

# New Drugs That Have Changed Medicine

## 3. Aspirin

**Makoto Shiragami**

**Fusayo Shiragami**

### ■ **A Drug That Has Been in Use in 3 Centuries**

Due to the efforts of pharmaceutical companies, many new drugs that improve the suffering of people with diseases are developed every year. However, drugs that make a grand entrance often have to eventually give up their starring role to newly developed drugs, and somewhere along the line they become extinct. Against such a background, aspirin has been used for more than 100 years. You must have received help from aspirin at least once. It was the year 1899, the end of the 19th century, when aspirin was first sold as a pain killer by Bayer, and thus it passed the 20th century, entering the third (21<sup>st</sup>) century and 114 years since it was first launched. Not very long ago, in 1950, it was recognized in the Guinness Book of World Records as the world's top-selling pain killer. Astronauts suffer headaches and muscle pains due to changes in the pressure, so the Apollo 11, which was the first space capsule to land on the moon in 1969, had aspirin on board. In 1999, it was

honored by the Smithsonian Institution's National Museum of American History as the "best known drug in the world with a unique history." It is said that 50 thousand tons, 100 billion tablets, of aspirin are even now being used per year in the world.

### ■ **The History of Aspirin**

Looking back on the history of aspirin, we must go back to the years before Christ, starting with the story of the willow tree. There is a record from around 400 B.C. that states that the father of modern medicine, Hippocrates of ancient Greek, used the bark of a willow tree to treat fever and pain. There is also a record in "De Materia Medica" of ancient Rome stating that the willow tree also has effects to stop bleeding and cure foot corn and calluses besides its pain killing actions. Meanwhile, in China, the tips of the branches of willow trees were broken into pieces and used to rub between the teeth for toothache. This is said to be the origin of the toothpick.

In the 19th century, salicylic acid, the active component of willow bark, was isolated and used as an analgesic antipyretic. However, salicylic acid had a strong, bitter taste, and strong gastrointestinal side effects. Acetylsalicylic acid, which is aspirin, was synthesized with the purpose of preserving its effect while reducing the side effects, and it was Bayer's young chemist Felix Hoffmann who succeeded in synthesizing adequately pure and stable acetylsalicylic acid that could be used as drug. It is said that his father's long suffering due to severe rheumatism as well as the side effects of salicylic acid had driven Hoffmann's research.



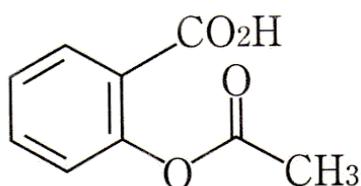
Hoffmann succeeded in synthesizing acetylsalicylic acid in 1897, and it was put on the market by Bayer under the brand name aspirin 2 years later. Aspirin was the world's first synthetically made drug. In 1900, the powder was made into a tablet, and it thus also became the world's first tableted drug. In the same year, 1900, there was already a newspaper article showing that aspirin was sold in Japan. At times it was sold under the kanji characters name, “阿斯泌林” (A-SU-PI-RIN) .



### ■ The Name Aspirin

The chemical name for aspirin is acetylsalicylic acid, and it has a relatively simple structure. “Aspirin” is the brand name of Bayer, but the name aspirin had become so popular that it has almost become a generic name. Even in the Japanese Pharmacopoeia, a book that regulates the quality standards of drugs widely used in Japan, aspirin is used as the official name.

In 1918, after World War I, the manufacturing rights for aspirin, the product of an enemy country, Germany, as far as the USA was concerned, were forfeited and auctioned in the United States. However, the American company that bought the rights continued selling aspirin under the name “Bayer aspirin,” keeping the company name, because the name aspirin was already so popular among the American citizens. It was not until 76 years later, in 1994, that Bayer bought back all the rights for aspirin.



### ■ **The Mechanism of Action of Aspirin**

You can use a drug without knowing how it works. However, if you do know its mechanism of action, you will be able to use the drug more efficiently and safely. The mechanism by which aspirin reduces fever, pain and inflammation only became known in 1971, more than 70 years after it was launched.

Aspirin inhibits the production of prostaglandin, a substance that is present in various tissues and organs of the human body. Prostaglandin has various functions, including those of increasing fever and pain. Prostaglandin is also produced when human body tissue is damaged, and causes symptoms of inflammation characterized by redness of the skin, fever, swelling, and pain. Aspirin inhibits the production of prostaglandin responsible for these actions, and can thus reduce fever, pain and inflammation. This mechanism was discovered by an English pharmacologist, John Vane. John Vane received the Nobel Prize for Physiology or Medicine in 1982 for discovering prostaglandin and the mechanism of the anti-inflammatory effect of aspirin.

### ■ **The Side Effects of Aspirin**

To use the drug properly, it is important to know its side effects. You should know that there are also serious side effects to aspirin, even if it was synthesized to reduce the side effects of salicylic acid and has been used for a long time as an analgesic antipyretic. Prostaglandin, of which aspirin suppresses the production, also has such functions as reducing the secretion of gastric acid and protecting the gastric mucosa, but aspirin also suppresses these functions and may therefore cause gastrointestinal disorders. In order to offset these side effects, a drug coated with a material called dialuminate, an acid suppressant, has been developed. Additionally, when children who are infected with influenza or chickenpox virus use aspirin, it may cause a life-threatening disease involving severe brain damage and accompanying liver dysfunction called Reye's syndrome. For this reason, there is a restriction on children taking aspirin when they have a cold.

### ■ **Continuously Developing Aspirin**

Aspirin was known as an analgesic antipyretic and anti-inflammatory drug, or should I say the term analgesic antipyretic and anti-inflammatory drug equaled aspirin, but in the late 1970s its application to the cerebral and cardiovascular fields began to attract attention, and an American research group discovered that aspirin inhibits the

aggregation of platelets, a component of blood. Platelets play an important hemostatic role by aggregating in case of bleeding, but when platelets aggregate inside vessels, they form blood clots and disturb the blood flow, which may eventually trigger myocardial or cerebral infarction with clogging of the vessels in the heart or brain. This new effect of aspirin can be explained by its mechanism of action. In 1988, the result of a large clinical trial involving 22,071 American doctors was reported, showing that aspirin decreases the risk for myocardial infarction by 44%. In Japan, aspirin's effect as an antiplatelet agent was added in 2000, and as a treatment of Kawasaki disease in 2005.

Aspirin is being continuously studied for its effect on cancer, Alzheimer's disease and other diseases, even now after more than 110 years after its birth, and it is continuing to develop as an old yet new drug.