Medicine Makers

Facilitator guidance notes

BIOCHEMICAL SOCIETY

BRITISH PHARMACOLOGICAL SOCIETY

Medicine Makers - facilitator guidance notes

Medicine Makers, a hands-on activity developed by the Biochemical Society and British Pharmacological Society, seeks to introduce participants to the basic mechanism of how painkillers work in our bodies; looking at how our bodies respond to pain and how these medicines help us to overcome it. We hope this activity pack will enable you to share scientific research in a fun and engaging way.

In this pack you will find a step-by-step guide on how to run Medicine Makers, and information on the scientific background for this activity. We have included a basic narrative to help you explain this, and you will also find curriculum links, discussion points and further resources for using this activity in schools, science clubs and workshops. We have found that children aged 10-14 years particularly enjoy the activity. If you successfully use the activity with children of other age ranges, please do let us know. We would value input about any modifications to the narrative that you found helpful.

When running an activity like Medicine Makers, it is important to tell a story. As well as a narrative, we have leaflets that describe the journey of a medicine through our bodies. These may help you describe this concept to visitors. You may need to adapt the narrative to engage with different participants; try to find ways to relate the topic to their experiences.

Contents

Background and set up

In this activity, visitors to the stand create their own model of a painkiller – aspirin, paracetamol or ibuprofen. Once they have built their model, visitors can 'bind' this to a model of the cyclooxygenase (COX) enzyme protein. Whilst visitors are making their painkillers, this is a great opportunity for facilitators to discuss mechanisms of pain relief with them.

In this section you will find a list of materials needed to run this activity, and step-by-step instructions. Later in this guide, you will find a narrative to help you explain the activity and more details on the scientific background.

When setting up your stand, it's important to be well organised, especially if you are expecting hundreds of people. In the image below, we have used two COX toober models, two pipecleaner stations and two bowls of Hama beads. This means two groups of visitors can build painkiller models at the same time. You may also find it helpful to prepare the materials before the event, cutting out the card painkiller models and pipecleaners for example.

Materials

- Toobers (amount depends on the size of your audience and stand. For most events, you will only need one pack of toobers). Where to buy: Timstar: £6.94 + shipping
- Pipe cleaners. Where to buy: Amazon or craft shops
- Coloured card. Where to buy: Amazon or craft shops
- Hama beads. Where to buy: Amazon or craft shops, 3000 beads for £5.99
- COX model - this can be made from Play Dough/modelling clay/plasticine
- Tape (matching colours to the toobers)
- The *Journey of a Medicine* leaflet
- Cards showing the structure of aspirin, ibuprofen and paracetamol. These can be left on the stand to aid visitors in making their painkiller models.

Image: Medicine Makers at Big Biology Day 2014

Method

Building the toober COX model
Please note, the toober model can be as big as you like! We usually create a larger model, as this allows for more visitors to attach painkiller models to it at the same time.

1. Straighten each toober to its full length. Decide which colours will form alpha helices and which will form beta sheets in your protein.
2. To make an alpha helix: coil your toober to make a right handed coil. You can make one longer coil, or several small ones. To make a longer coil, tape two toobers together and ensure you coil both of them the same way.
3. To make a beta sheet: beta sheets can be represented in a zigzag pattern. Make one or two folds in your toober to create this shape.
4. Cut pipe cleaners into short sections. Use colours that complement the toobers, as shown in the image below. Attach the pipe cleaners to the toober model.
5. Thread one Hama bead on to the end of each pipe cleaner. These will be the binding sites on your COX model. Try to have as big a range of colours as possible.

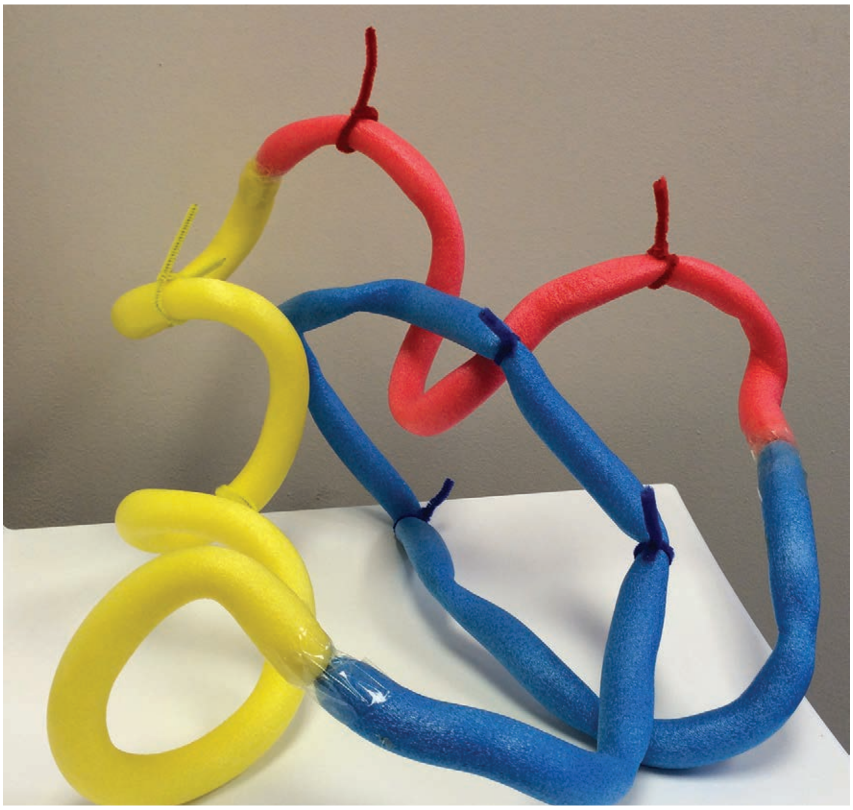
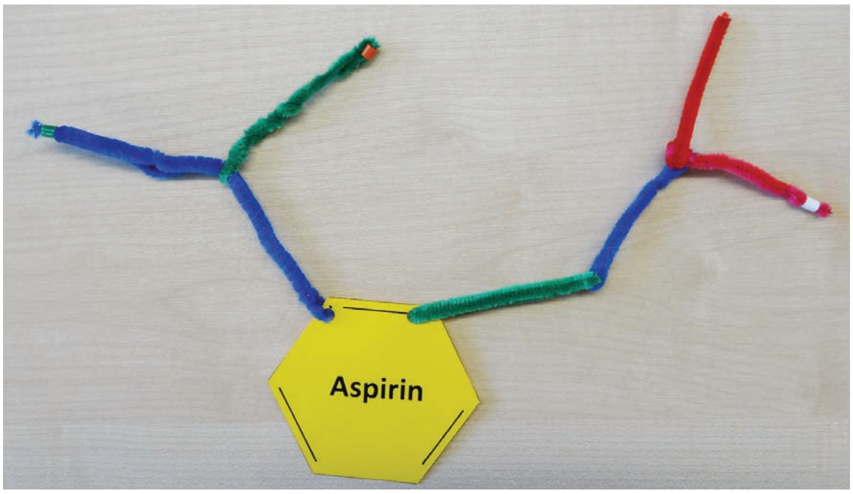
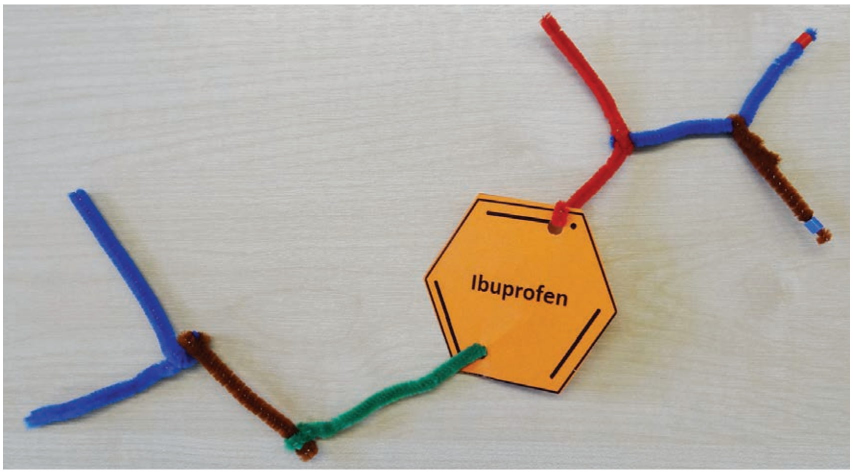


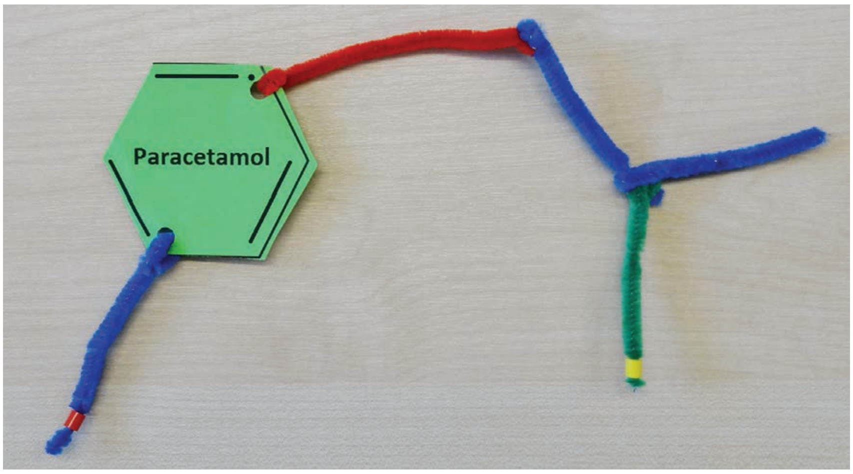
Image: An example COX model made of toobers. The blue and red toobers represent a beta sheet and the yellow toober represents an alpha helix.

Making the model painkillers

1. Print the painkiller template onto coloured card and cut these out. Using a hole punch, make holes in the corners of the templates where the black dots are.
2. Cut the pipe cleaners into different lengths. You will need some to be 3/4s of their original lengths, and some to be ¼ of their original length.
3. Using the templates of the molecular structure, create the shape of each painkiller by threading pipe cleaners through the holes in the template and twisting pipe cleaners around each other to make the branches.
4. The Hama beads will represent the oxygen and hydroxide groups on your painkiller; aspirin should have three, ibuprofen two and paracetamol two hama beads. Refer to the molecular structure and the pictures below for details.







Images: How to make your painkiller structure models

Running the activity

1. Ask a visitor to make a painkiller model; aspirin, paracetamol or ibuprofen
2. To show how your painkiller interacts with COX, 'bind' the painkiller to the model. The Hama beads will show the specificity of this binding; for example, if your model has green beads on, it can only bind to green beads on your COX toober model.
3. To attach the painkiller model to the toober model, wrap the pipe cleaners around each other and show how the painkiller is tightly bound to the protein.
4. You can also explain the interaction between COX and a painkiller using a 3D printed or play-dough model of COX.

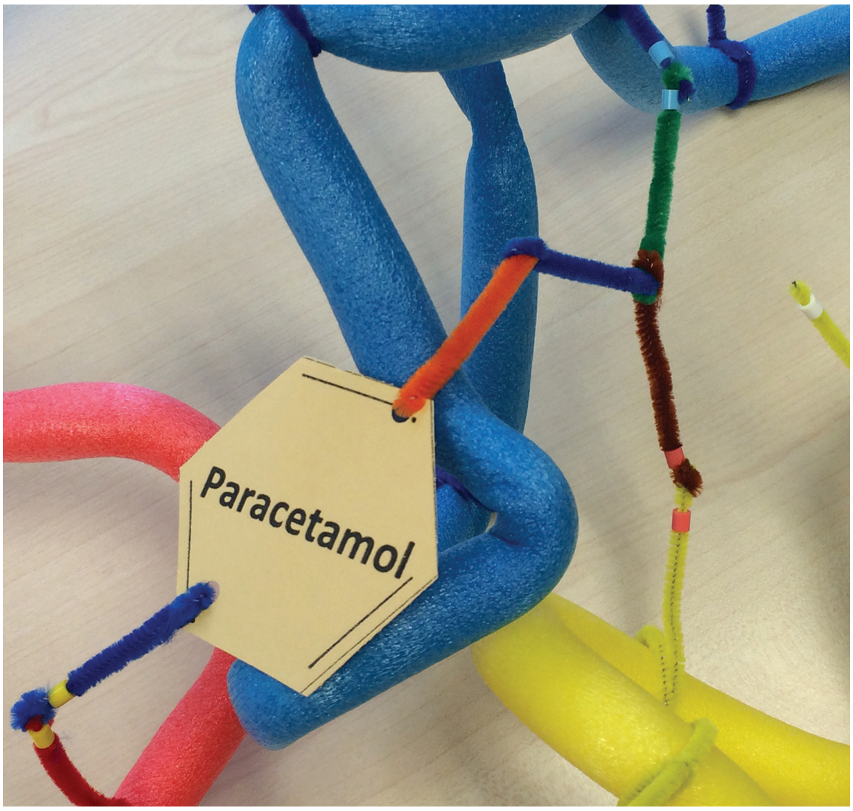


Image: a paracetamol model attached to COX

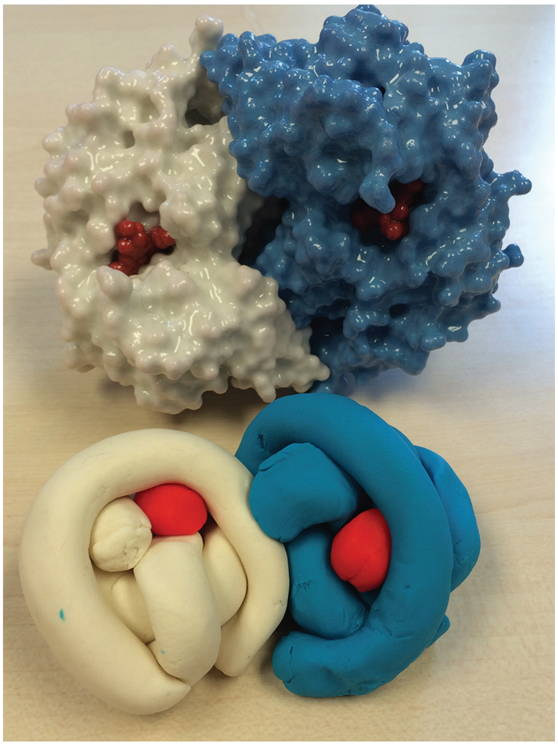


Image: a 3D printed model of COX and a play-dough model of COX

Image: using the COX model to explain protein-drug interactions

Explaining the activity

This basic narrative is something we give to volunteers ahead of running Medicine Makers. Experiment with a few different narratives during the activity until you find one that works for you and your audience.

Imagine you have a headache, and decide to take a painkiller to get rid of it. When you swallow a painkiller, it travels into your stomach where it dissolves and is absorbed into the bloodstream. Medicines are made up of molecules, which are so tiny you can't see them with the naked eye. Molecules are made when two or more atoms stick together.

The molecules of painkiller travel all around your body in your blood, looking for a specific enzyme called cyclooxygenase (COX). Enzymes are proteins, and help to make chemical reactions happen in your body. When your body gets injured or damaged, your cells release chemicals called prostaglandins, which stimulate your nerve endings and cause you to feel pain, heat and swelling. COX helps to make prostaglandins.

Painkillers such as ibuprofen and aspirin work by blocking the COX enzyme, stopping your body from producing prostaglandins and relieving pain so your headache goes away.

Paracetamol is a bit more complicated. It is thought to partly work through the COX enzyme. However, it works in another way too. Your body breaks down paracetamol into other molecules – and these new molecules are also painkillers. Pain is a really important signal for your body; it helps keep you safe. So, there are lots of other proteins in your body that help this signal get through – not just COX. Scientists think that it is some of these other proteins that are affected by the new molecules made when paracetamol is broken down. We still don't know for sure, it's a bit of a mystery. If you like mysteries and decide to become a scientist, perhaps you could help find out!

Scientific background

What are painkillers?

A painkiller is a drug or medicine which causes relief from pain or discomfort. In this activity, we will focus on paracetamol, ibuprofen and aspirin, which are examples of weak painkillers. Strong painkillers (opioids) include morphine and oxycodone.

Aspirin

- Aspirin reduces pain, fever and inflammation and is a very common painkiller. Under 16s should not take aspirin.
- Aspirin works by blocking the production of prostaglandins and other molecules by the COX enzyme.
- A molecule very similar to aspirin, salicylic acid, is found in the bark of the willow tree and is the active ingredient in preparations of the bark used as a painkiller throughout history. Aspirin was developed from this.

Ibuprofen

- Ibuprofen is a painkiller similar to aspirin, which is used to reduce pain, fever and inflammation.
- Ibuprofen also works by blocking the cyclooxygenase enzyme.
- Ibuprofen was developed by scientists in the 1960s.

Paracetamol

- Paracetamol reduces pain and fever and is a very common painkiller.
- The way in which paracetamol works is still not fully understood, but it is currently thought that it works in two main ways: -
  1. Paracetamol blocks the activity of the cyclooxygenase enzyme. The ability of paracetamol to block cyclooxygenase varies depending on the environment (or

part of the body) that the enzyme is in. Paracetamol is only a weak inhibitor of prostaglandins in the body, and this is why it doesn't have anti-inflammatory activity.
2. Paracetamol is also metabolized (changed by the body) into a variety of related molecules. These molecules appear to act on various other enzymes to reduce pain, often in the central nervous system. It is unclear which of these two ways is more important in reducing pain. This may help to explain why paracetamol is less effective at reducing inflammation than aspirin and ibuprofen.

- Paracetamol was discovered by chance when a similar molecule which was being developed as a fever-reducing drug was found to reduce pain too. Paracetamol was developed from this molecule.

What are enzymes?
Enzymes are biological catalysts; they speed up chemical reactions in our bodies. They are a type of protein, and work by allowing smaller molecules (called substrates) to fit into them in a very specific way. Enzymes are highly selective, so each enzyme will speed up one specific reaction in your body. Enzymes are involved in a wide range of reactions, for example some break down larger molecules into smaller ones to be absorbed by the body.

How do painkillers work?
Some substrates can reduce or completely stop the activity of enzymes. These chemicals are called inhibitors, and can block or distort the enzymes active site preventing further substrates from interacting with the enzyme. Medicine Makers looks at Non-Steroidal Anti-Inflammatory (NSAIDs) painkillers such as aspirin and ibuprofen, and paracetamol (which is not an NSAID). These painkillers are thought to inhibit the COX enzyme, preventing it from catalysing the conversion of arachidonic acid in to prostaglandins.

Watch this video from TED-Ed to find out more about how painkillers work.

Information about NSAIDs from the NHS

How paracetamol and ibuprofen work by the British Pharmacological Society

How safe are painkillers?
Like all medicines, painkillers are carefully tested before they are approved for use. They can have some side-effects, which will vary person to person, but most people will be able to use them safely. It is important not to exceed the stated dose, which means that you should always check to see if paracetamol is included as an ingredient in other medicines.

Image: Medicine Makers at Big Biology Day 2014

FAQs

Some of the most common questions asked by visitors are shown below with ideas of how to answer.

1.How does aspirin reduce blood clotting?
Although aspirin is a painkiller it also has anticoagulant, or "blood-thinning", properties which can help prevent blood clots from forming. This is because there are two types of COX enzyme and the other one can be found in your platelets, which are part of your blood. They don't have a nucleus, so they are not a cell – rather they are cell-fragments.

When a clot is needed, platelets release thromboxane, a chemical which attracts other platelets. The platelets are drawn to each other and create a clot. Blood clots stop us bleeding from a cut, but they can also cause strokes (where a blood clot forms in the brain) or heart attacks (where a blood clot prevents blood flow to the heart, stopping it from working to full capacity).

Aspirin prevents platelets from producing thromboxane, reducing the rate at which a clot forms. This is why aspirin is often prescribed to those who are more likely to have a stroke or a heart attack, for example people with high blood pressure or high cholesterol.

Anti-clotting agents explained

An animation showing the formation of a blood clot

2. Why do we only feel pain sometimes?
Cyclooxygenase is an enzyme. Like a light switch, it can be turned 'on' and 'off'. COX is usually turned off, but can be turned on by immune stimuli, hormones and growth factors. Damage to our bodies usually switch it on.

3. Why do different people respond differently to medicines?
Everyone is slightly different due to their genes and the environment they live in. Just like how the colour of our eyes is determined by genes, other genes can affect how we react to different medicines. This can mean that a medicine that works very well for one person doesn't work at all for someone else. For example, about 8% of people don't have an enzyme that helps the body break down codeine, which is a different painkiller. Just like paracetamol, codeine needs to be broken down to produce the painkiller molecules. Those people who don't have the enzyme can't break codeine down – and so they don't get the benefit. Hopefully in the future, more research into genetics and medicine will mean that doctors can pick the best medicine for each individual person.

From genes to personalised medicine

Personalising medicine

Issues surrounding personalised medicine

4. How do pharmaceutical companies decide on the colour and name of medicine?
There are two (or more) names for the majority of medicines. The drug name, which is the active ingredient in the medicine (this usually comes from the name of the chemical), and a brand name which the pharmaceutical company usually bases on the drug name. For example:

Chemical name	Drug name	Brand name
Isobutylphenylpropanoic acid	Ibuprofen	Nurofen
Para-acetylaminophenol	Paracetamol	Panadol
Acetylspirsäure	Aspirin	Anadin

Colours (and shape) are used to allow people to identify tablets easily. This is particularly important for people who need to take many different tablets.

Psychology and the colour of medication

A video on naming conventions

5. How do medicines know where to work?
They don't. Painkillers are not attracted to a specific part of the body. However, a majority of medicines have chemical properties that prevent them from entering the brain, or make them more likely to be concentrated in specific organs, therefore affecting their use. No matter where they are in the body, painkillers can only work if the protein they act on is present there.

The 'active ingredient' part of a medicine helps us to feel better. The active ingredient is a chemical with a very specific shape, like a jigsaw piece. This shape means the active ingredient can only interact with specific enzymes in the body. The active ingredient moves around the body, until it finds the specific enzyme it can interact with. In Medicine Makers, the active ingredients of ibuprofen and aspirin specifically interact with the COX enzyme. Paracetamol appears to work in different parts of the body in different ways. This is part of the reason it is hard to determine exactly how it works.

Enzymes: the lock and key model

Targeted painkillers vs generic painkillers

The psychology of targeted painkillers

Further resources

Articles about painkillers and pain
Lower-risk painkillers
How our bodies respond to pain

Clinical trials and animal research further resources
Clinical trials **– Sciberbrain (this activity is available for standard and advanced levels)**
Understanding animal research **– teaching ideas and resources**

Educational resources about drug discovery:
Find out about medicines **– ABPI**
Making medicines **– ABPI**
How new medicines are discovered **– Glaxosmithkline**
Where do medicines come from? **– Understanding Animal Research**

Educational resources about drug development:
The Big Picture on drug development **– The Wellcome Trust**
How to make molecules from MolyMods **– Keele University**

Educational resources about medicines
BBC bitesize KS2
BBC bitesize GCSE

Contact us

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British Pharmacological Society
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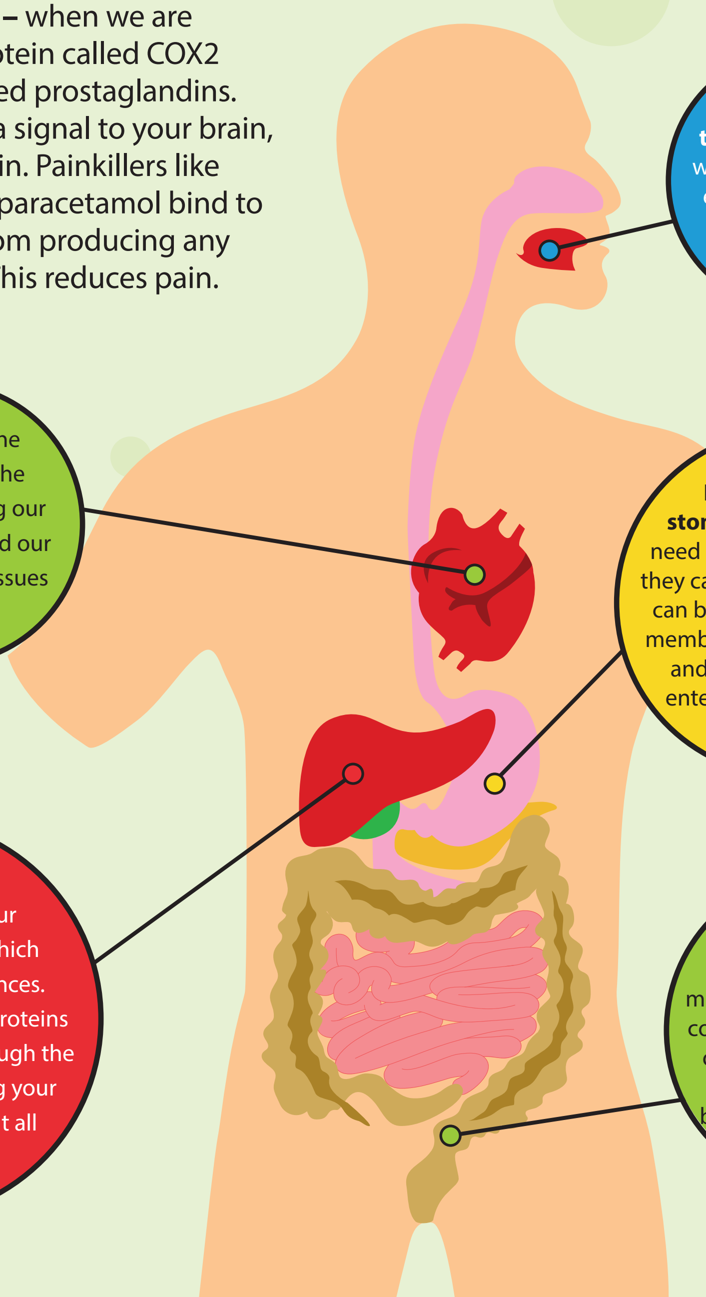
Medicine Makers

The journey of a medicine

How painkillers work – when we are in pain or injured, a protein called COX2 releases chemicals called prostaglandins. These chemicals send a signal to your brain, telling you you're in pain. Painkillers like aspirin, ibuprofen and paracetamol bind to COX2 , preventing it from producing any more prostaglandins. This reduces pain.



Swallowing a tablet – a common way for painkillers to enter our bodies is via swallowing or chewing.

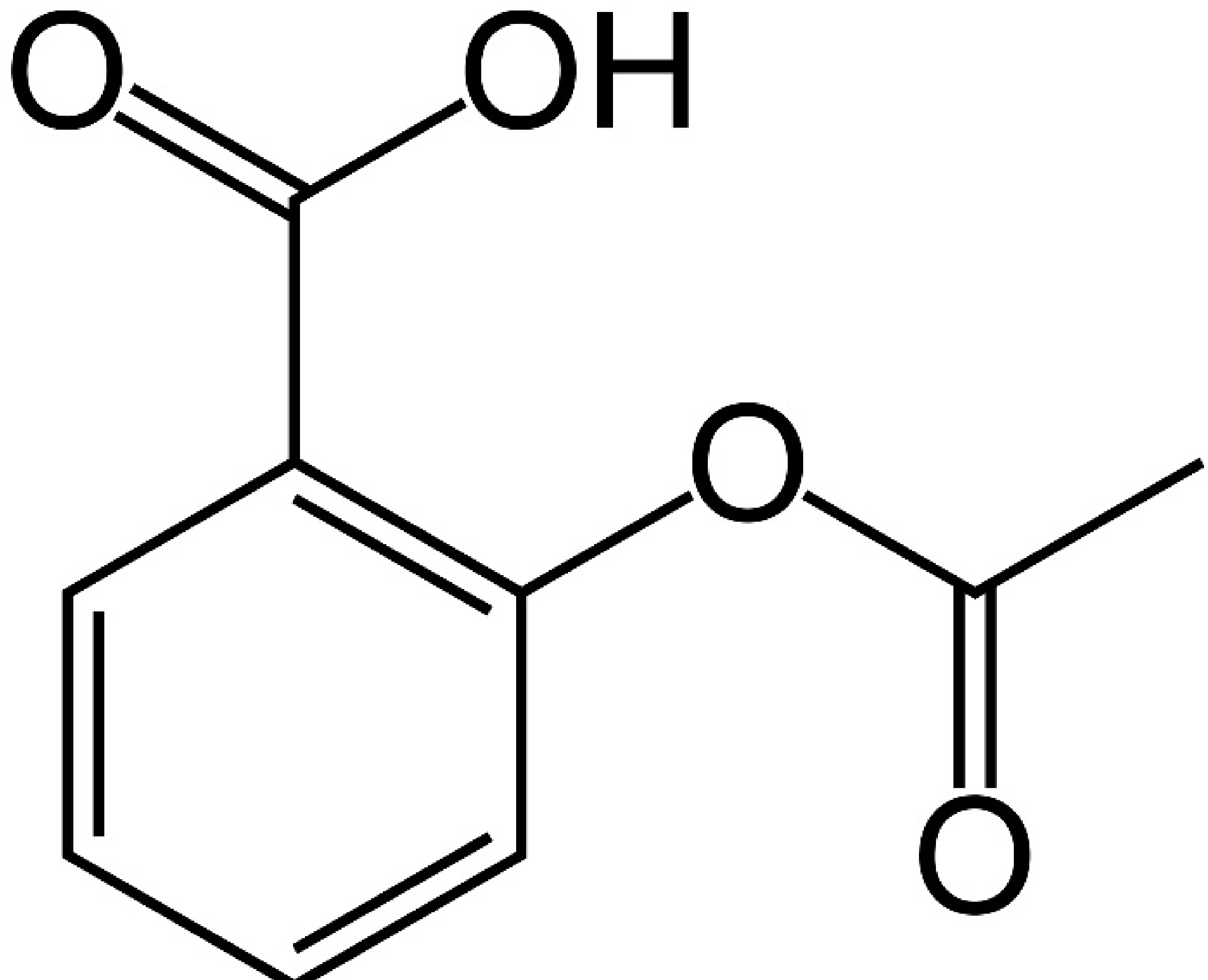
The heart – the heart pumps the blood containing our medicines around our body to all the tissues and organs.

Dissolved in the stomach – all medicines need to be dissolved before they can be absorbed. Aspirin can be absorbed across the membranes of your stomach and small intestine, and enter your blood stream.

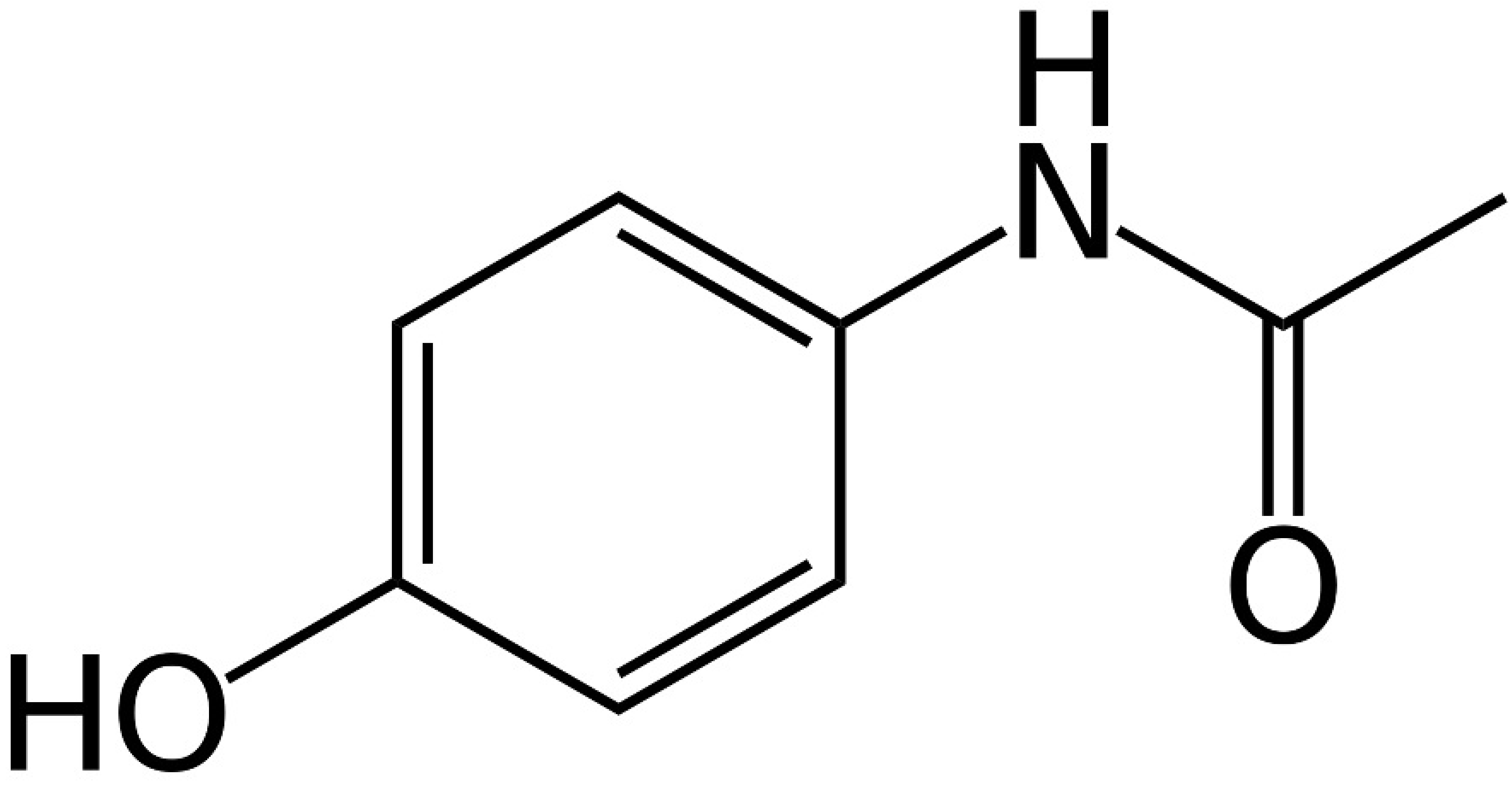
Through the liver – blood travels from your stomach to your liver, which removes harmful substances. Drugs like aspirin bind to proteins in your blood and pass through the liver undetected, meaning your liver doesn't dispose of it all straight away.

Disposal – five to six hours after taking the medicine, the liver will have completely removed it from our blood stream. This is then excreted from the body via the kidneys and in bile.

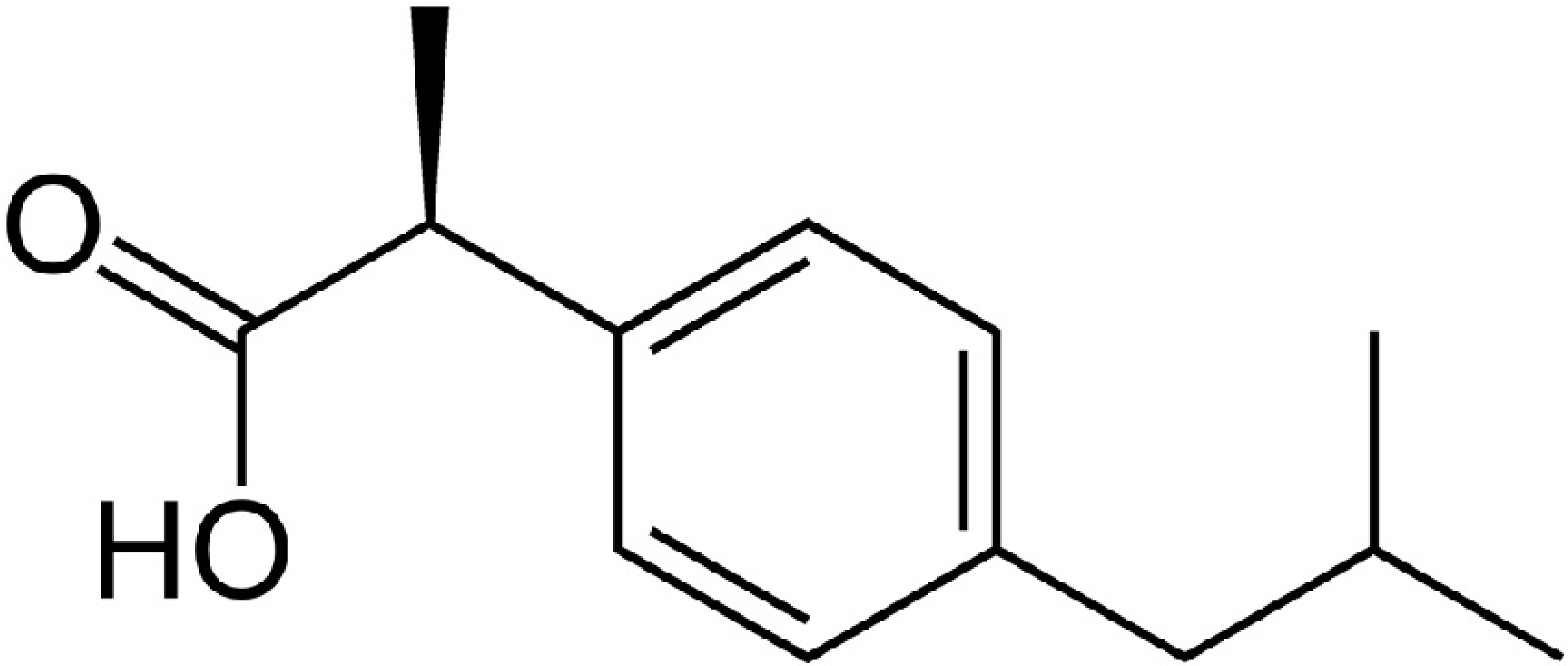
Aspirin

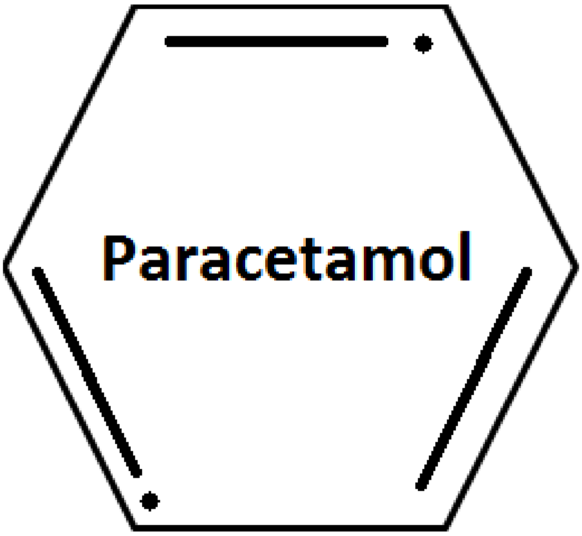


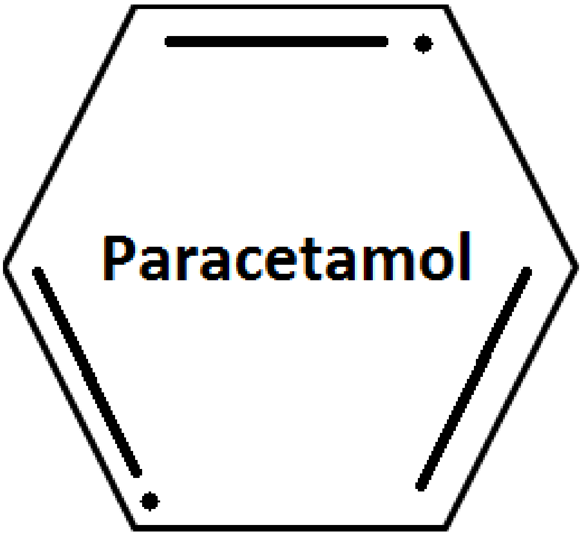
Paracetamol

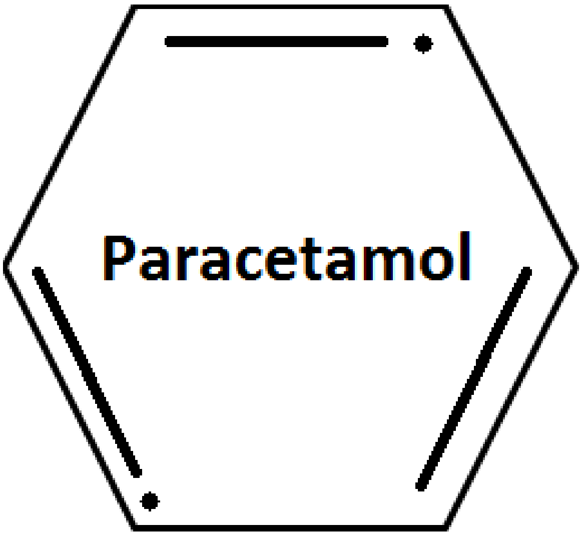


Ibuprofen




Paracetamol


Paracetamol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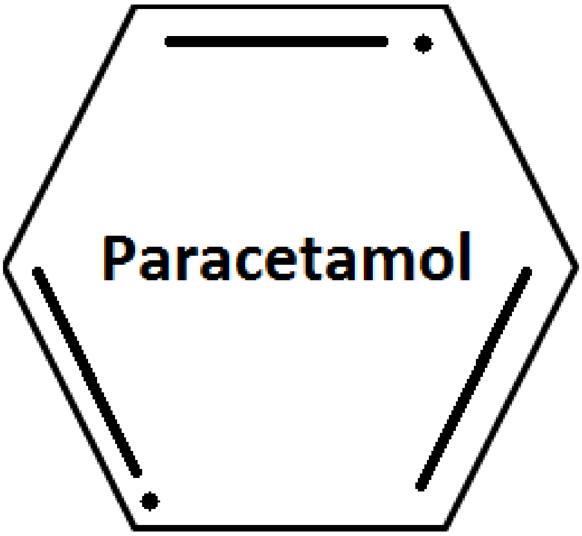
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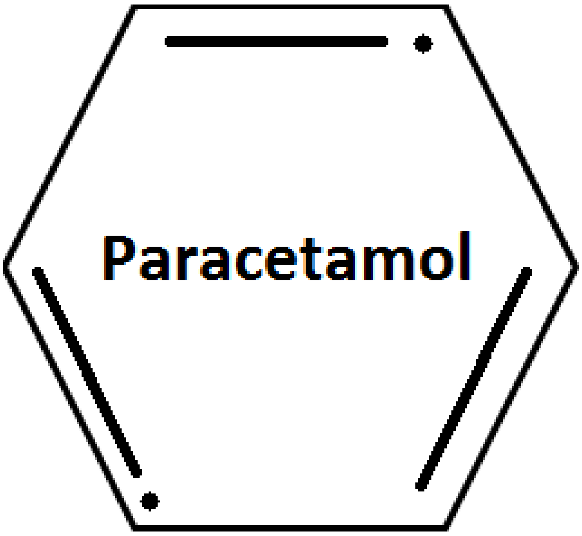
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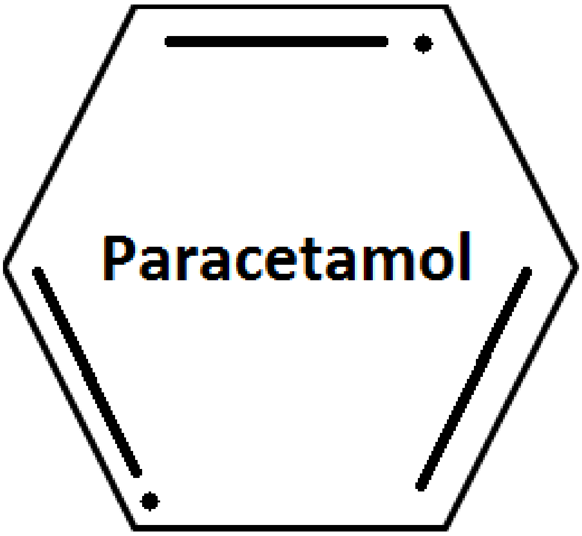
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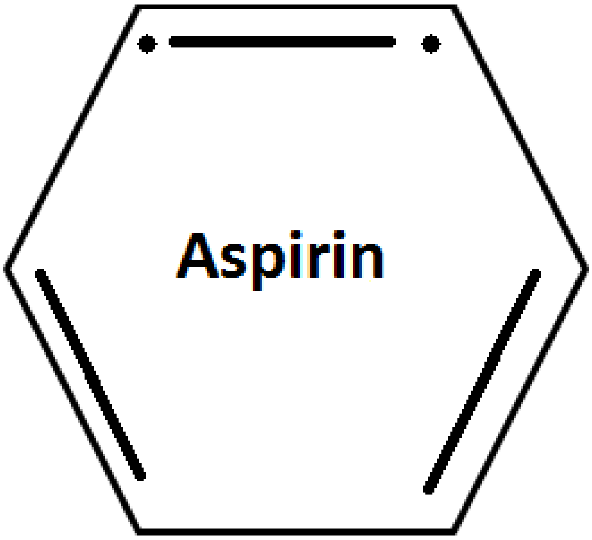
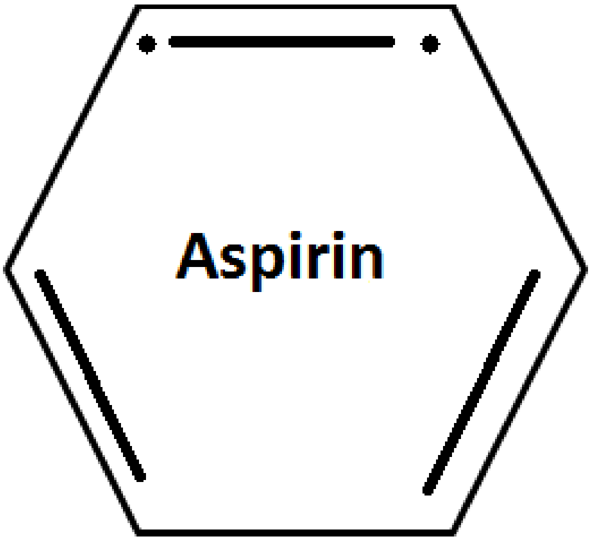

Aspirin

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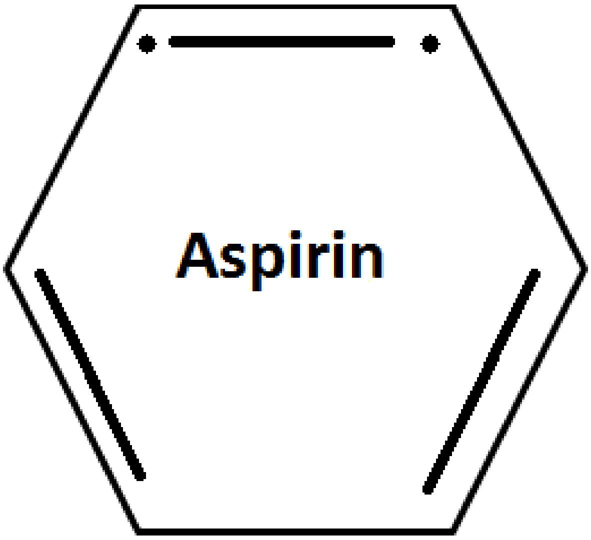
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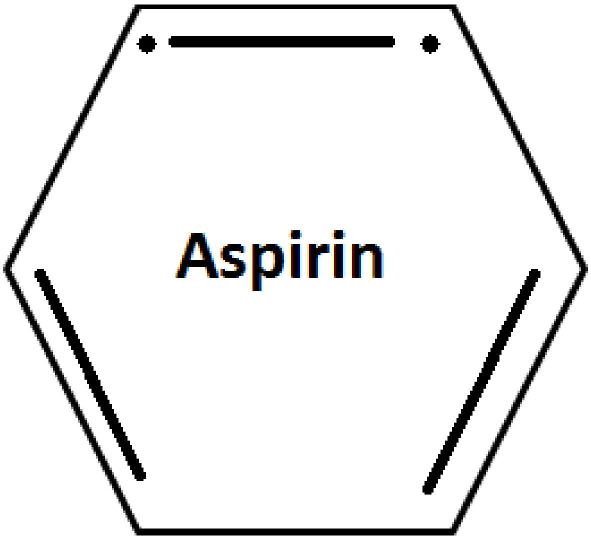
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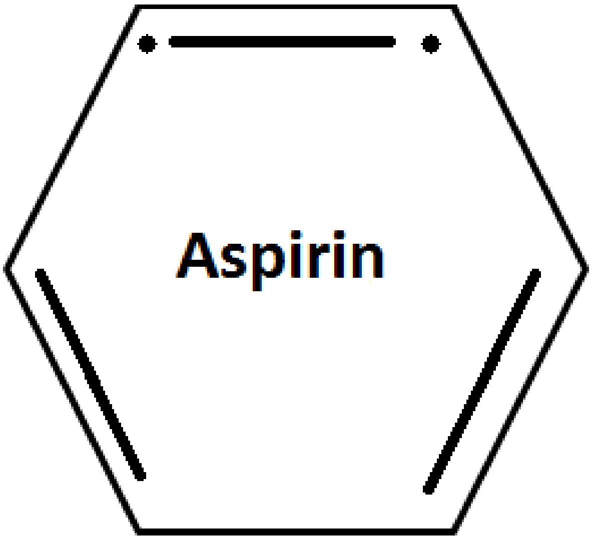
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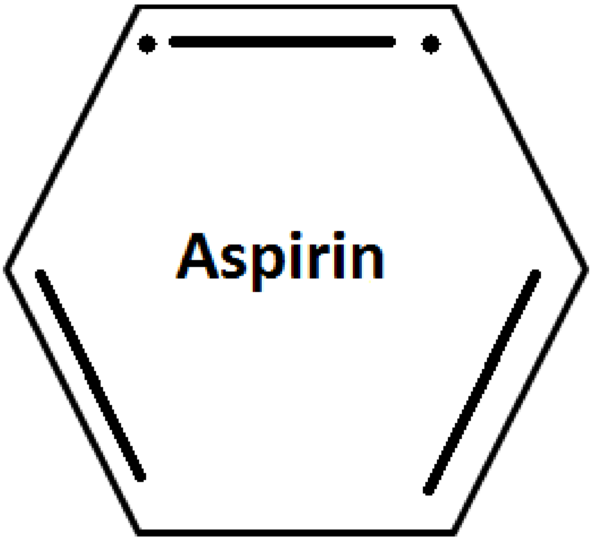
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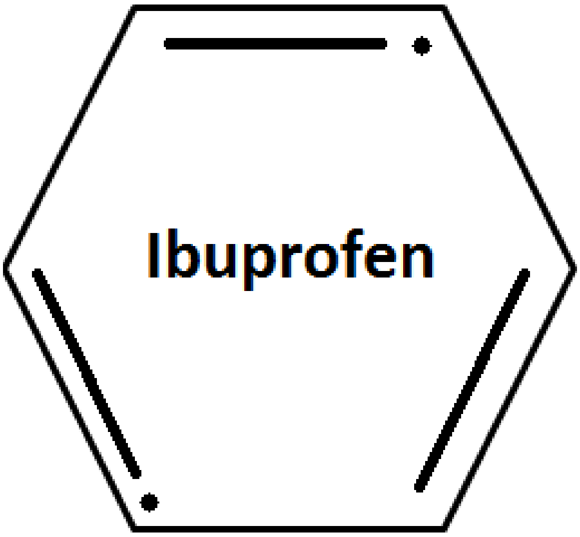
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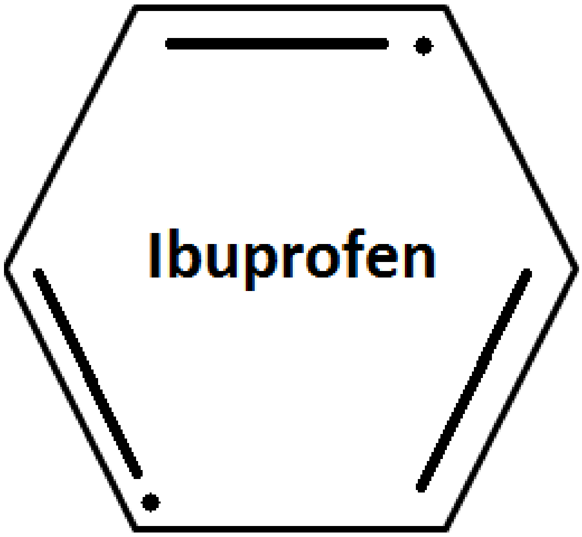
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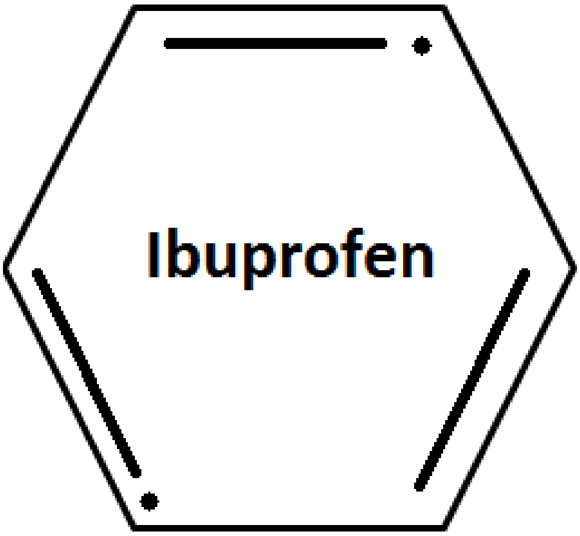
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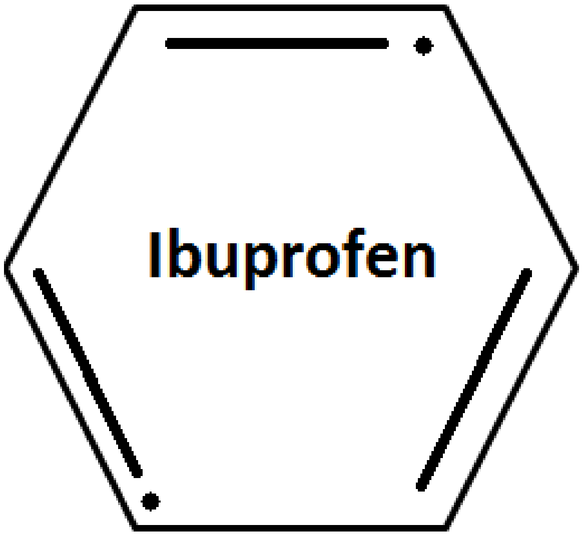
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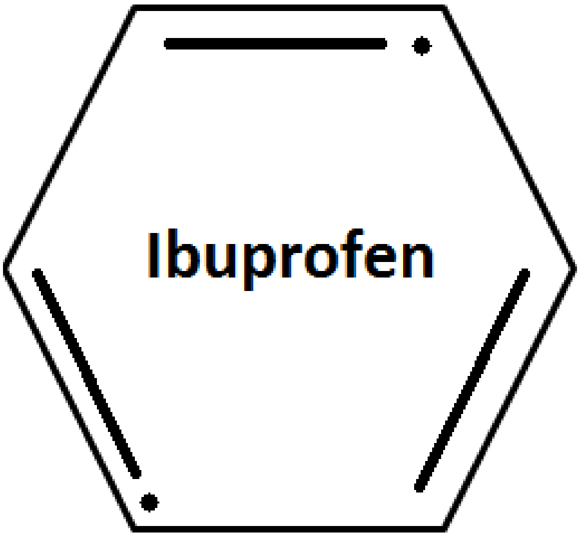
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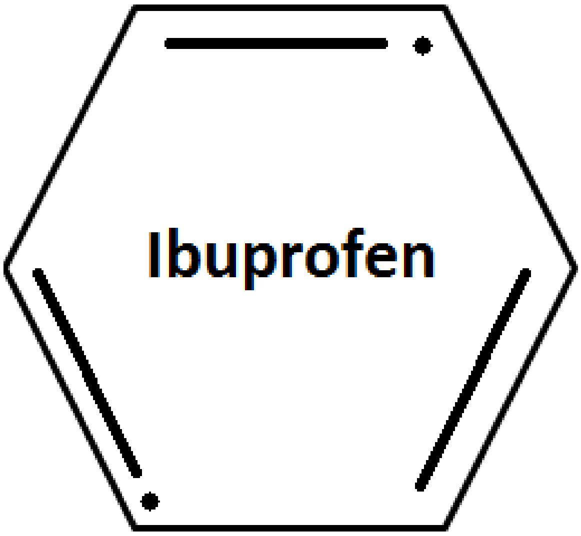
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