

## Year 12 Chemistry: Chapter 14 From Organic Molecules to Medicines

One very useful application of organic reaction pathways is in the design and synthesis of medicines. The main ingredients of medicines are **drugs**- substances that affect how the body functions.

A drug is any substance that alters a chemical process in the body.

### 14.1 Aspirin: a modern painkiller from a herbal remedy

Pharmaceutical products are often developed from substances found in a plant that has been used as a traditional medicine.

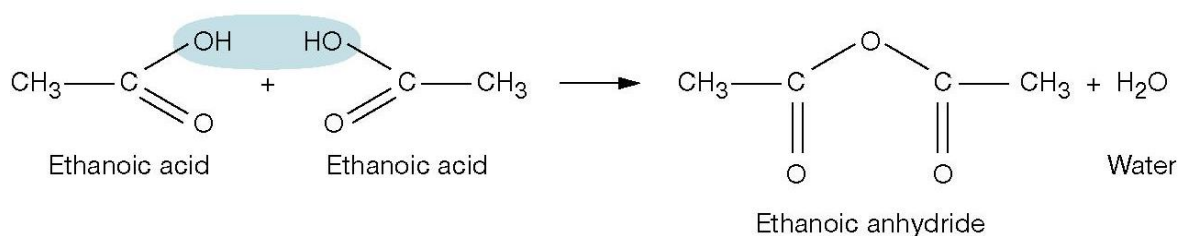
**Aspirin** is one such substance. It is found naturally occurring in the leaves and bark of willow trees and in the herb meadowsweet.

It is now known that the body converts salicin into **salicylic acid** and this is the active substance that helps reduce fever and acts as a painkiller.

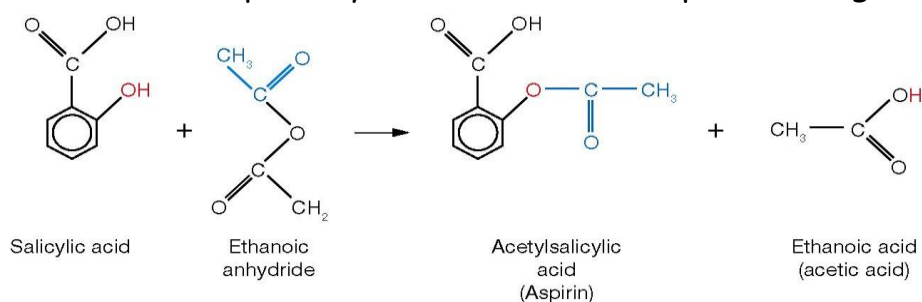
Felix Hoffman synthesis salicylic acid and replaced the OH functional group with an ester functional group to form **acetylsalicylic acid**. This is known commercially as **aspirin**.

The production of a substance to be used as a medicine usually requires a number of chemical steps, known as **synthetic pathways**.

The below reaction could be used to form acetylsalicylic acid, though it is **slow** and produces a **low** yield:

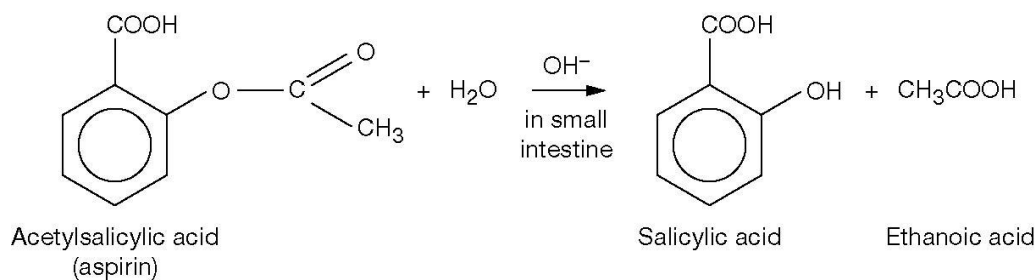


An alternative reaction pathway, which is **faster** and produces **higher** yields.



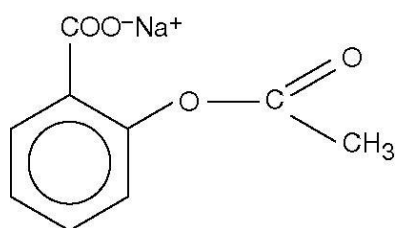
Acetylsalicylic acid is virtually tasteless and is much less irritating to the stomach than salicylic acid itself. It is not until after it has passed through the stomach that it reacts

with water (hydrolyses) in the alkaline conditions in the small intestine and returns to the more effective salicylic acid.



### Soluble aspirin

Pure acetylsalicylic acid (aspirin) is not very soluble in water. However, converting the carboxylic acid functional group into the sodium salt changes the molecule into an ion and makes it much more soluble.



### PolyAspirin: a polymer to prevent pain

A recent development is to make a polymer structure using a condensation reaction between salicylic acid and 1,8-octanedioic acid.

This larger molecule passes through the stomach to the small intestines where it enters the bloodstream before it is hydrolysed to salicylic acid, therefore does **not** irritate the stomach.

PolyAspirin has a number of potential advantages and applications:

- ☺ It can be used as a controlled-release pain killer - polymer breaks down slowly.
- ☺ It can be made into a thread - used to stitch cuts or wounds together as it breaks down it can fight pain and reduce inflammation.
- ☺ It has potential to be used as a plastic coating for an injured bone or joint - could promote bone growth as well as reduce pain.

**Penicillin:** read the section, though 99% it will not be on the exam!

### 14.3 Proteins as Medicines

We do not yet have the technology to use chemical reaction pathways to manufacture **therapeutic proteins**.

Pharmaceutical and biotechnology companies use **recombinant DNA** technology to manufacture a required medicinal protein using bacteria, yeast, fungi or animals cells that have been genetically modified.

**Insulin** is a protein that controls the storage and use of glucose in the body. Insulin-dependent diabetes is a disease caused by the body's inability to produce insulin.

In the past insulin was obtained from the pancreas of pigs and cattle. Today cloning or **genetic engineering** techniques are used to manufacture human insulin. The insulin gene is inserted into the DNA of a bacterial cell.

Other biosynthetic proteins:

- ☺ Etanercept: treatment of rheumatoid arthritis
- ☺ Clotting factor VIII: helps blood clot in haemophiliacs
- ☺ Erythropoietin (EPO): treatment of acute anaemia - it is a protein that controls production of red blood cells.

#### 14.4 A cleaner, greener future

$\% \text{ atom economy} = \frac{\text{Molar mass of atoms used in the products}}{\text{molar mass of all reactants}} \times 100$
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*\*Look at figure 14.17 (pg 232)*

The old process: 6 step method

- ☺ 40% of reactant atoms end up as product
- ☺ 60% being wasted.

Example: Its like saying that 70 million kg of the common ibuprofen produced gives over 100 million kg of useless wasted by-products.

New process:

- ☺ 77% in a three step method
- ☺ Can be raised to 99% for the recycling of acetic acid (by-product)

#### 14.5 Developing a new drug

Substances that can potentially be development into drugs care called 'lead' compounds. Some drugs have been developed from herbal or traditional remedies. Some chemicals are derived from plants and animals:

- ☺ Brazilian arrowhead viper venom: lead to the development of a drug to treat high blood pressure.
- ☺ Sponges (chemical extracted): developed AIDS drug (AZT)
- ☺ Californian yew trees: cancer medication

Other chemicals for screening for potential use as a drug are developed using an automated chemical process called **combinatorial chemistry**.

Computer modelling has led to the development of specifically designed drugs that match the size and shape of active sites in specific target proteins.

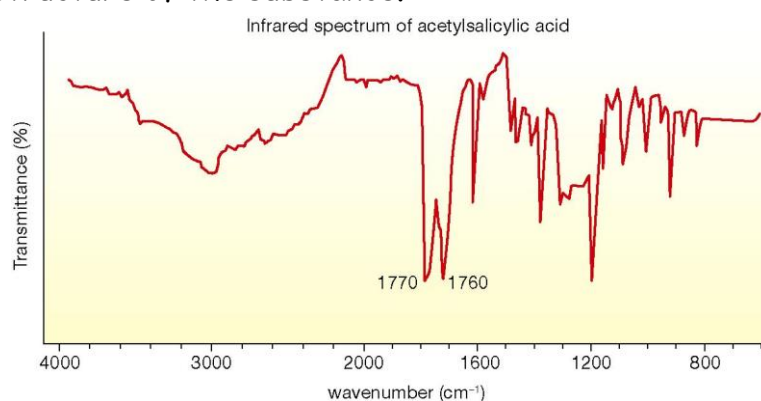
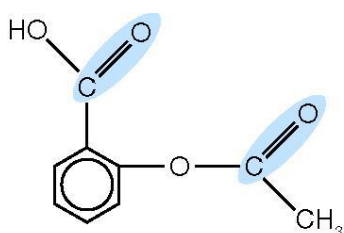
The potential medicine is tested on cell cultures and on animals to establish effectiveness, suitable doses and potential side effects. The medicine then goes through a number of clinical trials. Finally the results are submitted to the government's Therapeutic Goods Administration for approval before the new drug is made available to the public.

The development of a drug is expensive. About one in ten thousand compounds screened for pharmacological activity is actually developed into a drug for use.

### Analysis in Action

Instrumental methods such as mass spectroscopy, infrared spectroscopy, nuclear magnetic resonance spectroscopy and X-ray spectroscopy all contribute information that together confirms the exact structure of the substance.

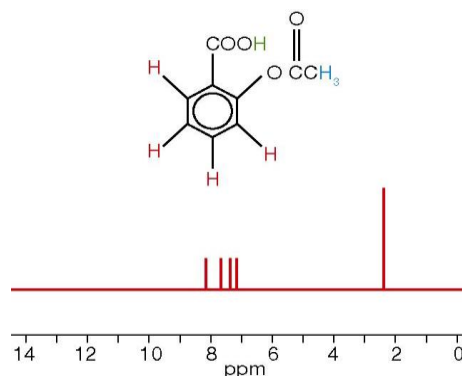
### Infrared Spectroscopy



There are two carbonyl,  $C=O$ , functional groups. One is part of the ester functional group and the other is found in the carboxy group.

### Nuclear Magnetic Resonance (NMR) spectroscopy

- ☺ Four hydrogens around the benzene ring - give the four peaks (different environments)
- ☺ Three hydrogens in the  $CH_3$  group - gives one large peak (same environment)
- ☺ One hydrogen on the  $OH$  group - would give a small peak (but not shown on this spectrum)



### Mass Spectroscopy

The peak at 180 is the molecular ion peak,  $M(C_9H_8O_4) = 180.0$ . The masses of the various fragments are used to confirm the structural formula.