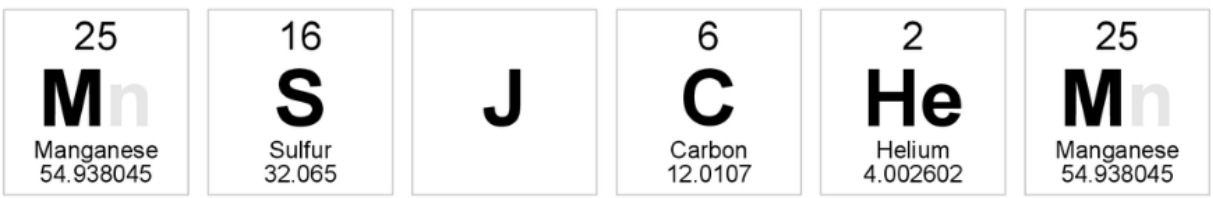
Option D Medicinal chemistry SL

IB CHEMISTRY SL



D.1 Pharmaceutical products and drug action

Understandings:

- In animal studies, the therapeutic index is the lethal dose of a drug for 50% of the population (LD_{50}) divided by the minimum effective dose for 50% of the population (ED_{50}).
- In humans, the therapeutic index is the toxic dose of a drug for 50% of the population (TD_{50}) divided by the minimum effective dose for 50% of the population (ED_{50}).
- The therapeutic window is the range of dosages between the minimum amounts of the drug that produce the desired effect and a medically unacceptable adverse effect.
- Dosage, tolerance, addiction and side effects are considerations of drug administration.
- Bioavailability is the fraction of the administered dosage that reaches the target part of the human body.
- The main steps in the development of synthetic drugs include identifying the need and structure, synthesis, yield and extraction.
- Drug–receptor interactions are based on the structure of the drug and the site of activity.

Applications and skills:

- Discussion of experimental foundations for therapeutic index and therapeutic window through both animal and human studies.
- Discussion of drug administration methods.
- Comparison of how functional groups, polarity and medicinal administration can affect bioavailability.

Guidance:

- For ethical and economic reasons, animal and human tests of drugs (for LD_{50}/ED_{50} and TD_{50}/ED_{50} respectively) should be kept to a minimum.

Introduction to medicines and drugs

Medicines and drugs are chemical substances that do one or more of the following:

- alter incoming sensory sensations
- alter a person's mood or emotions
- alter the physiological state of the body including consciousness and coordination.

Drugs

- A drug is a substance that causes a physiological change in the body.
- Pharmaceutical drugs are used for the treatment or prevention of disease.
- Recreational drugs are chemical substances taken for enjoyment, or leisure purposes, rather than for medical reasons.
- Examples include alcohol, nicotine, cannabis and ecstasy.

Medicines

- Medicines (pharmaceutical drugs) are substances used for the treatment or prevention of disease.
- Medicines contain beneficial drugs.
- The beneficial effect of a medicine is known as its therapeutic effect.
- Examples of medicines include aspirin, penicillin and ibuprofen.

Therapeutic window

- The therapeutic window is a measure of the safety of a drug.
- The wider the therapeutic window, the safer the drug.
- A wide therapeutic window means that there is a wide margin between doses that are effective and doses that are toxic.
- A narrow therapeutic window means that only a small increase in the effective dose may produce toxic effects.
- The therapeutic window can be quantified by the therapeutic index.
- The therapeutic index is the ratio between the dosage of a drug that causes a toxic (or lethal) effect and the dosage that causes a therapeutic effect.

$$\text{TI (humans)} = \frac{\text{TD}_{50}}{\text{ED}_{50}} \qquad \text{TI (animals)} = \frac{\text{LD}_{50}}{\text{ED}_{50}}$$

- ED_{50} (effective dose) is the dose that produces the therapeutic effect in 50% of the population.
- TD_{50} / LD_{50} (toxic/lethal dose) is the dose that is toxic / lethal to 50% of the population.

Example question:
Discuss the term therapeutic window. Your answer should include its meaning, a quantitative description and an explanation of wide and narrow therapeutic windows.
Answer:

- A measure of the relative margin of safety of a drug.
- Ratio of the lethal dose (LD_{50}) to effective dose (ED_{50}).
- Wide therapeutic window means a greater margin between effective and toxic dose (a safer drug).
- Narrow therapeutic window means there is a higher risk of an overdose.

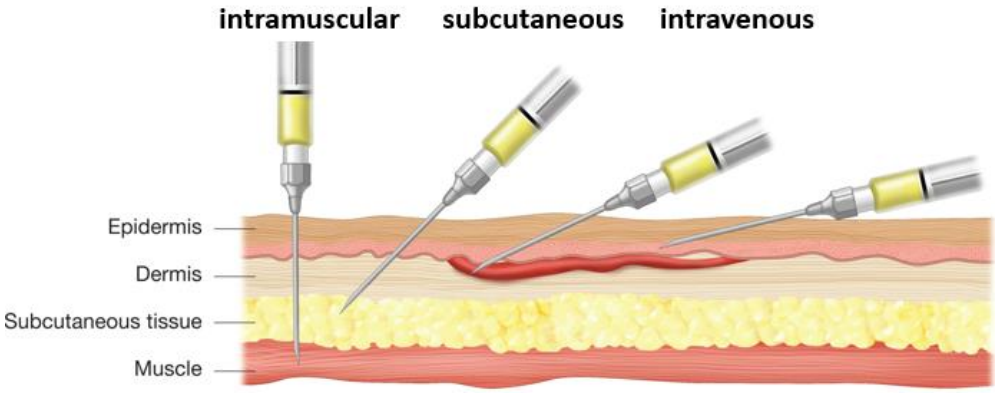
Stages of drug development
Main stages of drug development:

- Drug is synthesized in the laboratory.
- The drug is tested on animals to determine the LD_{50}.
- The drug is tested on humans – half of the group are given the real drug, the other half are a given a placebo.
- Placebo contains none of the drug being tested.
- Patients and administrators do not know who has received the drug and who has received the placebo.
- Placebo effect is when the body is fooled into healing itself naturally.
- Other factors that must be determined during clinical drug trials are:
  risk: benefit ratio – balance between the risks and benefits of the drug
  unwanted side effects
  drug tolerance – person needs to take ever larger quantities of a drug to gain the original effect.

Methods of drug administration

Method	Description	Example
Oral	Taken by mouth	Tablets, capsules, pills
Inhalation	Vapour breathed in smoking	Asthma medication Drugs such as nicotine
Skin patches	Absorbed through the skin into the blood	Hormone patches
Suppositories	Inserted into the rectum	Laxatives for constipation
Eye or ear drops	Liquids administered into eyes or ears	Treatment of eye or ear infections
Injection (parenteral)	Injected into the muscle, blood or under the skin	Vaccines, local anesthetics

Parenteral methods of drug administration



- Intramuscular – drug is injected directly into the muscle.
- Subcutaneous – drug is injected directly under the skin.
- Intravenous – drug is injected directly into the bloodstream.

Bioavailability

Bioavailability is the fraction of the administered dosage of a drug that enters the bloodstream thereby accessing the site of action.

The factors that affect the bioavailability of a drug are:

- the method of drug administration
- the polarity (solubility) of the drug
- the type of functional groups present in the drug.

Method of drug administration

- Drugs that are administered intravenously have a bioavailability of 100% as they are delivered directly into the bloodstream.
- Drugs that are administered orally are often broken down during digestion before reaching the bloodstream.
- In general, an oral dose of a drug needs to be about four times higher than the dosage of the same drug that is administered intravenously.

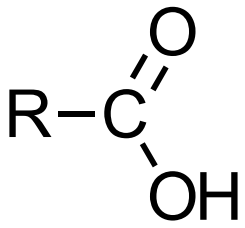
The polarity of a drug affects its solubility

- Very hydrophilic (polar) drugs are soluble in aqueous body fluid but are poorly absorbed because of their inability to cross cell membranes (which are composed of lipids).
- Very hydrophobic (non-polar) drugs are also poorly absorbed because they are insoluble in aqueous body fluids.
- For a drug to be readily absorbed, it must be largely hydrophobic, but also have some solubility in aqueous solutions.

Functional group and solubility in water and fat

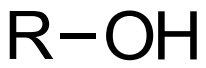
- The two major properties that contribute to the water solubility of a functional group are its ability to ionize and to form hydrogen bonds.

Carboxyl group

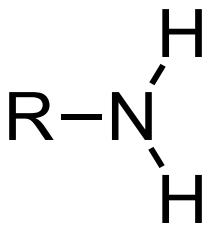


Acidic functional group

Hydroxyl group



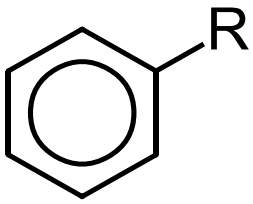
Amine group



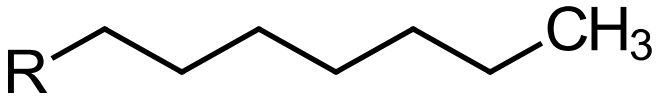
Basic functional group

- Functional groups that enhance the lipid solubility of a drug are non-polar.
- They lack the ability to ionize or to form hydrogen bonds.

Phenol group

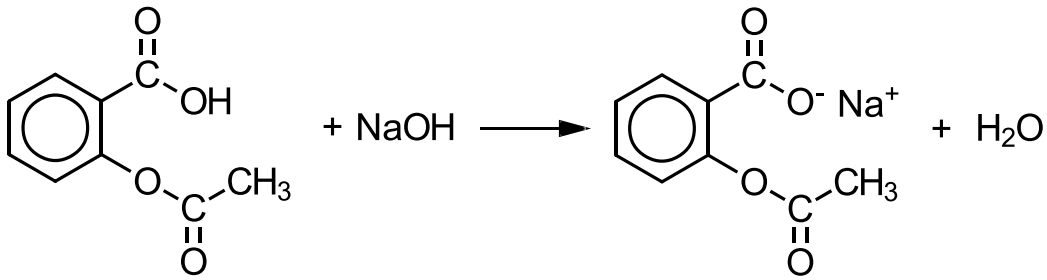


Hydrocarbon chain



Solubility of aspirin

- Aspirin is a largely non-polar molecule and therefore has low solubility in water.
- The solubility of aspirin can be increased by reacting it with aqueous NaOH forming an ionic salt.



- Drugs which contain an acidic or basic group can be chemically modified to form an ionic salt (increasing their bioavailability).

D.2 Aspirin and penicillin

Understandings:

Aspirin:

- Mild analgesics function by intercepting the pain stimulus at the source, often by interfering with the production of substances that cause pain, swelling or fever.
- Aspirin is prepared from salicylic acid.
- Aspirin can be used as an anticoagulant, in prevention of the recurrence of heart attacks and strokes and as a prophylactic.

Penicillin:

- Penicillins are antibiotics produced by fungi.
- A beta-lactam ring is a part of the core structure of penicillins.
- Some antibiotics work by preventing cross-linking of the bacterial cell walls.
- Modifying the side-chain results in penicillins that are more resistant to the penicillinase enzyme.

Applications and skills:

Aspirin

- Description of the use of salicylic acid and its derivatives as mild analgesics.
- Explanation of the synthesis of aspirin from salicylic acid, including yield, purity by recrystallization and characterization using IR and melting point.
- Discussion of the synergistic effects of aspirin with alcohol.
- Discussion of how the aspirin can be chemically modified into a salt to increase its aqueous solubility and how this facilitates its bioavailability.

Penicillin

- Discussion of the effects of chemically modifying the side-chain of penicillins.
- Discussion of the importance of patient compliance and the effects of the over-prescription of penicillin.
- Explanation of the importance of the beta-lactam ring on the action of penicillin.

Guidance:

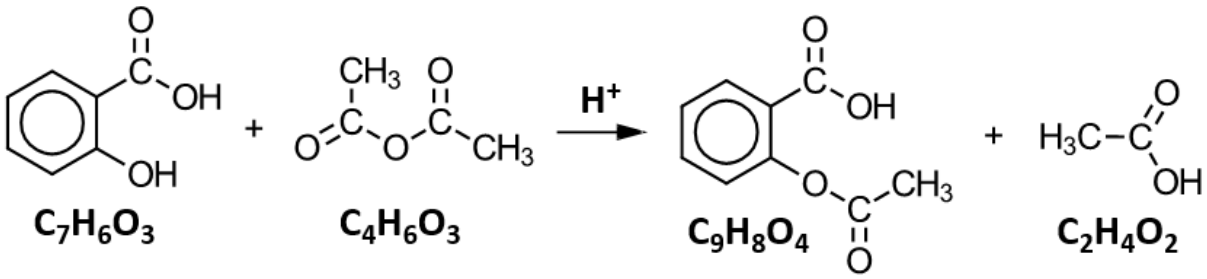
- Students should be aware of the ability of acidic (carboxylic) and basic (amino) groups to form ionic salts, for example soluble aspirin.
- Structures of aspirin and penicillin are available in the data booklet in section 37.

Uses of aspirin

- Aspirin is a mild analgesic (painkiller).
- Mild analgesics block the sensation of pain at the source.
- Aspirin works by blocking the action of the enzymes that produce prostaglandins.
- Prostaglandins are involved in the transmission of pain impulses to the brain, as well as causing fever and swelling.
- Aspirin prevents the prostaglandins from being synthesized, thereby reducing or eliminating the pain.
- Aspirin is also used as an anticoagulant.
- Anticoagulants are a class of drugs that work to prevent the blood from clotting.
- They are effective in the prevention of the recurrence of heart attacks and strokes.
- Due to its anti-inflammatory properties, aspirin is also taken for arthritis and rheumatism.
- The most common side effect of aspirin is that it can cause bleeding of the lining of the stomach.
- This effect is increased by drinking alcohol (ethanol) at the same time as taking aspirin, which is known as a synergistic effect.
- Two drugs can have a synergistic effect if they increase each other's effectiveness when taken together.
- The synergistic effects of alcohol and aspirin can cause increased bleeding of the stomach lining.

Synthesis of aspirin

- Aspirin (acetylsalicylic acid) is produced by reacting salicylic acid with ethanoic anhydride.



salicylic acid + ethanoic anhydride → aspirin + ethanoic acid

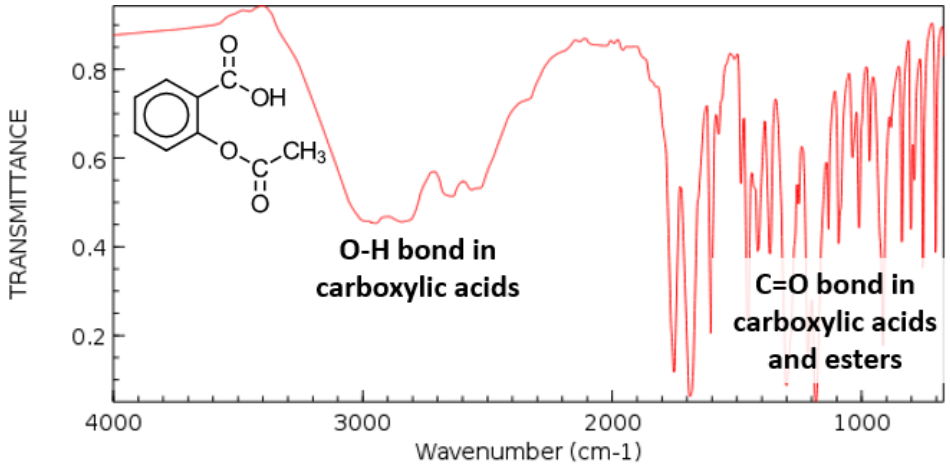
- Concentrated H_2SO_4 is added to the reaction mixture which is warmed gently.
- The product is cooled to form crystals which are then suction filtered and washed with cold water.
- Aspirin has very low solubility in cold water, so this process removes the soluble acids but not the aspirin.

- The aspirin is purified in a process known as recrystallization; this involves dissolving the impure crystals in a small volume of hot ethanol.
- Water is then added and the solution is cooled slowly and then chilled.
- The acetylsalicylic acid will recrystallize, and the unreacted salicylic acid remains dissolved in the solution.

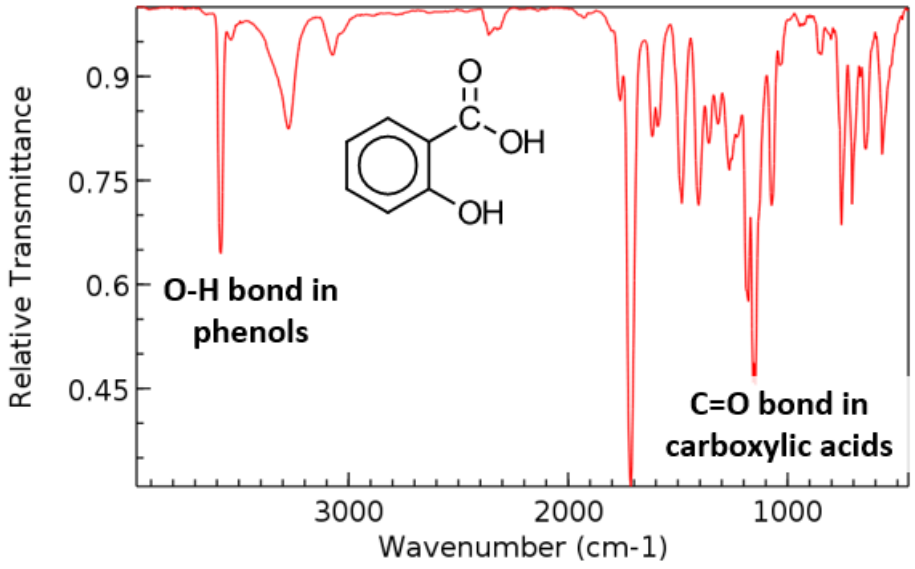
Determining the purity of aspirin

- The purity of the aspirin can be determined by its melting point and also its infrared spectrum.
- Pure aspirin has a melting point of between 128-140^{o}C.
- Impurities lower the melting point and cause it to melt over a wider temperature range.

Infrared spectrum of aspirin



Infrared spectrum of salicylic acid



Bioavailability of aspirin

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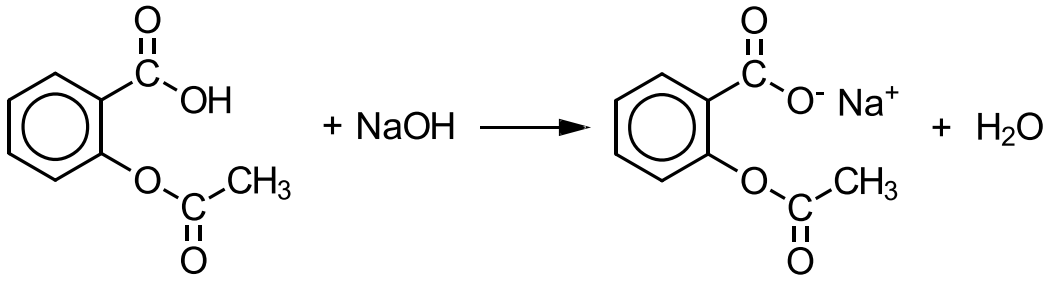
- The solubility of aspirin can be increased by reacting it with aqueous NaOH forming an ionic salt.



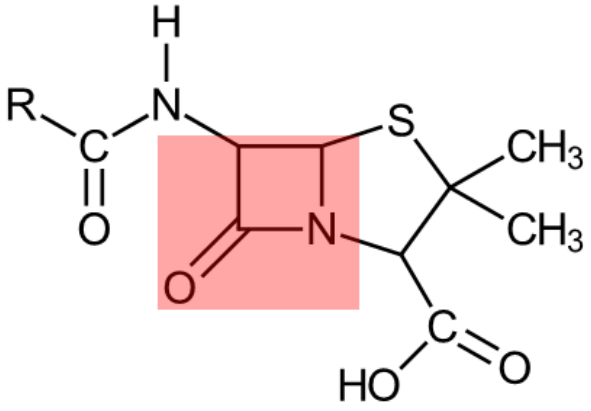
- Drugs which contain an acidic or basic group can be chemically modified to form an ionic salt (increasing their bioavailability).

Discovery of penicillin

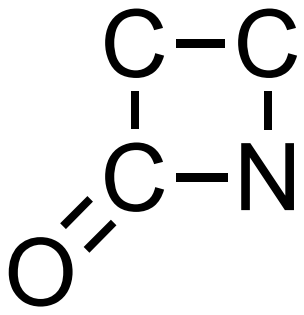
- Penicillins are a group of antibiotics used to treat a range of bacterial infections.
- They are derived from Penicillium fungi and can be taken orally or via injection.
- Penicillin was discovered in 1928 by Sir Alexander Fleming, a Scottish microbiologist, whilst working with bacteria cultures.
- He noticed that a fungus (Penicllium notatum) had contaminated some of his cultures and left a clear region where no bacteria colonies were growing.
- Fleming came to the conclusion that something in the fungus was inhibiting the growth of the bacteria.
- Despite Flemings' discovery, it wasn't until the 1940s that the true potential of penicillin was realized when it was used to save thousands of lives in World War Two.

Penicillin mode of action

- Penicillins (beta-lactam antibiotics) are characterized by the presence of a beta-lactam ring.
- The beta-lactam ring is the part of the molecule responsible for penicillin's anti-bacterial properties.



Two C atoms and the N atom in the ring are sp^3 hybridized (bond angle of 109.5^o)



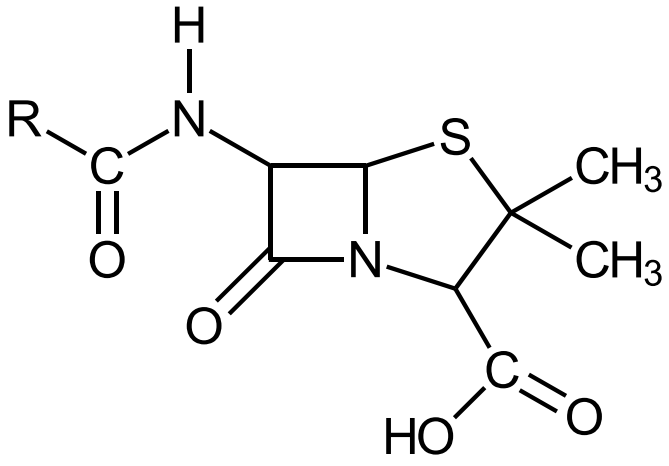
One C atom in the ring is sp^2 hybridized (bond angle of 120^o)

- The bond angles in the ring are reduced to about 90^o which puts a strain on the bonds.
- Due to the strain in the beta-lactam ring, it breaks relatively easily.
- Beta-lactam antibiotics disrupt the formation of cell walls in bacteria by inhibiting the enzymes responsible for creating cross-links in the cell wall.
- When the beta-lactam comes into contact with bacteria, the ring opens and binds irreversibly at the active site of the enzyme responsible for catalyzing cross-linking in the cell wall of the bacteria.
- Water enters the cell, increasing the osmotic pressure inside the cell, causing it to burst.

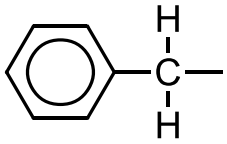
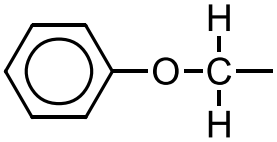
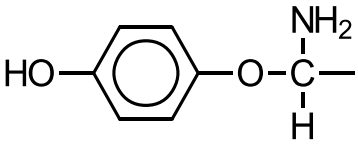
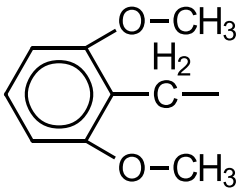
Antibiotic resistance

- Antibiotic resistance is the ability of bacteria to resist the effects of an antibiotic.
- Bacterial resistance to antibiotics is caused by the misuse or overuse of antibiotics.
- Examples of misuse include the over-prescription of penicillin for minor illnesses and the failure of patients to complete the course of antibiotics as prescribed by the doctor.
- Modifying the side-chain (R) results in penicillins that are more resistant to the penicillinase enzyme.

Basic structure of penicillin



Examples of different R groups and drug name

R group	Drug name
	Penicillin G
	Penicillin V
	Amoxicillin
	Methicillin

- The different side-chains reduce the occurrence of penicillin resistant bacteria.
- Modified penicillins are able to withstand the action of the penicillinase enzyme.
- For treating certain diseases (tuberculosis), a 'cocktail' of different types of antibiotics are required.
- The bacteria that cause TB are extremely resistant to penicillins, therefore a mixture of different antibiotics must be used.
- The side chain can also be modified to give increased resistance to breakdown by stomach acid, which means that the antibiotic can be taken orally.
- Penicillin G had to be injected as it was broken down by stomach acid.
- Ampicillin is a modified penicillin and can be taken orally.

D.3 Opiates

Understandings:

- The ability of a drug to cross the blood–brain barrier depends on its chemical structure and solubility in water and lipids.
- Opiates are natural narcotic analgesics that are derived from the opium poppy.
- Morphine and codeine are used as strong analgesics. Strong analgesics work by temporarily bonding to receptor sites in the brain, preventing the transmission of pain impulses without depressing the central nervous system.
- Medical use and addictive properties of opiate compounds are related to the presence of opioid receptors in the brain.

Applications and skills:

- Explanation of the synthesis of codeine and diamorphine from morphine.
- Description and explanation of the use of strong analgesics.
- Comparison of the structures of morphine, codeine and diamorphine (heroin).
- Discussion of the advantages and disadvantages of using morphine and its derivatives as strong analgesics.
- Discussion of side effects and addiction to opiate compounds.
- Explanation of the increased potency of diamorphine compared to morphine based on their chemical structure and solubility.

Guidance:

- Structures of morphine, codeine and diamorphine can be found in the data booklet in section 37.

Strong analgesics

- Morphine and codeine are examples of opiates and are used as strong analgesics.
- Opiates are natural analgesics that are derived from opium, which is found in poppy seeds.
- Opiate analgesics work by temporarily bonding to receptor sites in the brain, preventing the transmission of pain impulses without depressing the central nervous system.
- Strong analgesics are given to relieve severe pain caused by injury, heart attacks, or diseases such as cancer.
- Opiate analgesics can cause side-effects and can also lead to dependency and addiction.
- For these reasons, they are only available on prescription and their usage is monitored through medical supervision.

Advantages:

- Strong analgesics provide relief for acute or extreme pain.
- They have a wide therapeutic window.
- They can relieve anxiety, induce relaxation, or improve the quality of life.
- Because they are administered intravenously there is a faster distribution of the drug.

Disadvantages:

- Users feel euphoria, a lack of self-control, and can indulge in dangerous behaviour.
- Regular usage can lead to addiction, dependence and withdrawal symptoms.
- Users build up a tolerance to the drug with increased risk of overdose upon prolonged use.
- Increased risks associated with intravenous drug administration.

Blood-brain barrier

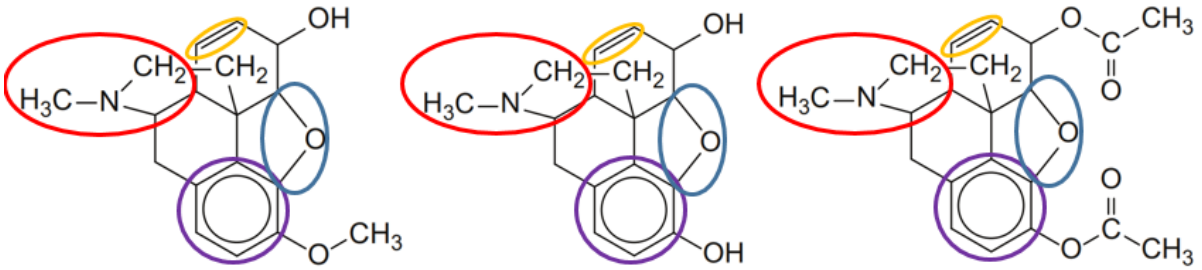
- The blood-brain barrier is a layer of tightly packed cells that protect the brain by restricting the passage of substances from the bloodstream into the brain.
- It is largely composed of lipids which are non-polar, hydrophobic molecules.
- The blood-brain barrier is not easily crossed by polar, hydrophilic molecules.
- For a drug to penetrate the blood-brain barrier and enter the brain, it must be non-polar and lipid soluble.
- The analgesic properties of opiates depend on their ability to move from the blood, where aqueous solubility is important, to the brain, where lipid solubility is important (to cross the blood-brain barrier).
- The solubility of the opiates is determined by their chemical structures.
- Once in the brain, opiates attach to opioid receptors. When opiates attach to the opioid receptors, they reduce the perception of pain.

- Opiates can also produce drowsiness, mental confusion, nausea, constipation, and, depending upon the amount of drug taken, can also depress respiration.
- Long-term use of opiates can cause addiction and tolerance (higher dose required to give same effect).

Structures of codeine, morphine and diamorphine

- The structures of these 3 compounds can be found in section 37 of the data booklet.

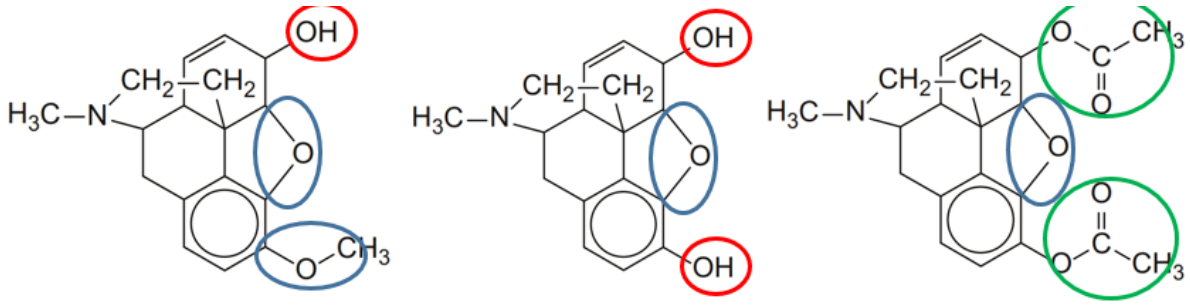
Comparison of functional group (similarities)



codeine morphine diamorphine (heroin)

- All three compounds have an alkenyl group (outlined in yellow)
- All three compounds have a tertiary amine group (outlined in red)
- All three compounds have an ether group (outlined in blue)
- All three compounds have a phenyl group (outlined in purple)

Comparison of functional group (differences)



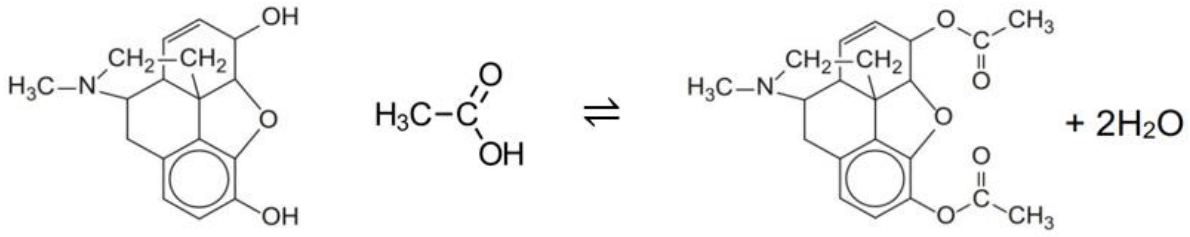
codeine morphine diamorphine (heroin)

- Codeine has one hydroxyl group, morphine has two hydroxyl groups but diamorphine has none.
- In diamorphine, the two hydroxyl groups have been replaced by ester groups.
- The presence of the two hydroxyl (OH) groups in morphine make it a polar molecule.
- Polar molecules are more soluble in water, but less soluble in lipids which limits their ability to cross the blood-brain barrier.

Synthesis of diamorphine and codeine

- Diamorphine is produced from morphine in an esterification reaction in which both OH groups are converted into ester (ethanoate) groups.

Diamorphine

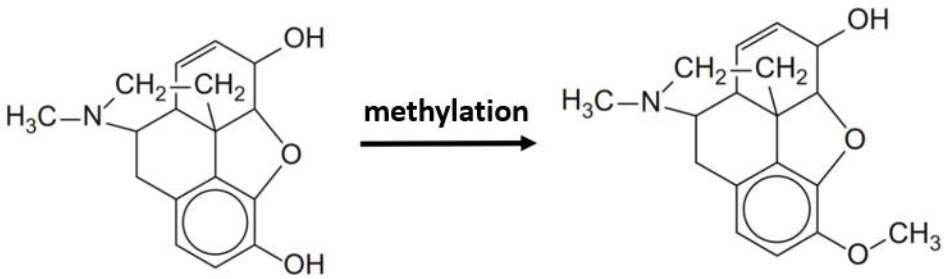


morphine diamorphine (heroin)

- Because of its higher lipid solubility, diamorphine is able to cross the blood-brain barrier more rapidly, and in higher concentrations, than morphine.
- As a result, it is much more potent than morphine, but its effects do not last as long.
- Heroin is used as a recreational drug for its euphoric effects.
- Frequent use of heroin causes tolerance and physical dependence.

Codeine

- Codeine is produced from morphine in a methylation reaction.
- An OH group is converted into a methoxy (OCH_3) group.



morphine codeine

- This reaction makes codeine a less polar molecule than morphine and more able to cross the blood-brain barrier.
- However, this reaction also reduces the ability of codeine to bond at the opioid receptors, which makes codeine a weaker analgesic than morphine.

D.4 pH regulation of the stomach

Understandings:

- Non-specific reactions, such as the use of antacids, are those that work to reduce the excess stomach acid.
- Active metabolites are the active forms of a drug after it has been processed by the body.

Applications and skills:

- Explanation of how excess acidity in the stomach can be reduced by the use of different bases.
- Construction and balancing of equations for neutralization reactions and the stoichiometric application of these equations.
- Solving buffer problems using the Henderson–Hasselbalch equation.
- Explanation of how compounds such as ranitidine (Zantac) can be used to inhibit stomach acid production.
- Explanation of how compounds like omeprazole (Prilosec) and esomeprazole
- (Nexium) can be used to suppress acid secretion in the stomach.

Guidance:

- Antacid compounds should include calcium hydroxide, magnesium hydroxide, aluminium hydroxide, sodium carbonate and sodium bicarbonate.
- Structures for ranitidine and esomeprazole can be found in the data booklet in section 37.

Antacids

- Antacids are used to reduce excess stomach acid.
- The stomach contains hydrochloric acid (HCl) that kills bacteria present in food and also provides the optimum pH for digestive enzymes.
- Excess stomach acid can cause health effects such as acid indigestion, heartburn, and stomach ulcers.
- Antacids work by neutralizing the excess hydrochloric acid in the stomach (neutralization reactions).
- Antacids are weak bases such as calcium hydroxide ($CaOH_2$), magnesium hydroxide ($MgOH_2$), aluminium hydroxide ($AlOH_3$), sodium carbonate (Na_2CO_3), and sodium bicarbonate ($NaHCO_3$).
- Strong bases such as sodium hydroxide (NaOH), and potassium hydroxide (KOH) cannot be used as antacids as they are strong bases and harmful to the body.

$$Ca(OH)_{2(aq)} + 2HCl_{(aq)} \rightarrow CaCl_{2(aq)} + 2H_2O_{(l)}$$

$$Mg(OH)_{2(aq)} + 2HCl_{(aq)} \rightarrow MgCl_{2(aq)} + 2H_2O_{(l)}$$

$$Al(OH)_{3(aq)} + 3HCl_{(aq)} \rightarrow AlCl_{3(aq)} + 3H_2O_{(l)}$$

$$NaHCO_{3(s)} + HCl_{(aq)} \rightarrow NaCl_{(aq)} + CO_{2(g)} + H_2O_{(l)}$$

$$Na_2CO_{3(s)} + 2HCl_{(aq)} \rightarrow 2NaCl_{(aq)} + CO_{2(g)} + H_2O_{(l)}$$

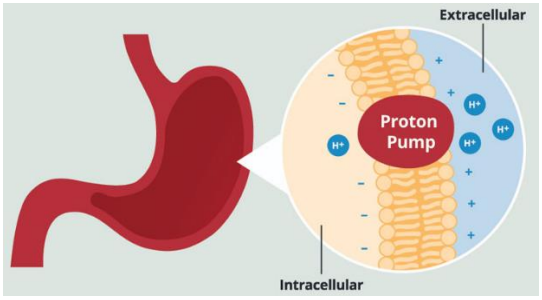
- A group of medicines called alginates are found in some brand of antacid medication.
- Alginates produce a neutralizing layer which prevents acid in the stomach from rising into the oesophagus (heartburn).
- Dimethicone is added to some antacids as an anti-foaming agent to prevent bloating and flatulence.

Stomach acid inhibitors

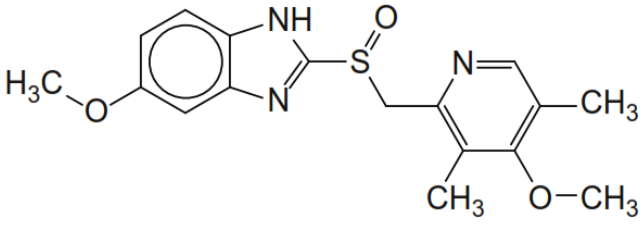
- Stomach acid inhibitors inhibit the production of stomach acid.
- Proton pump inhibitors (PPIs) and H_2 receptor antagonists (H_2 blockers) are both stomach acid inhibitors.
- PPIs inhibit the proton pumps in the stomach.
- H_2 blockers work by blocking the histamine receptors in acid-producing cells in the stomach.

Proton pump inhibitors

- The gastric proton pump pumps protons (H^+) into the stomach.



- PPIs inhibit the proton pump which prevents the release of protons into the stomach.
- PPIs have a longer-lasting effect (up to 3 days).
- They are used to treat stomach ulcers and also provide relief from the symptoms of acid-reflux.
- Omeprazole is an example of a proton pump inhibitor (PPI)



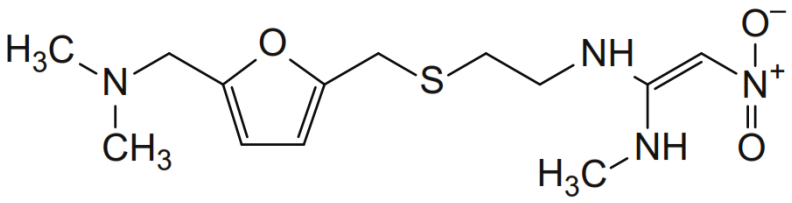
omeprazole

Comparison of PPIs and antacids

- Both compounds relieve the symptoms of acid reflux, heartburn and indigestion.
- PPIs (Omeprazole) inhibit the production of stomach acid and antacids ($Mg(OH_2)$) neutralize excess acid in stomach.
- PPIs have a longer-lasting effect than antacids.

H_2 blockers

- H_2 blockers reduce the amount of acid produced by the cells in the lining of the stomach.
- Histamine in the stomach stimulates the secretion of stomach acid by interacting at receptors (H_2) in the stomach lining.
- H_2 blockers compete with histamine for binding at the H_2 receptors.
- They block the interaction between histamine and the H_2 receptors, preventing the release of stomach acid.
- Ranitidine is an example of a H_2 receptor antagonist.



ranitidine

D.5 Antiviral medications

Understandings:

- Viruses lack a cell structure and so are more difficult to target with drugs than bacteria.
- Antiviral drugs may work by altering the cell's genetic material so that the virus cannot use it to multiply. Alternatively, they may prevent the viruses from multiplying by blocking enzyme activity within the host cell.

Applications and skills:

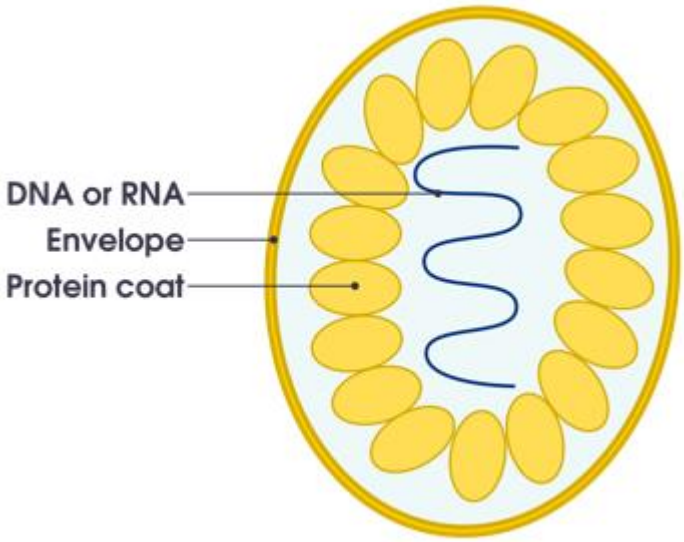
- Explanation of the different ways in which antiviral medications work.
- Description of how viruses differ from bacteria.
- Explanation of how oseltamivir (Tamiflu) and zanamivir (Relenza) work as a preventative agent against flu viruses.
- Comparison of the structures of oseltamivir and zanamivir.
- Discussion of the difficulties associated with solving the AIDS problem.

Guidance:

- Structures for oseltamivir and zanamivir can be found in the data booklet in section 37.

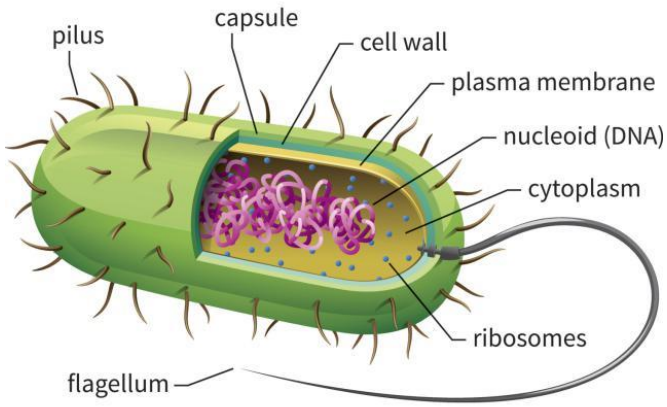
Viruses

- Viruses are sub-microscopic organisms that replicate inside the living cells of other organisms.
- Viruses have two main components, a protein coat and nucleic acid (either DNA or RNA).
- Viruses do not carry out metabolic processes and are considered to be non-living.
- They derive their energy from the host cell.



Bacteria

- Bacteria are single-celled microorganisms.
- Unlike viruses, bacteria are self-reproducing units (they do not require a host to reproduce).
- Bacteria contain various cell subunits (organelles) together with a cell wall.
- Bacteria carry out metabolic processes and are considered to be living.



Comparison of viruses and bacteria

- Bacteria are self-reproducing units while viruses need living hosts to multiply.
- Bacteria carry out metabolic processes while viruses do not.
- Bacteria contain organelles that perform specific functions while viruses consist only of genetic material and a protein coat.
- Bacteria are many times larger than viruses.

Antiviral drugs

- Viruses lack a cell structure and so are more difficult to target with drugs than bacteria.
- Antibiotics are effective against bacteria and work by disrupting the formation of the bacteria cell wall.
- Antibiotics are ineffective against viruses because they lack a cell wall.
- Viral infections are treated by medicines known as antivirals.

Viruses are more difficult to treat than bacteria for the following reasons:

- viruses mutate quickly so adapt to drugs
- bacteria are more complex and can be targeted in more ways, whereas viruses lack subunits that can be targeted by antibacterials.
- bacteria can be killed by simple chemical agents but viruses must be targeted on a genetic level.

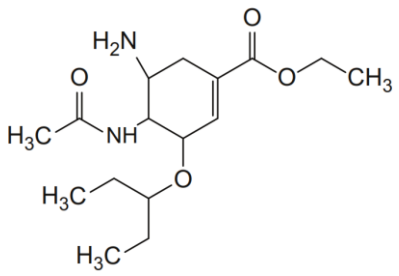
Antiviral drugs may work in the following ways:

- alter the cells genetic material so that the virus cannot use it to multiply
- prevent viruses from multiplying by blocking enzyme activity within the host cell
- bind to cellular receptors targeted by viruses
- prevent or hinder the release of viruses from the cell.

Oseltamivir and zanamivir

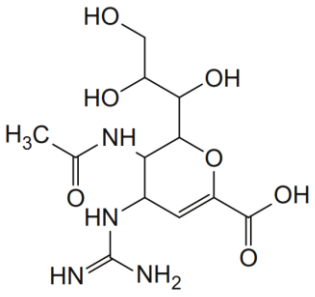
- Oseltamivir (Tamiflu) and zanamivir (Relenza) are both used as antivirals to prevent the spread of the flu virus.
- Zanamivir is taken by inhalation due to its low bioavailability when taken orally.
- Oseltamivir can be taken orally as its bioavailability is not affected by this method of administration.

Functional groups present in oseltamivir and zanamivir



oseltamivir

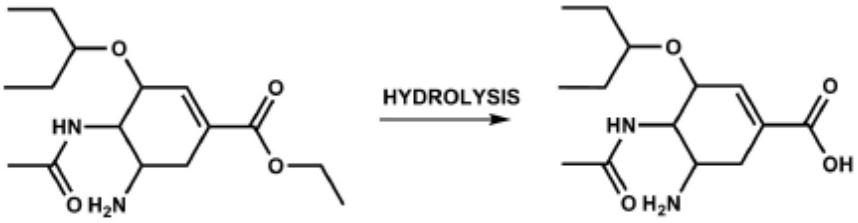
Alkenyl, carboxamide, amine, ester, ether



zanamivir

Alkenyl, carboxamide, amine, ether, carboxyl, hydroxyl

In the human body, the ester group in oseltamivir is hydrolysed to a carboxyl group.



OSELTAMIVIR GS4071

- Both oseltamivir and zanamivir work by inhibiting the enzyme neuraminidase by binding to its active site.
- Neuraminidase is an enzyme found on the surface of the influenza virus that enables.
- the virus to be released from the host cell.
- By inhibiting this enzyme, the virus is prevented from leaving the host cell and cannot infect other cells.

Solving the AIDS problem

The difficulties associated with treating HIV:

- HIV destroys T-cells (the cells that protect the body from infection)
- HIV can mutate rapidly
- HIV uses host cells to replicate
- Drugs used to treat HIV may also harm the host cell
- High price of antiretroviral drugs

Sociocultural factors related to the AIDS problem:

Condom use	availability / cost / cultural resistance
Cultural factors	Ignorance / misinformation / social stigma
Illegal activities	drug use / prostitution
Resources / medical factors	availability of medical services / cost of drugs

D.6 Environmental impacts of medications

Understandings:

- High-level waste (HLW) is waste that gives off large amounts of ionizing radiation for a long time.
- Low-level waste (LLW) is waste that gives off small amounts of ionizing radiation for a short time.
- Antibiotic resistance occurs when micro-organisms become resistant to antibacterials.

Applications and skills:

- Describe the environmental impact of medical nuclear waste disposal.
- Discussion of environmental issues related to left-over solvents.
- Explanation of the dangers of antibiotic waste, from improper drug disposal and animal waste, and the development of antibiotic resistance.
- Discussion of the basics of green chemistry (sustainable chemistry) processes.
- Explanation of how green chemistry was used to develop the precursor for
- Tamiflu (oseltamivir).

Guidance:

- The structure of oseltamivir is provided in the data booklet in section 37.

Radioactive waste

- Radioactive waste can be classified as low-level, intermediate-level or high-level waste.
- High-level waste (HLW) gives off large amounts of ionizing radiation for a long time (long half-life).
- Low-level waste (LLW) gives off small amounts of ionizing radiation for a short time (short half-life).

Type of radioactive waste	Examples	Disposal method
Low-level waste	Gowns / protective clothing / shoe covers / tissues / needles / mops	Stored in shielded containers until the isotopes have decayed and then disposed of as non-radioactive waste.
Intermediate-level waste	Radioactive sources (Co-60, Cs-137)	Stored in shielded containers in underground repositories.

Antibiotic waste

- Antibiotics are medicines used to prevent and treat bacterial infections.
- Antibiotic resistance occurs when bacteria are able to resist the effects of antimicrobial drugs.
- When antibiotic resistant bacteria infect humans or animals, the infections they cause are more difficult to treat than those caused by non-resistant bacteria.
- An example is MRSA (superbug) which is resistant to many commonly used antibiotics.

Antibiotics are released into the environment in three ways:

- the use of antibiotics in animal feeds – healthy animals are given antibiotics to prevent livestock diseases.
- improper disposal of antibiotic medicines by hospitals and households.
- antibiotics excreted by humans in urine.

- Antibiotics in agricultural waste such as manure and water run-off can carry antibiotics into the soil and groundwater.
- Antibiotics in urine and pharmaceutical waste enter the sewage system at low concentrations.
- Sewage treatment plants are rarely equipped to remove antibiotics from wastewater, therefore they can ultimately end up in the drinking water supply.

Solvent waste

- The majority of medicines and drugs are produced by chemical synthesis.
- The production of these medicines and drugs requires multiple steps such as reaction, separation and purification to form the end product.
- Solvents are used as reaction media and in product recovery and purification.
- These solvents must be disposed of carefully to avoid causing harm to the environment.

Taken from the Green Chemistry solvent guide:

Preferred solvent	Useable solvent	Undesirable solvent
Water	Cyclohexane	Pentane
Propan-1-ol	Octane	Dichloromethane
Ethyl ethanoate	Ethanenitrile	Dichloroethane
Methanol	Ethanoic acid	Trichloromethane
Ethanol	Methyl benzene	Carbon tetrachloride

- Many undesirable solvents are VOCs (volatile organic compounds).
- VOCs are used as solvents due to their high volatility (easy to remove by evaporation).
- VOCs in the environment have the potential to cause nose and throat discomfort, nausea and fatigue.
- They can also result in the formation of low-level ozone and smog.

Principles of Green Chemistry

1. Prevent waste
2. Maximize atom economy
3. Design less hazardous chemical syntheses
4. Design safer chemicals and products
5. Use safer solvents and reaction conditions
6. Increase energy efficiency
7. Use renewable feedstocks
8. Avoid chemical derivatives
9. Use catalysts, not stoichiometric reagents
10. Design chemicals and products to degrade after use
11. Analyze in real time to prevent pollution
12. Minimize the potential for accidents