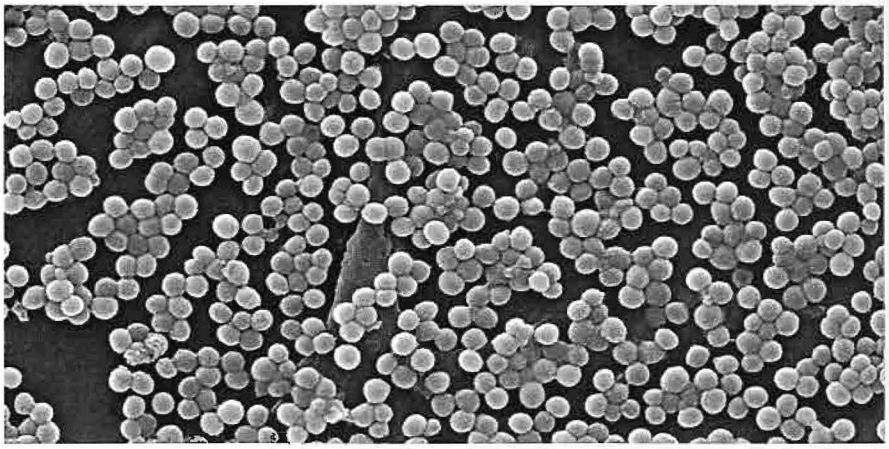
15 Medicines and drugs: Option D

Records from Egypt and from Greece written over three thousand years ago document medical properties in extracts from animal organs, plant tissue and minerals. Chinese medicine too has its roots in ancient times. These insights into the healing properties of natural substances, often based on knowledge of the local environment, have typically been passed on from generation to generation within communities. This continues to be an important aspect of health management for many people today.

The 20th century, however, saw a major new development in health care – that of the production of synthetic molecules specifically for the treatment of illnesses. Without question this has been one of the most significant achievements of the last 100 years. Development of targeted drugs and vaccines has meant that diseases such as smallpox have been eradicated, countless millions have survived infections such as malaria and tuberculosis, and other diseases like polio are on their way to extinction. Untold numbers of people today owe their lives to the action of medicines.

At the same time, and as with other great innovations, the pharmaceutical industry has brought its own challenges. Abuses, problems arising from excesses and new problems like antibiotic resistance all have to be faced. As global travel becomes more commonplace and new diseases such as avian 'flu and ebola appear, the potential exists for pandemics (epidemics across a large region of human population), as we have already seen with HIV. In addition, there are huge discrepancies in the availability of drugs in different parts of the world, which means that many diseases for which effective treatments exist are still inflicting suffering and death in some places.

As most medicines and drugs are organic in nature, you will gain a greater understanding of this chapter if you have first studied Chapter 10, Organic chemistry. It is hoped that this option will help you to apply your chemistry knowledge to the many topical issues discussed, as well as to be better prepared to make important decisions about the management of your own health.



Coloured scanning electron micrograph of MRSA (methicillin-resistant *Staphylococcus aureus*) bacteria. These bacteria are resistant to most commonly prescribed antibiotics and have become a serious problem in many hospitals. The search for new antibiotics to fight resistant bacteria is a major aspect of research by the pharmaceutical industry.

Assessment statements

D.1 Pharmaceutical products

D.1.1 List the effects of medicines and drugs on the functioning of the body.

D.1.2 Outline the stages involved in the research, development and testing of new pharmaceutical products.

D.1.3 Describe the different methods of administering drugs.

D.1.4 Discuss the terms *therapeutic window*, *tolerance* and *side-effects*.

D.2 Antacids

D.2.1 State and explain how excess acidity in the stomach can be reduced by the use of different bases.

D.3 Analgesics

D.3.1 Describe and explain the different ways that analgesics prevent pain.

D.3.2 Describe the use of derivatives of salicylic acid as mild analgesics and compare the advantages and disadvantages of using aspirin and paracetamol (acetaminophen).

D.3.3 Compare the structures of morphine, codeine and diamorphine (heroin, a semi-synthetic opiate).

D.3.4 Discuss the advantages and disadvantages of using morphine and its derivatives as strong analgesics.

D.4 Depressants

D.4.1 Describe the effects of depressants.

D.4.2 Discuss the social and physiological effects of the use and abuse of ethanol.

D.4.3 Describe and explain the techniques used for the detection of ethanol in the breath, the blood and urine.

D.4.4 Describe the synergistic effects of ethanol with other drugs.

D.4.5 Identify other commonly used depressants and describe their structures.

D.5 Stimulants

D.5.1 List the physiological effects of stimulants.

D.5.2 Compare amphetamines and epinephrine (adrenaline).

D.5.3 Discuss the short- and long-term effects of nicotine consumption.

D.5.4 Describe the effects of caffeine and compare its structure with that of nicotine.

D.6 Antibacterials

D.6.1 Outline the historical development of penicillins.

D.6.2 Explain how penicillins work and discuss the effects of modifying the side-chain.

D.6.3 Discuss and explain the importance of patient compliance and the effect of penicillin overprescription.

D.7 Antivirals

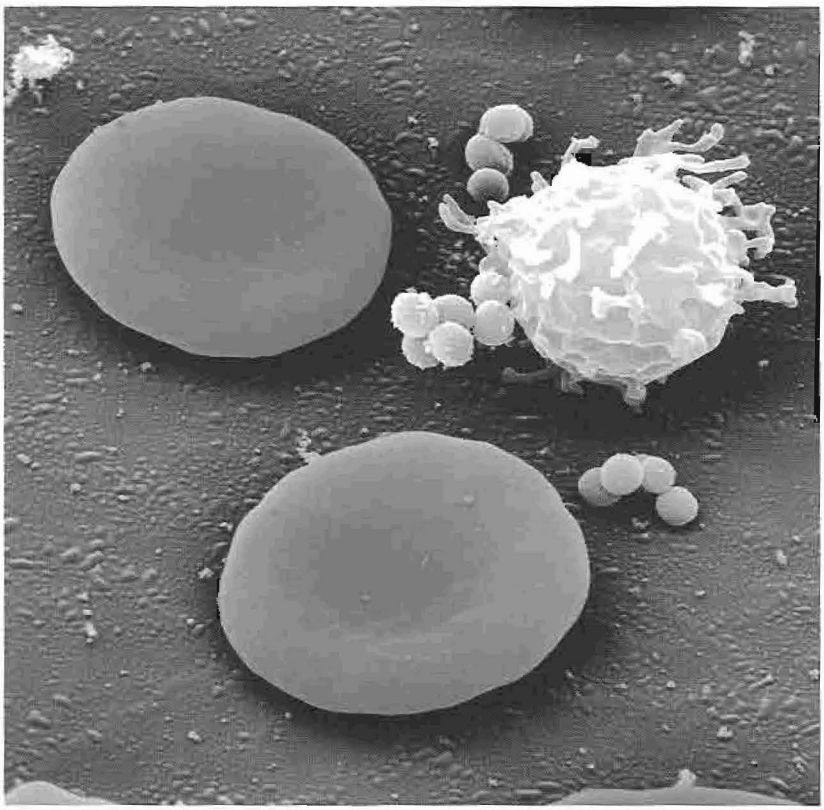
D.7.1 State how viruses differ from bacteria.

D.7.2 Describe the different ways in which antiviral drugs work.

D.7.3 Discuss the difficulties associated with solving the AIDS problem.

D.1 Pharmaceutical products

The human body has many natural systems of defence



▲ Coloured scanning electron micrograph of bacteria, shown in yellow, in the blood alongside red blood cells and a white blood cell. The white blood cell will destroy the bacteria, protecting the body from disease.

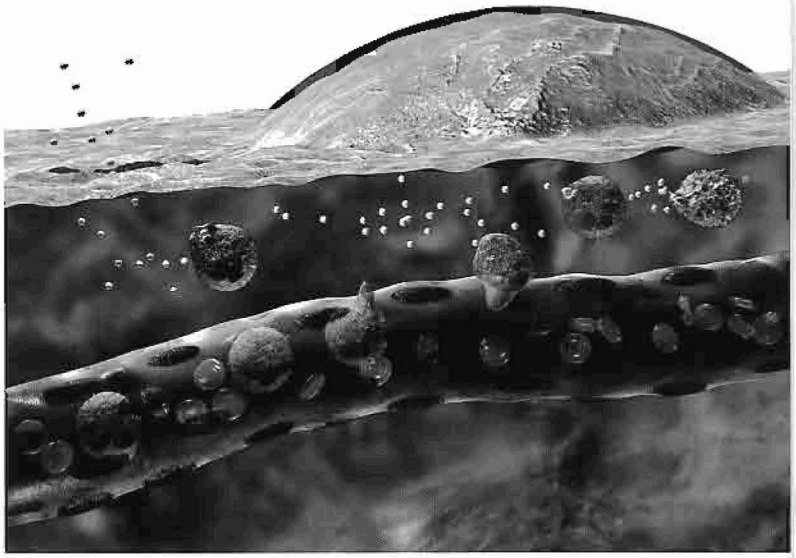
The functioning of the human body involves an incredibly intricate balance of thousands of different reactions occurring simultaneously. All of these must respond to the changing demands of the individual's activities and environment – it is truly complex chemistry! The remarkable fact is that for most people most of the time, the functioning of the body works effectively – the situation when we describe ourselves as 'healthy'. However, inevitably the system can suffer from many types of defect and breakdown, through injury, through genetically or environmentally caused abnormalities and through accumulated changes with age. In addition, we are constantly under attack from microorganisms which can enter the body, alter its functioning and so cause disease.

Happily, the human body is well equipped with equally complex systems of defence and healing processes to try to minimize the effects of these challenges. Rather like in a battle in a war, we describe attacking microorganisms as **invaders** and the body's responses as different **lines of defence**, activated as the invaders penetrate more deeply. Some of the key aspects of the natural defence mechanisms are described in the table below.

Non-specific defence mechanisms		Specific defence mechanisms
First line of defence: barriers to prevent entry	*Second line of defence: attack invaders*	*Third line of defence: immune system*
• skin	• white blood cells engulf invaders (phagocytosis)	• white blood cells produce specific proteins called **antibodies** to recognize and destroy the invaders
• mucous membranes	• blood clotting to prevent loss of blood and further invasions	• memory cells enable the body to fight a repeat invasion of the same organism more effectively
• closures and secretions of natural openings such as lips, eyelids, ear wax etc.	• the inflammatory response	

Often the responses of the body to an invading organism manifest themselves as symptoms of disease. For example, we may experience excess mucus from the nasal passages, or a fever as the body raises its temperature to fight the infection of a common cold. Although these symptoms generally need to be monitored, as for example a high body temperature can be dangerous, they are not usually themselves cause for concern.

When considering how best to fight disease, it is essential that we keep the focus on maximizing the effectiveness of the body's natural defence systems, rather than in any way defeating it or inhibiting its effect. At best, medicines work by supplementing our natural healing processes.



Computer artwork of the inflammatory response. Bacteria, shown in gold, are seen entering the body through a cut in the skin and the blood capillary beneath the site of entry is releasing white blood cells, shown in purple and green, into the tissue. These cells will destroy the bacteria and activate the immune response.

There are many different types of medicines and drugs

The terms 'medicines' and 'drugs' are sometimes used interchangeably and sometimes have slightly different meanings in different parts of the world. They are most clearly defined as follows.

Drug: a chemical that affects how the body works. This includes changes for the better and for the worse. The term is sometimes associated with substances which are illegal in many countries, such as cocaine, ecstasy and heroin, but its usage is not limited to these cases.

Medicine: a substance that improves health. Medicines, which may be natural or synthetic, therefore contain beneficial drugs. Synthetic medicines also contain other ingredients, which are non-active but help in the presentation and administration of the drug. The beneficial effect of a medicine is known as its **therapeutic** effect.

In general, the effects on the body of drugs include the following:

- alteration of the physiological state, including consciousness, activity level and coordination
- alteration of incoming sensory sensations
- alteration of mood or emotions.

Given the complexity of the chemical reactions in the body, most drugs have more than one effect and so can be difficult to classify precisely. However, the drugs considered in this chapter are those which primarily:

- target the nervous system and brain, including the perception of stimuli; these include **analgesics**, **stimulants** and **depressants**
- target metabolic processes; these include **antacids**
- aim to supplement the body's ability to fight disease-causing organisms; these include **antibacterials** and **antivirals**.

The placebo effect – the power of suggestion?

The word *placebo* is Latin for 'I will please'. The term *nocebo*, Latin for 'I will harm', is sometimes used to describe a condition worsened by a belief that a drug used is harmful. One example is a person dying of fright after being bitten by a non-venomous snake.

The placebo effect is when patients gain therapeutic effect from their belief that they have been given a useful drug, even when they have not.

It has been known for years that a significant number of patients receive therapeutic and healing effects from medicines that are pharmacologically inert, when they *believe* they are taking an effective drug. This effect, called the **placebo effect**, has been the subject of much research and analysis, but remains controversial. To date, no rigorous clinical explanation exists for the placebo effect. Nonetheless, many medical reports validate the phenomenon, in particular the ability of placebos to reduce pain. Recent research using brain scans has shown that some patients who believed they were taking pain medication were actually releasing opioids or natural pain relief, so providing some biological basis to explain the effect. It is generally accepted that about one-third of a control group taking a placebo show some improvements, a fact used in all major clinical trials, which will be discussed below.

Studies on the placebo effect are fraught with difficulties of interpretation as there are many other factors that could have contributed to the claimed therapeutic effects. These include spontaneous improvement, fluctuation of symptoms, answers of politeness and patient misjudgement. Consider what other factors might be involved in interpreting such research and how experiments to produce reliable and reproducible data could be conducted.

Drugs can be administered in several different ways

The manner in which a drug is delivered to the patient's body depends on many factors. These include the chemical nature of the drug, the condition of the patient and the most effective way of getting the drug to the target organ. For example, some chemicals (including proteins such as insulin) are decomposed by the action of the digestive enzymes in the gut, so they cannot be administered as pills, but must instead be injected directly into the blood. Likewise, a patient in a coma might be unable to swallow an ingested pill so the drug must be delivered in another way.

The following methods are all used to administer drugs.

Method of administering drug	Description	Example
oral	taken by mouth	tablets, capsules, pills, liquids
inhalation	vapour breathed in; smoking	medications for respiratory conditions such as asthma; some drugs of abuse such as nicotine and cocaine
skin patches	absorbed directly from the skin into the blood	some hormone treatments e.g. estrogen, nicotine patches
suppositories	inserted into the rectum	treatment of digestive illnesses, haemorrhoids
eye or ear drops	liquids delivered directly to the opening	treatments of infections of the eye or ear
parenteral – by injection (see diagram on the next page)	intramuscular	many vaccines
	intravenous: fastest method of injection	local anaesthetics
	subcutaneous	dental injections

You can listen to some leading researchers on placebos discussing their results and some of the ethical issues raised by the use of placebo treatment in the medical profession.

Now go to www.heinemann.co.uk/hotlinks, insert the express code 4259P and click on this activity.

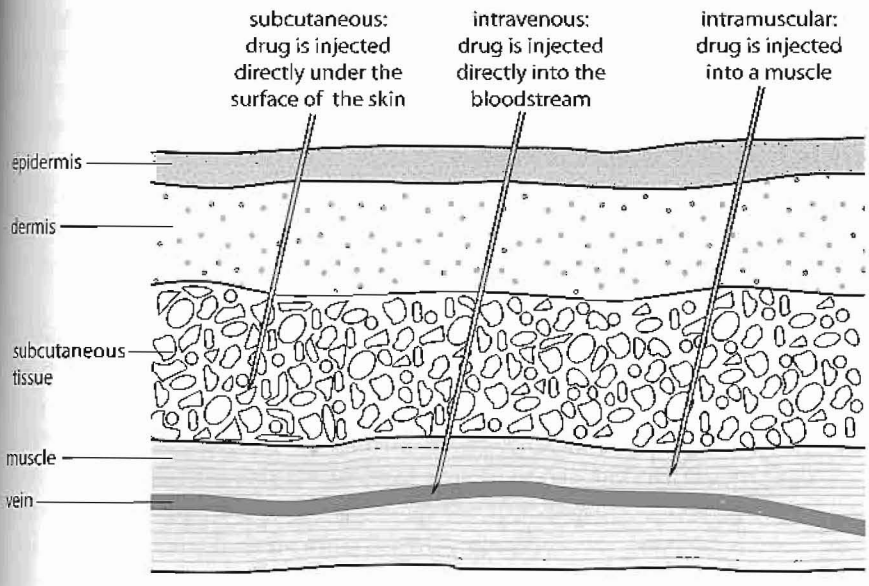


Figure 15.1 Methods of injection. (parenteral administration)

Physiological effects of drugs are complex and depend on the dosage

Because of the complexity of the chemical reactions in the body, a drug can interact in many different ways. This means that usually a drug will produce more than one physiological effect and these can be classified as follows:

physiological effects of drug in body

therapeutic effect	side-effects
the intended physiological effect	unintended physiological effects

Side-effects are defined as physiological effects which are not intended and vary greatly from one drug to another and with the same drug in different people. Sometimes side-effects may be beneficial, such as the fact that aspirin, taken for pain relief, helps protect against heart disease. Other times, the side-effects may be relatively benign, such as causing drowsiness, nausea or constipation. But of greater concern are side-effects which are much more adverse, such as causing damage to organs. The impact of these side-effects must be evaluated throughout the drug treatment. Patients must also be made aware of the possible side-effects of a drug to help in the monitoring of the treatment and to make possible adjustments in lifestyle, for example in some cases not driving or operating machinery. One of the most dramatic – and tragic – examples of adverse side-effects was the deformities produced in unborn children resulting from the thalidomide drug discussed below.

The **dosing regime** for a drug refers to the amount of drug used for each dose and the frequency of administration. Determining this is usually quite difficult as there are so many variables involved – for example the age, sex and weight of the patient, as well as factors such as diet and environment. Interaction with other drugs must also be considered. Ideally the dosage should result in constant levels of the drug in the blood, but this is almost impossible to achieve other than by a continuous, intravenous drip. Drugs administered by the other methods described

The therapeutic window is the range of a drug's concentration in the blood between its therapeutic level and its toxic level.

will inevitably lead to fluctuations in the blood drug level between doses. The important thing is that the concentration in the bloodstream must remain within a certain range: above this range, unacceptable side-effects may occur, whilst below this range there may not be effective therapeutic outcomes. This target range is referred to as the **therapeutic window**.

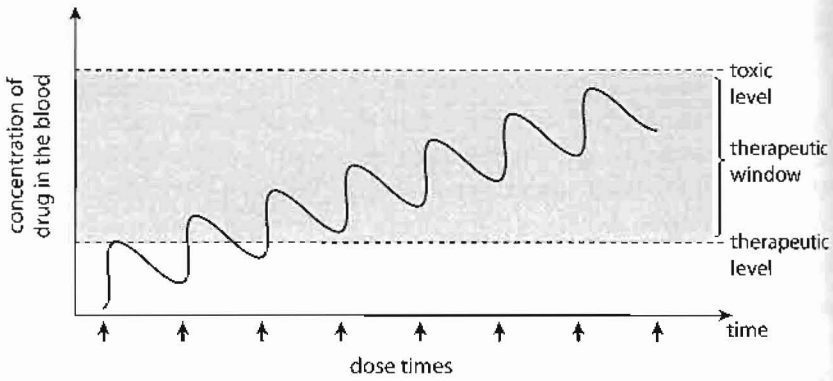


Figure 15.2 The therapeutic window.

Tolerance occurs when repeated doses of a drug result in smaller physiological effects.

The range of concentrations that defines the therapeutic window varies greatly from one drug to the next.

When a person is given repeated doses of a drug, it sometimes happens that **tolerance** develops, that is a reduced response to the drug. So higher doses are needed to produce the same effect and this increases the chances of there being toxic side-effects. The mechanism by which tolerance to a drug develops is not always understood – it could be that the body has become able to metabolize and break down the drug more efficiently, or that the drug receptors in cells become less effective. For some drugs, tolerance develops to one effect of the drug and not to other effects.

A related but different condition is **dependence** or **addiction**. This occurs when a patient becomes dependent on the drug in order to feel normal and suffers from **withdrawal symptoms** if the drug is not taken. Symptoms can be mild, such as headaches suffered on withdrawal from dependence on caffeine, or serious if the drug is toxic or shows tolerance, such as opiates, alcohol and barbiturates.

It is possible to experience addiction even to one's own hormones and neurotransmitters (chemicals used for communication in the nervous system). For example, some people are addicted to exercise as this leads to the release of chemicals that can produce a 'high'. Susceptible people are driven to exercise increasingly and they suffer withdrawal symptoms such as depression if they cannot fulfil this need.

Research, development and testing of new pharmaceutical products is a long and costly process

Pharmaceutical companies and research groups are constantly developing new drugs in response to demand. The goal is usually to develop drugs that are more effective and have fewer toxic side-effects than pre-existing drugs for the same condition, as well as drugs for new conditions such as SARS (severe acute respiratory syndrome). Every new drug developed represents a major investment of money, which makes the industry very selective in its focus. Hence a large amount of research goes into drugs to treat conditions such as obesity, depression, cancer, cardiovascular disease and ulcers, which are prevalent in the developed world where the market can support the cost. Much less attention and resources are given to researching drugs for conditions such as tropical diseases which are prevalent in the developing world.

Most drugs have wide ranging, varied and potentially harmful effects, so it is clear that there must be stringent controls over the development and licensing of what is developed for the market. The details of this vary greatly from one country to

Malaria is a disease that is both curable and preventable. But a child dies of malaria every 10 seconds; more than one million people die of malaria every year. Why do you think this is?

Find out more about the spread of malaria, the problems of drug resistance in its treatment and the programmes aimed at ending the suffering caused by this disease.

Now go to www.heinemann.co.uk/hotlinks, insert the express code 4259P and click on these activities.

another, so only general principles that are widely followed will be described here. The essential point is that as much information as possible about the full effect of the drug in an individual, including long-term effects, must be gathered before a drug can be approved and this is usually monitored at the governmental level. For every new drug that reaches the market, thousands of candidate molecules fail to meet the criteria and are rejected. This is one of the reasons why drug development is so costly. The average time for development of a drug from its first identification to its appearance on the market is about 10–12 years.

Discovery research

The first stage in drug development involves identifying and extracting compounds that have been shown to have biological activity and are known as **lead compounds** (pronounced to rhyme with 'need', not the element Pb!). Often these compounds have only low levels of activity, or possibly give negative side-effects, but they can still provide a start for the drug design and development process. Lead compounds are often derived from plants; for example, an anti-cancer agent extracted from yew trees led to the development of Taxol, and digitalis extracted from the foxglove flower led to heart medications. Microorganisms too have provided rich sources of lead compounds, particularly in the development of antibiotics, which we will study later.

Next the effectiveness of the lead compound is optimized by making and testing many chemically related compounds known as **analogues**. This process is often now fast-tracked by two relatively new techniques: **combinatorial chemistry** and **high-throughput screening**. These processes enable the production and testing of vast numbers of candidate medicines in a very short time. Following extensive laboratory tests, a potential medicine is then tested on animals, under strict legislative control. These tests help scientists to determine the dose to be administered in human trials.

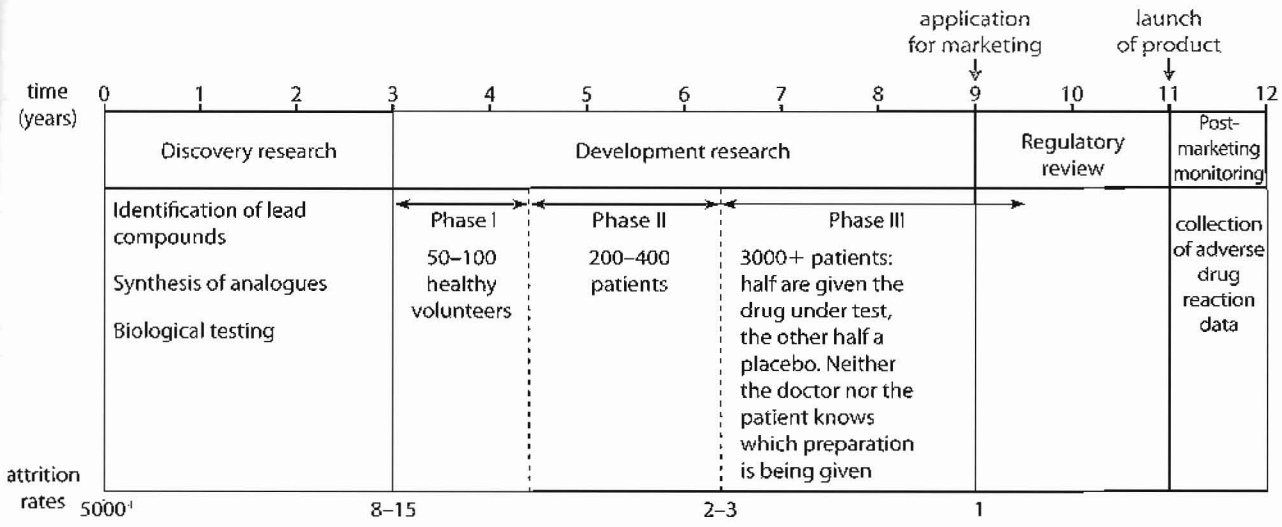
Development research

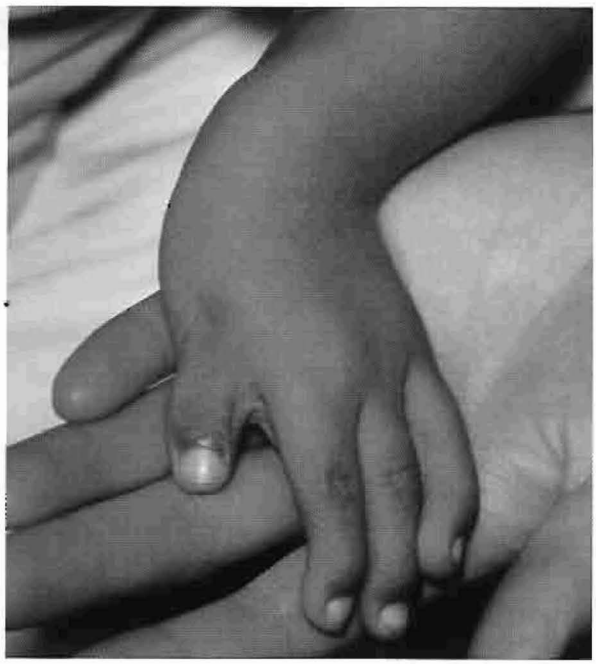
There are usually three phases in the subsequent human trials, as shown in Figure 15.3, involving an increasing number of patients. The effectiveness of the drug is judged by the relative improvement in the patients who have received the real medication compared with those on a placebo in Phase III.

The use of animals in drug trials is highly controversial and raises many questions for pharmaceutical researchers and legislators across the world. Supporters of the practice argue that almost every medical achievement over the last 100 years has involved the use of animals in some way. For example, the US and British governments both support the advancement of medical and scientific goals using animal testing, provided that the testing minimizes animal use and suffering. Opponents argue that the practice is intrinsically cruel and that animals have a right to freedom from such inflicted suffering. Many also consider it to be poor scientific practice since animal responses to drugs may not be a reliable predictor of human reactions. Concerns are also raised that the regulation of the use of animals in many countries is not well monitored.

Find out more about the opposing sides in the debate on drug testing on animals
Now go to www.heinemann.co.uk/hotlinks, insert the express code 4259P and click on these activities.

Figure 15.3 Stages in the discovery and development of a new medicine.





Close-up of the deformed hand and forearm of a 'thalidomide baby'. Thalidomide is a sedative drug that was administered to many pregnant women in the 1960s. It was withdrawn from the market after it was found to cause serious foetal abnormalities. This tragedy led to major changes in drug testing protocols.

Owing largely to the high rates of attrition (the fact that many trial drugs have to be rejected), the total cost of this process for every new drug that reaches the shelves is many hundreds of millions of dollars.

Over the last 50 years, many countries have adopted an additional regulatory step in this process, triggered by the disaster involving use of the drug **thalidomide**. During the late 1950s and early 1960s this drug was marketed initially in Germany as a sedative and anti-inflammatory medication and later prescribed to pregnant women in many countries to help reduce 'morning sickness' in their early months of pregnancy. Tragically, the drug had devastating effects on the development of the foetus and up to 12 000 children were born with severe birth defects, most notably missing or malformed limbs. In addition, many babies did not survive infancy. By the time the deformities in the newborns were linked with the thalidomide drug, it had been widely marketed in at least 46 countries.

Regulators realized then that it was not sufficient only to establish the safety and effectiveness of a drug *before* it went on the market. An additional system was needed to track medications once the population had access to them, when effects in different groups of people, including long-term effects, become known. Today, many countries maintain post-marketing safety surveillance programmes for all approved drugs and databases are available that give details of adverse drug reactions. This has sometimes led to the withdrawal of a drug from the market after years of usage. This happened, for example, in the USA with the Vioxx anti-inflammatory drug in 2004, following concerns that its long-term use caused an increased risk of heart attack and stroke. In November 2007, the pharmaceutical company Merck was forced to pay almost US$5 billion to settle lawsuits from people who claimed that the drug Vioxx had caused their heart attacks and strokes.

You can watch the documentary 'Cancer Warriors' with selective short chapters on developing and testing drugs and on thalidomide.

Now go to www.heinemann.co.uk/hotlinks, insert the express code 4259P and click on this activity.

You can watch a short documentary news clip about the issues surrounding the withdrawal of Vioxx from the market.

Now go to www.heinemann.co.uk/hotlinks, insert the express code 4259P and click on this activity.

All drugs carry risks as well as benefits. Who should ultimately be responsible for assessing the risk-to-benefit ratio of a drug in an individual – the pharmaceutical company, a government watch body, the doctor, or the patient?

The thalidomide drug was never marketed in the USA because of the intervention of Frances Kelsey, a pharmacologist working at the Food and Drug Administration (FDA). Despite pressure from thalidomide's manufacturer and the fact that it was already approved in over 20 European and African countries, she registered concerns about the drug's ability to cross the placenta into the foetal blood. Her insistence that further tests be carried out was dramatically vindicated when the effects of thalidomide became known. For her insightful work in averting a similar tragedy in the USA she was given a Distinguished Federal Service Award by President Kennedy.

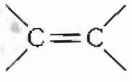
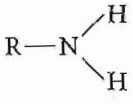
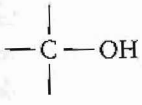
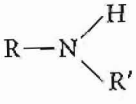
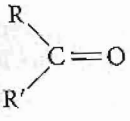
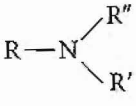
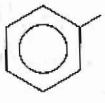
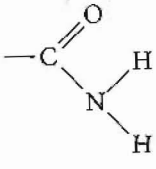
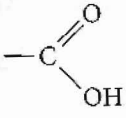
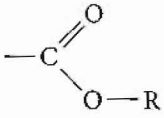
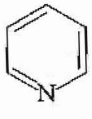
Exercises

1 List the three different ways in which drugs can be injected into the body. Predict, giving a reason, which of the three methods will result in the drug having the most rapid effect.

2 State what is meant by tolerance towards a drug and explain why it is potentially dangerous.

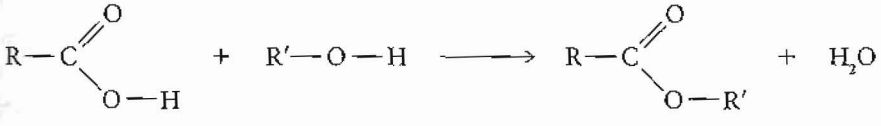
Quick reference for functional group identities and some important organic reactions

In the following sections on different classes of drugs, reference will be made to the functional groups of the molecules which are generally associated with their activity. It is important that you can recognize and identify these groups in different molecules. Some but not all of them were introduced in Chapter 10, so a brief summary of the important ones found in drugs is given here. (Note that R and R′ refer to carbon-containing or alkyl groups.)

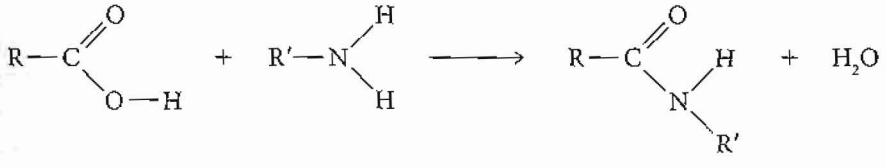
Structure of functional group	Name of functional group	Structure of functional group	Name of functional group
	alkene; carbon–carbon double bond		primary amine
	alcohol; hydroxyl		secondary amine
	ketone		tertiary amine
	benzene or phenyl ring		amide
	carboxylic acid		ester
R—O—R′	ether		a heterocyclic ring containing atoms other than C, usually N
—Cl	chloro	$-NO_2$	nitro

In addition, there are two common condensation reactions in organic chemistry that you should be able to recognize:

(i) Acid + alcohol → ester + water



(ii) Acid + amine → amide + water



● **Examiner's hint:** It is easy to confuse *amine* and *amide*. Amines are organic derivatives of ammonia, NH_3. In amides, the N is attached to a carbonyl carbon (C=O), so these are derivatives of carboxylic acids. There is no —C=O group in amines.

D.2 Antacids

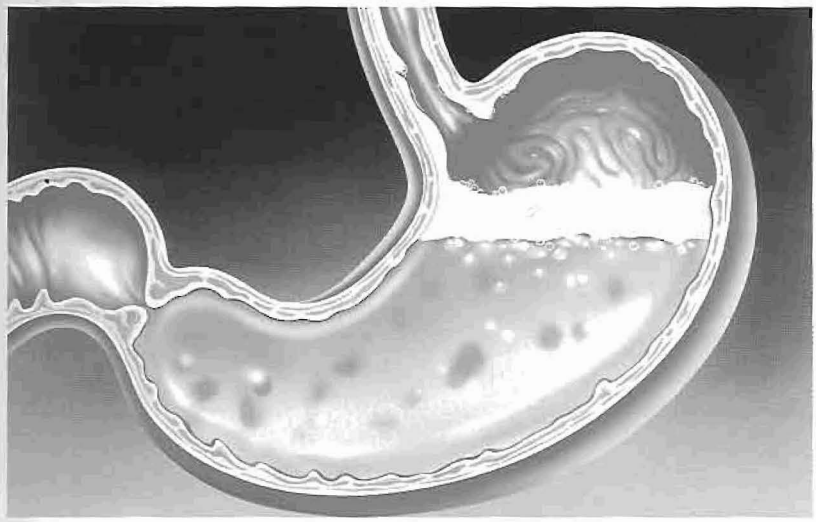


Illustration of a raft of foaming antacid on top of the contents of a human stomach. Heartburn is caused when the stomach's acidic contents rise into the oesophagus, shown in the upper centre, causing inflammation and a sense of pain. Antacids neutralize the acid to bring relief.

Acidity in the stomach is normal, but excess acidity is potentially harmful

The body keeps a tight control over the pH in cells and extra-cellular fluids, as changes in the H^+ concentration have significant effects on the activity of many molecules, especially catalysts known as enzymes. The gastro-intestinal tract, or gut, generates and maintains different pH environments along its length, which play an important role in controlling the activity of digestive enzymes.

The stomach is unusual in that it generates a pH as low as 1–2 by the production of hydrochloric acid from structures in the lining of the walls, known as gastric glands. The acid environment not only kills bacteria that may have been ingested with food, but also provides the optimum environment for the action of its digestive enzymes. However, some factors, such as excess alcohol, smoking, stress and some anti-inflammatory drugs, can cause excess production of this acidic secretion known as gastric juice. This can lead to the following problems:

- acid indigestion: a feeling of discomfort from too much acid in the stomach
- heartburn: acid from the stomach rising into the oesophagus – often called acid reflux
- ulcer: damage to the lining of the stomach wall, resulting in loss of tissue and inflammation.

Antacids are weak bases which neutralize excess acid

Drugs to help combat such excess acid are known as **antacids**. They work by neutralizing the hydrochloric acid, hence relieving the symptoms. Antacids are usually weakly basic compounds, often metal oxides or hydroxides, carbonates or hydrogencarbonates, which react with the acid to produce a salt and water. Note that these drugs do not directly coat ulcers or induce healing, but according to the dictum 'no acid, no ulcer', they do allow the stomach lining time to mend. For example:

Aluminium hydroxide $Al(OH)_3$

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

Magnesium hydroxide $Mg(OH)_2$

$$Mg(OH)_2(s) + 2HCl(aq) \rightarrow MgCl_2(aq) + 2H_2O(l)$$

Several antacid formulations contain both aluminium and magnesium compounds as they complement each other well. Magnesium salts tend to be faster acting, but because aluminium compounds dissolve more slowly they tend to provide longer lasting relief. In addition, magnesium salts tend to act as a laxative, whereas aluminium salts cause constipation. Aluminium has been linked with

Ulcers can occur in different regions of the gut and there are distinct differences in the relative frequency of occurrence of the different types of ulcer. For example, in the British population duodenal ulcers are more common, whereas in Japan gastric ulcers predominate. The reasons for the different occurrences are probably based on diet, but there are many other possible causes. Consider what some of these might be.

the development of Alzheimer's disease and although this is by no means proven, many people carefully limit its intake.

Other antacids contain metal carbonates and hydrogen carbonates which react with the acid to produce a salt, water and carbon dioxide. The latter can cause bloating of the stomach and flatulence. To avert this, **antifoaming agents** such as dimethicone are often added to the formulation.

Sodium hydrogen carbonate $NaHCO_3$

$$NaHCO_3(aq) + HCl(aq) \rightarrow NaCl(aq) + H_2O(l) + CO_2(g)$$

Calcium carbonate $CaCO_3$

$$CaCO_3(s) + 2HCl(aq) \rightarrow CaCl_2(aq) + H_2O(l) + CO_2(g)$$

Some antacids also contain **alginates** which float to the top of the stomach, forming a 'raft' which acts as a barrier preventing reflux into the oesophagus.

Note that because antacids change the pH of the stomach, they can alter other chemical reactions, including the absorption of other drugs. They should never therefore be taken for an extended period without medical supervision.

● **Examiner's hint:** In stoichiometry questions concerning antacids, remember that the molar ratio of antacid to acid will vary with different antacids. So make sure you are basing your answer on the correct balanced equation.

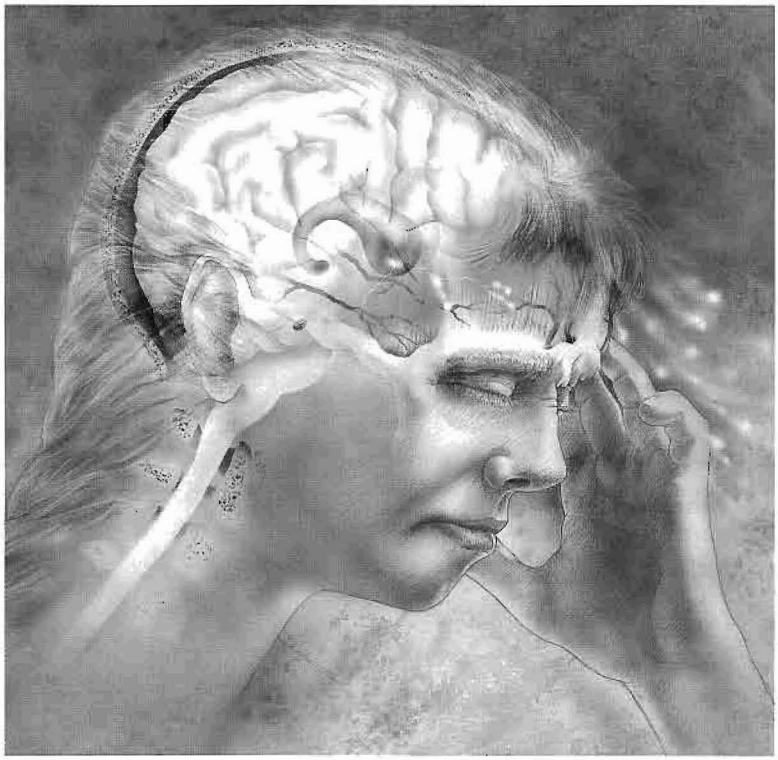
Exercise

3 Magnesium hydroxide and aluminium hydroxide can act as antacids.
- (a) Write an equation for the reaction of hydrochloric acid with each of these antacids.
- (b) Identify which antacid neutralizes the greater amount of acid if 0.1 mol of each antacid is used.
- (c) Suggest why potassium hydroxide is not used as an antacid.

D.3 Analgesics

Our body's ability to perceive pain is one of our very best defence mechanisms. We act immediately to try to eliminate the source of pain – and thus to reduce further damage to ourselves. Removing our hand from a hot plate, being aware that a sharp object has pierced our skin, or being virtually incapable of moving a broken limb are all examples of our innate abilities to protect ourselves.

But we all know that the sensation of pain is unpleasant – at best. At worst, it can dominate the senses and cause a debilitating effect, especially as many people have medical conditions that result in chronic pain. Therefore there is a need for painkillers, a class of drugs known as **analgesics**. Note though that pain is a symptom of a bigger problem – an injury or a disease – and therefore long-term relief is dependent on treating the underlying cause.



Conceptual artwork of a person suffering from a headache showing inflamed blood vessels and nerves around the brain. Analgesics work in different ways to block the pathway between the source of pain and perception by the brain.

It is estimated that chronic pain afflicts about 20% of the population of developed countries. Musculoskeletal and joint disorders and neck and back pain account for most of this, with headaches, migraines and cancer accounting for most of the remainder.

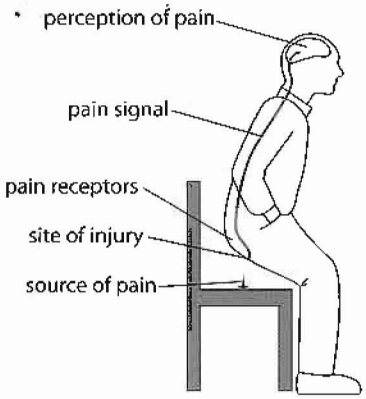


Figure 15.4 Pathways of pain in the body.

It could be argued that whereas mild analgesics seek to eliminate pain at source, strong analgesics only alter our ability to perceive pain. Consider the relative value of these two approaches to pain management.

Pain is detected as a sensation by the brain when nerve messages are sent from various **pain receptors** located around the body. These receptors are themselves stimulated by chemicals known as **prostaglandins**, which are released from cells damaged by thermal, mechanical or chemical energy. Once released, prostaglandins also mediate the **inflammatory response** by causing the dilation (widening) of blood vessels near the site of injury. In turn this can lead to swelling and increased pain. In addition, prostaglandins have an effect on the temperature regulation of the body which may result in increased temperature known as fever.

To be effective, a painkiller must somehow intercept or block this pathway somewhere between the source of pain and its perception in the brain.

Different analgesics work by blocking pain at different sites

Mild analgesics, including aspirin and non-steroidal anti-inflammatory drugs (NSAIDs) such as ibuprofen, act by preventing stimulation of the nerve endings at the site of pain. They inhibit the release of prostaglandins from the site of injury and so give relief to inflammation and fever as well as to pain. (Paracetamol is an exception as it inhibits prostaglandin release in the brain rather than at the site of injury.) Because these analgesics do not interfere with the functioning of the brain, they are also known as **non-narcotics**.

Strong analgesics include the drugs related to morphine, known as the opioids. This refers to their ability to bind to so-called opioid receptors in the brain, which then blocks the transmission of pain signals between brain cells and so alters the *perception* of pain. Because these analgesics act on the brain, they may cause drowsiness and possible changes in behaviour and mood, so are also known as **narcotics**. They are the most effective painkillers for severe pain, but owing to their side-effects and potential problems with dependence, their usage must be monitored through medical supervision.

In response to the fact that too often patients suffering with conditions such as advanced cancer were not receiving optimal pain control medication, the World Health Organization (WHO) developed a three-step 'analgesic ladder'. This simple guideline has had a great impact in achieving better standards of pain management.

1 use mild analgesics
2 add a weak opioid such as codeine or tramadol
3 in severe intractable pain, use strong opioids such as morphine, fentanyl or methadone.

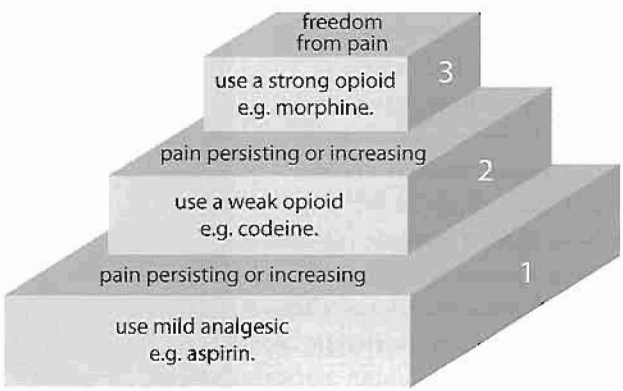


Figure 15.5 The WHO three-step analgesic ladder.

Despite the fact that cost-effective methods of pain control exist, they are not widely used everywhere. There are cultural, societal, political and economic factors that influence the availability of painkillers globally. Recognizing this as a deep problem, coalitions of doctors in many countries are pushing towards the goal of making access to pain management a universal human right. In 2004 a 'Global Day against Pain' was organized in Geneva, Switzerland, by several international organizations including the WHO.

Mild analgesics

Aspirin

From the time of Hippocrates in about 400 BC, it was known that chewing willow bark could give relief to pain and fever. But it was not until the early 1800s that it was demonstrated that the active ingredient in the bark is salicin which is converted to **salicylic acid** in the body (*salix* is the Latin name for willow). Although salicylic acid proved to be effective in treating pain, it tasted awful and caused the patient to vomit.

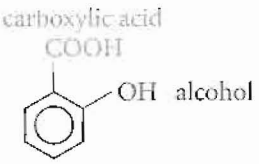


Figure 15.6 The structure of salicylic acid (2-hydroxybenzoic acid).

In 1890 the Bayer Company in Germany made an ester derivative of salicylic acid, which was more palatable and less irritable to the stomach, while still effective as an analgesic. It was named **aspirin**, in recognition of the plant spirea which produces a similar compound. Aspirin manufacture began that year and it became one of the first drugs to enter into common usage. Today it continues to hold its place as the most widely used drug in the world with an estimated production of over 100 billion standard tablets every year. It is widely used in the treatment of headaches, toothaches and sore throats. Also, because it is effective in reducing fever (known as an antipyretic) and inflammation, it is used to provide relief from rheumatic pain and arthritis.

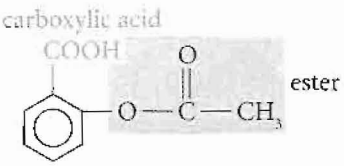


Figure 15.7 The structure of aspirin (2-ethanoyloxybenzenecarboxylic acid or acetyl salicylic acid, ASA).

In 1982 the British chemist John Vane won the Nobel Prize in Medicine for his discovery that aspirin works by blocking the synthesis of prostaglandins. This finding explains the analgesic effects of aspirin, as well as its effectiveness in reducing fever and inflammation and some of its significant side-effects. The latter can be both positive and negative as discussed below.

Aspirin reduces the ability of the blood to clot and this makes it useful in the treatment of patients at risk from heart attacks and strokes. Many people take a low daily dose of aspirin for this purpose. But this same side-effect means that aspirin is not suitable (and could be potentially dangerous) if taken by a person whose blood does not clot easily, or for use following surgery when blood clotting must be allowed to occur.

Recent research has also shown that regular intake of a low dose of aspirin may reduce the risk of colon cancer, although additional data are needed before aspirin is routinely recommended for this use.

Negative side-effects of aspirin include irritation and even ulceration of the stomach and duodenum, possibly leading to bleeding. This effect can be more acute when it is taken with ethanol in alcoholic drinks. A large number of people, especially those prone to asthma, are also allergic to aspirin, so it must be used with caution. It is not recommended for children under 12 because its use has been linked to Reye's syndrome, a rare and potentially fatal liver and brain disorder.

Aspirin is available in many formulations, which include various coatings and buffering components. These can delay the activity of the aspirin until it is in the small intestine to help alleviate some of its side-effects.

The name 'Aspirin' was originally a trademark belonging to the pharmaceutical company Bayer. After Germany lost World War I, Bayer was forced to surrender this trademark (and also the one for 'Heroin') to Britain, France, Russia and the USA as part of the reparations of the Treaty of Versailles in 1919.

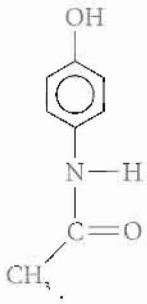


Figure 15.8 Structure of paracetamol (acetaminophen).

Paracetamol (also known as acetaminophen)

Paracetamol is a much younger drug than aspirin, having been marketed only since 1953.

Paracetamol is different from other mild analgesics as it is thought to act by reducing the production of prostaglandins in the *brain*, but does not affect prostaglandin production in the rest of the body. This means that it is not effective in reducing inflammation. It is one of the safest of all analgesics when taken correctly. It does not usually irritate the stomach and allergic reactions are rare. These are reasons why its use might make it favoured over aspirin, especially for children. However, an overdose or chronic use of paracetamol can cause severe and possibly fatal damage to kidneys, liver and brain. Also, when used in combination with ethanol by heavy drinkers, its toxic effect may be increased.

The table below summarizes and compares the relative advantages and disadvantages of aspirin and paracetamol.

	Aspirin	Paracetamol
analgesic properties (painkiller)	yes	yes
antipyretic properties (reduces fever)	yes	yes
reduces inflammation	yes	no
side-effects	stomach wall irritant, blood anti-coagulant	does not irritate stomach wall
severe side-effects (over-dosage)	Reye's syndrome in children	serious kidney, liver and brain damage
synergistic effect with alcohol	increased risk of stomach bleeding	toxic side-effects can be increased
allergic reactions	relatively common	rare
recommended use for children	no; can cause Reye's syndrome (although 'baby aspirin' is available)	yes

Flower and seed head of *Papaver somniferum*, the opium poppy.

Strong analgesics

These drugs, the opioids, also known as narcotics, are all related to **opium** – an extract of poppy seeds. The first records of cultivation of the opium poppy go back to Mesopotamia more than 5000 years ago, the start of the long, complex and bloody history of this crop. It seems likely that no chemical product ever has been responsible for more wars, economic fortunes and legislative changes, and this continues to be true today.

The so-called opium wars involving China, Britain, France and India in the late 19th century erupted from trade disputes involving opium. They ended in the imposition of several treaties by western countries on China, including the yielding of Hong Kong to Britain (which ended in 1997). Still today, opium production is a major, if illegal crop, particularly in South West Asia. It is estimated that Afghanistan produces 93% of the world's opiates and increasingly is processing more of the crop into heroin within the country. This market, estimated at US$4 billion a year, is approaching record levels. Most of the profits are, however, made outside the country by criminal gangs and networks. The government's eradication efforts have been largely ineffective and the USA plans to spray poppy plants with herbicides are highly controversial. The United Nations has called for an international effort to help address the problem of the Afghan opium trade.

The narcotic drugs derived from opium are primarily morphine and its derivatives. We will consider three of these here: **codeine**, **morphine** and diamorphine, known as **heroin**. These are powerful analgesics, acting on the central nervous system to block the perception of pain.

In addition, they have several other effects that can sometimes be used for therapeutic purposes, but sometimes are considered adverse side-effects. They include:

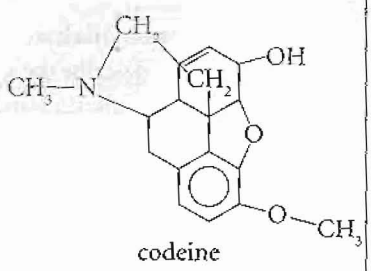
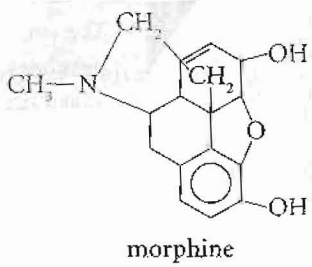
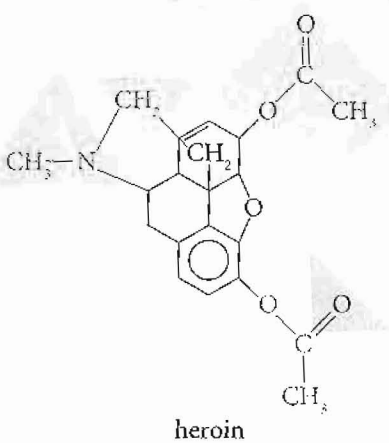
- causing constipation
- suppressing the cough reflex
- causing constriction of the pupil in the eye
- narcotic effects – to be discussed below.

Heroin is one of the best painkillers known. Its name dates from the end of the 19th century when it was believed to be the 'heroic' drug that would banish pain forever. It went on the market in 1898 but was withdrawn from general distribution five years later when its addictive properties became evident.

The three drugs differ in their effectiveness as follows:

Codeine	increasing strength as analgesics
Morphine	increasing narcotic effects
Heroin	increasing side-effects

The table below compares the structure and effects of codeine, morphine and heroin.

	Codeine	Morphine	Diamorphine (heroin)
structure	 codeine	 morphine	 heroin
functional groups	benzene ring **ether** (2) alkene alcohol (1) tertiary amine	benzene ring **ether** alkene alcohol (2) tertiary amine	benzene ring **ether** alkene ester – ethanoate (2) tertiary amine
obtained from	raw opium (0.5%)	raw opium (10%)	found in opium but usually obtained by reaction of morphine, so is known as a **semi-synthetic** drug
therapeutic uses	Sometimes used in a preparation with a non-narcotic drug such as aspirin or paracetamol in the second stage of the pain management ladder. Also used in cough medications and in the short-term treatment of diarrhoea.	Used in the management of severe pain, such as in advanced cancer. Can be habit forming and can lead to dependence, so use must be regulated by a medical professional.	Used medically only in a few countries legally (Britain and Belgium) for the relief of severe pain The most rapidly acting and the most abused narcotic. Initially produces euphoric effects, but very high potential for causing addiction and increasing tolerance. Dependence leads to withdrawal symptoms and many associated problems.

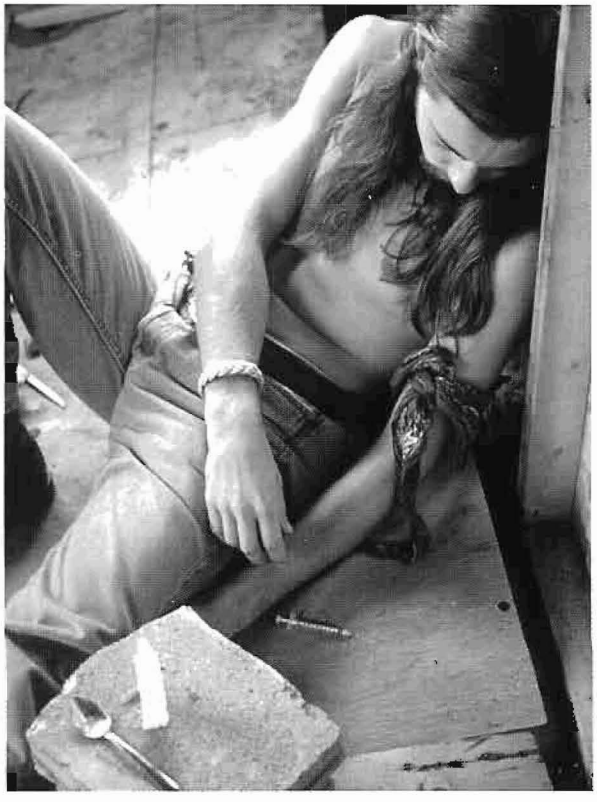
Notice that these three drugs have a common basic structure that accounts for their similar properties, as well as some different functional groups.

Meet people deep in the throes of heroin addiction with no way out.

Now go to www.heinemann.co.uk/hotlinks, insert the express code 4259P and click on this activity.

The conversion of morphine into heroin involves an esterification reaction in which both its –OH groups are converted into ethanoate (ester) groups by reaction with ethanoic acid CH_3COOH. The loss of the two polar –OH groups means that heroin is less polar and so more lipid-soluble than morphine. This enables it to cross the blood–brain barrier quickly which is why it is faster acting than the other opioid drugs. In the brain it is hydrolysed to morphine by reversing the esterification reaction.

The blood–brain barrier was first discovered by the German scientist Paul Ehrlich in the late 19th century, when he observed that a blue dye introduced into the blood of an animal coloured all its organs blue except the brain. Later experiments involved injecting the dye into the spinal fluid, when it was found that the brain became dyed but the rest of the body did not. This tight control over the movement of substances between fluids in the brain and blood vessels, the blood–brain barrier, is now known to be a membranic structure that helps to protect the brain. It is crossed more easily by small, lipid-soluble molecules than by larger and more polar molecules. One of the challenges in treating brain diseases such as tumours involves outwitting this natural defence of the brain so that it will allow therapeutic chemicals to enter.



Heroin user slumped after injecting himself with heroin (diamorphine). The tourniquet around his arm is used to make the veins stand out to ease injection.
Heroin, a strong analgesic, is a highly addictive drug with powerful narcotic effects. Heroin abuse is associated with serious health conditions, including collapsed veins, spontaneous abortion, infectious diseases and can lead to fatal overdose.

Narcotic effects

The word *narcotic* is derived from a Greek word meaning numbness or stupor. It is used to describe the strong analgesics because of their effects on brain functioning. All three of the drugs described above produce narcotic effects, but heroin does so most acutely, so this will be discussed here.

In the short term, heroin induces a feeling of well-being and contentment, as it causes a dulling of pain and a lessening of fear and tension. There is often a feeling of euphoria in the initial stages after intake. Long-term regular use leads to constipation, reduced libido, loss of appetite and poor nutrition. Heroin users start to show dependence relatively quickly, so they cannot function properly without the drug and suffer from withdrawal symptoms such as cold sweats and anxiety when it is withheld. This is compounded by an increasing tolerance to the drug, so higher doses are needed to bring about relief. In most countries, access to the drug usually involves dealing in an illegal market and the cost of the supply often is beyond the individual's means. This in turn may lead to crime and other social problems. As the drug is taken by injection, the user commonly picks up infections such as HIV and hepatitis from unclean needles. In short, the life of the heroin addict is usually profoundly altered by the drug.

Visit this site for the research report 'Heroin abuse and addiction' from the American National Institute on Drug Abuse.

Now go to www.heinemann.co.uk/hotlinks, insert the express code 4259P and click on this activity.

Helping heroin addicts to break their dependence is a slow and difficult process. Sometimes an alternative analgesic, **methadone**, is administered. It is taken orally and has a longer duration of action. This can reduce drug craving and prevent symptoms of withdrawal. Although its use is controversial in some countries, research has shown that methadone maintenance is the most effective treatment for opioid dependence, reducing the death rates of addicts receiving it to about one-tenth.

Exercises

4 Aspirin and paracetamol (acetaminophen) are described as mild analgesics.
   (a) Explain the difference in the method of action of mild analgesics and strong analgesics.
   (b) Give one therapeutic effect of aspirin, other than reducing pain, which is common to paracetamol.
   (c) Give one therapeutic effect of aspirin which is not common to paracetamol.

5 Codeine, morphine and heroin are described as strong analgesics.
   (a) State two functional groups common to codeine, morphine and heroin.
   (b) A patient has been prescribed morphine following surgery. State the main effect and a major side-effect she will experience.

D.4 Depressants

Depressants are drugs that act on the brain and spinal cord (known as the central nervous system or CNS). The action of these drugs changes the communication between brain cells by altering the concentration or the activity of chemicals called **neurotransmitters**. As a result they cause a depression, or a *decrease* in brain activity that in turn influences the functioning of other parts of the body, such as the heart and the mechanisms determining breathing rate. (The analgesics discussed earlier are also examples of depressants.)

Be warned that the language here can be a little confusing. This is because the term 'depression' is also used to describe a clinical condition characterized by mood changes and loss of interest in normal activities. Individuals who suffer from this might have insomnia, fatigue, a feeling of despair and an inability to concentrate. Clinical depression is associated with a high proportion of all suicides. The drugs used to treat this are hence known as 'antidepressants'.

Depressants include drugs also classified as tranquilizers, sedatives and hypnotics and the differences between these is often a question of dosage as shown below.

Dosage	Low to moderate dose	High dose	Extremely high doses
effect	calmness relief from anxiety very relaxed muscles	slurred speech staggering gait altered perception sleep induced	respiratory depression coma death

Description: tranquilizer — sedative — hypnotic — lethal dose

increasing dosage

We can see that in high doses these drugs can have very serious effects and so they must always be used with caution. In addition, many drugs of this type can elicit responses of tolerance and dependence and regular users can therefore suffer from withdrawal when a drug is not continued. As a specific example of a widely used depressant we will focus here on ethanol.

Ethanol

Ethanol, C_2H_5OH, is the alcohol present in beer, wine and hard liquor. Ingestion of fermented beverages containing ethanol was first recorded in the Egyptian Book of the Dead, dated approximately 5000 years ago. It was probably first discovered in the natural fermentation products from plants and microorganisms and then more systematically prepared from different natural substrates such as grapes

and grains. The concentration of ethanol can be increased through distillation, yielding hard liquors such as vodka, whisky and gin. Today ethanol is the most widely used psychoactive drug and is legal in most countries, although often with age restrictions on its purchase.

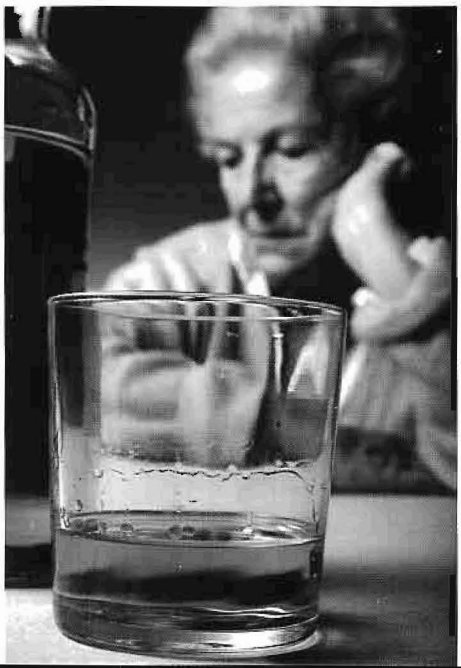
Uses of ethanol

Ethanol has some antiseptic properties, so can be used on the skin before an injection or to clean a small wound. For this reason it is often carried in first aid kits. It also has the effect of hardening the skin, so it can be rubbed on to feet to prevent the formation of blisters, for example. Ethanol in alcoholic drinks is an important part of many diets and cultures, adding a sense of occasion to meals, rituals and festivities. In low doses it can help to create a mild excitement and users become more talkative, confident and relaxed. There is also some evidence that low doses of ethanol might have a beneficial effect on the circulation and diminish cardio-vascular diseases, perhaps owing to its mild anti-clotting effect.

Abuses of ethanol

As a CNS depressant, ethanol brings about changes in behaviour and these quickly become adverse as the dose increases. The effects of ethanol abuse are obviously multiplied by the duration over which it occurs and these are summarized here.

Short-term effects of ethanol abuse	Long-term effects of ethanol abuse
• loss of self-restraint; memory, concentration and insight are impaired • loss of balance and judgment • violent behaviour associated with domestic abuse and family breakdown • dangerous risk-taking behaviour leading to many accidents involving motor vehicles and machinery • dehydration caused by increased urine output leading to 'hangover' and loss of productivity • at high doses can cause vomiting, loss of consciousness, coma and death	• dependence known as alcoholism, associated with withdrawal symptoms • liver disease, e g. cirrhosis, liver cancer • coronary heart disease • high blood pressure • fetal alcohol syndrome • permanent brain damage

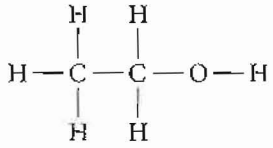


In summary, chronic consumption of large amounts of ethanol is a major source of social and physiological problems. It has been said that if ethanol were to be discovered today it would probably not pass the regime of drug testing and would be a restricted drug.

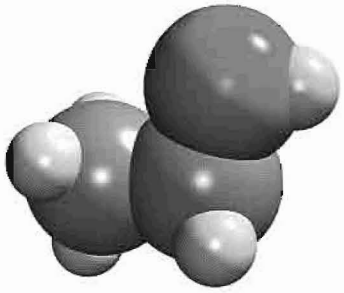
◀ Alcohol is a depressant and long-term use of large quantities can have a radical impact on a person's health and lifestyle.

Metabolism of ethanol

Ethanol C_2H_5OH has the structure



The polar –OH group enables it to form hydrogen bonds with water, making it readily soluble in aqueous solution. As a small organic molecule it is also able to dissolve in lipids, which enables it to cross cell membranes with relative ease. Following ingestion, ethanol passes quickly from the gut into the blood, mostly through the stomach wall, and then circulates to all tissues of the body. This accounts for the short time interval between ingestion and the onset of ethanol-mediated effects. Approximately 90% of an ethanol load is broken down in the liver, with the remainder being eliminated by the kidneys and lungs. Ethanol also readily passes across the placenta to the fetus when consumed during pregnancy. In addition it passes readily into breast milk and is transmitted to the nursing infant.



▲ Space-filled model of ethanol C_2H_5OH. The atoms are represented as colour-coded spheres: carbon (blue), hydrogen (yellow) and oxygen (red). Ethanol is the intoxicating component of all alcoholic beverages.

Synergistic effects of ethanol

Ethanol has the potential to increase the activity of other drugs when taken at the same time. This effect is known as **synergy**. It means that care must be taken when consuming alcoholic drinks alongside other medications, as the synergistic effects can lead to very serious, even fatal, results. One of the problems is that because ethanol is such a widely consumed and socially available drug, many people do not consider its interaction with other prescription and non-prescription drugs.

Here are some important examples:

- with aspirin, ethanol can cause increased bleeding of the stomach lining and increased risk of ulcers
- with other depressants such as barbiturates, including sleeping pills, ethanol can induce heavy sedation, possibly leading to coma
- with tobacco, ethanol appears to increase the incidence of cancers, particularly of the intestines and liver
- with many other drugs, ethanol can interfere with their metabolism by the liver, which can cause greater and more prolonged drug effects.

Visit the World Health Organization's site on substance abuse from where you can access the Global Alcohol Database which has comprehensive data, interactive maps and so on. You can also download the very interesting publication *Alcohol, Gender and Drinking Problems – Perspectives from Low and Middle Income Countries*.

Now go to www.heinemann.co.uk/hotlinks, insert the express code 4259P and click on this activity.

Techniques used for the detection of ethanol

Because of the potentially damaging effects that an individual's alcohol intake can have on other people, most countries have instituted processes to test for the presence of ethanol in the body. This is linked to legislation that sets limits for body ethanol concentration for the performance of certain activities. For example, an upper limit of 80 mg ethanol per 100 cm^3 of blood is commonly set for driving a motor vehicle. Analysis of ethanol concentration is usually based on samples of the breath, blood or urine – or sometimes a combination of these. Recently, techniques have been developed which may make it possible to detect ethanol concentration in saliva or eye fluids.

Ethanol analysis of breath

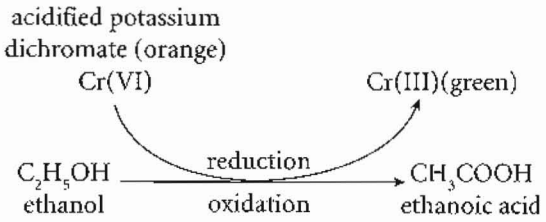
Ethanol is a volatile compound and at body temperature in the lungs it establishes equilibrium between being dissolved in the blood and released into the air in the exhaled breath.

$$\underset{\text{in blood}}{C_2H_5OH(aq)} \rightleftharpoons \underset{\text{in air spaces}}{C_2H_5OH(g)}$$

Alcohol breath test. The roadside breathalyser gives an immediate reading of whether the level of alcohol in the motorist's blood is over the legal limit

The equilibrium constant K_c for this reaction has a fixed value at a particular temperature so measurement of the ethanol in the breath can be used to assess the blood alcohol concentration.

The simplest test involves a roadside **breathalyser** which contains crystals of potassium dichromate(VI) which are orange, but are changed to green chromium(III) Cr^{3+} as they oxidize the ethanol to ethanal and ethanoic acid (see oxidation of alcohols in Chapter 10).



The extent of the colour change can be measured using a photocell and so used to determine the ethanol concentration. However, this test is not very accurate and will usually lead to further, more accurate tests being carried out in a laboratory.

A more accurate technique for breath analysis uses **infrared spectroscopy** in an apparatus called an **intoximeter**. The principle here (see Chapter 12) is that different molecules cause different absorption bands in the infrared part of the spectrum, as a result of vibrations of their particular bonds and functional groups. Hence ethanol has a characteristic absorption band at 2950 cm^{-1} owing to its C–H bonds. (Note that the O–H bond also gives a characteristic band but this bond is also present in water vapour, which will be a component of the breath sample.) The size of the peak can be used to measure ethanol concentration, when compared with a reference taken from the ambient air.

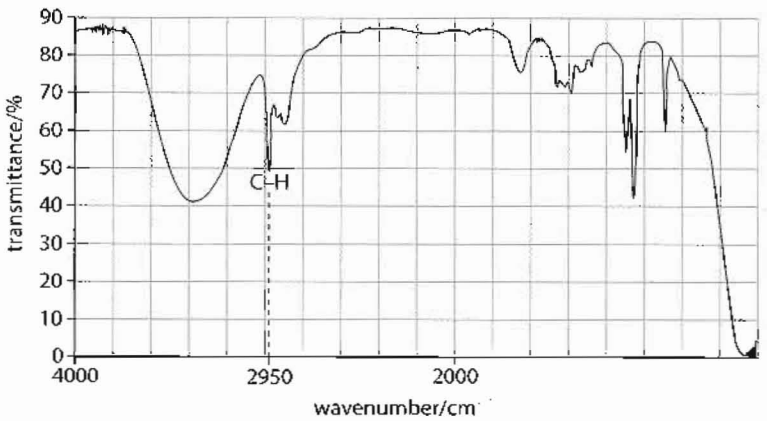


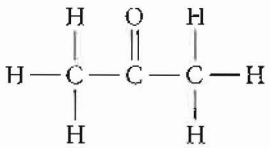
Figure 15.9 Infrared absorption spectrum of ethanol in the gas phase.

Worked example

People who suffer from diabetes often exhale propanone vapour in their breath. Explain why this can give a positive result in the infrared test for ethanol even if they have not consumed alcohol. Refer to the structure of propanone in your answer.

Solution

Propanone has the structure:



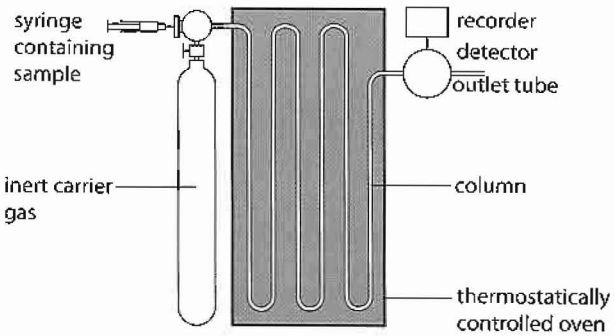
and so contains C—H bonds which will give the same characteristic band at 2930 cm^{-1} as ethanol.

A different version of the intoximeter uses a **fuel cell**. This works on the principle that in the presence of a catalyst, ethanol is oxidized in the air first to ethanoic acid and then to water and carbon dioxide. A fuel cell converts the energy released when oxidation occurs into a detectable electrical voltage that can be used to measure ethanol concentration very accurately.

Starting in 2008, the car manufacturer Volvo plans to incorporate the option of an 'alcolock' into their new cars. This is a fuel cell intoximeter which will automatically read the alcohol content of the driver's breath and accordingly determine whether the car will start or not. The feature aims to reduce the number of alcohol-related traffic accidents, which are responsible for millions of deaths worldwide every year.

Ethanol analysis in blood and urine

The most established method for ethanol analysis is **gas–liquid chromatography**, which must be carried out in a laboratory. In this technique, blood or urine is vaporized and injected into a stream of an inert gas (known as the mobile phase) over the surface of a non-volatile liquid (known as the stationary phase). The components of the vapour, including ethanol gas, move at different rates depending on their boiling points and relative solubility in the two phases. As a result, each leaves the column holding the liquid phase after a specific interval of time known as its **retention time**. So a peak at the retention time corresponding to ethanol can be used to confirm its presence in the vapour. The area under the peak is a measure of ethanol concentration relative to a known standard in the mixture such as propan-1-ol. The method allows for an accurate assessment of ethanol levels.



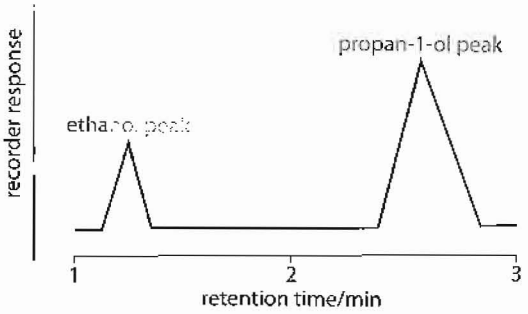
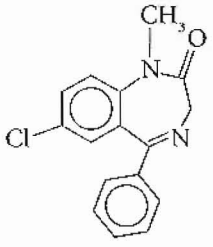


Figure 15.10 Gas–liquid chromatography apparatus and a gas–liquid chromatograph of an alcohol mixture.

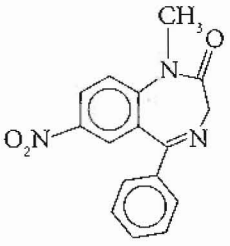
Other depressants

The **benzodiazepines** are a major group of depressants. These drugs depress activity in the part of the brain that controls emotion and so are used as tranquilizers in the treatment of anxiety disorders and related insomnia. As well as being the most commonly used class of sleeping pill, they are also used as muscle relaxants. Although they are usually well tolerated by most people and cause relatively few side-effects, they can cause dependence. For this reason, they are used mostly in short-term treatments. Some widely used benzodiazepine drugs are

diazepam, marketed as Valium® and nitrazepam, marketed as Mogadon®. Their structures are shown here.



diazepam (Valium®)



nitrazepam (Mogadon®)

You can see that, as the name benzodiazepine implies, they contain both benzene rings and the diazepine structure, which is a seven-membered heterocyclic ring containing carbon and two nitrogen atoms. As these molecules are largely non-polar, they have high lipid solubility and so are able to cross the brain–blood barrier.

Worked example

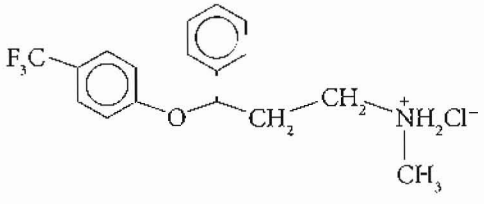
Name three structural features that these molecules of diazepam and nitrazepam have in common. Identify and name one different group in the two molecules.

Solution

Both molecules have two benzene rings, an amide group and a carbon–nitrogen double bond. The one difference is in the substitution in one of the benzene rings: chloro- in diazepam and nitro- in nitrazepam.

A widely used anti-depressant drug is fluoxetine hydrochloride, marketed as Prozac®. It functions by increasing the levels of serotonin – an important neurotransmitter in the brain. It is used in the treatment of depression, as well as eating and panic disorders. (Note that Prozac® does not depress the activity of the CNS so it is not a depressant.) Its structure is shown here.

• **Examiner's hint:** The structures of these drugs are given in the IB Data booklet so they do not have to be learned. However, you should be able to recognize different functional groups and compare structures.



fluoxetine hydrochloride (Prozac®)

Exercises

6 Depressants include tranquilizers and sedatives.

(a) State two effects on the body of taking:

(i) a low dose of a tranquilizer

(ii) a high dose of a sedative.

(b) Explain why depressants are sometimes described as anti-depressants.

7 Ethanol is the most widely used depressant.

(a) Discuss the harmful effects of a regular intake of large amounts of ethanol.

(b) Ethanol can be detected using a breathalyser containing acidified potassium dichromate(VI). Explain what happens to both the ethanol and the dichromate(VI) ion in the reaction and the colour change that occurs.

(c) Briefly describe two other methods that can be used for analysis of ethanol in the breath.

D.5 Stimulants

Stimulants are a different class of drugs that affect the central nervous system. Their function is largely opposite to that of depressants, as they *increase* the activity of the brain and hence the person's state of mental alertness. They are used to prevent excessive drowsiness through the day and so allow greater concentration and thought processes to be possible.

As with other nervous system drugs, stimulants have physiological effects on other parts of the body including the following:

- They can help to facilitate breathing by causing relaxation of the air passages and are used in the treatment of respiratory infections such as severe bronchitis.
- They may reduce appetite and so have been used as part of a treatment for obesity.
- They may cause palpitations or tremors to occur.
- When used in excess they can cause extreme restlessness, sleeplessness, fits, delusions and hallucinations.

Different stimulant drugs function in different ways but most commonly they alter the levels of **neurotransmitters**, chemicals that act as messengers in the nervous system. A few different examples will be discussed here.

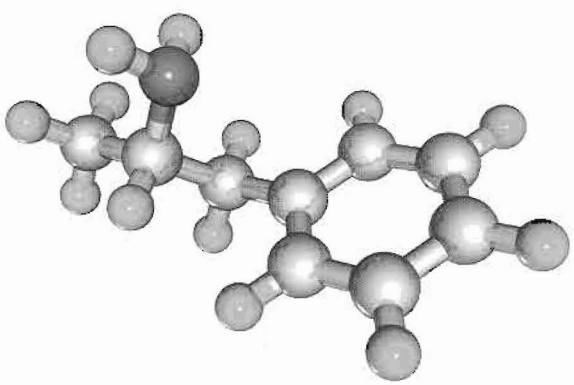
Amphetamines: stimulants that mimic adrenaline

Adrenaline (also called epinephrine) is the hormone that is released in times of stress and enables the body to cope with sudden demands imposed by pain, shock, fear, cold and so on. If you have ever experienced a cold sweat when watching a scary movie, or had a racing pulse during a difficult exam, then you know the effects of adrenaline. The response, sometimes called the 'fight or flight' reaction, stimulates the pathways that:

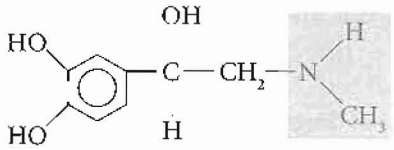
- increase the heart rate and blood pressure
- increase the blood flow to the brain and muscles
- increase the air flow to the lungs
- increase mental awareness.

Adrenaline is very similar in both its structure and its physiological effects to a neurotransmitter called **noradrenaline** (or norepinephrine) which is responsible for communication in the part of the nervous system known as the **sympathetic nervous system**. Here its role is to stimulate the pathways described above.

One major group of stimulant drugs acts to mimic and enhance these effects of adrenaline and noradrenaline. They are known as the **amphetamines** and have a structure quite similar to that of adrenaline and noradrenaline.

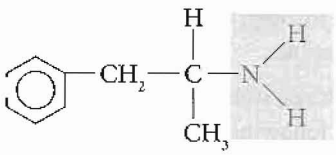


Computer model of a molecule of the drug amphetamine. Carbon atoms are shown in grey, hydrogen atoms in light blue and the nitrogen atoms in dark blue.



secondary amine

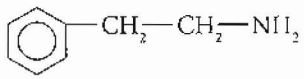
structure of adrenaline



primary amine

structure of amphetamine

You can see that both molecules are derivatives of the phenyl ethyl amine structure.



phenyl ethyl amine

substituted benzene ring — two carbon chain — NH_2 group attached to carbon

Because of their role in stimulating the sympathetic nervous system, the amphetamines are called **sympathomimetic** drugs. In small doses, amphetamines increase mental alertness and physical energy. Side-effects include dilation of the pupils of the eyes and decreased appetite, as well as possible blurred vision and dizziness. Regular use of these drugs leads to the rapid development of both tolerance and dependence, coupled with serious long-term effects such as severe depression and reduced resistance to infection. Abuse of amphetamines through overuse is a serious problem.

Modifications to the amphetamine structure have produced some so-called **designer drugs** that are very powerful – and dangerously addictive stimulants. These include **methamphetamine**, known as 'speed' and 'crystal meth', and the drug 'ecstasy', which although illegal in most countries has markedly increased in distribution globally since the 1980s. It is believed that long-term use of these drugs causes serious brain damage and that in some people even smaller doses can be fatal.

Watch the ABC News Special video 'Ecstasy rising'.

Now go to www.heinemann.co.uk/hotlinks, insert the express code 4259P and click on this activity.

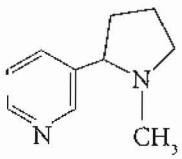
Methamphetamine is dangerous not only to the user but to society at large. It is estimated that every kilogram of methamphetamine produced leaves behind about seven kilograms of toxic waste.

Nicotine: stimulant and highly addictive drug

Drying tobacco leaves in Thailand.

The tobacco plant can grow in a wide variety of warm, moist climates and is farmed on most continents. China has the biggest production, followed by India, Brazil, the USA and Zimbabwe. It is estimated that tobacco is used to make the 5.5 trillion cigarettes that are smoked around the world every year.

Nicotine is one of the most widespread and abused stimulants. It is obtained from tobacco plants but is also found at low concentrations in tomato, potato, eggplant and green pepper plants. Usually it is taken in by inhalation of smoke from cigarettes, cigars and pipe tobacco, but it can also be taken by chewing. Its structure is



nicotine

As a lipid-soluble molecule, nicotine is able to cross the blood–brain barrier bringing about rapid effects on brain activity. Its action is to increase the levels of adrenaline as well as to alter the concentrations of certain neurotransmitters in the brain. As with other drugs, its effects change with increased consumption over time. These are summarized below.

Short-term effects of nicotine consumption	Long-term effects of nicotine consumption
• increases concentration • relieves tension and boredom • helps to counter fatigue • increases heart rate and blood pressure • decreases urine output	• high blood pressure • increases risk of heart disease including angina • coronary thrombosis • increases the level of fatty acids in the blood which can lead to atherosclerosis and stroke • over-stimulation of stomach acids which can lead to increased risk of peptic ulcers

Nicotine is a habit-forming drug, quickly leading to dependence or addiction. The addiction means that the person suffers withdrawal symptoms if they cease intake and these may include nausea, weight gain, drowsiness, inability to concentrate, depression and craving for cigarettes. One of the problems of nicotine addiction is that it is often linked to social factors such as peer pressure.

Burning cigarettes release poisonous chemicals into the air, including nicotine, tar, soot and carbon monoxide. These are inhaled into the lungs of smokers and are also taken in by non-smokers breathing the same air.

Tobacco is the second major cause of death in the world. It is currently responsible for about 5 million deaths each year (that is about 1 in 10 adult deaths worldwide). The World Health Organization states that if current smoking patterns continue this figure will rise to about 10 million deaths each year by 2020. Half the people who smoke today – that is about 650 million people – will eventually be killed by tobacco. In addition, the long-term inhalation of second-hand smoke (sometimes called passive smoking) is now known to have similarly harmful effects on health.

The World Health Organization Framework Convention on Tobacco Control was the world's first international public health treaty when it came into force in February 2005. It aims to help countries strengthen their tobacco control programmes, such as indoor smoking bans, and encourages comprehensive tobacco advertising bans and restrictions on distribution. Currently it has been ratified and is legally binding in 151 countries. Notable non-parties to the agreement are Russia, which has not signed it, and the USA, which has not ratified it.

Nicotine is consumed in tobacco smoke as part of a cocktail of chemicals that include other noxious components such as tar and carbon monoxide. It is now known that long-term smoking is strongly correlated with increased risk of chronic lung diseases, adverse effects on pregnancy and cancers of the lung, mouth and throat. This is in addition to the high cost of obtaining tobacco in most parts of the world and the fact that it stains skin and nails, and leaves a lingering smell on clothing.

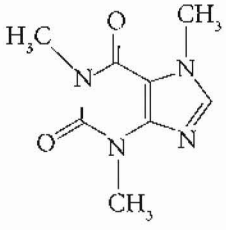
In short, tobacco smoking and nicotine intake can significantly compromise a person's health and well-being. This is perhaps best reflected in the fact that no serious athlete is a smoker and the safe pursuit of many activities such as diving and high altitude mountaineering preclude smokers.

Caffeine: the world's most widely used stimulant

Woman drying coffee beans in the sun in Laos. After picking, the beans are pulped, fermented, washed in water and finally dried in the sun, producing 'milled beans'.

In the last ten years or so, lawsuits in the USA against the tobacco industry have won some successes in claiming compensation for people affected by deaths attributable to tobacco use. The suits claimed that the industry knew of the carcinogenic effects of tobacco smoking but failed to make this information available. It is likely that similar law suits will follow. Now that more information about the effects of tobacco smoking is available, who should be responsible for the impact that it has on an individual's health?

Caffeine is present in coffee, tea, chocolate and colas. It is legal and unregulated almost everywhere; it is estimated that in North America 90% of adults consume caffeine daily. It acts to reduce physical fatigue and restore mental alertness, and is commonly used to help people work longer hours and cope with body clock changes. Its structure is shown here.



caffeine

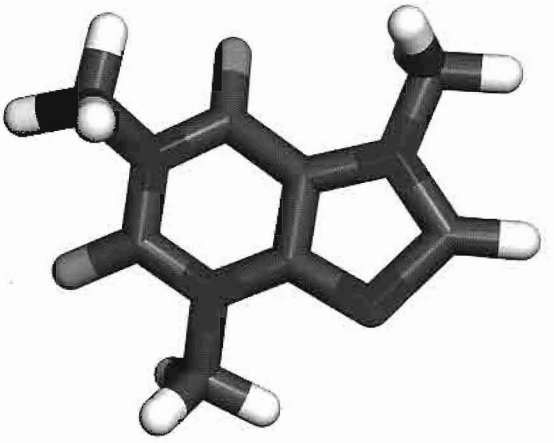
Note that, like nicotine, caffeine contains heterocyclic rings (containing both carbon and nitrogen) and a tertiary amine group. In addition, caffeine contains two amide groups.

For some light relief enjoy this humorous recording depicting how Sir Walter Raleigh, who introduced tobacco to Britain, may have explained the use of tobacco to his boss in London in the 16th century.

Now go to www.heinemann.co.uk/hotlinks, insert the express code 4259P and click on this activity.

Caffeine is found in the beans, leaves and fruit of over 60 plants where it acts as a natural pesticide, paralysing and killing certain insects that feed on the plants.

The main source of coffee beans is the Arabica plant which is grown in over 70 countries. The top coffee producers are Brazil, Colombia, India, Indonesia, Mexico, Puerto Rico and Vietnam. Although coffee has experienced a spike in popularity over the last 20 years, it has often been at the expense of the producers who have experienced a dramatic fall in price and often live in impoverished conditions. The 'fair trade coffee' movement has attempted to address the inequalities by assuring its customers that the coffee was purchased under fair conditions.



Model of a molecule of caffeine: nitrogen is shown in blue, oxygen in red and hydrogen in white. Notice the positions of the tertiary amine and amide groups.

Caffeine acts as a respiratory stimulant increasing the rate of energy release within cells. It also intensifies and prolongs the effects of adrenaline. Some of the main effects of caffeine, depending on the amount consumed, are summarized below.

Consumption of caffeine in small amounts	Consumption of caffeine in large amounts
• enhancement of mental energy, alertness and ability to concentrate • acts as a diuretic, increasing the volume of urine; can cause dehydration	• can cause anxiety, irritability and insomnia • can cause dependence; side-effects on withdrawal include headaches and nausea

In general, an intake of more than four cups of coffee per day may be considered non-beneficial. Pregnant women are advised to limit their caffeine intake.

Caffeine helps the body to absorb some analgesics and is often included in the formulation of headache pills and other medications.

There are many ways of preparing decaffeinated coffee but usually the beans are first soaked in hot water which dissolves out the caffeine. The water is then passed over activated charcoal which removes the caffeine by adsorption, but allows other components of the coffee, essential for its flavour, to remain. The water is then returned to the beans. Other processes use solvents to absorb caffeine selectively from the infused water. The extracted caffeine is used in soft drinks and in the preparation of caffeine tablets.

Alka-Seltzer tablets are used to treat indigestion, heartburn and associated aches and pains. They contain aspirin (analgesic), sodium hydrogen carbonate (antacid) and caffeine. The tablets effervesce in water, as seen on the packet.

Exercise

8 Look at the structures of caffeine and nicotine which are given in Table 20 of the IB Data booklet.

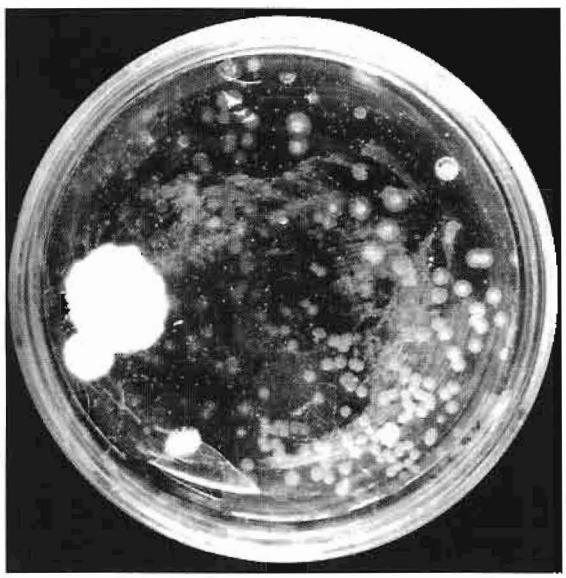
(a) Describe two similarities in their structure, not including the presence of double bonds, methyl groups and nitrogen atoms.

(b) Discuss the problems associated with nicotine consumption with reference to both short-term and long-term effects.

D.6 Antibacterials

The first example of a chemical used to kill pathogens came from the observation that certain dyes used in the dyestuffs industry were able to kill some microorganisms. In 1891 this led to the treatment of malaria using methylene blue. Paul Ehrlich of Berlin (page 344) introduced the concept of a 'magic bullet', a chemical designed to target a specific disease but not touch the host cells, and successfully treated syphilis patients with an arsenical drug. Systematic screening for other potential antimicrobials led to the discovery of the **sulfonamide** drugs, such as Prontosil®, in 1933 with their seemingly miraculous ability to cure septicaemia. By 1940, the use of sulfonamides had dramatically reduced the number of deaths of mothers in childbirth.

However, it was the discovery of the chemicals known as **penicillins** that truly revolutionized modern medicine, as this gave birth to drugs now known as **antibiotics**. These are chemicals, usually produced by microorganisms, which act against other microorganisms. Their discovery is generally credited to Alexander Fleming, who was a Scottish microbiologist, working in 1928 on bacteria cultures. He noticed that a fungus (or mould) known as *Penicillium notatum* had contaminated some of his cultures and was therefore about to discard them as spoiled. However, his eye was drawn to the fact that the mould had generated a clear region around it where no bacterial colonies were growing. He concluded that something produced by the mould was specifically inhibiting the bacterial growth. Fleming published his findings, but as he and his collaborators were not chemists, they did not pursue the work of isolating and identifying the active ingredient.



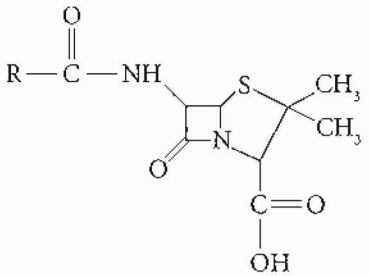
Fleming's original culture plate contaminated by the fungus *Penicillium notatum*, photographed 25 years after the discovery in 1928. The clear region around the fungus where bacterial growth is inhibited can be clearly seen.

In the early 1940s the Australian bacteriologist Howard Florey and German-born biochemist Ernst Chain, working in Oxford, England, picked up the research and successfully isolated penicillin as the antibacterial agent produced by the penicillium mould. It was used for the first time in human trials in 1941 – in the midst of World War II when there was an unprecedented demand for such a treatment for bacterial infections resulting from war wounds. Its rapid development and distribution is known to have saved thousands of lives in the later years of the war. For their work in discovering penicillin, Fleming, Florey and Chain shared the Nobel Prize in Medicine in 1945.

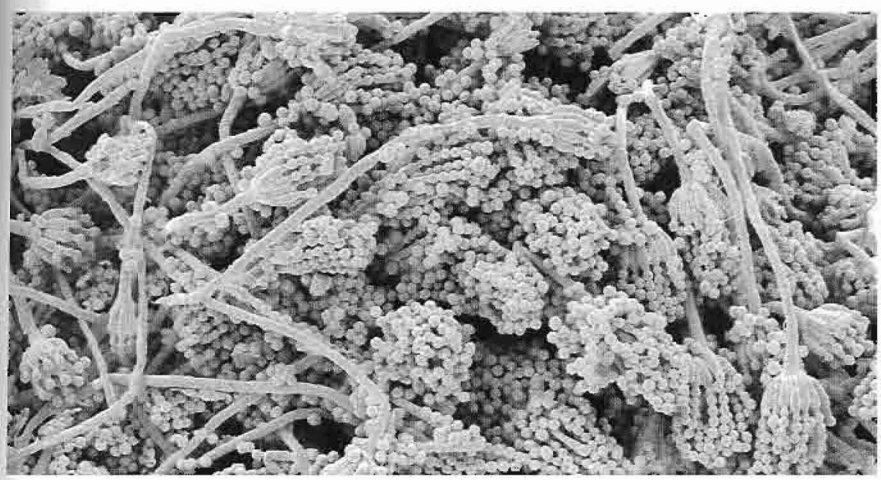
Fleming's discovery of penicillin is often described as serendipitous – a fortunate discovery made by chance or by accident. However, as Louis Pasteur once famously said 'Chance favours only the prepared mind'. Consider to what extent scientific discoveries are only possible by scientists who are trained in the principles of observation and interpretation.

The main research and production of penicillin was moved to the USA in 1941 to protect it from the bombs pounding Britain during the war. Large-scale production methods were developed using deep fermentation tanks containing corn steep liquor through which sterile air was forced.

The isolation and development of penicillin occurred, however, before there was any understanding of its chemical structure or its mode of action. It was the work of British biochemist Dorothy Hodgkin in 1945 using X-ray crystallography, which determined the structure of **penicillin G**, the major constituent of the mould extract. Its structure is shown here.



Its core structure is a four-membered ring consisting of a nitrogen atom and three carbon atoms. Its antibacterial action lies in the fact that it inhibits the development of cross-links in bacterial cell walls, so weakening the walls and causing the bacteria to rupture and die during their reproductive phase. Its action is effective against a wide range of bacteria, many of which are responsible for infections of the ear, nose, throat and mouth, as well as at the sites of infection from wounds.



A disadvantage of penicillin G is that it is broken down by stomach acid and has to be injected directly into the blood. Different forms of penicillin have been developed by modifying the side chain (the part denoted as 'R' in the diagram above) and these enable the drug to retain its activity even when ingested in pill form.

Antibiotic resistance: are we killing the cures?

A major problem with the use of penicillin – and also other antibiotics – is that of **bacterial resistance**. This was observed as early as the 1940s when penicillin proved to be ineffective against some populations of bacteria. It is now known that these resistant bacteria produce an enzyme, **penicillinase**, which can open penicillin's four-membered ring and render it inactive.

During World War II, when the supply of penicillin could not meet demand, it became a practice to collect the urine from patients being treated to isolate and reuse the penicillin it contained. It was estimated that as much as 80% of early penicillin formulations was lost from the body in the urine.

Dorothy Hodgkin (1910–1994), the British X-ray crystallographer who discovered the structures of penicillin, vitamin B_{12} and insulin. She was awarded the Nobel Prize in Chemistry in 1964.

Coloured scanning electron micrograph of *Penicillium* sp growing on bread. This is the mould that is used to produce the antibiotic penicillin.

Antibiotic resistance has become a major problem for some strains of tuberculosis (TB) and treatment may now require the use of several different antibiotics together. It is estimated today that one in seven new TB cases is resistant to the drugs most commonly used to treat it. In crowded conditions such as prisons in Russia, resistance rates are higher still, although the World Health Organization has had some success in introducing tough measures to stem a TB epidemic there. Antibiotic resistance must be faced on a global scale, as no country can protect itself from the importation of resistant pathogens through travel and trade.

Antibiotic resistance arises by genetic mutation in bacteria and would normally account for a very small proportion of the population. But the number of resistant organisms increases dramatically with increased exposure to the antibiotic. So the very success of antibiotics in fighting disease has led to this major challenge from widespread resistant strains, which today threatens their very usefulness. So-called **superbugs** are bacteria which carry several resistant genes and are a serious problem in many hospitals.

The problem of resistance has been compounded by the wide use of penicillins (and other antibiotics) in animal feeds to lower the incidence of disease in the stock. It is estimated that more than 55% of antibiotics produced in North America and Europe are given to food animals in the absence of disease. This has caused the antibiotics to enter the human food chain and hence increase the proportion of resistant bacteria.

Responses to the challenge of antibiotic resistance have included the following:

- developing different forms of penicillin, with modified side chains able to withstand the action of penicillinase
- controlling and restricting the use of antibiotics by legislation to make them prescription-only drugs; also encouraging doctors not to over-prescribe
- education and encouragement of patients in the importance of completing the full course of treatment with an antibiotic, referred to as 'patient compliance'. This is essential to prevent resistant bacteria prolonging the disease or spreading into the community.

Exercise

9 (a) State how penicillins prevent the growth of bacteria and explain why scientists continue to develop new penicillins.
(b) Explain the specific effects of modifying the side chain in penicillin.
(c) Discuss three ways in which human activities have caused an increase in the resistance to penicillin in bacteria populations.

D.7 Antivirals

Viruses: nature's most successful parasites

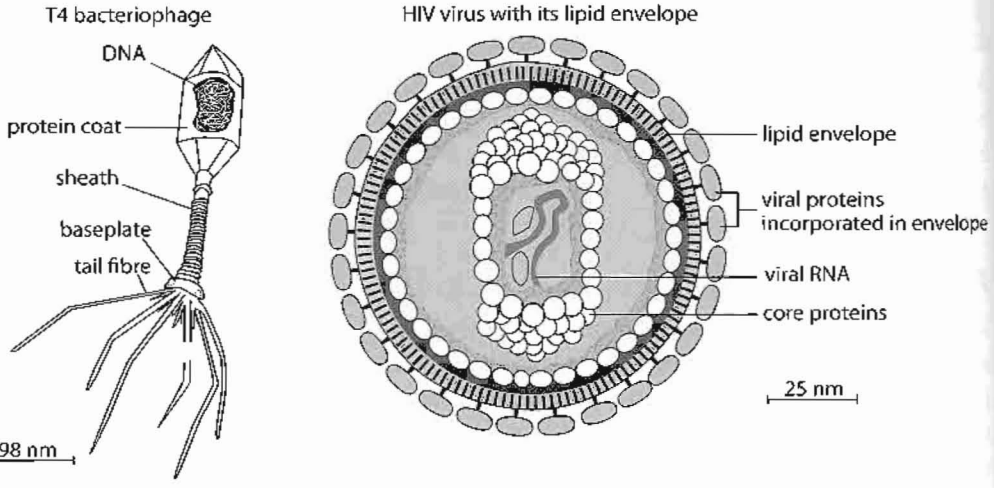


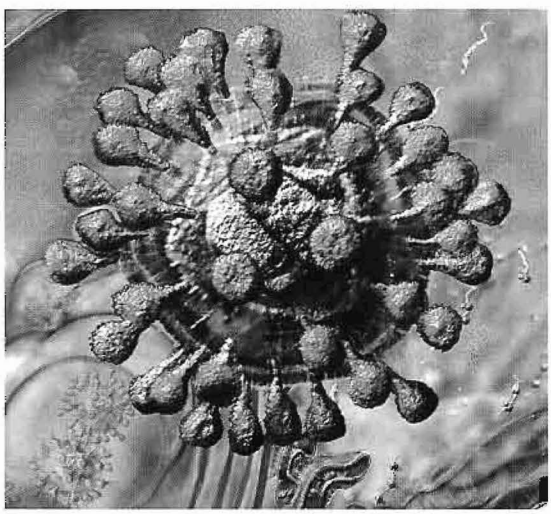
Figure 15.11 Examples of viruses

Viruses are such small and simple structures that there is debate about whether they can be classified as living organisms in their own right. They contain only the two components protein and nucleic acid (either RNA or DNA), have no cellular structure and are only capable of reproducing inside another living cell. In all of these ways they are different from bacteria with their more complex cellular structure and ability to survive and reproduce independently from other living cells.

Viruses are in fact the original hijackers – they literally take over the functioning of another cell (the so-called 'host' cell) and use it to carry out their own reproduction. The host cell's components are used in the assembly of new viral particles and in the process the cell eventually dies, releasing thousands of viral particles into the body.

The war against viruses

Viral infections claim the lives of millions of people each year and are responsible for an even greater number of illnesses, many of them serious. Diseases such as measles, meningitis and polio are caused by viruses as well as relatively new diseases such as AIDS (acquired immune deficiency syndrome) and avian 'flu. Developing effective antivirals is therefore one of the most pressing challenges of modern medicine.



Artwork of a SARS virus particle inside a cell. SARS (Severe Acute Respiratory Syndrome) is an often fatal lung disease that first appeared in China in late 2002 and spread rapidly through the world via air travel. The virus is related to the type that causes the common cold. Like all viruses it cannot replicate by itself but instead uses the machinery of the host cell to produce more copies of itself.

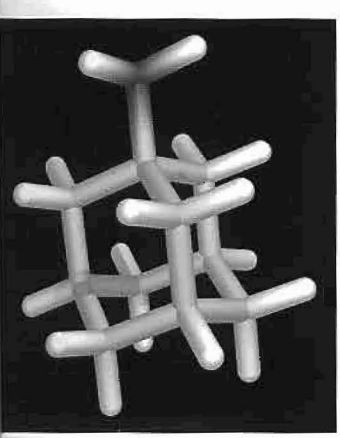
Treating viral infections is a challenge because the viruses live within cells and so cannot be easily targeted. Lacking the cell structure of bacteria, they are not attacked by antibiotics. Another problem is the speed at which they can multiply which means that they have often spread throughout the body by the time that symptoms appear. In addition, virus particles have a tendency to mutate rapidly (make small changes in their genetic material) and this changes their susceptibility to drugs. This is why, for example, different types of 'flu vaccine are developed each year according to the most abundant strain of virus around.

Polio was a common disease in the industrialized world until a successful vaccination was developed in the 1950s. It most commonly affected children under five years old, leaving many who survived crippled and paralysed. Immunization programmes have led to the eradication of the disease from most of the world, although some countries, notably India, Nigeria and Pakistan, remain polio-endemic. The Global Polio Eradication Initiative was launched in 1988 and tracks all new cases on a weekly basis.

Nonetheless there have been significant successes in the treatment of viral infections. Successful vaccination programmes, which generally enable the body to prepare specific **antibodies** against a virus, have reduced the incidence of diseases such as cholera, polio and measles. In 1980, the World Health Organization declared smallpox an eradicated disease.

Some antivirals work by altering the cell's genetic material (DNA) so that the virus cannot use it to multiply. Others block enzyme activity within the host cell, which prevents the virus from reproducing. In this case the progression of the disease will be halted and there will be relief from symptoms, but note that the virus is not completely eradicated from the body. This can cause a flare up on another occasion – this is what happens, for example, with some herpes infections that cause cold sores.

One reasonably effective antiviral drug is **amantadine**, which causes changes in the cell membrane that prevent the entry of the virus into the cells. It is therefore best used as a prophylactic (preventative) treatment or given before the infection has spread widely. It has been used in this way quite effectively in the treatment of influenza.

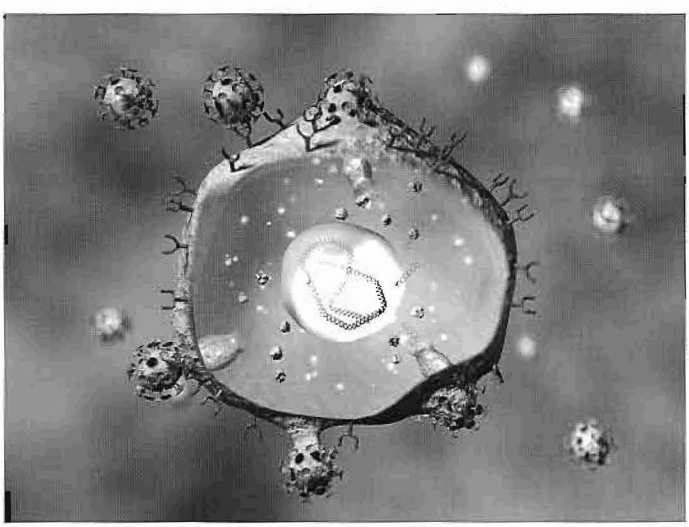


Molecular model of amantadine antiviral drug. The drug is used to treat Influenza A infection in adults, as it prevents the ability of the virus to replicate its genetic material.

AIDS: a viral pandemic

The condition known as AIDS, caused by the virus HIV (human immunodeficiency virus), was first diagnosed in humans in 1981. It is characterized by a failure of the immune system, so that the body falls prey to life-threatening opportunistic infections such as pneumonia and forms of cancer. The infection has spread at an alarming rate through the global population and it is estimated that 40 million people are currently **HIV positive**, with a likelihood of developing AIDS. In some countries in sub-Saharan Africa it is believed that as many as one-third of the adult population may be affected.

HIV primarily infects vital white blood cells in the immune system called **$CD4^+$ T cells** by binding to specific receptor proteins on their surface and then penetrating the cell. As HIV is a **retrovirus** (having its genetic material in the form of RNA rather than DNA), it releases its RNA into the cell and the enzyme **reverse transcriptase** controls the synthesis of viral DNA from the RNA. The HIV DNA integrates into the cell's own DNA and replicates with it when the cell divides. Viral particles are produced within the host cell and are released in large numbers when the cell dies.



Computer artwork of HIV replication. The viral particles, shown in green, surround the white blood cell, shown in blue, and attach themselves to its surface using specific proteins for recognition. RNA, shown in pink, is then injected into the cell and, using reverse transcriptase, synthesizes DNA, which integrates into the host's chromosome (this can be seen to the right of the white cell nucleus. New viral particles are assembled within the cell and are shown at the bottom budding from the cell, taking part of the membrane as an envelope.

There are three main reasons why HIV is proving even more challenging than other viruses to defeat.

1 The virus destroys T helper cells, the very cells in the immune system that should be defending the body against it.
2 The virus tends to mutate very rapidly even within a patient. It is thought that there is more variation in HIV in a single patient than in influenza worldwide in a year! These variations mean that the virus 'escapes' the immune response, so the patient has to make a response to the new virus.
3 The virus often lies dormant within host cells, so the immune system has nothing to respond to.

Drugs to help in the fight against HIV, known as **antiretroviral drugs**, act at different stages in the HIV lifecycle. One target is to inhibit the enzyme reverse transcriptase, as this is specific to the virus and does not affect the host cell. The drug AZT, also known as zidovudine, works in this way and was the first antiretroviral drug approved for use in AIDS treatment. It does not destroy the HIV infection, but it has been effective in delaying the progression of the disease. It is also used as part of a regimen to prevent mother to child transmission of HIV during pregnancy. Other antiretrovirals act to block the binding of HIV to cell membranes or to inhibit the assembly of new viral particles within the cell. Although these drugs all produce side effects ranging from unpleasant to serious, they are proving successful in helping to prolong the length and quality of life of people infected with HIV.

Intense research into developing a vaccine for HIV/AIDS has so far failed to produce a fully effective result. This is mainly because of the problem of the variable nature of the virus within cells and the fact that the immune response seems to act too slowly in the case of HIV infection.

Antiretroviral drugs usually need to be taken in combination with each other and over a long period of time to be effective. This is one of the reasons why they are generally expensive to administer and have been very poorly distributed in the countries where they are needed the most. However, in May 2007 the Clinton Foundation HIV/AIDS Initiative announced a commitment from major drug companies that reductions in price to US$1 per day would apply to the provision of antiretrovirals in 65 developing countries in Africa, Asia and Latin America.

Practice questions

1 Acidified potassium dichromate(VI) is commonly used in roadside tests for ethanol in the breath of persons operating motor vehicles. It reacts with the ethanol present to form ethanoic acid.

(a) State the function of potassium dichromate(VI) and give the colour change that takes place in this reaction. (2)

(b) Identify **two** other methods for the detection of ethanol in a person's breath or blood that are considered to be more accurate. (2)

(c) State **one** harmful effect of aspirin that is more likely to occur if it is taken with ethanol. (1)

(d) Diazepam and nitrazepam are two depressants that are very similar in their structures. State the name of **two** different functional groups present in both depressants. (2)

(Total 7 marks)

2 (a) State the purpose of using an antacid. (1)

(b) State and explain which would be more effective as an antacid, 1.0 mol of magnesium hydroxide or 1.0 mol of aluminium hydroxide. Support your answer with balanced equations. (3)

(Total 4 marks)

3 Analgesics can be classified as mild or strong.

(a) State and explain how each type of analgesic prevents pain. (4)

(b) Aspirin is a common mild analgesic.

(i) Outline **one** advantage and **one** disadvantage of using aspirin. (2)

(ii) Acetaminophen (paracetamol) is often used as a substitute for aspirin. State **one** disadvantage of using acetaminophen. (1)

(Total 7 marks)

4 The structures of some analgesics are shown in Table 20 of the IB Data booklet. Refer to this table when answering parts (a) and (b) of this question.

(a) State the name of the nitrogen-containing functional group in each of the following molecules. (2)

paracetamol heroin

(b) Naturally occurring morphine can be converted into synthetic heroin by reaction with ethanoic acid. Identify the group in the morphine molecule that reacts with ethanoic acid, the name of the type of reaction and the other product of the reaction. (3)

(Total 5 marks)

5 Penicillins are molecules that can kill harmful microorganisms. Their general structure is shown in Table 20 of the IB Data booklet.

(a) State the type of microorganism killed by penicillins and explain how they do this. (4)

(b) Explain the effect of over-prescription of penicillins. (3)

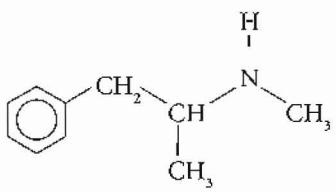
(Total 7 marks)

6 (a) Describe the differences between bacteria and viruses by referring to their structures and the way they multiply. (4)

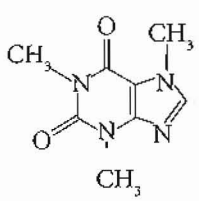
(b) Outline **two** ways in which antiviral drugs work. (2)

(Total 6 marks)

7 Methylamphetamine (also known as methamphetamine or 'speed') and caffeine are stimulants with the following structures.



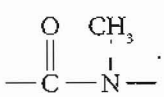
methylamphetamine



caffeine

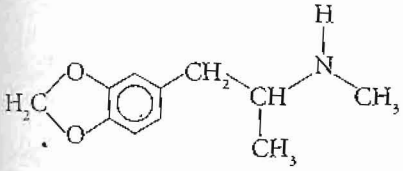
(a) (i) On the structure for methylamphetamine above, draw a ring around the amine group. (1)

(ii) Determine whether both amine groups in caffeine are primary, secondary or tertiary. (1)

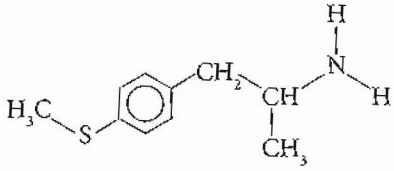
(b) Caffeine contains the group  .

State the general name for this functional group. (1)

(c) A 'designer drug' with a structure related to methylamphetamine is ecstasy. Ecstasy tablets are sometimes contaminated with a substance called 4-MTA.



ecstasy



4-MTA

(i) Methylamphetamine, ecstasy and 4-MTA are sympathomimetic drugs. Identify the structural similarity between the three drugs and adrenaline, the structure of which is given in the IB Data booklet. (1)

(ii) Outline what is meant by the term *sympathomimetic drug* and state **one** example of a short-term effect sympathomimetic drugs have on the human body. (2)

(iii) State **one** example of a long-term effect of taking stimulants. (1)

(Total 7 marks)

8 (a) Many drugs are taken orally. State three other ways in which drugs may be taken by a patient. (2)

(b) State what is meant by the term *side-effect*. (1)

(c) One common type of drug taken orally is the antacid. Antacids such as sodium hydrogencarbonate are taken to reduce stomach acidity.

(i) State the names of **two** metals, other than sodium, whose compounds are often used in antacids. (1)

(ii) Give an equation for the neutralization of hydrochloric acid in the stomach by sodium hydrogencarbonate. (1)

(iii) Explain how heartburn is caused. (1)

(iv) Explain why dimethicone is added to some antacids. (1)

(Total 7 marks)

9 (a) Aspirin is a widely used analgesic.

(i) State the general names of the **two** functional groups attached to the benzene ring in a molecule of aspirin. (2)

(ii) The use of aspirin can have beneficial effects for the user, but can also produce some unwanted side-effects. State **one** beneficial effect (other than its analgesic action) and **one** unwanted side-effect. (2)

(b) Morphine is a naturally occurring analgesic that can be converted into codeine.

(i) Calculate the difference in relative formula mass between morphine and codeine. (1)

(ii) Explain what is meant by developing tolerance towards codeine and state why this is dangerous. (2)

(Total 7 marks)