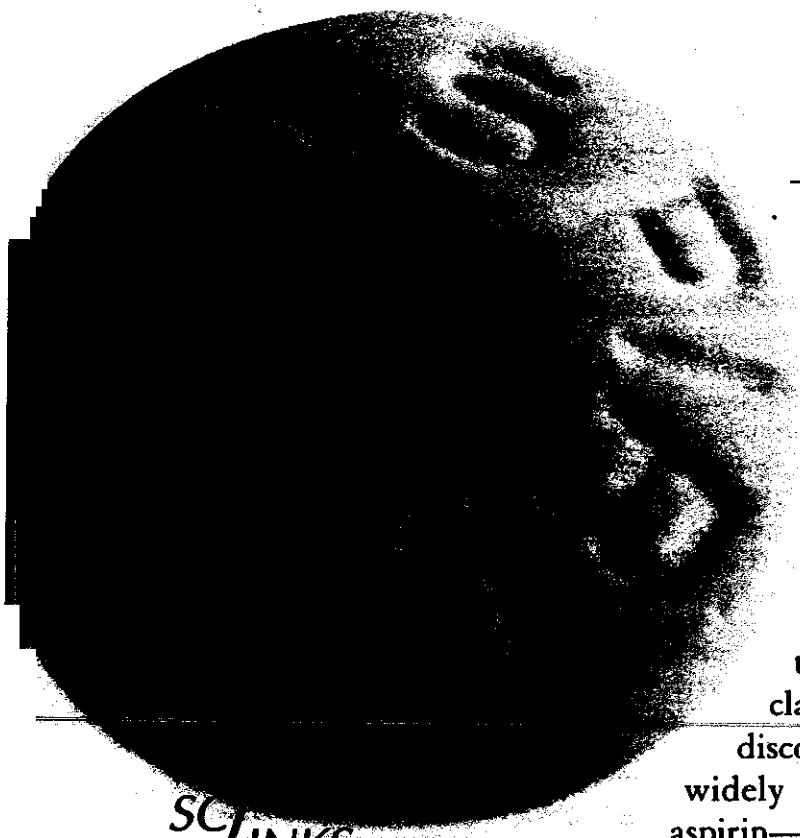
Aspirin

History and Applications

Cross-curricular instructional strategies, ideas, and applications for teaching about aspirin in the science classroom



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Of the thousands of drugs and medicines available for the prevention, treatment, and control of human disease and discomfort, the most widely used is aspirin. The primary reason for aspirin's popularity is its capabilities as a pain reliever, fever reducer, and anti-inflammatory agent.

This article explores the historical development of aspirin and provides teachers with instructional strategies, ideas, and applications for teaching about aspirin in the science classroom. The historical account of the scientific discoveries and breakthroughs that led to the most widely used and beneficial medicine worldwide—aspirin—serves not only as an interesting history lesson but also an excellent opportunity for science teachers to apply this knowledge to lessons in science and other curricular subjects.

History

The history of aspirin is just as fascinating as its immense popularity and effectiveness as a "drug for all ailments." One of the earliest documented uses of aspirin can be traced back to about 400 BC when Hippocrates (ca460–370 BC) recommended chewing on the bark of a willow tree to relieve the pain associated with the labor of childbirth. The bark of a willow tree, as it would be discovered centuries later, contains salicin, a member compound of the salicylate family and the active ingredient of aspirin.

The bark from the willow tree was recognized as an effective treatment for symptoms such as pain and fever but no one had ever considered it as a therapeutic agent for a particular ailment until the 18th century. In 1763, English physician and clergyman Edward Stone reported on the use of willow tree bark to specifically treat the symptoms of rheumatic fever experienced by 50 parishioners and expanded the prospects to include malaria and febrile (fever) disorders, providing the first written account of the therapeutic effects of willow bark (Stone 1763).

In the 19th century, scientists began to unlock the mysteries of willow bark and identified the compound that was responsible for the commonly observed therapeutic effects. In 1828, Johann Buchner was the first scientist to successfully isolate salicin from the willow tree bark in crystalline form (Weissmann 1991).

Although salicylic acid was widely heralded as an effective pain reliever of its time, this enthusiasm was diminished by unpleasant side effects that included irritation and damage to the inner lining of the digestive tract, mouth, and stomach. The internal damage was attributed to the acidic nature of the salicylic acid molecule. Thus, attempts were made to experimentally neutralize the acidity of salicylic acid by synthesizing its corresponding salt. This was done by replacing the hydrogen atom of the carboxyl group (COOH) with an atom of a metal, for instance, sodium. The result was sodium salicylate, which was less irritating to the digestive tract but was not palatable to the general population.

Up to this point, the synthesis of salicylic acid and related salicylates involved complicated experimental procedures to extract and purify quantities derived from the various plant sources. In light of this, Wilhelm Gerland, in 1852, made another significant discovery when he successfully developed a method by which salicylic acid could be synthesized exclusively in the laboratory without the laborious extraction procedure from plant sources (Mueller and Scheidt 1994). In 1860, German chemists Hermann Kolbe and Eduard Lautemann discovered an organic synthesis reaction that yielded large quantities of salicylic acid from phenol using the organic reactant, acetic acid (Kolbe and Lautemann 1860). This reaction, known as the Kolbe synthesis (Figure 1), eventually led to the inexpensive production of acetylsalicylic acid (ASA), or aspirin, and is used today in the commercial production of aspirin.

In 1893 an industrial chemist at Bayer named Felix Hoffmann synthesized the chemical compound (ASA) and, more importantly, devised an efficient process by which it could be commercially produced (Mueller and Scheidt 1994). Hoffman successfully synthesized ASA (Figure 2)—the chemical name of the compound that has come to be known as aspirin in a pure and stable form—that minimized devastating side effects but remained just as effective at relieving pain. Hoffman is credited as the discoverer of aspirin.

Although ASA was synthesized by Hoffman in 1893, it wasn't until 1897 that Bayer mass produced the compound ASA without a brand name. In 1899, Bayer provided ASA with the name *aspirin,* derived as a combination of the following roots: *a* representing acetyl chloride; *spir* representing the plant *Spiraea ulmaria* from which salicylic acid was extracted; and *in* was a common attachment to medicine names founded during that time (Weissmann 1991)

In 1899, Heinrich Dreser, an official at Bayer, eventually published the first article on aspirin in which he demonstrated that aspirin was just as efficacious as salicylic acid without the unpleasant side effects (Dreser 1899). Publication of these results in a scientific journal provided an objective account of the therapeutic potential of aspirin based on scientific evidence. Also that year, Bayer patented the

FIGURE 1

The Kolbe synthesis

The organic synthesis reaction discovered by Kolbe and Lautemann in which large quantities of salicylic acid are obtained from phenol, using acetic acid.

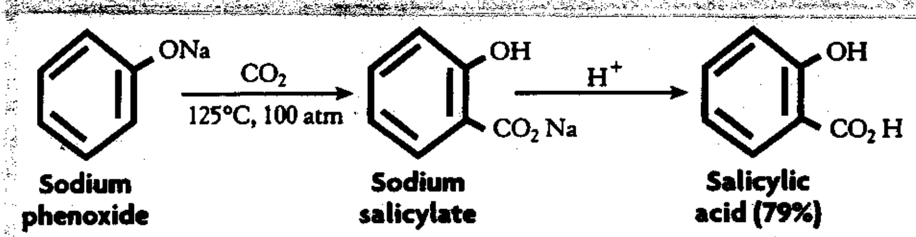

FIGURE 2

Aspirin

Chemical structure of acetylsalicylic acid, the active ingredient in aspirin.

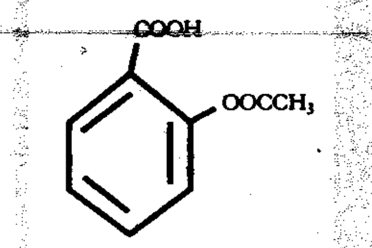

FIGURE 3

Aspirin-related research questions and activities in curricular areas to foster inquiry-based learning.

[All references to the Aspirin Adventures website, along with complete activities, can be found at *www.chemheritage.org/EducationalServices/pharm/asp/asp00.htm* (CHF 2001).]

Biology

Sources of drugs

- The discovery of aspirin was a long and arduous process. Ask students to explore the following questions: How are drugs developed for a specific illness or disease? What is the process and general timeline for such a task? What are the difficulties in accomplishing such a task in the search for a treatment or cure for AIDS or cancer?
- Assign students a disease and ask them to research the history and timeline of a particular drug or family of drugs developed to treat the disease.
- Aspirin, or the active ingredient in aspirin, was a drug rooted in ancient times. Ask students: What were some of the sources for drugs in ancient times and what was the rationale for their use? How did the search for various sources of drugs change over time?

Treatment of disease/illness

- Aspirin belongs to a family of drugs known as nonsteroidal anti-inflammatories (NSAIDs), which include ibuprofen (Advil) and naproxen (Aleve). Ask students: How is aspirin similar to these drugs? How is aspirin different from these drugs? How do the risks and benefits compare among these drugs (Weissmann 1991)?
- Students can visit the Aspirin Adventures website and click on "A Festival of Analgesics." Students will explore the wide variety of pain relievers and, based on the recommendations on the label, match the appropriate pain reliever to an individual with a specific ailment.

Chemistry

Synthesis of aspirin and stoichiometry

- In order for a method of synthesis to be commercially viable, purity, number, and cost of reactants must be considered (Olmsted 1998). Ask students to identify other factors that might be important in the commercial production of aspirin. How can researchers improve upon the efficiency of aspirin production?
- In stoichiometric calculations, the chemist must balance a reaction equation on the premise of the conservation of mass. In the lab, students can synthesize aspirin (ASA) from salicylic acid and acetic anhydride. (Details can be found by visiting the Aspirin Adventures website and clicking on "Making Aspirin.") Students can write and balance the chemical equation for this synthesis reaction, and calculate the theoretical yield of ASA from the amounts of reactants used. (Details can be found by visiting the Aspirin Adventures website and clicking on "Aspirin Math for High Schoolers.") Students also can calculate the mass of salicylic acid needed to produce one aspirin tablet (325 mg ASA).

Titration and quantitative analysis

- Often, one interchanges the terms aspirin and ASA. The terms are different in that ASA is the active ingredient of aspirin. In order to quantify the amount of ASA in an aspirin tablet, a titration can be performed. Give students an aspirin tablet and have them devise and perform a titration experiment to determine the amount of ASA in the aspirin (Chemtutor 2005). Ask students: What calculations would one perform to quantify the mass/percentage of ASA in aspirin? Would the same approach, methods, and calculations apply for pain relievers such as ibuprofen and acetaminophen?
- Students can visit the Aspirin Adventures website and click on "About Acids." Because the major component of aspirin is ASA, students will learn about the basic chemistry of acids.

Qualitative analysis

- Students can visit the Aspirin Adventures website and click on "Real or Phony." Students will determine whether the unknown sample contains ASA using the ferric chloride test.
- Editor's note: For an additional chemistry-related aspirin activity, please see the November 2004 issue of *The Science Teacher* (McKinney and Michalovic 2004).

Anatomy and physiology

Toxicology

- Although routinely given in prescribed amounts to assist patients with pain relief, individuals have been known to overdose on aspirin. An overdose of aspirin, as is the case with any drug overdose, can cause serious problems, including death (Azer and Bailey 2005). Ask students: In the event of an aspirin overdose, what symptoms are emergency room physicians usually looking for? How are aspirin overdose cases treated?

Heart and the circulatory system

- In addition to its role as an effective pain reliever, fever reducer, and anti-inflammatory agent, aspirin has also been shown to effectively treat heart disease by preventing heart attacks (AHA; Hoffman 2005; Awtry and Loscalzo 2000). Ask students: What is a heart attack and how common is it? How does a heart attack occur? What are the underlying processes that increase the likelihood of a heart attack? How does aspirin prevent heart attacks?

Blood coagulation

- Aspirin can prevent a heart attack because it is a platelet antiaggregant, an agent that prevents the blood platelets from sticking together at the site of an injury (AHA; Hademenos 1999). Ask students: What are the major steps or components of the blood coagulation process? What causes the body to activate the blood coagulation processes? How does aspirin affect the blood coagulation processes? What other drugs act to affect blood coagulation?

Mathematics

Graphical analysis

- The ability to create, interpret, and evaluate a graph of data from an experiment with aspirin allows scientists to acquire important information about the identity, concentration, and behavior of aspirin. Examples of graphs that a scientist might see include: titration curves, absorption vs. concentration and absorption vs. wavelengths graphs from spectrophotometry, and dose response curves (Borer and Barry 2000). Ask students: How are these graphs created and what information do they reveal?

Cost of analysis of production

- Because of the enormous popularity of aspirin as an effective drug, the costs of producing the drug to meet its worldwide demands while attempting to generate a profit are daunting. Ask students: How would one derive a mathematical equation relating profit versus expenditure?
- Students can visit the Aspirin Adventures website and click on "Aspirin Math for High Schoolers," where students will perform stoichiometric calculations related to the chemical equations for the synthesis of ASA, or "Compare the Aspirins," where students will compare several brands of aspirin.

Physics

Fluid dynamics

- Aspirin is effective in preventing heart attacks for patients suffering from atherosclerosis—a process that results in the development of fatty deposits along the artery wall (Hademenos 1997; Hajjar and Nicholson 1995; Malek, Alper, and Izumo 1999). Ask students: What are the properties of fluid dynamics in normal blood flow? How does the fatty deposit change blood flow through the vessel? How does the Bernoulli effect apply to blood flow through an obstructed blood vessel?

History and government

Historical context of drugs

- History provides an important perspective on how seemingly inconsequential substances are used over time to treat symptoms and illnesses common to the time and location of a population. Have students investigate the history of the development of other important drugs such as insulin in the treatment of diabetes.
- Students can visit the Aspirin Adventures website and click on "Timeline of Discovery." Students will explore the major historical events involved in the discovery of aspirin.

Federal Drug Administration

- A major role of the FDA is to ensure all drugs distributed in the United States are effective yet safe in treating a particular symptom or disease (FDA 1998). Ask students: What is the federal role in the approval of drugs? How was the FDA formed and what branch of government is responsible for its oversight? What laws govern the patent process with drugs?

Business and marketing

Marketing of drugs

- Science and medicine are responsible for the discovery and production of aspirin. However, in order to reach individuals who would benefit from aspirin, business and marketing specialists must become involved. Ask students: How is aspirin marketed to the general public? What laws govern the marketing of drugs domestically? Internationally? How was aspirin advertised in the 19th century and how has the advertising of aspirin evolved over time?
- Students can visit the Aspirin Adventures website and click on "The Aspirin Label." Given a hypothetical aspirin label, students are first asked to identify particular claims and properties followed by evidence to support these claims and properties.

name *aspirin* and marketed the drug first as a powder and then in tablet form the following year. In 1915, aspirin was available in the United States without a prescription and, in 1939, aspirin was officially approved by the Food and Drug Administration (FDA) for widespread human consumption (Mann and Plummer 1991).

A curricular potpourri

The history of aspirin can be applied toward interesting lessons in science and other curricular subjects. For example, chemistry students can synthesize aspirin or quantitatively determine the amount (mass and percentage) of ASA in aspirin through acid/base titration procedures. Biology students might investigate the mechanisms of aspirin as a pain reliever, fever reducer, anti-inflammatory agent, and platelet antiaggregant (an agent that prevents blood platelets from clumping together—the first step in blood clot formation). To integrate mathematics, students can perform stoichiometric calculations from the chemical equation for the synthesis of aspirin, given the mass of a substrate or reaction yield.

Examples of the various subjects and topics applicable to aspirin can be found in Figure 3 (p. 32), along with possible stimulus questions to base the lesson and engage students in solving the problem. [Safety note: The Material Safety Data Sheet (MSDS) for aspirin can be found at *www.jtbaker.com/msds/englishhtml/a7686.htm*.] Many activities related to the topics found in Figure 3 are derived from the Aspirin Adventures website at *www.chemheritage.org/EducationalServices/pharm/asp/asp00.htm* (CHF 2001). The types of assignments that originate from these examples can be adjusted to accommodate students at different levels of science and according to various levels of higher-order, problem-solving skills as described by Bloom's Taxonomy (Bloom 1956), limited only by the efforts, resources, and creativity of the teacher.

CAUTION

Aspirin has had a very eventful and remarkable history and has played a critical role in medicine. Aspirin is unique in that it provides a wealth of instructional ideas and strategies across the curriculum for science teachers to readily engage and challenge their students, as well as fosters collaborations between teachers of other subjects.

Connecting to the Standards

The content and activities of this article are aligned with several of the National Science Education Standards including:

- Content Standard A: Science as Inquiry (NRC 1996, p. 173)
- Content Standard B: Physical Science (NRC 1996, p. 176)
- Content Standard E: Science and Technology (NRC 1996, p. 190)
- Content Standard G: History and Nature of Science (NRC 1996, p. 200)

Given over a century of activity in understanding aspirin and its associated effects on the human body in health and disease, one can only wonder what will the next 100 years bring to medicine—and to the classroom. ■

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