. Give the systematic names of citral and citronellal. 2 MARKS

b. Evaluate and explain whether citral and citronellal could easily be separated from each other using solvent extraction or steam distillation. 3 MARKS

c. One impurity often found in lemon myrtle is myrcene.



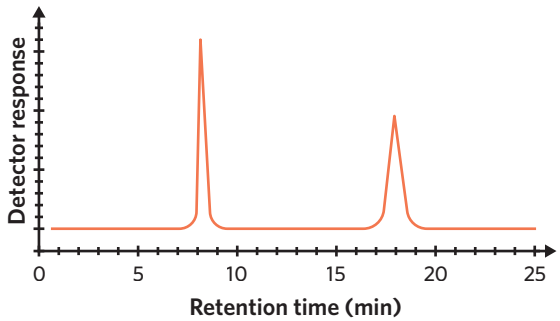
Myrcene

Explain how myrcene could be removed from a citral/citronellal mixture. 2 MARKS

FROM LESSONS 7B & 7C

Question 19 🌶🌶🌶 (10 MARKS)

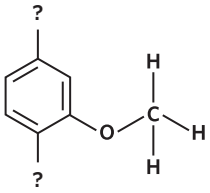
A group of researchers are investigating the properties of vanilla essence, a plant extract believed by some to have calming properties. Initially, HPLC is performed to determine the major compounds present. The HPLC results for vanilla extract, as well as those for some candidate compounds tested under identical conditions, are shown below.



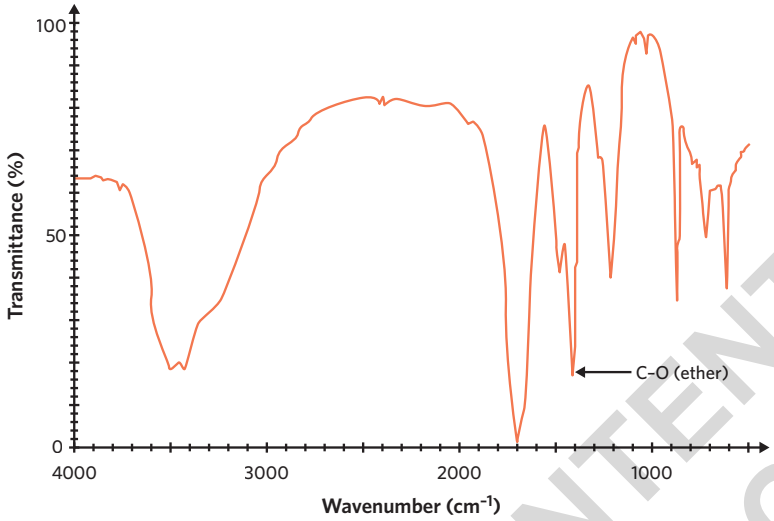
Compound	Retention time (mins)
Phenol	7
Vanillin	8
Coumarin	18
Glycerol	20

a. Besides vanillin, use the information provided to identify one other compound present in vanilla essence. Explain your answer. 2 MARKS

b. The researchers conduct a number of preliminary tests. From these, they determine that vanillin has empirical formula $C_xH_xO_3$ and the partial structure shown:

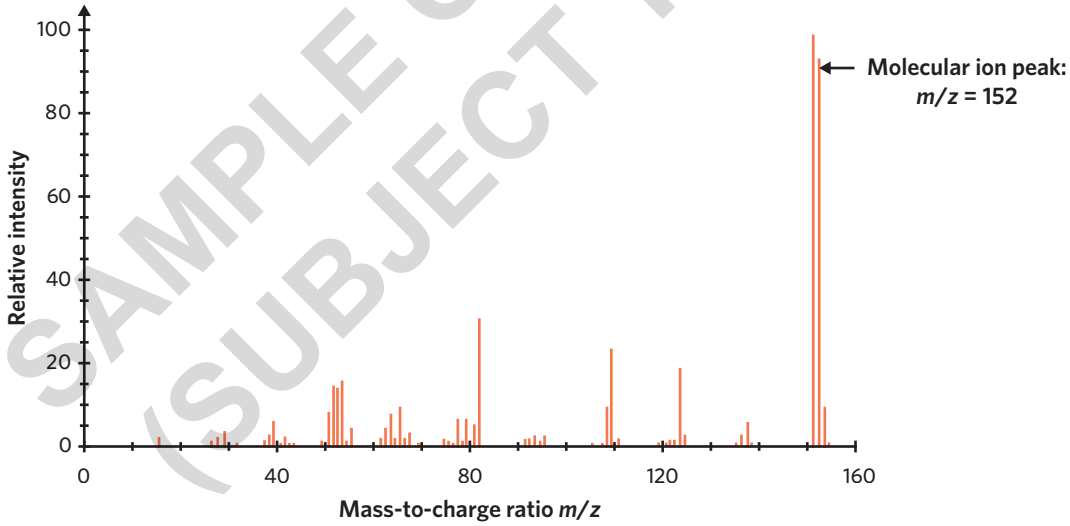


Vanillin was then analysed using infrared spectroscopy, producing the spectrum shown.



Identify two functional groups (besides the C–O–C ether group, labelled on the IR spectrum) potentially present in vanillin. Justify your choices using the information presented in the IR spectrum. 4 MARKS

c. The mass spectrum for vanillin was also determined.



Identify the molecular mass of the compound. 1 MARK

d. Using all the information provided, give the molecular formula and draw a possible skeletal formula of vanillin. 3 MARKS

FROM LESSON 10F

11B Enzymes and medicines

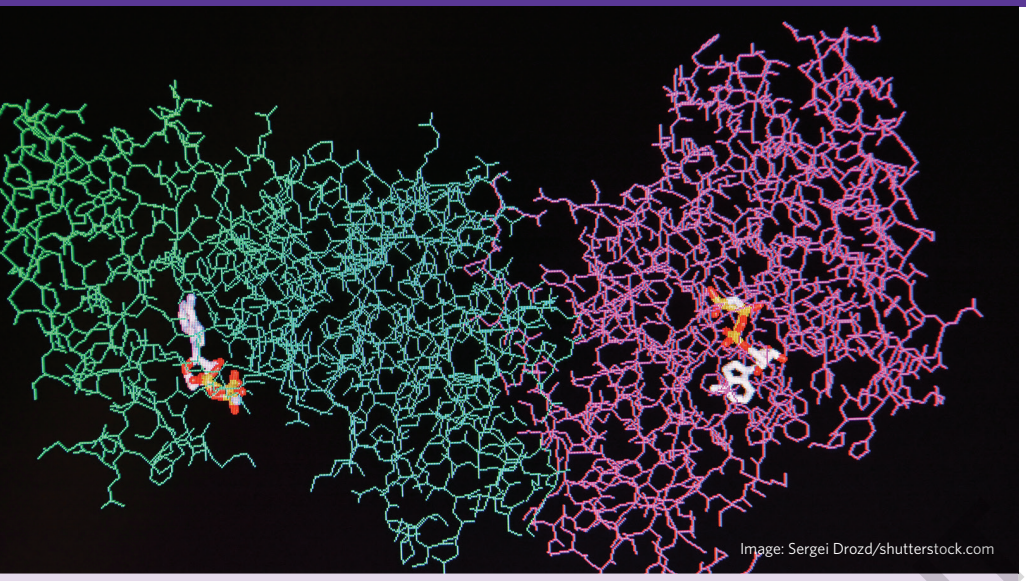


Image: Sergei Drozd/shutterstock.com

How do some medicines actually work?

There are thousands of different **enzymes** found in human cells that are essential for a healthy life. These are often very complex molecules, and computers are often used to visualise these structures. As enzymes are classified as proteins, we will look at the different structural levels and how changes in conditions affect these structures, including how medicinal enzyme inhibitors control the catalytic activity of reactions in the body.

KEY TERMS AND DEFINITIONS

Acidic amino acid amino acid with a carboxyl group in its side chain

Active site region of an enzyme where the substrate molecule binds to the enzyme and undergoes a chemical reaction

Basic amino acid amino acid with an amino group in its side chain

Competitive inhibitor molecule that competes with the substrate for binding to an active site in an enzyme

Denaturation process where proteins lose their quaternary, tertiary and/or secondary structure due to factors such as pH and temperature change

Deprotonation loss of a proton

Enzymes protein-based catalysts in living systems

Enzyme-substrate complex the unit which has the substrate bound to the active site of an enzyme

Lock-and-key model theory of enzyme-substrate binding where the substrate perfectly fits the active site of the enzyme

Optimal temperature temperature at which enzyme activity is at its greatest

Polypeptide chain chain of amino acids bonded by amide links (peptide bonds)

Primary structure linear sequence of covalently bonded amino acids in a polypeptide chain

Protonation gain of a proton

Quaternary structure combination of two or more interacting tertiary chains

Secondary structure arrangement of a primary protein structure in a way that results in an α-helix or β-pleated sheet due to hydrogen bonding

Substrate molecule which an enzyme acts upon

Tertiary structure overall three-dimensional structure of a protein

Zwitterion neutral molecule that has a positively charged $-NH_3^+$ and a negatively charged $-COO^-$ on the number two carbon

STUDY DESIGN DOT POINT

- enzymes as protein-based catalysts in living systems: primary, secondary, tertiary and quaternary structures and changes in enzyme function in terms of structure and bonding as a result of increased temperature (denaturation), decreased temperature (lowered activity), or changes in pH (formation of zwitterions and denaturation)
- medicines that function as competitive enzyme inhibitors: organic molecules that bind through lock-and-key mechanism to an active site preventing binding of the actual substrate

11A — 11B

- 4.2.15.1 The different protein structures
- 4.2.15.2 Principles of enzymes
- 4.2.15.3 Effect of temperature on enzyme function
- 4.2.15.4 Effect of pH on enzyme function
- 4.2.16.1 Medicinal enzyme inhibitors

ESSENTIAL PRIOR KNOWLEDGE

- 2-amino acid (α-amino acid)
- Amphiprotic
- 4A Rate of reaction

See questions Xx – Xx.

The different protein structures 4.2.15.1

As we learned in lesson 8A, proteins are made up of repeating units called amino acids. These building blocks are responsible for the four main types of structures found in proteins:

- primary
- secondary
- tertiary
- quaternary.

How are the four types of protein structure formed?

Primary structure

The simplest level of protein structure, the **primary structure**, is a sequence of amino acids linked by covalent bonds (called either amide links, amide bonds or peptide bonds) in a linear **polypeptide chain** (figure 1). As there are 20 different types of amino acids, a number of different polypeptide chain combinations can be formed.

USEFUL TIP

Amino acids are linked by a special type of covalent bond called an amide bond; this bond is a functional group and can also be referred to as an amide linkage or a peptide bond.

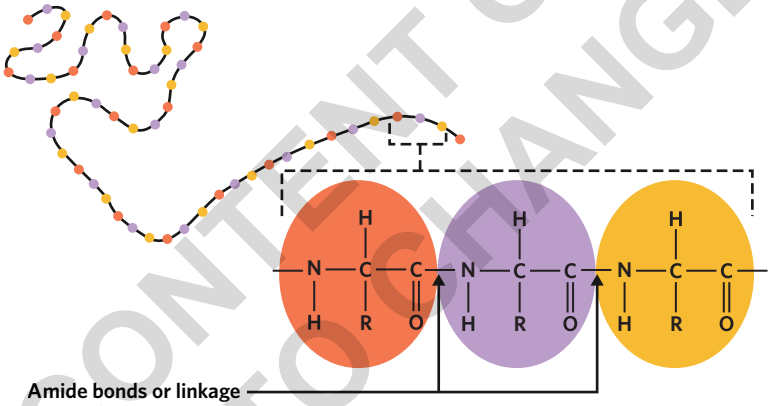


Figure 1 Covalent bonds between carbon and nitrogen create the primary structure in proteins.

Secondary structure

The next level of protein structure, the **secondary structure**, occurs when the polypeptide chains that form the primary structure fold into different shapes as a result of hydrogen bonding within the polypeptide chain. There are two main types of secondary structures:

- The α-helix structure is stabilised by the hydrogen bonds formed between the oxygen of the C=O group in each peptide bond and the hydrogen of the N-H group in the peptide bond four amino acids below it in the helix (figure 2.1).
- A β-pleated sheet is formed by linking two or more adjacent sections of the polypeptide by hydrogen bonds between the oxygen in one peptide bond and the hydrogen in the other peptide bond (figure 2.2).

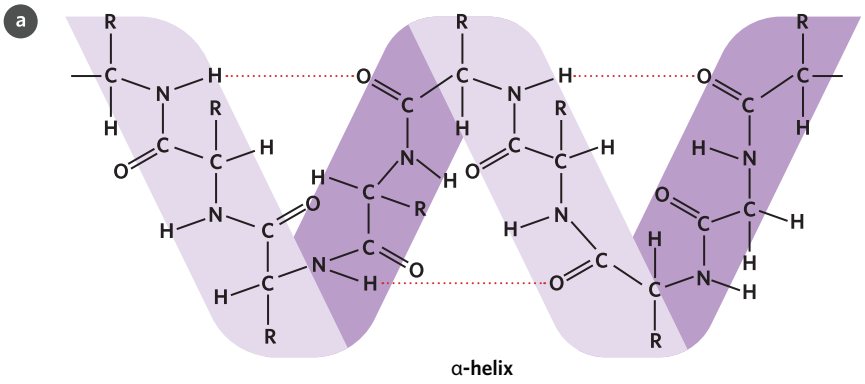


Figure 2.1 Hydrogen bonds (dotted red lines) create the secondary structure **(a)** α helix

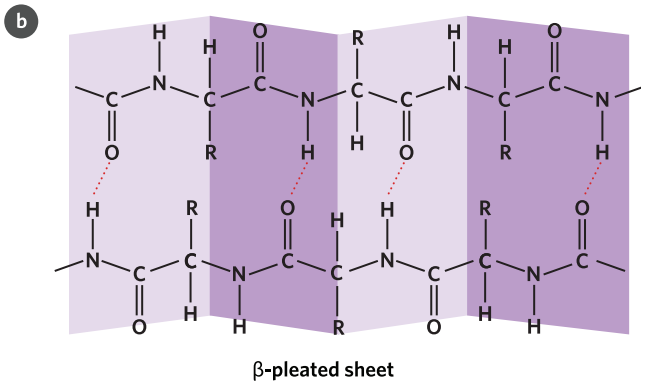


Figure 2.2 Hydrogen bonds (dotted red lines) create the secondary structure **(b)** β-pleated sheet.

Tertiary structure

The **tertiary structure** is the overall 3D shape of a polypeptide chain. A tertiary structure is stabilised by a combination of the forces shown in table 1.

Table 1 Forces that hold the tertiary structure of a protein together

Type of force	Example of attractions (figure 3)	Energy required to break attraction (kJ mol^{-1})
Ion-ion interactions	a) NH_3^+ and COO^- on adjacent side chains	Varies greatly: ~100-600
Disulfide bridges (a type of covalent bond)	b) Two cysteine –SH side chains only	~250
Hydrogen bonds	c) N and H, O and H	~20
Dispersion forces	d) Non-polar side chains	~1-5

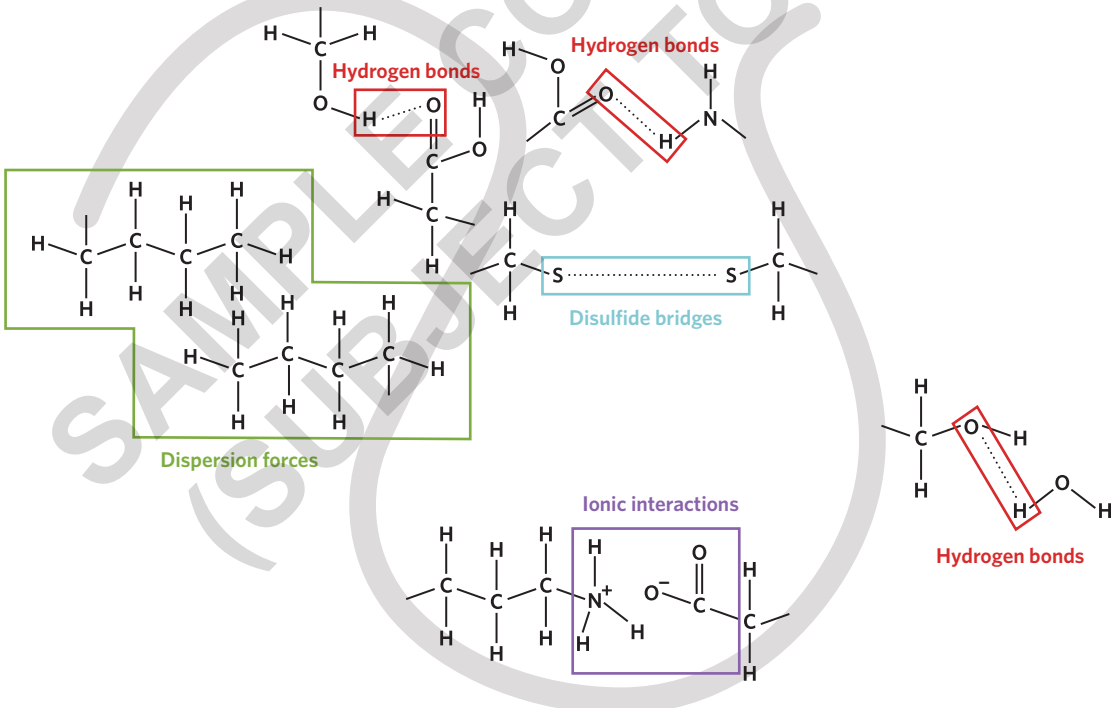


Figure 3 Different combinations of electrostatic forces of attraction create the tertiary structure.

Not all tertiary structures will contain each type of electrostatic force of attraction; it will depend on the type of side chain present in the amino acids. The tertiary structure of a protein is considered to be the functional structure of protein; hence, proteins will lose their functions if their tertiary structures are disrupted.

The unique properties of each side-chain – and thus the many different interactions possible between them – give rise to the vast range of structures and functions of proteins in the body.

Quaternary structure

The **quaternary structure** comprises the combination and interactions between two or more tertiary chains (figure 4). It is important to note that not all proteins have quaternary structures.

USEFUL TIP

Although dispersion is the weakest force in general, it actually has the largest effect on protein folding. Recall that dispersion strength increases as molecule size increases. Proteins are very large molecules, meaning dispersion forces have significant effects on the tertiary and quaternary structures.

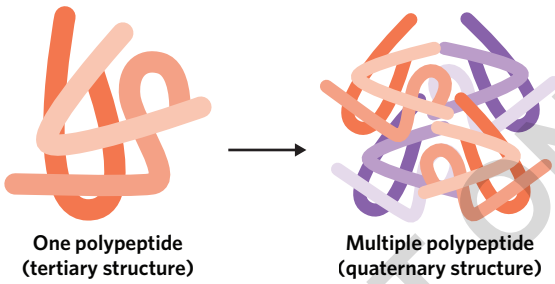


Figure 4 Quaternary structures are held together by the same forces as the tertiary structure.

PROGRESS QUESTIONS

Question 1

Aside from the 'R' side chain, the functional groups found in an amino acid are

A. amino and hydroxyl.
B. amino and carboxyl.
C. carbonyl and esters.
D. carboxyl and amide.

Question 2

The type of force(s) present in the tertiary structure of a protein are

A. dispersion.
B. ion-ion.
C. covalent.
D. All of the above

Question 3

When referencing the structures of proteins, hydrogen bonds can be found only in

A. primary structures.
B. α–helices and primary structures.
C. primary structures and tertiary structures.
D. α–helices, β–pleated sheets, tertiary structures and quaternary structures.

Principles of enzymes 4.2.15.2

Enzymes are biological catalysts made of proteins that play an essential role in the functioning of the human body.

How do enzymes alter the rate of reaction?

Enzymes are crucial to the body's function as they catalyse chemical reactions necessary to sustain life that would otherwise occur too slowly. Specifically, an enzyme catalyses a reaction by providing an alternate reaction pathway that requires a lower activation energy. This has been covered in chapter 4 and is shown in the energy profile diagram in figure 5.

An enzyme functions by binding to the reactant(s) of a reaction, known as the **substrate**. The region of the enzyme to which the substrate binds is known as the **active site** (figure 6).

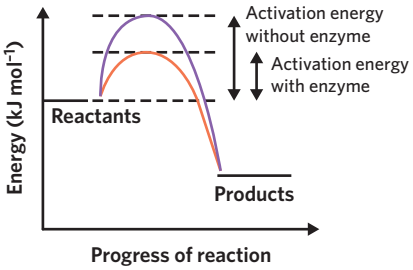


Figure 5 Enzymes can lower the activation energy of specific reactions.

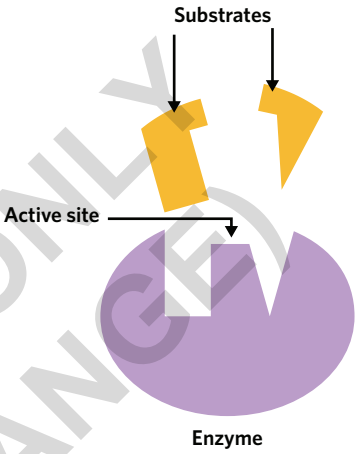


Figure 6 The general model of an enzyme and substrates

MISCONCEPTION

'Enzymes are used up in reactions.'

Enzymes are not used up in the reactions they catalyse and do not change the yield of a reaction - they simply speed up the rate of reaction.

USEFUL TIP

The word 'bind' applies to electrostatic forces of attraction that are both reversible (temporary attraction) and irreversible (bond).

Unlike inorganic catalysts, enzymes are highly specific in that each enzyme is only responsible for catalysing one or a small number of chemical reactions. This explains why there is an immense number of different enzymes catalysing reactions in the body.

The size, shape, chemical behaviour, and three-dimensional nature of the active site is very important to the functioning of the enzyme, as for the substrate to successfully bind to the active site, the substrate must form a temporary bond with the enzyme.

One of the major models[1] that scientists have developed to explain enzyme activity is the **lock-and-key model** which, as the name suggests, is where the substrate fits perfectly into the active site of the enzyme, just as a key perfectly fits a lock. As shown in figure 7, the shape of the substrate is perfectly complementary to the shape of the enzyme's active site. After successful binding, the entire structure is known as an **enzyme-substrate complex**. As a complex, the enzyme's action will begin, which may catalyse a reaction breaking down larger molecules into smaller ones, or building larger molecules from smaller ones. After the reaction has occurred, the enzyme will release the substrate and it is free to bind to a new substrate.

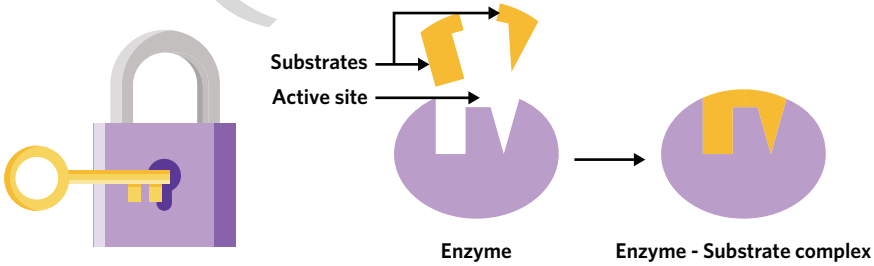


Figure 7 The lock-and-key model

USEFUL TIP

Enzymes can be categorised as either positive or negative catalysts. A positive catalyst increases the rate of a reaction, whilst a negative catalyst decreases the rate. Negative catalysts are also known as inhibitors.

KEEN TO INVESTIGATE?

1 **What is the other main model used to explain the function of enzymes?**
Search: Models of enzyme function

PROGRESS QUESTION

Question 4

The lock-and-key model states that

A. an enzyme will change the shape of its active site to fit the substrate.

B. the substrate perfectly fits the enzyme's active site.

C. an enzyme cannot differentiate between isomers.

D. an enzyme can only be used once.

Effect of temperature on enzyme function 4.2.15.3

Enzyme activity is heavily dependent on the temperature of the chemical reaction.

How do different temperatures affect the function of enzymes?

As discussed in lesson 4A, an increase in temperature causes an increase in the rate of reaction. However, the activity of enzymes does not always increase in response to an increase in temperature.

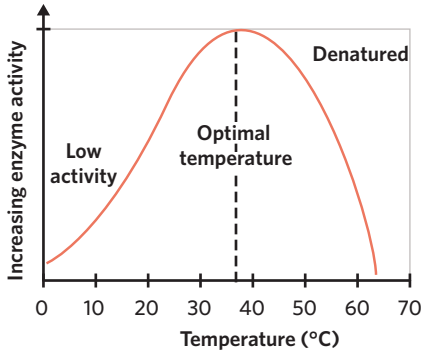


Figure 8 Graph of enzyme activity and temperature in humans

As we can see in figure 8, as temperature increases, there is a general increase in enzyme activity. This is consistent with our knowledge of reaction rates, because at higher temperatures, not only is the average kinetic energy of the particles greater, but there are also more collisions per unit of time between enzymes and their respective substrate. However, after reaching the **optimal temperature** – the temperature at which an enzyme's activity is at its greatest – the enzyme activity begins to decrease rapidly, and eventually reaches zero. We can explain this in terms of the chemical composition of enzymes:

- Enzymes are proteins and will therefore be denatured at high temperatures.
- **Denaturation** is the process whereby the secondary, tertiary, and quaternary (if applicable) structures of the enzyme, which define the shape of the active site, are disrupted by the increase in temperature (figure 9).
- Lower temperatures do not denature the enzyme; rather, activity is minimised and protein stability is maximised.

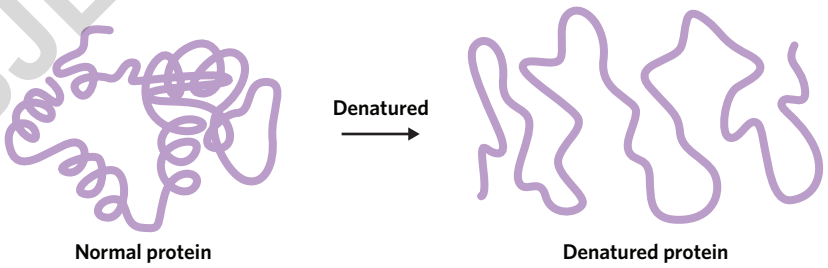


Figure 9 Denaturation of a protein's structure at high temperatures

Denaturation causes irreversible structural damage, meaning the enzyme is unable to function again; however at lower temperatures, the enzyme is not irreversibly damaged. Therefore, the function of an enzyme is very sensitive to temperature changes.

PROGRESS QUESTIONS

Question 5

When an enzyme is heated to 75 °C, the part of the enzyme's structure that will be least affected is the

A. primary structure.

B. secondary structure.

C. tertiary structure.

D. quaternary structure.

Question 6

An enzyme

A. is denatured at low temperatures.

B. is consumed in a reaction.

C. is always active.

D. is usually specific to a certain substrate.

Effect of pH on enzyme function 4.2.15.4

pH can denature an enzyme's tertiary (and quaternary if present) structure, impacting its binding capability to a substrate. Enzyme activity is also dependent on the pH of the environment in which it functions due to the effect of pH on the charges of certain functional groups.

How do changes in pH affect the function of an enzyme?

As we have learned so far, the active site of an enzyme binds to a substrate. Figure 10 illustrates the important role that the side groups of amino acids play in this temporary act of binding.

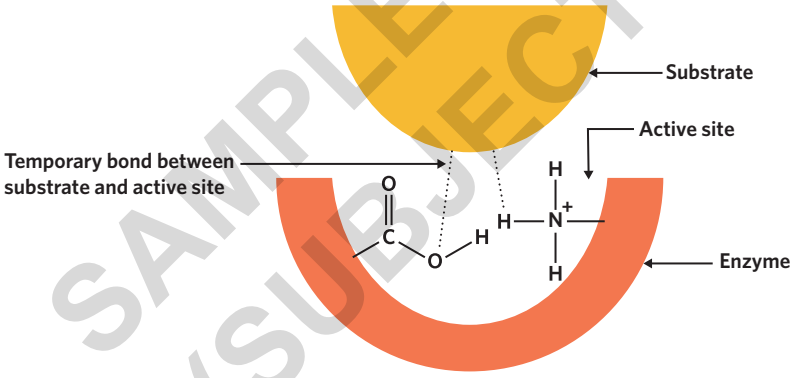


Figure 10 Interaction between substrate and amino acid side groups in the active site

The properties of the side groups on different amino acids are very important – in particular, whether they are acidic or basic.

An **acidic amino acid**, such as aspartic acid in figure 11, has a carboxyl group in its side chain, as circled on the figure.

As such, in a very basic solution where the pH is greater than 13, each carboxyl group will lose a hydrogen atom, giving aspartic acid a doubly negative charge as shown in figure 12. This process, known as **deprotonation**, occurs when a large number of OH^- ions are present.

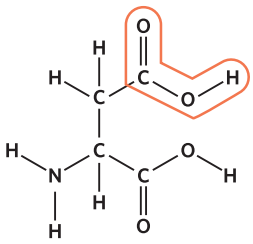


Figure 11 Aspartic acid has a carboxyl functional group in its side chain.

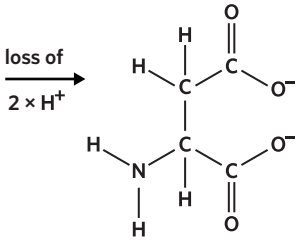


Figure 12 The deprotonation of aspartic acid from figure 11 to give a net charge of −2

Furthermore, a **basic amino acid**, such as lysine in figure 13, has an amino functional group in its side chain, circled on the figure.

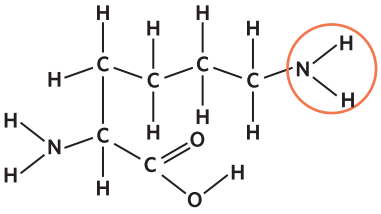


Figure 13 Lysine has an extra amino functional group.

In a very acidic solution, where the pH is less than 1, the two amino groups in lysine will each gain a proton and become doubly positively charged, as shown in figure 14. This process, termed **protonation**, occurs when a large number of H^+ ions are present.

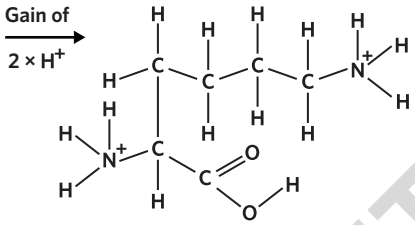
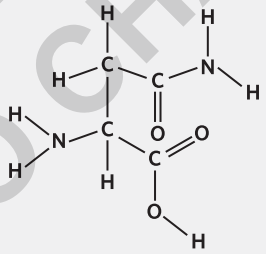


Figure 14 The protonation of lysine from figure 13 to give a net charge of +2

WORKED EXAMPLE 1

The structural formula of the amino acid asparagine is shown below. Draw the structural formula of asparagine at a pH of 1.0.



What information is presented in the question?

The structure of the amino acid asparagine.

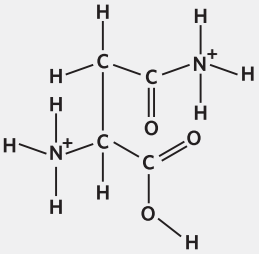
What is the question asking us to do?

Draw the structure of the amino acid when the pH is 1.0.

What strategies do we need in order to answer the question?

1. Determine whether the concentration of H^+ or OH^- is high when the pH is low.
2. Based on step 1, determine whether the NH_2 group or COOH group is altered.
3. Draw the structure of the amino acid based on step 2.

Answer



When the pH is low, an amino acid has as many H^+ added to it as possible. All bonds must be shown in a structural formula. The asparagine now has an overall net charge of +2.

A change in the pH in the enzyme's environment may alter enzyme activity due to:

- Changes in the charges of the side chains of an enzyme's constituent amino acids, shown in figure 10 and figure 12.
- Different interactions between an enzyme and its substrate due to disruption to the enzyme's tertiary structure.
- Secondary, tertiary, and quaternary forces that maintain the structures being disrupted causing denaturation.

Consequently, most enzymes function only in a narrow pH range.

How are zwitterions formed?

All amino acids are amphoteric, meaning they can accept or donate a proton depending on the pH of the environment. In an environment of neutral pH, where $[H^+] = [OH^-]$, neither the protonated or deprotonated species dominates. Instead, the NH_2 group can accept a H^+, forming NH_3^+, and the COOH group can donate its H atom, forming COO^-. This results in the formation of a **zwitterion** due to the presence of both a negative and positive charge on functional groups attached to the second carbon; hence, zwitterions have no net charge. This idea is summarised in figure 15. It is important to note that different amino acids change in structure at a different pH level.[2]

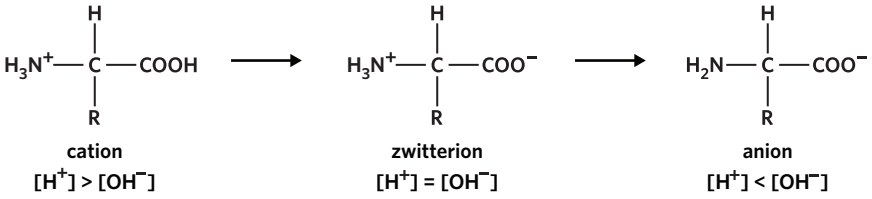


Figure 15 The structure of an amino acid depends on the pH of the solution.

KEEN TO INVESTIGATE?

[2] **What is the isoelectric point of zwitterions?**
Search YouTube:
Are zwitterions charged?

WORKED EXAMPLE 2

Met-enkephalin is a small protein found in the central nervous system and the gastrointestinal tract of the human body. Which of the following are the correct structures for the two terminal ends of met-enkephalin at a very low pH?

A.	$-NH_2$	$-COOH$
B.	$-NH_2$	$-COO^-$
C.	$-NH_3^+$	$-COO^-$
D.	$-NH_3^+$	$-COOH$

What information is presented in the question?

The pH is low and the chemical is a protein and so has an amino acid structure.

What is the question asking us to do?

Identify the terminal groups of this protein.

What strategies do we need in order to answer the question?

1. Determine whether the concentration of H^+ or OH^- is high when the pH is low.
2. Based on step 1, determine whether the NH_2 group or COOH group is altered

Answer

D. α-amino acids or 2-amino acids have the general structure $H_2NCH(R)COOH$. At very low pH, i.e. in acidic solutions, basic $-NH_2$ groups become protonated to form $-NH_3^+$ groups. At low pH $-COOH$ groups are unaffected. So, the correct structures for the terminal ends of met-enkephalin and any protein are $-NH_3^+$ and $-COOH$.

Adapted from VCAA 2016 exam Multiple choice Q11

PROGRESS QUESTIONS

Question 7

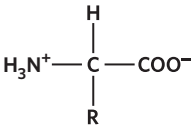
Which of the following statements is **incorrect** regarding enzymes?

A. Enzyme activity differs with a change in temperature.
B. Enzymes are biological catalysts.
C. Enzymes are consumed in chemical reactions.
D. Enzyme activity differs with a change in pH.

Continues →

Question 8

The following structure is an example of a



A. tertiary structure.

B. quaternary structure.

C. zwitterion.

D. protein.

Medicinal enzyme inhibitors 4.2.16.1

Many of the small-molecule medicines approved by the Therapeutic Goods Administration (TGA - Australia) are **competitive inhibitors** of enzymes. These molecules can 'mimic' an enzyme's usual substrate by being similar in shape and chemical property, and therefore fit into the active site and block the binding of the substrate.

How do some enzyme inhibitors work?

Angiotensin-Converting-Enzyme Inhibitors (ACEIs)

ACEIs are some of the most widely used enzyme inhibitors in modern medicine. They are used to treat hypertension (also known as high or raised blood pressure), heart failure, diabetes, and kidney disease.

Mechanism of action

As the name suggests, ACE inhibitors work by inhibiting the angiotensin-converting enzyme that leads to smooth muscle contraction (figure 16). This is the cause of hypertension, a condition in which the blood vessels have consistently raised pressure, which is a major cause of heart-attacks and strokes.

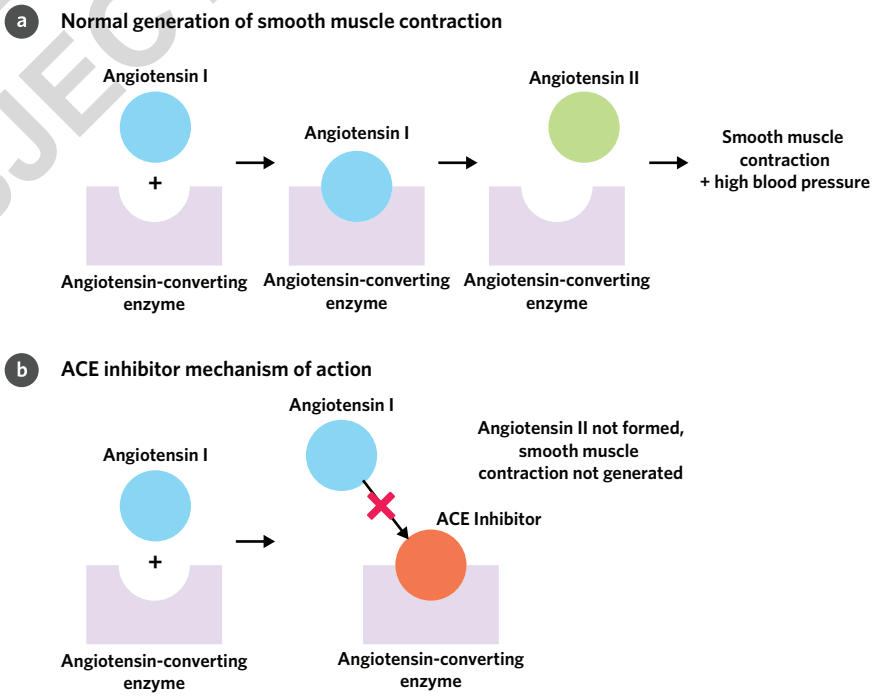


Figure 16 **(a)** Using the lock-and-key model to show the normal process **(b)** and mechanism of action of ACEIs

Donepezil

Donepezil is a competitive, reversible enzyme inhibitor used for the treatment of Alzheimer's. Alzheimer's is a brain disease that gradually destroys memory and cognitive skills. Alzheimer's is associated with decreased acetylcholine levels and donepezil selectively inhibits the enzyme that breaks down acetylcholine (called acetylcholinesterase - this enzyme has two active sites, one exhibiting ion-ion interactions and one exhibiting hydrogen bonding with the substrate). Figure 17 shows the normal process by which acetylcholine is broken down in the body and figure 18 models how donepezil inhibits this process.

Mechanism of action

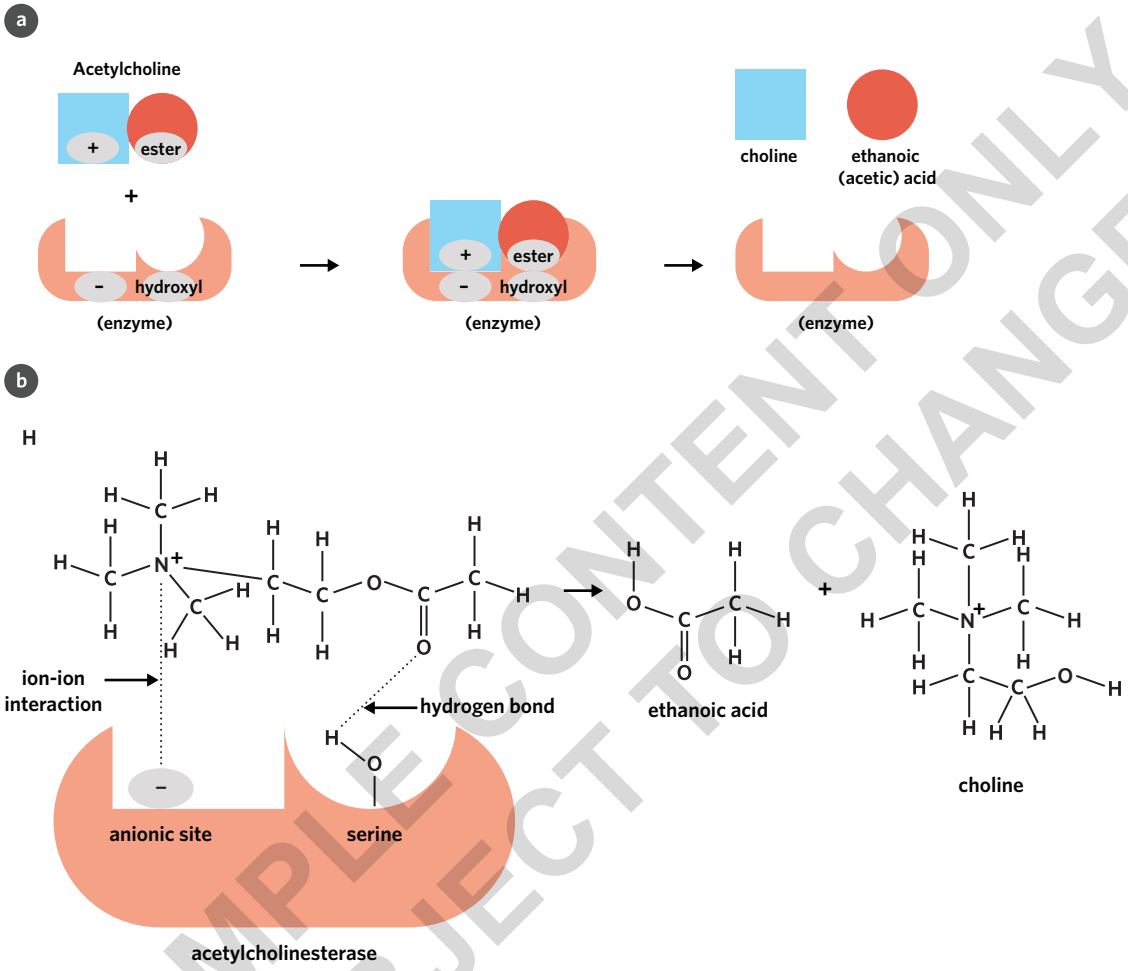


Figure 17 The lock-and-key model **(a)** and structural formula **(b)** can be used to show the normal breakdown of acetylcholine.

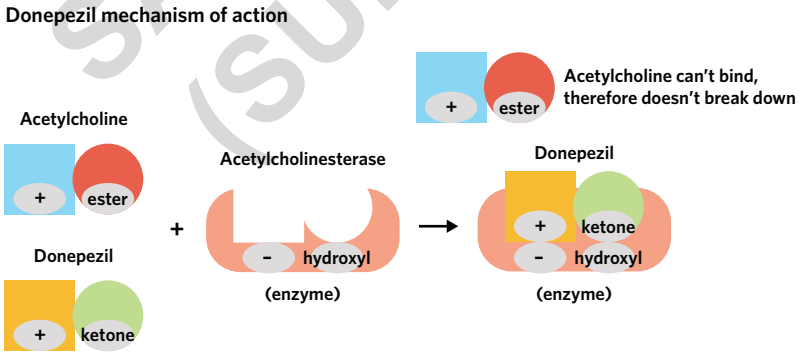


Figure 18 Lock-and-key model of donepezil inhibiting the breakdown of acetylcholine

PROGRESS QUESTION

Question 9

Enzyme inhibitors work by

A. increasing the activation energy.

B. decreasing the activation energy.

C. binding to active sites.

D. creating a second active site.

Theory summary

- There are four levels to the structure of a protein: primary, secondary, tertiary, and quaternary.
- The lock-and-key model proposes that a substrate fits perfectly into the active site of an enzyme.
- Enzymes are biological catalysts which consist of an active site which binds to a substrate.
- Enzymes require the exact physical (3D shape) and chemical (electrostatic attractions) characteristics to function with a specific substrate.
- An increase in temperature increases the enzyme activity up to the optimal temperature, above which there is a sharp decrease in activity due to denaturation of the enzyme.
- A decrease in temperature lowers enzyme activity but does not denature it.
- The charges of an amino acid change depending on the pH of the solution:
  - In an acidic solution, amino acids appear as a cation.
  - In a basic solution, amino acids appear as an anion.
  - In a neutral solution, amino acids appear as a zwitterion.
- When an amino acid is in the form known as a zwitterion, it has both positive and negative charges on the second carbon atom, with no net charge (the side-chains are not charged in a zwitterion).
- A change in pH can affect enzyme function by causing an enzyme to become denatured, as the H^+ or OH^- disrupt the forces that maintain the specific shape of the enzyme.
- Many medicines work by competitively (and reversibly) inhibiting important enzymes in the body, improving the quality of life for millions of humans.

11B Questions

Mild Medium Spicy

Deconstructed

Use the following information to answer questions 10–12.

Consider the following statements about the structure of proteins.

I. The primary structure of a protein is determined by the sequence of amino acid residues.

II. The secondary structure of a protein is the result of hydrogen bonding between −NH and −CO groups.

III. The tertiary structure of a protein involves bonding between the side chains on the amino acid residues.

Question 10 (1 MARK)

The primary structure of amino acids in a polypeptide chain is held together by

A. hydrogen bonds.

B. covalent bonds.

C. ionic bonds.

D. metallic bonds.

Question 11 (1 MARK)

The secondary structure of a protein is determined by

A. dispersion forces.

B. ionic interactions.

C. hydrogen bonds.

D. disulfide bridges.

Question 12 (1 MARK)

Of these statements

A. only I and III are true.

B. only I and II are true.

C. only II and III are true.

D. I, II, and III are all true.

VCAA 2012 Exam 1 Multiple choice Q5

Exam-style

Question 13 (1 MARK)

Botox is a neurotoxic protein that causes paralysis. The toxin acts by disrupting the disulfide bonds of cell receptors, which are made from proteins. By doing so, botox disrupts the

A. primary structure.

B. secondary structure.

C. tertiary structure.

D. All of the above

Question 14 (1 MARK)

Which of the following does not affect the rate of a reaction involving enzymes?

A. A change in pH

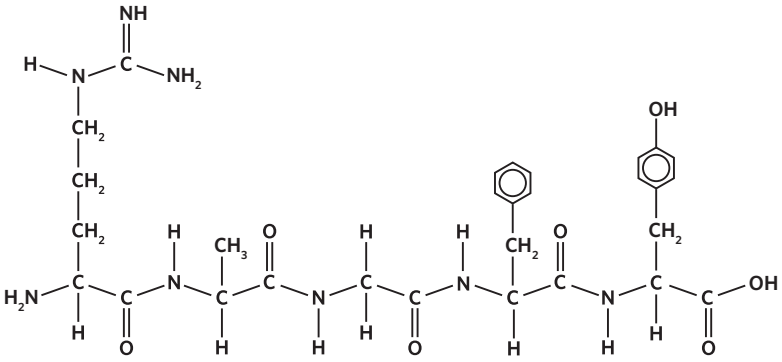
B. An increase in the concentration of an enzyme when all the substrate molecules are bound

C. A change in temperature

D. An increase in the concentration of an enzyme when not all the substrate molecules are bound

Question 15 (1 MARK)

The number of amide bonds (linkages) in the following polypeptide is



A. 2

B. 3

C. 4

D. 5

Question 16 (1 MARK)

More than 200 million people worldwide rely on taking statins to help improve their heart health. Statins lower artery-clogging cholesterol by inhibiting enzymes involved in the synthesis of cholesterol. They do this by competing with a chemical precursor to cholesterol for the active site of the HMG-CoA reductase enzyme.

Given that the body does need a small amount of cholesterol to function, medicinal enzyme inhibitors used to treat high cholesterol must be

A. cheap and easy to manufacture.

B. readily available and easily distributed.

C. irreversible competitive inhibitors.

D. reversible competitive inhibitors.

Question 17 (3 MARKS)

Alanine behaves differently depending on the environment of the solution to which it is added. It has the formula $CH_3CH(NH_2)COOH$.

a. Draw the structural formula of alanine in a solution with a pH of 9. 1 MARK

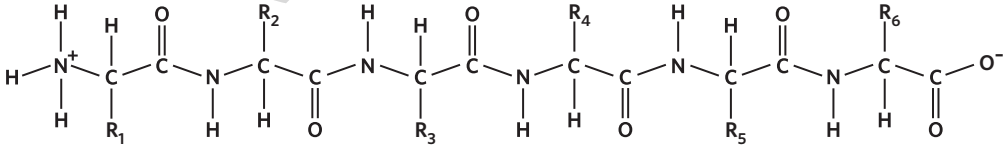
b. Alanine is commonly found in β-pleated sheets. Describe the bonds that contribute to maintaining this structure. 2 MARKS

Question 18 (4 MARKS)

The DNA in our cells gives instructions for the production of functional proteins found in our body. This process occurs progressively in different areas of the cell. Depending on the stage, the structure of the protein can look different.

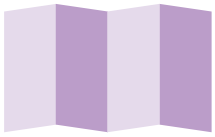
The image below shows different forms of the same protein.

i.



ii.

α-helix



β-pleated sheet

iii.

iv.

Identify the name of each structure and the bonds that hold each structure together.

Key science skills

Question 19 (7 MARKS)

Boglárka, a VCE chemistry student, would like to determine the effect of pH on enzyme activity. They use the enzyme lipase which is essential in the breakdown of lipids. This enzyme has an optimum pH range of 4.0–5.0, and they set up 3 test tubes each with a few drops of lipase. One test tube has a pH of 1.0, the second has a pH of 4.5, and a third has a pH of 14.0. Boglárka then places a cube of fat of the same size in each test tube.

a. Using your knowledge of pH and enzyme activity, predict what Boglárka would observe in each test tube, justifying your reasons. 2 MARKS

b. Does this experiment have control test tubes? If not, explain what could be done to improve the validity of the results. 2 MARKS

c. The enzyme α-amylase is produced by the salivary glands and secreted into the mouth. Explain why α-amylase can only function in the mouth, given that different parts of the digestive tract all vary with respect to pH. 2 MARKS

d. What structure(s) of a protein is changed when an enzyme becomes denatured? 1 MARK

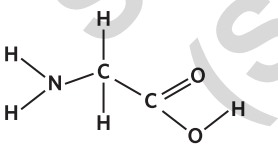
FROM LESSON 12D

Questions from multiple lessons

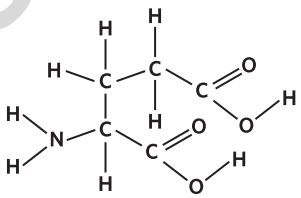
Question 20 (3 MARKS)

Due to the trends of supplemented protein intake, many foods claim to have increased levels of protein.

Dominykas wanted to determine the protein content in a packet of chips that claimed to have 'only added glycine and glutamic acid'.



Glycine



Glutamic acid

a. After some extraction techniques, Dominykas conducted mass spectrometry on the sample. He found that the molecular ion had a mass to charge ratio of 147 m/z. Identify the amino acid that was present in his sample. 1 MARK

b. To confirm, Dominykas made another sample of his chips for HPLC analysis. Given that a polar stationary phase was used, which amino acid - glycine or glutamic acid - would have the greatest retention time? Explain. 2 MARKS

FROM LESSONS 10A & 10E

Question 21 🌶🌶🌶 (7 MARKS)

The following is a student's summary of catalysts. It contains some correct and incorrect statements.

I. A catalyst increases the rate of a reaction.

II. All catalysts are solids.

III. The mass of a catalyst is the same before and after the reaction.

IV. A catalyst lowers the enthalpy change of a reaction, enabling more particles to have sufficient energy to successfully react.

V. A catalyst increases the value of the equilibrium constant, thus favouring the extent of the forward reaction, resulting in a greater yield of product.

VI. All catalysts align the reactant particles in an orientation that is favourable for a reaction to occur.

VII. The effectiveness of a metal catalyst is not dependent upon its surface area.

VIII. Enzymes are biological catalysts that catalyse a specific biochemical reaction once only.

IX. The effectiveness of an enzyme is independent of temperature.

a. Identify two correct statements. 1 MARK

b. Evaluate the student's summary by identifying three incorrect statements. In each case, explain why it is incorrect. 6 MARKS

i. Incorrect statement one

ii. Incorrect statement two

iii. Incorrect statement three

VCAA 2013 Exam 2 Short answer Q11

FROM LESSONS 4A, 4B & 5B

Chapter 11 review

Multiple choice (10 MARKS)

Question 1 (1 MARK)

Below are a number of statements regarding medicines.

I. No medicines approved for use in Australia are extracted from plants.

II. Medicines can work by stopping an enzyme from acting.

III. Repeating the distillation process decreases the purity of medicines.

IV. Competitive inhibitors enhance enzymes' usual catalytic activity.

Which of these statements is/are correct?

A. I, III, and IV only

B. II only

C. III only

D. II and IV only

Question 2 (1 MARK)

Which of the following is a correct statement about the process of protein denaturation?

A. High temperatures denature proteins by disrupting forces and bonds between polypeptide chains.

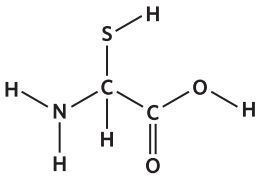
B. Changes in pH result in denaturation by disrupting the protein's primary structure.

C. Denaturation is a reversible process.

D. Denaturation involves the disruption of all forces and bonds in the protein's secondary, tertiary and quaternary structures.

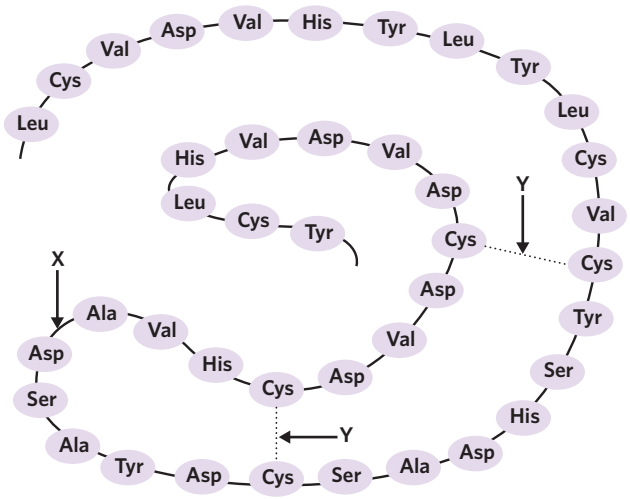
Use the following information to answer questions 3–5.

Cysteine is one of the two amino acids that contain sulfur atoms. A scientist has developed a new medicine that selectively breaks the covalent bonds between two sulfur atoms of non-adjacent amino acids in a protein.



Question 3 (1 MARK)

The following is a diagram of a section of a protein chain.



The bonds/forces represented by X and Y are

A. X: amide bond; Y: disulfide bond

B. X: covalent bond; Y: ionic bond

C. X: hydrogen bond; Y: peptide bond

D. X: dipole-dipole force; Y: covalent bond

Adapted from VCAA 2011 Exam 1 Multiple choice Q5

Question 4 (1 MARK)

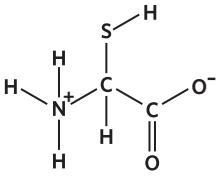
What level of protein structure would be most directly affected by the medicine?

A. Primary **B.** Secondary **C.** Tertiary **D.** Quaternary

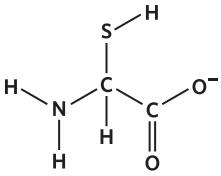
Question 5 (1 MARK)

The pH in the bloodstream is approximately neutral. Which of the following represents the structure of cysteine in the bloodstream?

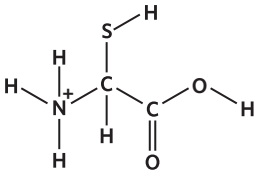
A.



B.



C.



D. Cysteine's structure would not change in a solution of neutral pH.

Question 6 (1 MARK)

Which of the following is true of amino acids?

A. In basic solutions, the amino group attached to the α-carbon exists in the $-NH_3^+$ form.

B. Amino acids only contain the elements C, H, O, and N.

C. In solutions of high pH, amino acids form zwitterions.

D. Amino acids are amphiprotic.

Question 7 (1 MARK)

The protein haemoglobin acts as an oxygen carrier in the bloodstream and consists of four subunits that form its complex quaternary structure. A student tested four separate samples of pure haemoglobin in the form of 1 M aqueous solutions.

In which of the following tests would the primary structure of haemoglobin most likely be disrupted?

A. Blend the solution at very high speed

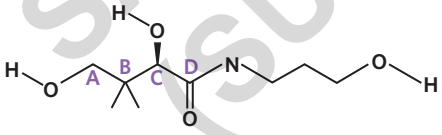
B. Warm the solution and test for gas(es) evolved

C. Add concentrated hydrochloric acid to the solution then boil the solution

D. Add methanol that will disrupt the hydrogen bonding in haemoglobin

Use the following information to answer questions 8–9.

Panthenol is a compound which can be applied to the skin as a moisturiser.
One of its two optical isomers, dexpanthenol (shown), has been shown to be an effective medicine for gastrointestinal conditions.



Question 8 (1 MARK)

Which of the following is a chiral centre?

A. Carbon atom A

B. Carbon atom B

C. Carbon atom C

D. Carbon atom D

Question 9 (1 MARK)

Which of the following best explains why dexpanthenol is separated from panthenol's other optical isomer when used as a gastrointestinal medicine?

A. Using a single optical isomer uses less energy, hence saving money for medicine manufacturers.

B. Dexpanthenol has more polar groups than its optical isomer, enabling it to dissolve better in the body.

C. Dexpanthenol's optical isomer may interact differently in the body and hence have different medicinal properties.

D. Dexpanthenol is achiral, whereas its optical isomer is chiral and more difficult to manufacture.

Question 10 (1 MARK)

A manufacturer wishes to extract salicin to make aspirin. To determine the best method, the manufacturer has access to the following table of data on organic compounds commonly present in plants.

Compound	Melting point (°C)	Boiling point (°C)	Solubility in hexane	Solubility in ethanol	Solubility in water
Salicin	207	240	low	moderate	high
Globulol	89	293	high	high	low
Verbenone	7	229	high	high	low
Oxalic acid	190	365	low	high	high

Based on the data in the table, which of the following extraction and purification methods would be most appropriate for separating salicin from verbenone?

A. Simple distillation

B. Steam distillation

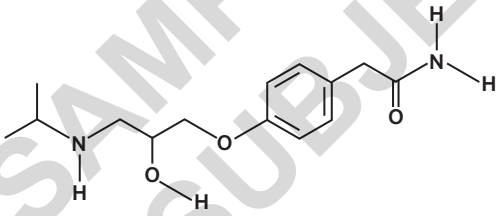
C. Solvent extraction using water and ethanol

D. Solvent extraction using water and hexane

Short answer (30 MARKS)

Question 11 (5 MARKS)

Atenolol is a medicine used to treat high blood pressure. It acts by dissolving in the (aqueous) bloodstream, then blocking receptors in the heart to decrease heart rate.



a. Describe what techniques a chemist could use to identify atenolol's:

i. Functional groups 1 MARK

ii. Structure 1 MARK

b. Considering atenolol's mode of action, why are polar functional groups necessary to its function? 1 MARK

c. The binding of medicines to receptors can be considered in terms of the lock-and-key model. Explain, according to this model, how atenolol blocks receptors in the heart. 2 MARKS

Question 12 (7 MARKS)

A protein's overall shape is maintained by intermolecular forces in its secondary, tertiary and quaternary structure.

a. Describe the different intermolecular forces and arrangements involved in a protein's secondary and tertiary structure. 4 MARKS

b. The protein transferrin is used as an iron carrier in the bloodstream. A sample of transferrin was isolated and then dissolved in a solution with a pH of 2.3. After a few minutes, significant 'clumps' were observed in the solution. Explain this observation. 3 MARKS

Question 13 (3 MARKS)

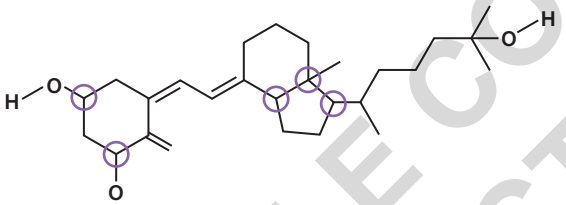
A chemist has designed a medicine that exists as a racemate (a 50/50 mixture of two optical isomers). In order for it to have the desired effect, the medicine needs to be able to be broken down by enzymes in the body. However, the chemist soon discovers that only half the medicine is broken down in the body. Using your knowledge of optical isomers and enzymes, suggest a reason why this might be the case.

Question 14 (3 MARKS)

Hyperthermia is a medical condition where the body's temperature exceeds the normal range and hypothermia is a medical condition where the body's temperature is below that of the normal range. With reference to enzyme activity and temperature, justify why doctors consider both of these conditions to be life-threatening.

Question 15 (10 MARKS)

The enzyme 24-hydroxylase catalyses the breakdown of the active form of vitamin D in the body. The structure of the active form of vitamin D is shown, with five of its six chiral centres circled.



a. Identify the sixth chiral centre. 1 MARK

b. Explain why this molecule is chiral. 2 MARKS

c. Explain why this enzyme would not break down a different optical isomer of vitamin D. 2 MARKS

d. With specific reference to the energy of the reactant molecules, describe how an enzyme catalyst acts to increase the rate of a chemical reaction. 3 MARKS

e. Describe the process of this enzyme catalysis, assuming 24-hydroxylase acts via the lock-and-key model. 2 MARKS

Question 16 (2 MARKS)

E. coli bacteria, which are made up of proteins (like enzymes), cause severe food poisoning when ingested. Explain one way you could minimise the risk of food poisoning from meat that contains *E. coli* bacteria.

Key science skills (10 MARKS)

Question 17 (5 MARKS)

Captopril is the earliest example of a competitive enzyme inhibitor used as a medicine primarily to treat high blood pressure. It acts by inhibiting an enzyme which converts angiotensin I to angiotensin II (a substance that increases blood pressure).

A major pharmaceutical company was seeking to market captopril as a treatment for numbness of fingers in cold weather. To test its effectiveness while saving on costs, they tested the medication on 30 company employees, of whom 17 reported a reduction in numbness of their fingers when using the medication.

a. Scientists often use models to communicate chemical ideas. Using the lock-and-key model, draw diagrams to represent this enzyme's usual action, and how captopril acts to inhibit it. 3 MARKS

b. Evaluate the validity of this study, based on the excerpt given. 2 MARKS

FROM LESSONS 12D & 12E

Question 18 (5 MARKS)

Every year, thousands of medicines reach the trial phase, yet in Australia, only around 40 medicines are approved for use annually.

a. Explain why it is particularly difficult to approve the safety and effectiveness of chiral medicines. 2 MARKS

b. Describe one factor relevant to the approval of medicines under each of the following themes:

i. Social 1 MARK

ii. Legal 1 MARK

iii. Economic 1 MARK

FROM LESSON 12B

11A Extraction, purification and identification of medicinal molecules

Progress questions

1. B. Generally in solvent extraction, solvents with significant differences in polarity are used.

2. A. Distillation (using a heating mantle, for fuels) can be used to separate compounds with similar polarities yet significantly different boiling points.

3. D. Since oils have high boiling points, high temperatures are necessary for simple distillation, and these may cause decomposition of oils.

4. D. Medicinal molecules are often large, have polar groups, and contain rings.

5. C. The broad trough at 3200-3600 is indicative of an O—H (alcohol) bond, most likely in an —OH (hydroxyl) group.

6. B. Carbon atom B is attached to four unique environments (do not forget the hydrogen atom, which is not shown in skeletal structures), whereas carbon atoms A, C, and D are attached to three, two, and two unique environments respectively.

7. C. The molecule in option C contains a single chiral centre (the second carbon).

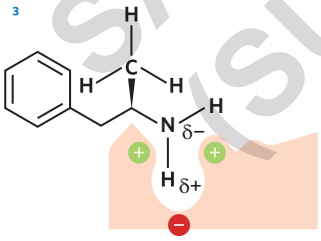
8. C. Single bonds can rotate and hence the two structures are 180° rotations of each other.

9. D. Optical isomers can bind differently to receptors, but always rotate a plane of polarised light in opposite directions (a physical property). It is not always possible to separate optical isomers of a compound.

Deconstructed

10. D 11. B

12. [Since dextroamphetamine is chiral, its mirror image is non-superimposable.[1]][As a result, this mirror image (optical isomer) is less likely to bind to the receptor, and will hence likely be less effective as a medicine.[2]]



✓ ✗ I have explained that dextroamphetamine has an optical isomer.[1]

✓ ✗ I have explained that this optical isomer would be less likely to bind to this receptor.[2]

✓ ✗ I have supported my response with a diagram.[3]

Exam-style

13. a. i. [Solvent extraction could be used to separate (largely non-polar) tea tree oil from polar impurities,[1]][and steam distillation could be used to further purify it with minimal decomposition of the oil.[2]]

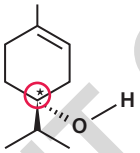
✓ ✗ I have identified that solvent extraction could remove polar impurities.[1]

✓ ✗ I have identified that steam distillation could purify tea tree oil.[2]

ii. HPLC could be used to qualitatively and quantitatively determine the compounds in tea tree oil.

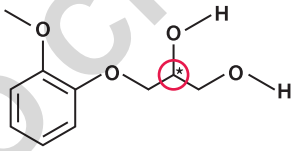
iii. MS, ^{13}C-NMR, ^{1}H-NMR, and IR could be used to determine the structures and functional groups of the compounds in tea tree oil.

b. i.

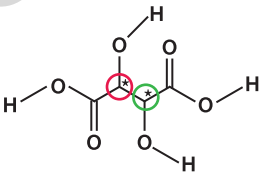


ii. For chiral medicinal molecules, one optical isomer may bind differently to receptors in the body compared with the other optical isomer, leading to potentially differing effectiveness and safety between optical isomers.

14. a. i.



ii.

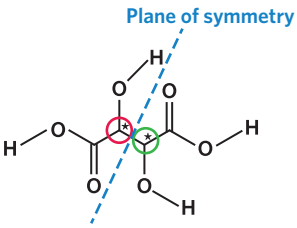


b. i. [Guaifenesin is chiral,[1]][since it contains exactly one chiral centre OR since it has a non-superimposable mirror image.[2]]

✓ ✗ I have identified guaifenesin as chiral.[1]

✓ ✗ I have explained why guaifenesin is chiral.[2]

ii. [Tartaric acid is achiral,[1]][since although it contains two chiral centres, it also has a plane of symmetry / since its mirror image is superimposable.[2]]



✓ ✗ I have identified tartaric acid as achiral.[1]

✓ ✗ I have explained why tartaric acid is achiral.[2]

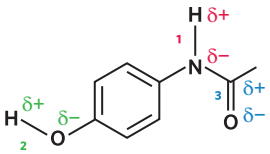
15. a. [Salicin is predominantly polar, whereas flavone is mostly non-polar.[1]][As a result, both water and a less polar solvent such as acetone (propanone) or hexane could be placed in a separating funnel to undertake solvent extraction.[2]][Salicin would largely dissolve in the water, whereas flavone would largely dissolve in the less polar solvent, allowing separation.[3]]

- I have identified the polarity of the two compounds.[1]
- I have identified a suitable pair of solvents for solvent extraction.[2]
- I have explained how these solvents would allow separation of the two compounds.[3]

b. [A temperature towards the middle of the range 367–549 °C would be appropriate for distillation,[1]][as at this temperature, salicin is a liquid whereas flavone is a gas, allowing separation of the two compounds.[2]]

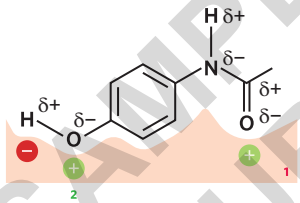
- I have identified a suitable temperature for distillation.[1]
- I have explained why this temperature is suitable.[2]

16. a.

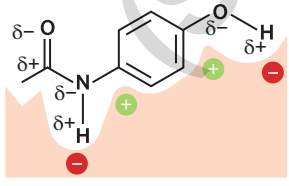


- I have identified the partial charges of the amino group.[1]
- I have identified the partial charges of the hydroxyl group.[2]
- I have identified the partial charges of the carbonyl group.[3]

b.



OR



- I have drawn a possible shape for the receptor.[1]
- I have drawn the possible charges of sites on the receptor.[2]

c. [Paracetamol is achiral,[1]][since each of its atoms is attached to a maximum of three unique environments, and hence paracetamol has no chiral centre.[2]]

- I have identified paracetamol as achiral.[1]
- I have explained why paracetamol is achiral.[2]

d. Since paracetamol is achiral, its mirror image is superimposable and is hence not likely to bind differently to receptors in the body.

Key science skills

17. a. i. Picking leaves from a eucalyptus tree could harm the tree.

Alternative answers:

- Collect already-fallen leaves if possible.
- Pick as few leaves as possible from the tree, minimising waste.

ii. Steam distillation requires high temperatures and can be energy-intensive.

Alternative answers:

- Ensure the distillation apparatus is well-insulated.
- Use renewable energy to heat the substances.

b. [Dry and grind the collected eucalyptus leaves to a powder, then dissolve them in an appropriate solvent.[1]][Place this solution in a distilling flask and feed water into the distillation apparatus to be vaporized.[2]][Heat the solution until eucalyptol evaporates, allowing it to recondense separately and be collected.[3]]

- I have given a method step for the conversion of eucalyptus leaves to a distillable form.[1]
- I have given a method step for the setup of the steam distillation apparatus.[2]
- I have given a method step for separation and collection of eucalyptol.[3]

FROM LESSONS 12B & 12E

Questions from multiple lessons

18. a. [Citral: 3,7-dimethylocta-2,6-dienal.[1]]
[Citronellal: 3,7-dimethyloct-6-enal.[2]]

- I have given the correct systematic name of citral.[1]
- I have given the correct systematic name of citronellal.[2]

b. [As both compounds are very similar in structure and size, they likely have similar boiling points.[1]][Moreover, since they each contain one polar aldehyde group and a large, non-polar hydrocarbon chain, they also have very similar polarities.[2]][These factors combine to make it very difficult to separate these compounds using solvent extraction or steam distillation.[3]]

- I have identified the two compounds as having similar boiling points.[1]
- I have identified the two compounds as having similar polarities.[2]

I have evaluated the difficulty of separating the two compounds.[3]

c. [Myrcene is entirely non-polar, whereas citral and citronellal are slightly polar.[1]][As a result, solvent extraction using a non-polar solvent (e.g. hexane) and a somewhat polar solvent (e.g. ethanol) could potentially be used to separate myrcene from citral and citronellal.[2]]

I have identified the difference in polarities of myrcene and citral/citronellal.[1]

I have explained how solvent extraction could exploit this difference in polarities.[2]

FROM LESSON 7B

19. a. [Coumarin is also present in the vanilla essence sample.[1]] [This can be ascertained because there is a peak on the HPLC chromatogram for vanilla essence at retention time = 18 minutes, which is the retention time of coumarin determined under identical conditions.[2]]

I have identified that coumarin is present in the vanilla essence sample.[1]

I have explained how HPLC can be used for qualitative analysis.[2]

b. [The IR spectrum for vanillin shows a broad trough at approximately 3500 cm^{-1}.[1]][This indicates the presence of an O—H bond in an alcohol, corresponding with an hydroxyl group.[2]][The IR spectrum for vanillin also shows a narrow yet significant trough at approximately 1660 cm^{-1}.[3]] [This indicates the presence of a C=O bond, likely corresponding with a carbonyl group in an aldehyde.[4]]

I have identified the broad trough at 3500 cm^{-1}.[1]

I have identified the presence of an hydroxyl group.[2]

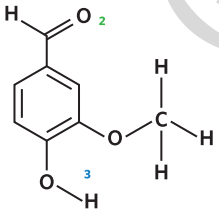
I have identified the narrow trough at 1660 cm^{-1}.[3]

I have identified the presence of a carbonyl group.[4]

c. 152 $g\ mol^{-1}$

d. [Molecular formula: $C_8H_8O_3$.[1]]

Skeletal formula:

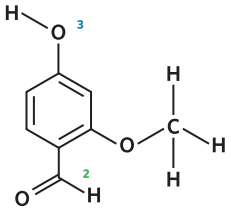


I have correctly identified the molecular formula of vanillin.[1]

I have correctly drawn —CHO attached to the ring.[2]

I have correctly drawn —OH attached to the ring.[3]

Alternative answer:



FROM LESSON 10F

11B Enzymes and medicines

Progress questions

1. B. Amino acids all have an amino group and a carboxyl group positioned on the second carbon and are called 2-amino acids or α-amino acids.

2. D. All of the forces (along with hydrogen bonding) maintain the tertiary structure of a protein.

3. D. Hydrogen bonds are found in the secondary, tertiary, and quaternary structures.

4. B. The shapes of most enzymes are specific to particular substrates.

5. A. The covalent bonds in the primary structure of an enzyme will not be broken at temperatures as low as 75 °C.

6. D. Most enzymes are very specific to a particular substrate.

7. C. Enzymes can be reused as they are not broken down or used up when they catalyse a reaction.

8. C. Zwitterions have a COO^- and an NH_3^+ group but no overall net charge.

9. C. They block unwanted reactions that can threaten the health of a human.

Deconstructed

10. B

11. C

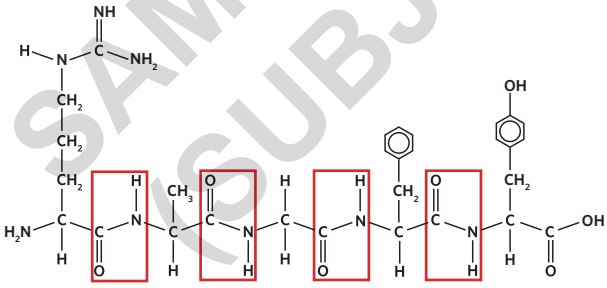
12. D. The primary, secondary and tertiary structures are accurately described in statements I, II, and III respectively.

Exam-style

13. C. Disulfide bridges are responsible for maintaining both the tertiary and quaternary structures.

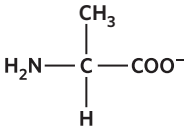
14. B. The enzyme is in excess and thus will not affect the rate if the concentration is increased further.

15. C. The amide linkage —CONH— joins the chain together.



16. D. If the enzyme activity were irreversible, the body would not have enough cholesterol (very important in making hormones and vitamin D) to maintain proper function.

17. a.



b. [Hydrogen bonds.[1]][They form between the N and H & the O and H on different peptide bonds within the same polypeptide chain.[2]]

✓ ✗ I have identified the bonds.[1]

✓ ✗ I have explained how these are formed.[2]

18. [Primary structure: amide/peptide/covalent bonds.[1]] [Secondary structure: hydrogen bonds.[2]][Tertiary structure: hydrogen bonds, ionic interactions , disulfide bridges, permanent dipole-dipole forces, and dispersion forces.[3]] [Quaternary structure: hydrogen bonds, ionic interactions, disulfide bridges, dipole-dipole, and dispersion forces.[4]]

✓ ✗ I have determined the bonds present in the primary structure.[1]

✓ ✗ I have determined the bonds present in the secondary structure.[2]

✓ ✗ I have determined the bonds and forces of attraction present in the tertiary structure.[3]

✓ ✗ I have determined the bonds and forces of attraction present in the quaternary structure.[4]

Key science skills

19. a. [Since enzymes only operate in a narrow pH range, test tubes 1 & 3 with a pH of 1 and 14 respectively would result in lipase being denatured, meaning it would not function.[1]][As a result, Boglárka should still observe the cube of fat in test tubes 1 and 3, but in test tube 2 it should be broken down. [2]]

✓ ✗ I have stated the effect of pH on enzyme activity.[1]

✓ ✗ I have stated what Boglárka should observe.[2]

b. [A control has not been carried out, and the pH of the solution around the cube of fat could be affecting the results.[1]] [This could be remedied by setting up another 3 test tubes without the enzyme lipase, of pH 1.0, 4.5, and 14.0 respectively, to see if the pH itself has any effect on the size of the cube of fat.[2]]

✓ ✗ I have stated whether a control was carried out.[1]

✓ ✗ I have explained how the experiment could be improved in light of this.[2]

c. [The enzyme α-amylase's optimum pH range is very close to the pH of the mouth.[1]][Since an enzyme functions in a narrow pH range and the pH throughout the digestive tract varies, α-amylase can only function in the mouth.[2]]

✓ ✗ I have identified the optimum pH range of α-amylase.[1]

✓ ✗ I have explained why α–amylase can only function in the mouth.[2]

d. Denaturation affects the secondary, tertiary, and quaternary structures of an enzyme. It does not affect its primary structure.

FROM LESSON 12D

Questions from multiple lessons

20. a. The amino acid present in the sample was glutamic acid as it has an m/z of 147, whereas glycine has an m/z of 75.

b. [Glutamic acid has the greatest retention time.[1]][Due to the presence of an extra carboxyl group, glutamic acid is more polar than glycine. Therefore, it is more strongly adsorbed to the polar stationary phase and would in turn have the greater retention time.[2]]

✓ ✗	I have determined the amino acid with the greatest retention time.[1]
✓ ✗	I have compared the structure of both amino acids and the interaction with the stationary phase.[2]

FROM LESSONS 10A & 10E

21. a. I and III

b. i. [II. 'All catalysts are solid.'[1]][Catalysts can be solids, liquids, gases or aqueous solutions; for example, sulfuric acid/enzymes/H_3PO_4, etc.[2]]

✓ ✗	I have identified an incorrect statement.[1]
✓ ✗	I have explained why it is incorrect.[2]

ii. [IV. 'A catalyst lowers the enthalpy change of a reaction, enabling more particles to have sufficient energy to successfully react.'[1]][A catalyst does not change the relative energy contents of reactants and products. It does, however, lower the activation energy/increases the proportion of successful collisions/provides an alternative reaction pathway with the same overall ΔH.[2]]

✓ ✗	I have identified an incorrect statement.[1]
✓ ✗	I have explained why it is incorrect.[2]

iii. [V. 'A catalyst increases the value of the equilibrium constant, thus favouring the extent of the forward reaction, resulting in a greater yield of product.'[1]][A catalyst increases the rate of the forward and reverse reactions equally and does not affect the extent of a reaction, only temperature changes affect the value of k.[2]]

✓ ✗	I have identified an incorrect statement.[1]
✓ ✗	I have explained why it is incorrect.[2]

Alternative answers:

- [VI. 'All catalysts align the reactant particles in an orientation that is favourable for a reaction to occur.'[1]][Enzymes/solid catalysts align (arrange) reactant particles into orientations that favour a reaction. However, liquid catalysts and gaseous catalysts do not arrange reactants in this way.[2]]
- [VII. 'The effectiveness of a metal catalyst is not dependent upon its surface area.'[1]][Reaction occurs on the catalyst surface. The larger the surface, the more 'effective' the catalysts.[2]]
- [VIII. 'Enzymes are biological catalysts that catalyse a specific biochemical reaction once only'.[1]][Enzymes continue to catalyse specific chemical reactions because they are not consumed in the reactions or the tertiary structure/active site is not changed as a result of the reaction.[2]]
- [IX. 'The effectiveness of an enzyme is independent of temperature.'1[1]][Enzyme effectiveness depends on the shape of the active site/enzymes have an optimum operating temperature. At high temperatures the active site is denatured (changes shape).[2]]

FROM LESSONS 4A, 4B & 5B

Chapter 11 review

Multiple choice

1. B. Competitive inhibitors (a type of medicine) act by blocking an enzyme's usual activity, rather than enhancing it; Paclitaxel is a medicine extracted from plants that is approved for use in Australia; repeating the distillation process generally increases the purity of medicines.

2. A. Denaturation, which may be caused by high temperatures, is the irreversible disruption of some forces and bonds in the protein's secondary, tertiary, and quaternary structures.

3. A. Amide bonds exist between amino acids within polypeptide chains, whereas disulfide bonds occur between non-adjacent cysteine amino acids.

4. C. The tertiary structure involves the interactions and bonds between side chains within a protein, including disulfide bonds, which are the target of this new medicine.

5. A. In solutions of neutral pH, amino acids form zwitterions, which contain $-NH_3^+$ and $-COO^-$.

6. D. Amino acids may donate or accept a proton, and they are hence amphiprotic. In basic solutions (of high pH), the α-carbon exists in the $-COO^-$ form. The amino acids methionine and cysteine contain the element S.

7. C. Very high temperatures and acidity can disrupt the primary structure of proteins.

8. C. Carbon atom C is attached to four unique environments: $-OH$, $-CONCH_2CH_2CH_2OH$, $-H$, and $-C(CH_3)_2CH_2OH$. Carbon atoms A, B, and C are all attached to only three unique environments.

9. C. Due to their different 3D shape, optical isomers can bind differently to substances in the body, leading to unpredictable biological effects.

10. D. Salicin and verbenone have similar boiling points, yet very different solubilities in both water and hexane.

Short answer

11. a. i. Infrared (IR) spectroscopy analysis of the compound

ii. A combination of IR, MS, ^{1}H–NMR, and ^{13}C–NMR analysis of the compound

b. Polar groups enable atenolol to dissolve in aqueous solution, and hence enter the bloodstream and reach the heart.

c. [Atenolol acts as the 'key' in the 'lock', which represents a receptor in the heart.[1]][According to this model, atenolol is of the exact three-dimensional shape to fit the receptor and hence block it.[2]]

- ✓ ✗ I have identified the 'lock' and the 'key' in this situation.[1]
- ✓ ✗ I have explained that atenolol's 3D shape must fit the receptor.[2]

12. a. [A protein's secondary structure is determined by hydrogen bonding between $-C{=}O$ and $-N{-}H$ of the amide linkages in different sections of the protein's amino acid sequence.[1]] [This results in the formation of either α-helices or β-pleated sheets.[2]][A protein's tertiary structure is determined by the interactions between each amino acid residue's side chain.[3]] [These intermolecular forces include hydrogen bonding, ionic interactions, dispersion forces, disulfide bridges, and dipole-dipole forces.[4]]

- ✓ ✗ I have identified the origin of a protein's secondary structure.[1]
- ✓ ✗ I have described the structures that result from this hydrogen bonding.[2]
- ✓ ✗ I have identified the origin of a protein's tertiary structure.[3]
- ✓ ✗ I have specified the types of intermolecular forces present in a protein's tertiary structure.[4]

b. [The presence of a highly acidic solution (H^+) causes dramatic changes to any ionic interactions between charged amino acid side chains, and this permanently alters the interactions in the protein's tertiary structure.[1]][The protein is denatured as a result,[2]][with long protein chains folding over each other forming the 'clumps' in the solution.[3]]

- ✓ ✗ I have identified the effect of pH on a protein's tertiary structure.[1]
- ✓ ✗ I have linked this idea to the process of denaturation.[2]
- ✓ ✗ I have related this theory to the observed outcome in the experiment.[3]

13. [Enzymes are specific to a certain optical isomer,[1]][because the particular three-dimensional shape of the enzyme's active site only matches one three-dimensional optical isomer.2][Since the enzyme can break down only one of these optical isomers, half of the medicine will not be broken down in the body.[3]]

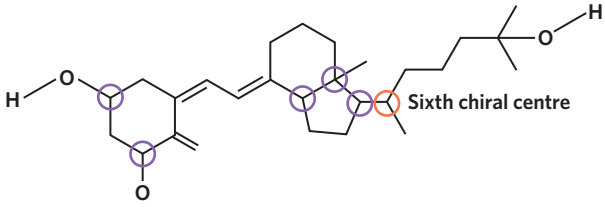
- ✓ ✗ I have identified enzymes as specific to a certain optical isomer.[1]
- ✓ ✗ I have explained why enzymes are specific to a certain optical isomer.[2]
- ✓ ✗ I have justified why this will result in the chemist's findings.[3]

14. [With elevated body temperatures, enzyme activity decreases, as more and more enzymes are denatured after exceeding their optimal temperatures.[1]][With lower body temperatures (below the optimal temperature), enzyme activity also decreases due to the lower kinetic energy.[2]][A decrease in enzyme activity is life-threatening because reactions that are necessary to sustain life proceed at a much slower rate.[3]]

- ✓ ✗ I have described the effect of higher temperatures on enzyme activity.[1]
- ✓ ✗ I have identified the effect of lower temperatures on enzyme activity.[2]

I have explained how decreased enzyme activity affects human function.[3]

15. a.



b. [Although the active form of vitamin D contains multiple chiral centres, it has no plane of symmetry.[1]][As a result, its mirror image is non-superimposable, and the molecule is chiral.[2]]

I have identified that the molecule has chiral centres but no plane of symmetry.[1]

I have explained that the molecule's mirror image is non-superimposable.[2]

c. [Enzymes have active sites that are specific to one particular substrate molecule.[1]][The 24-hydroxylase enzyme will not be able to bind to another optical isomer of vitamin D due to its different orientation in space, which makes it non-superimposable and thus preventing it from acting as a substrate.[2]]

I have described the specificity of an enzyme's active site.[1]

I have linked this specificity to the concept of optical isomerism.[2]

d. [An enzyme lowers the activation energy of a reaction by providing an alternate reaction pathway.[1]][This means that a larger proportion of reactant molecules possess sufficient energy to react,[2]][leading to a higher proportion of successful collisions, which increases the overall rate of reaction.[3]]

I have identified the effect of an enzyme on the activation energy of the reaction.[1]

I have explained how this affects the energy threshold of the reactant molecules.[2]

I have explained how this causes the overall change in reaction rate.[3]

e. [The lock-and-key model suggests that the enzyme has a very specific, rigid active site that binds with the substrate.[1]][Under this model, the substrate (vitamin D) binds to 24-hydroxylase's active site, catalysing vitamin D's breakdown without 24-hydroxylase changing shape.[2]]

I have described the key principles of the lock and key model.[1]

I have linked these principles to the reaction in the question.[2]

16. [Cooking the meat will minimise the risk of food poisoning by *E. coli*,[1]][as the high temperatures will denature the proteins in the bacteria, inhibiting their biological activity when ingested by the body.[2]]

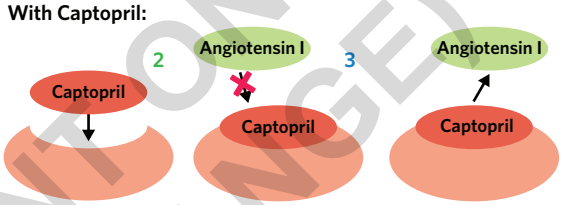
I have identified a method of preventing food poisoning from *E. coli*.[1]

I have explained how this method prevents food poisoning.[2]

Key science skills

17. a. **Normal enzyme action:**

With Captopril:



I have a drawn the enzyme's usual action according to the lock-and-key model.[1]

I have drawn captopril fitting the same 'lock' as angiotensin I.[2]

I have drawn captopril preventing angiotensin I from converting to angiotensin II.[3]

b. [This is not a valid study,[1]][because using only company employees in the trial will likely introduce bias to the results.[2]]

I have evaluated the study as invalid.[1]

I have explained that the presence of bias invalidates the study.[2]

FROM LESSONS 12D & 12E

18. a. [For chiral medicines, often only one optical isomer binds to the desired receptor, whereas the other optical isomer could bind to another receptor (with potentially dangerous consequences).[1]][Since chiral medicines are often produced as a racemate which may not be easily separable, it can be difficult to ensure that only one optical isomer is present in the medicine, and hence ensure its safety and effectiveness.[2]]

I have identified that optical isomers bind differently to receptors in the body.[1]

I have explained why optical isomers are often difficult to separate from a racemate.[2]

b. i. The medicine's potential side effects and harms to various groups in society (for example, pregnant people) must be thoroughly researched.

ii. Laws surrounding the distribution and prescription of the medicine must be developed prior to approval.

Alternative answer:

- Research must be conducted to ensure that the medicinal molecule cannot be used to synthesise illegal substances.

iii. Research companies must have sufficient funding to thoroughly trial the safety and effectiveness of potential medicines.

FROM LESSON 12B