The aspirin story

This resource accompanies the article **From plant to pill** in *Education in Chemistry* which delves into the science behind natural remedies and can be viewed at: rsc.li/42xZOw0

Learning objectives

1 Research, design and make a presentation.

2 Describe the discovery of aspirin and how its use has developed over time.

3 Explain the chemistry of aspirin.

The history of aspirin and other medicines dealing with pain, fever or inflammation reveals many interesting points about scientific methodology and the interaction of people and society with technology. One overriding theme that emerges when looking at the development of medicines is the importance of sharing information and cooperation in research. Time and again discoveries in one part of the world have been published, but not developed fully until another person reads and uses the information in another time and place.

The emphasis in this activity is on learners finding this scientific process out for themselves and presenting their findings to a suitable audience (LO1). Ask groups of learners to choose the format of their presentation from either a talk, poster or video. Find hints and tips for making each type of presentation on the student sheet.

Your role is to be supportive and offer advice. The fact sheet gives some background to the conditions treated, side effects, and methods for testing new drugs (LO2). There is also a brief outline of some of the chemistry of aspirin (LO3), but learners must find out more than is given to them here (all LOs).

Alternatively, you can set this task as a student-led group activity, where learners work on the project in their own time. Learners can then peer assess each other's work against the success criteria below.

- The conditions that aspirin helps to relieve or cure, including technical terms such as analgesic, antipyretic, anti-inflammatory and myocardial infarction.
- The side effects of aspirin, and the alternative treatments for people who are affected by them.
- How aspirin was developed over the past 260 years, including the achievements of those responsible for the main developments.
- The chemistry involved in developing the medicine in a usable form.
- The nature and importance of clinical trials.
- The overall quality of the presentation.
- The sources of information given.

Differentiation

The fact sheet contains information you can use to support and guide learners as needed. In addition, a timeline is given in a separate document that you can optionally use to support learners who may find it challenging to construct their own from research. Using some or all of the information in the fact sheet and timeline will cut down on the research time, allowing learners to concentrate on putting the presentation or poster together.

Resources

Groups will need:

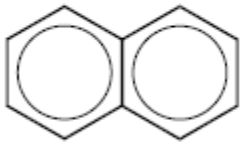
- Student sheet with instructions available from: rsc.li/3M1TmX9
- Fact sheet and timeline (optional).
- Internet access for groups to carry out their research.
- Presentation software, such as MS PowerPoint or equivalent for making a presentation.
- Poster paper, glue, scissors and a printer for making a poster.
- Recording equipment and software – eg tablet or mobile phone – for making a video.

Alternative pain relief

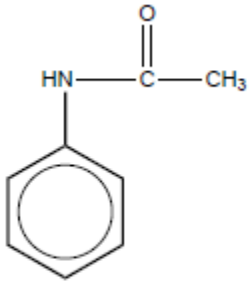
Paracetamol

At the University of Strasbourg in the 1880s, Adolf Kussmaul, of the Department of Internal Medicine, asked two assistants to give patients naphthalene as a treatment for intestinal worms.

The medicine had little effect on worms, but one patient had a great reduction in fever temperature. It was found that this patient had, in fact, been given acetanilide instead of naphthalene due to a mistake at the pharmacy!



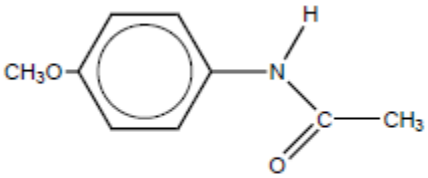
Naphthalene



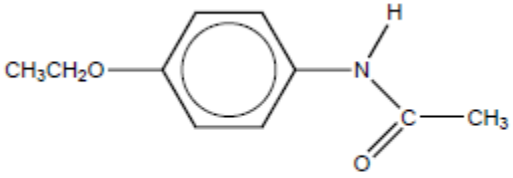
Acetanilide (*N*-Phenyl-ethanamide)

The young assistants quickly published the discovery of this new antipyretic. It was soon in production and remained in use for several years because it was so cheap to produce. However, it had a serious side effect involving the deactivation of some of the haemoglobin in red blood cells.

The publication of news about acetanilide immediately spurred a chemist at Bayer's dyeworks to make some derivatives:



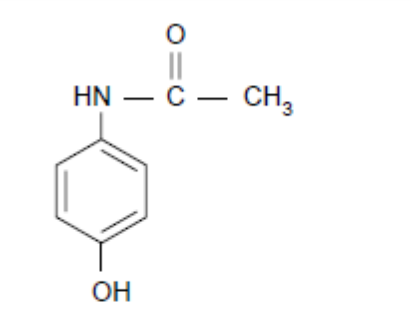
N-(4-Methoxyphenyl)ethanamide



N-(4-Ethoxyphenyl)ethanamide (Phenacetin)

These were both found to be antipyretic and *N*-(4-ethoxyphenyl)ethanamide was less toxic than acetanilide itself. It was promptly marketed as 'phenacetin' and has remained in use ever since. However, phenacetin's use is restricted due to kidney damage in long-term users.

Many medicines were synthesised to try to improve on phenacetin and as early as 1893 Joseph von Mering made paracetamol.



N-(4-Hydroxyphenyl)ethanamide
(Paracetamol)

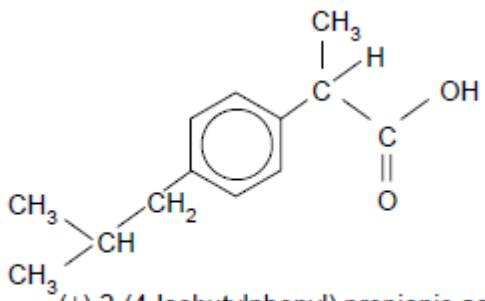
He found it to be an effective antipyretic and analgesic, but wrongly thought that it caused the same haemoglobin problem as acetanilide.

It was not until the 1940s that paracetamol was reinvestigated after it was found present in patients dosed with phenacetin. In 1953 Sterling-Winthrop Co marketed and promoted paracetamol as preferable to aspirin since it was safe to take for children and people with ulcers. However, chronic use causes liver damage.

Ibuprofen

In the 1960s researchers at Boots decided to synthesise a series of compounds with the aim of producing an alternative to aspirin. They based their new compounds around the benzene ring and carboxylic acid group of aspirin. They made and tested more than 600 compounds before ibuprofen was chosen as the medicine to market.

In 1983, after 15 years of use, ibuprofen became available as an over-the-counter medicine (not just on prescription) due to its minimal side effects.



(±)-2-(4-Isobutylphenyl) propionic acid
(Ibuprofen)

Ibuprofen – a case study in green chemistry

The original Boots synthesis has now been superseded by a more environmentally friendly (or green) synthesis. Full details can be found at bit.ly/3O4LqHb