ASPIRIN

Have you ever had a headache? Chances are you have; almost all of us do once in a while. And chances are you took some kind of medicine to ease your headache. That medicine was most likely a relative of **aspirin**.

You may also have taken aspirin or its relatives for other problems, like inflammation (swelling of joints or other parts of the body) or fever. But did you know that about **80 billion** aspirin tablets are taken per year for these problems, as well as many others? For example, millions of people take aspirin to help prevent heart attacks! There are good reasons a doctor might say, "Take two aspirin and call me in the morning"!

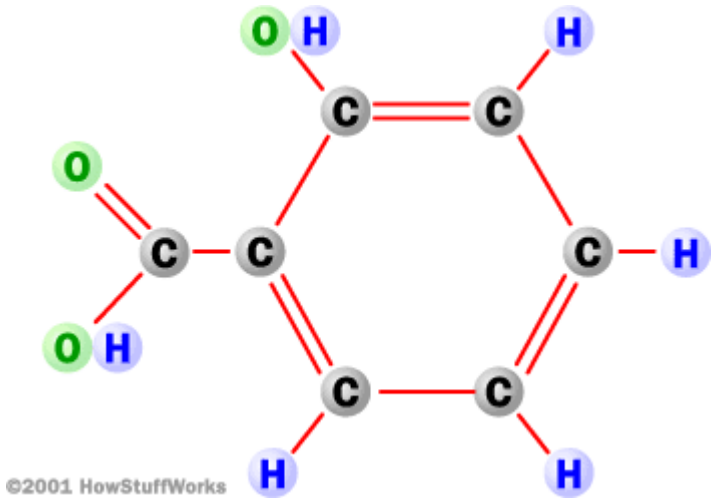
In this article, Dr. Luke Hoffman leads an exploration of aspirin. You will learn about the many benefits of aspirin, as well as some good reasons NOT to take this medication! You will also come to understand why Bayer has called aspirin "the wonder drug that works wonders!"

A Short History

Aspirin is a member of a family of chemicals called **salicylates** (see below for chemistry and structure). These chemicals have been known to people interested in medicine for centuries.

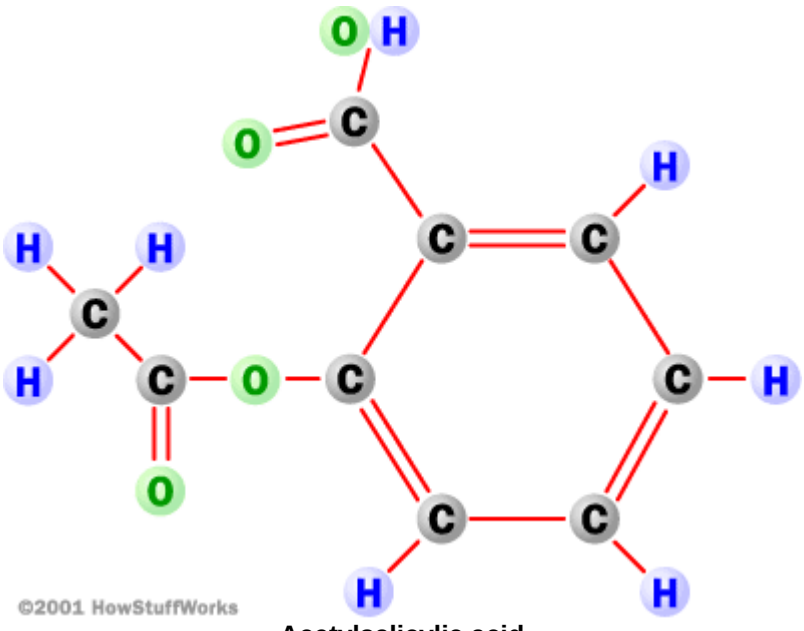
One of the first and most influential physicians, Hippocrates, wrote about a bitter powder extracted from willow bark that could ease aches and pains and reduce fevers as long ago as the fifth century B.C. In the 1700s, the scientist Reverend Edmund Stone wrote about the success of the bark and the willow in the cure of the "agues," or fevers with aches. With a bit of chemical detective work, scientists found out that the part of willow bark that was (1) bitter and (2) good for fever and pain is a chemical known as **salicin**.

This chemical can be converted (changed) by the body after it is eaten to another chemical, **salicylic acid**. It was a pharmacist known as Leroux who showed in 1829 that salicin is this active willow ingredient, and for many years it, salicylic acid (made from salicin for the first time by Italian chemist Piria), and close relatives were used at high doses to treat pain and swelling in diseases like arthritis and to treat fever in illnesses like influenza (flu).



Salicylic acid

The problem with these chemicals was that they upset the user's stomach fairly badly. In fact, some people had bleeding in their digestive tracts from the high doses of these chemicals needed to control pain and swelling. One of these people was a German man named Hoffmann. His arthritis was pretty bad, but he just couldn't "stomach" his salicylic acid. Enter this man's son, German chemist **Felix Hoffmann**, who worked for a chemical company known as Friedrich Bayer & Co. Felix wanted to find a chemical that wouldn't be so hard on his dad's stomach lining; reasoning that salicylic acid may be irritating because it is an acid, he put the compound through a couple of chemical reactions that covered up one of the acidic parts with an acetyl group, converting it to **acetylsalicylic acid** (ASA). He found that ASA not only could reduce fever and relieve pain and swelling, but he believed it was better for the stomach and worked even better than salicylic acid.



Acetylsalicylic acid

Unfortunately, Hoffmann had to wait for fame. He finished his initial studies in 1897, and his employers didn't pay much attention to it because it was new and they were cautious -- they didn't think it had been tested enough. By 1899, though, one of Bayer's top chemists, a scientist named Dreser, had finished demonstrating the usefulness of the potent new medicine and even gave it a new name: **aspirin**. It is believed that the name comes from a plant relative of a rose that makes

salicylic acid (several plants make this compound, not just the willow). The Bayer company could then support the tested medicine; they spread the word and marketed the new pill widely.

Over the next hundred years, this medicine would fall in and out of favor, at least two new families of medicines would be derived from it, and innumerable research articles would be published about aspirin. Thousands have been published in the past five years alone! One of the most important pieces of research about aspirin came in the early 1970s, when a British scientist named John Vane and his colleagues showed how aspirin works (see the following sections). His work was so important that he and his colleagues were awarded the Nobel Prize in Medicine in 1982. Dr. Vane was even made a British knight for his work!

What is a Headache?

No one completely understands how pain works. Actually, a lot is known about pain, but the more we find out the more questions arise. So let's take a simplified view.

Pain is really something you feel in your brain. For example, let's say you hit your finger with a hammer (please don't try this at home). The part of your finger that is damaged has **nerve endings** in it -- these are little detectors in your joints and your skin that feel things like heat, vibration, light touch from things like the mouse you're holding, and, of course, big crushing shocks like being hit with a hammer. There are different receptors for each of these types of sensations. The damaged tissue in your finger also releases some chemicals that make those nerve endings register the crushing shock even stronger -- like turning up the volume on your stereo so you can hear it better. Some of these chemicals are **prostaglandins**, and working cells in the damaged tissues make these chemicals using an enzyme called **cyclooxygenase 2** (COX-2).

Because of the **prostaglandins**, the nerve endings that are involved now send a strong signal through nerves in your hand, then through your arm, up your neck and into your brain, where your mind decides this signal means, "HEY! PAIN!" The prostaglandins seem to contribute just a portion of the total signal that means pain, but this portion is an important one. In addition, prostaglandins not only help you to feel the pain of the damaged finger, but they also cause the finger to swell up (this is called **inflammation**) to bathe the tissues in fluid from your blood that will protect it and help it to heal. Remember this is a simplified version of the pain story; lots of chemicals seem to be involved in this process, not just prostaglandins.

This pathway works very well as far as telling you your finger is hurt. The pain serves a purpose here: It reminds you that your finger is damaged and that you need to be careful with it and not use it until it's healed. The problem is that, sometimes, things hurt without the hammer or for any other good reason. For example, sometimes you get a headache, probably because your scalp and neck muscles are contracted from stress or because a blood vessel in your brain has a spasm. Many people have arthritis, which is swelling and pain in the joints such as the knuckles or knees, and this problem can not only make people uncomfortable, it can damage the joints permanently. And many women have pain in their abdomens during their periods, usually known as cramps, for no known useful reason. These processes appear to involve prostaglandins as well.

What Does Aspirin Do?

Aspirin helps these problems by stopping cells from making prostaglandins. Remember the enzyme, COX-2? It is a protein made by your body's cells whose job is to take chemicals floating around in your tissues and turn them into prostaglandins.

COX-2 can be found in lots of normal tissues, but much more of it is made in tissue that has been damaged in some way. Aspirin, it turns out, sticks to COX-2 and won't let it do its job; it's like a lock you put on your bicycle. The bicycle won't move with the lock on, and COX-2 can't work with aspirin stuck in it. So by taking aspirin, you don't stop the problem that's causing the pain, like the tight muscles in your scalp, or the cramping in your abdomen, or the hammer-damaged finger. But it does "lower the volume" on the pain signals getting through your nerves to your brain.

One common question about aspirin and other medicines is, "**How does it know how to get to where the pain is?**" The answer is that it doesn't! When you take aspirin, it dissolves in your stomach or the next part of the digestive tract, the small intestine, and your body absorbs it there. Then it goes into the bloodstream and it goes through your entire body. Although it is everywhere, it only works where there are prostaglandins being made, which includes the area where it hurts.

You may ask, "**How come I have to keep taking aspirin if it works so well?**" As with almost all chemicals, your body has ways of getting rid of aspirin. In this case, your liver, stomach, and other organs change aspirin to... surprise! Salicylic acid! This chemical then slowly gets changed a bit more by the liver, which sticks other chemicals onto the salicylic acid so that your kidneys can filter it out of your blood and send it out in your urine. This whole process takes about four to six hours, so you need to take another pill at that time to keep the effect going.

The problem with the fact that aspirin goes through your entire bloodstream is that your body needs prostaglandins for some reasons. One place they are useful is in the stomach; it turns out another enzyme called **COX-1** makes a prostaglandin that seems to keep your stomach lining nice and thick. Aspirin keeps COX-1 from working (it keeps most prostaglandins from being made equally well -- it's "nonselective"), and your stomach lining gets thin, allowing the digestive juice inside to irritate it. This is probably the biggest reason why aspirin and its relatives upset stomachs (not only because it's an acid, as Hoffmann had thought).

COX-2 also works in some normal tissues like the brain and kidney; at normal amounts, one dose of aspirin probably doesn't affect these areas much. And there are other places in the body where prostaglandins have a job in normal tissues, such as the blood...

What Else is it Good For?

In the last few decades, it has been found that aspirin's action of stopping prostaglandin production has effects on things besides pain, inflammation, and the stomach.

For example, some types of prostaglandins cause tiny particles in your blood (known as platelets) to stick together to form a **blood clot**. By inhibiting prostaglandin production, aspirin slows down clot production. Although this can be bad, such as with a bloody nose -- in which case you want a clot to form -- blood clots can be damaging as well, such as in causing heart attacks by clogging the blood vessels that bring oxygen and energy to the beating heart. For this reason, many adults now take aspirin to prevent heart attacks, and it also helps people who have already had a heart attack stay alive. Surely Hoffmann (and the Bayer company) could

never have predicted this effect. And as noticed at least as far back as Hippocrates in ancient Greece, aspirin and its relatives also lower **fevers**; this seems to be an effect on a part of the brain known as the hypothalamus, which controls temperature (as well as other body functions).

A lot of research is being done now to find out if aspirin can be used for other problems; it has already shown some promise in helping with problems as diverse as cataracts in the eyes, some cancers, gum disease, and high blood pressure during pregnancy!

Does it Have Side Effects?

Just like all medicines, aspirin isn't all good. It has effects on the body that you and your doctor don't want (**side effects**). Some of them have already been mentioned; for example, if you hit your finger with a hammer and it's bleeding, an aspirin may help the pain and swelling, but the wound may take longer to clot and stop bleeding. Also, it can be very upsetting to the stomach, especially at the high doses often used in arthritis.

Aspirin also isn't used as much for fevers in children since research has suggested that aspirin given to kids with flu, chickenpox, or other viral sicknesses may cause a potentially deadly problem called **Reye syndrome**.

Aspirin also changes the way your kidneys make urine, can cause some people to have trouble breathing (rarely), and can be dangerous at very high doses.

For these reasons, chemists have found other chemicals closely related to aspirin that have some of its good effects and lack some of its bad effects. For example, **ibuprofen** and **naproxen** (or Motrin and Naprosyn, respectively) also treat pain, swelling and fever, but they seem to have less of an effect on platelets than aspirin does. These medicines are called the **non-steroidal antiinflammatory drugs** (**NSAIDs**) because they decrease swelling but they aren't steroids, which are the most potent antiinflammatory chemicals we have. Another family of medicines related to aspirin includes **acetaminophen** (or Tylenol), which decreases fevers and pain, but it doesn't affect either swelling or your stomach as much as the true NSAIDs do.

Felix Hoffmann was sure that aspirin would make a good drug for arthritis. But as he struggled to prove it to his cautious employer, how could he have known it would save lives, and in so many ways? So the next time you get out the hammer, think of Felix and set aside an aspirin or two. He deserves the tribute, and it's best to be prepared for hitting the wrong nail.

Sources:

http://health.howstuffworks.com/aspirin.htm