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Aspartame:
History of the Artificial Sweetner

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Do you ever wonder how some of the processed foods you eat taste so sweet and yet claim to have less sugar than one would imagine? And sometimes you skip real sugar, thinking that the substance in the pink packet is a much better substitute that will help you keep your diet on track. Regardless of where you get your sweet taste from, humans have been attracted to sweetness throughout history. Furthermore, a study of newborns clearly showed a strong liking for sweet-tasting stimuli, signifying that the attraction is innate, rather than a learned one. Such importance has prompted chemists to discover the structures naturally occurring and artificial sweeteners to replace sugar. While sugary and starchy foods are dangerous to dental enamel, sugars do not contain carbohydrates and thus prevent teeth from attack (article 1). Artificial sweeteners are also advantageous to help combat diabetes and obesity, for many of them claim to contain less than 5 calories. While many scientists attempt to discover the artificial sweeteners systematically, analyzing possible structures and making models, it is fascinating to note that many sweeteners, including the first artificial sweetener, saccharin, have actually been discovered accidentally.

> *"Artificial sweeteners are advantageous to help combat diabetes and obesity."*

Discovery of Saccharine

The story of the discovery of saccharin goes two ways, perhaps depending on the storyteller's perspective. One story states that Professor Ira Remsen of Johns Hopkins University was lecturing to his class using samples of newly- prepared chemicals before him. During the lecture, "he unconsciously poked his pencil into several samples"(reword). Later, in his office, Professor Remsen happened to be troubled over a tough problem. While contemplating over it, he unconsciously touched the tip of the pencil to his lips and was amazed by the incredible sweetness. He rushed back to his lecture hall and systematically tasted all the chemicals until he found the one prepared by Fahlberg (article 7). Another story, told by Fahlberg at a 1904 chemical congress in Berlin, goes that Constantine Falhlberg discovered saccharin while working in Ira Remsen's laboratory at Johns Hopkins University. He spilled a chemical on his hand when he was researching new and interesting uses of coal tar derivatives. Later on in the day when he was eating dinner, he noticed his bread rolls tasted sweeter than normal. However, when he mentioned this fact to his wife, she told him that they tasted the same as usual. After realizing he hadn't washed his hands, Falhberg traced the sweet taste to be coming from the chemicals (article 5). Remsen and Fahlberg's original paper on the discovery of saccharin was published in 1879, one year after their experiments had been performed.

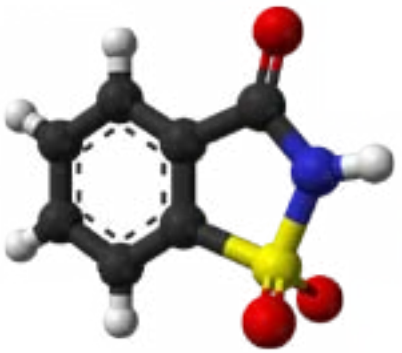

Figure 1. 3-dimensional model of saccharin, a calorie-free sweetner much sweeter than sucrose.

The Controversy of Saccharin's Risk and Saccharin's Rise to Popularity

Saccharin quickly rose to popularity as the first calorie-free sweetener, when it became known as the "poor man's sugar" during World War 2 when real sugar was in short supply and thus more expensive (article 2). Perhaps since saccharin is the oldest substitute, it is also the best researched out of all sweeteners. Although saccharin was

extremely sweet, it unfortunately had a bitter aftertaste, so there was an increasing demand for a new improved sweet substance (article 9). In 1937, 59 years after saccharin had been discovered, Michael Sveda, a graduate student at the University of Illinois, discovered another sweetener, cyclamate, accidentally. Sveda was working on antipyretic drugs in Audreith's laboratory when he unconsciously put his cigarette down on the lab bench. When he put it back in his mouth later, he noticed it tasted sweeter, and thus discovered another compound, now known as cyclamate, that could potentially be used as a substitute for sugar (article 6). The FDA approved cyclamate in 1951. Since it blended with saccharin, the two products were mixed together and were sold as "Sweet 'n' Low", which quickly became popular in the United States. Cyclamate was also used to sweeten soft drinks. (Article 9). However, in 1970, the Food and Drug Administration (FDA) banned cyclamate from all dietary foods in the United States, due to suspicion of inducing cancer in experimental animals. A study by Wagner found an increased incidence of bladder carcinomas in rats and it

"In 1970, the Food and Drug Administration (FDA) banned cyclamate from all dietary foods in the United States."

was discovered that cyclamate is converted to a metabolite, cyclohexylamine, which is very toxic.

Discovery of Aspartame

The third artificial sweetener, Aspartame, entered the market in 1981. Much like saccharin and cyclamate, it too was a product of chance. The story goes that a chemist at G.D. Searle, named Jim Schlatter, was synthesizing a tetrapeptide, a molecule containing four amino acids, in order to test drugs for treating gastric ulcers. Schlatter unintentionally got a small amount of a dipeptide intermediate, aspartyl-phenylalanine methyl ester, on his hands. Later, he unconsciously licked his finger before picking up a piece of paper and noticed its sweet taste. Having first dismissed it as coming from a donut he had eaten, he suddenly realized that he had washed his hands since then. Thus, like Fahlberg and Sveda, Schlatter traced the sweetness back to his laboratory.

Figure 2. Packets of Assugrin (Brand Name) artificial sweetner that is commercially sold in supermarkets.

Since aspartic acid and phenylalanine were naturally-occurring amino acids present in all proteins, he tasted the substance, noting its sweet taste without the bitter aftertaste of saccharin. The story also goes that Schlatter and his lab partner, Harman Lowrie, also tasted the material in 10 milliliters of black coffee, and their boss, Dr. Bob Mazur persuaded the company of its potential as a widely -distributed artificial sweetener (article 10).

Conclusion

Many chemists take a systematic approach when attempting to discover synthetic and natural sweeteners. Today, there are at least 50 structural classes of sweet-tasting organic compounds and the sweet compounds are very diverse in structure.(pubs.asc.org). Yet, it was hypothesized that there was a common pharmacore, or group of atoms, and Cohn described the earliest model in 1914, which argued that all sweet-tasting substances produce a common glucophore. Two centuries after the first artificial sweetener was discovered, chemists have advanced a broader array of models that can be utilized when designing new sweeteners that come even close to the unique taste of sugar--unless of course, serendipity strikes again.

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